Zirconium-Mediated Coupling Reactions of Amines and Enol or Allyl Ethers: Synthesis of Allyl- and Homoallylamines

José Barluenga,* Félix Rodríguez, Lucía Álvarez-Rodrigo, José M. Zapico, and Francisco J. Fañanás[a]

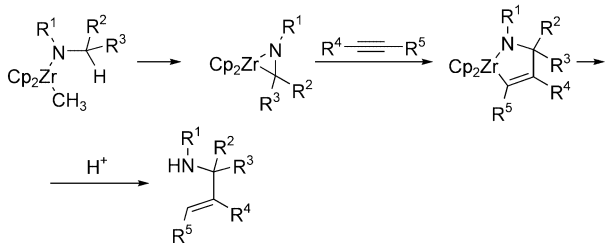
Abstract: An easy and efficient zirconium-mediated synthesis of allylamines from simple amines and enol ethers is described. This strategy also allows the synthesis of amino alcohol derivatives containing a *Z* double bond in their structure when 2,3-dihydrofuran is used. Simple conventional modification of these amino alcohols leads to 2-substituted piperidine derivatives. By applying this approach, a formal total synthesis of the alkaloid coniine is easily achieved from a protected butylamine. Finally, the zirconium-mediated reaction of amines and allyl phenyl ether furnishes homoallylamines or amino ethers depending on the structure of the starting amine.

Keywords: allylamines · C–C coupling · coniine · zirconium

Introduction

Nitrogen-containing organic molecules are without any doubt among the most important compounds in organic chemistry. Proof of this can be found in the fundamental biological activity of compounds such as amino acids[1] or alkaloids.[2] For the synthesis of these kinds of molecules, allylamines are considered ideal building blocks, and thus, in recent years many methods for the racemic and asymmetric synthesis of allylamines have appeared.[3] These compounds are also used as starting materials in important industrial processes.[4] In this context, Buchwald et al. described some years ago an elegant method to prepare allylamine derivatives from simple amines.[5] As shown in Scheme 1, this process relies on the formation of a η^2-imine–zirconocene complex from a methylzirconocene amide and its entrapment with an alkyne to give an azazirconacyclopentene derivative, which affords the desired allylamine on protic work-up.[6]

This sequence constitutes a powerful synthetic transformation since it accomplishes both a C–H activation and a carbometalation process, reactions which are difficult to achieve with conventional reagents. However, the method has some limitations. For example, simple allylamines, unsubstituted at the 2- and 3-positions are not experimentally easy (or are impossible) to obtain since it would require the use of acetylene as the alkyne counterpart. Also, the use of unsymmetrical alkynes generally leads to mixtures of regioisomers. Finally, the method always affords geometrically pure *E* allylamines but *Z* allylamines cannot be obtained.



Scheme 1. Zirconium-mediated coupling of amines and alkynes. Cp = cyclopentadiene.

As part of a program concerned with the development of new reactions involving zirconocene complexes,[7] we wish to report herein our findings on the reaction of enol ethers with η^2-imine–zirconocene complexes. This unprecedented reaction allowed us to overcome some of the limitations mentioned above to obtain unsubstituted allylamines and *Z* allylamines. Moreover, an extensive study on the reaction of the zirconocene complexes with allyl ethers is presented.

Results and Discussion

Insertion reactions of enol ethers and imine–zirconocene complexes: Successive treatment of amines **1** with one equivalent of butyllithium at −40 °C and zirconocene methyl

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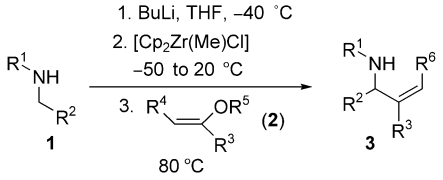
chloride at temperatures ranging between −50 and 20 °C, followed by addition of the appropriate enol ether **2** and further heating to 80 °C in a sealed tube, led after 18 h to allyl amines **3** with high yields in most cases (Scheme 2 and Table 1).



Scheme 2. Zirconium-mediated coupling of amines **1** and enol ethers **2**. Synthesis of allylamines **3**. THF = tetrahydrofuran.

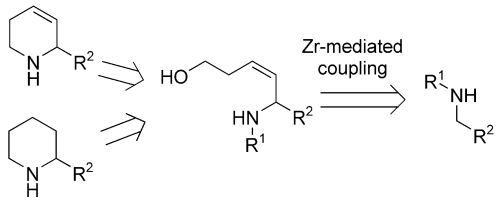
Table 1. Zirconium-mediated synthesis of allylamines **3** from amines **1** and enol ethers **2**.

Entry	Starting amine	R^1	R^2	Enol ether	R^3	R^4	R^5	Product	R^6	Yield [%][a]
1	**1a**	Ph	H	**2a**	H	H	Bu	**3a**	H	83
2	**1b**	Ph	Me	**2a**	H	H	Bu	**3b**	H	68
3	**1c**	Ph	Pr	**2a**	H	H	Bu	**3c**	H	70
4	**1d**	Ph	Ph	**2a**	H	H	Bu	**3d**	H	96
5	**1e**	Bn[b]	Ph	**2a**	H	H	Bu	**3e**	H	85
6	**1f**	Ph	Ar[c]	**2a**	H	H	Bu	**3f**	H	87
7	**1g**	Ph	Ar[d]	**2a**	H	H	Bu	**3g**	H	84
8	**1a**	Ph	H	**2b**	Me	H	Me	**3h**	H	61
9	**1a**	Ph	H	**2c**	H	$(CH_2)_2$		**3i**	$(CH_2)_2OH$	68
10	**1b**	Ph	Me	**2c**	H	$(CH_2)_2$		**3j**	$(CH_2)_2OH$	60
11	**1d**	Ph	Ph	**2c**	H	$(CH_2)_2$		**3k**	$(CH_2)_2OH$	62
12	**1e**	Bn	Ph	**2c**	H	$(CH_2)_2$		**3l**	$(CH_2)_2OH$	64
13	**1f**	Ph	Ar[c]	**2c**	H	$(CH_2)_2$		**3m**	$(CH_2)_2OH$	75
14	**1g**	Ph	Ar[d]	**2c**	H	$(CH_2)_2$		**3n**	$(CH_2)_2OH$	70

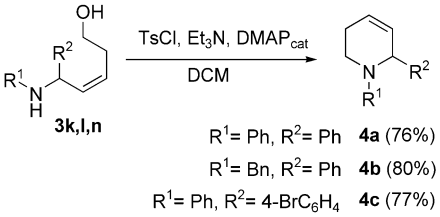
[a] Yield based on starting amine **1**. [b] Bn = benzyl. [c] Ar = 4-$MeOC_6H_4$. [d] Ar = 4-BrC_6H_4.

The first examples were performed with butyl vinyl ether (**2a**) and the results were satisfactory in all the cases attempted (Table 1, entries 1–7). When the reaction was carried out with an α-substituted enol ether, 2-methoxypropene (**2b**), the reaction only proceeded with *N*-methylaniline (**1a**; Table 1, entry 8). With all the other amines tried the reaction did not produce the expected allyl amines analogous to **3h** and unreacted starting amine was recovered. Interesting results were obtained when cyclic enol ethers were used. Thus, the reaction with 2,3-dihydrofuran (**2c**) led to amino alcohols **3i–n** (Table 1, entries 9–14). It is important to note that in all cases we observed the exclusive formation of the allylamine with *Z* stereochemistry in the double bond. This stereochemistry is opposite to that obtained from the previously reported coupling of alkynes and η^2-imine–zirconocene complexes, where the exclusive formation of *E* olefins was observed.[5] Next, we tried to extend this reaction to other cyclic enol ethers such as 3,4-dihydro-2*H*-pyran. However, the reaction did not produce the expected coupling products and unreacted starting amines **1** were recovered in all cases.[8]

Synthesis of 2-substituted piperidines: Formal total synthesis of coniine: Taking into account the results described above about the zirconium-mediated coupling reactions of amines and 2,3-dihydrofuran (**2c**) to give compounds **3i–n** containing a *Z* double bond in their structures, we devised a simple method to easily transform these products into 2-substituted piperidines (Scheme 3).[9] Thus, for example, the reaction between amino alcohols **3k**,**l**,**n**, obtained from the zirconium-mediated reaction described above, and tosyl chloride in dichloromethane led to piperidine derivatives **4a–c** in a single step and high yield, as shown in Scheme 4.



Scheme 3. Strategy devised for the synthesis of 2-substituted piperidines.

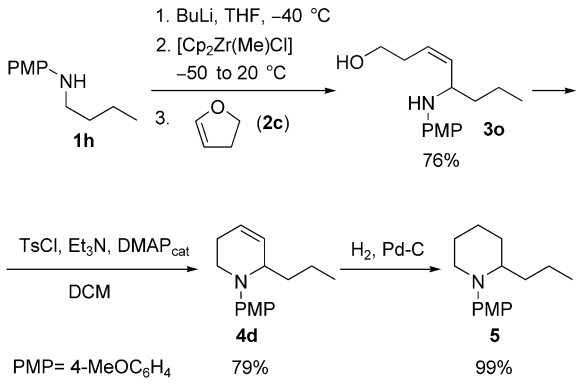


Scheme 4. Synthesis of 2-substituted piperidines **4**. Ts = toluene-4-sulfonyl = tosyl, DMAP = 4-dimethylaminopyridine, DCM = dichloromethane.

Next, we decided to apply this strategy to the synthesis of the alkaloid coniine.[10] Thus, starting from PMP-protected butylamine **1h**, we carried out the coupling reaction with 2,3-dihydrofuran (**2c**) to obtain allylamine **3o** in 76% yield

Abstract in Spanish: *Se describe una síntesis fácil y eficiente de alilaminas a partir de aminas sencillas y enol éteres promovida por zirconio. Esta estrategia también permite la síntesis de derivados de aminoalcoholes que contienen en su estructura un doble enlace con estereoquímica Z cuando se usa 2,3-dihidrofurano. Una modificación simple y convencional de estos aminoalcoholes da lugar a derivados de piperidina sustituidas en posición 2. Aplicando esta aproximación, se ha logrado la síntesis formal del alcaloide coniína a partir de una butilamina protegida. Finalmente, la reacción de aminas y alil fenil éter promovida por zirconio genera homoalilaminas o aminoéteres dependiendo de la estructura de la amina de partida.*

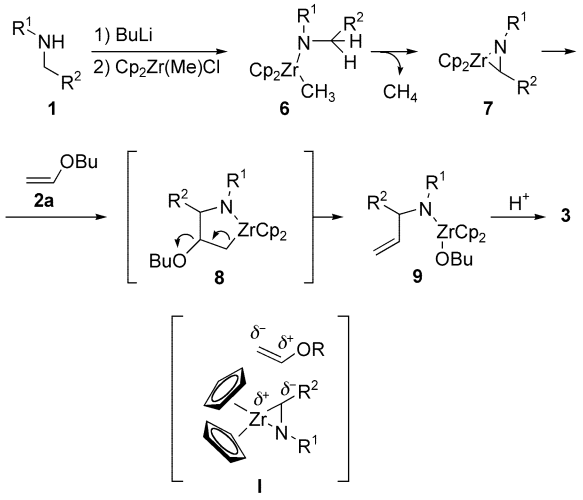
(Scheme 5). Tosylation of the hydroxy group and subsequent cyclization led, in a single step, to unsaturated piperidine **4d** in 79% yield. Further hydrogenation of the double bond quantitatively gave the *N*-protected piperidine **5** (PMP-protected coniine).



Scheme 5. Formal total synthesis of coniine. PMP = *para*-methoxyphenyl.

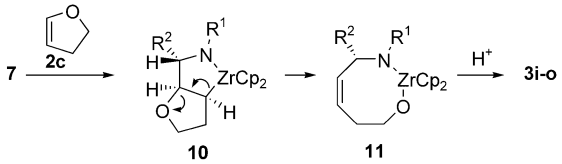
Thus, this sequence describes the formal synthesis of the alkaloid coniine from protected butylamine **1h** in only three steps (Scheme 4; note that the zirconium-mediated coupling is a one-pot process and can be considered as a single step). Following this strategy, many other biologically active compounds and natural products with structures related to **4** or **5** can be easily prepared.

Mechanism of the insertion reaction of enol ethers and imine–zirconocene complexes: The zirconium-mediated formation of allylamines **3** from amines **1** can be explained by the mechanism depicted in Scheme 6. Treatment of amine **1** with butyllithium generates the corresponding lithium amide, which reacts with zirconocene methyl chloride to give zirconocene complex **6**. A cyclometalation with subsequent elimination of methane leads to η^2-imine complex **7**. Insertion of the double bond of enol ether **2a** takes place regioselectively on the zirconium–carbon bond of **7**. Moreover, the insertion of enol ether **2a** occurs with the appropriate orientation to furnish the zirconaazacyclopentane derivative **8**. Both electronic and steric effects favor this orientation of the enol ether as depicted in **I** (bottom of Scheme 6).[11] The intermediate **8** can undergo β elimination of the alkoxy group to give zirconocene derivative **9**, which after hydrolysis gives rise to allylamine **3**.



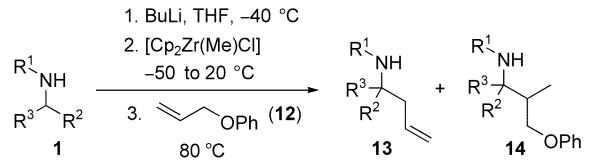
Scheme 6. Top: Proposed mechanism for the formation of allylamines **3**. Bottom: Orientation of the allyl ether during the insertion process.

The mechanism for the reaction of amines **1** with 2,3-dihydrofuran (**2c**) is analogous to that described above. However, the exclusive formation of *Z* amino alcohols **3i–o**, could be justified by the formation of bicyclic intermediate **10**, which after the β elimination process leads to the *Z*-oxaazazirconacyclooctene **11** and finally to amino alcohols **3i–o** with *Z* configuration in the double bond (Scheme 7).



Scheme 7. Prposed mechanism for the formation of *Z* alkene derivatives **3i–o**.

Insertion reactions of allyl ethers and imine–zirconocene complexes: After our study on the coupling reactions of enol ethers and η^2-imine–zirconocene complexes we turned our attention to the behavior of allyl ethers with this kind of complexes. In a paper that appeared in 1990,[12] Whitby and co-workers described a single example of the reaction of the η^2-imine complex derived from tetrahydroquinoline and an allyl ethyl ether to give a mixture of two products (a homoallylamine and an amino ether). As far as we know this is the only example of this reaction reported in the literature. We decided to initiate a study into the zirconium-mediated coupling reaction of different amines **1** and allyl phenyl ether (**12**). Thus, successive treatment of amines **1** with one equivalent of butyllithium and zirconocene methyl chloride in the conditions described above, followed by addition of excess allyl phenyl ether (**12**) and further heating to 80 °C in a sealed tube, led to mixtures of homoallylamines **13** and amino ethers **14** in different ratios depending on the structure of the initial amine **1** (Scheme 8 and Table 2).



Scheme 8. Zirconium-mediated coupling of amines **1** and allyl phenyl ether **12**.

Analysis of Table 2 showed us several interesting features. For example, the use of *N*-methylaniline (**1a**) as starting material basically led to amino ether **14a** in 70% yield (ratio

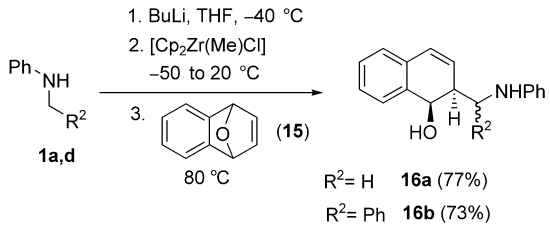
Table 2. Zirconium-mediated synthesis of homoallylamines **13** and amino ethers **14** from amines **1** and allyl phenyl ether **12**.

Entry	Starting amine	R^1	R^2	R^3	Product	Yield [%][a]
1	**1a**	Ph	H	H	**14a**	70[b]
2	**1b**	Ph	Me	H	**13b**/**14b**	18/52
3	**1c**	Ph	Pr	H	**13c**/**14c**	26/52
4	**1i**	Ph	*i*Pr	H	**13d**	81
5	**1j**	Ph	Me	Me	**13e**	73
6	**1d**	Ph	Ph	H	**13f**	96
7	**1e**	Bn	Ph	H	**13g**	86
8	**1f**	Ph	4-$MeOC_6H_4$	H	**13h**	95
9	**1g**	Ph	4-BrC_6H_4	H	**13i**	84

[a] Yield based on starting amine **1**. [b] The crude mixture of the reaction showed a 14:1 mixture of **14a**/**13a** by ^{1}H NMR spectroscopy. The major diastereisomer **14a** was easily separated.

14a:**13a**, 14:1; Table 2, entry 1). It has to be noted that the starting amine **1a** is unsubstituted in the α position ($R^2=R^3=H$). Moreover,'more substituted' amines **1b** ($R^2=Me$) and **1c** ($R^2=Pr$) led to mixtures of homoallylamines **13b,c** and amino ethers **14b,c**, respectively (Table 2, entries 2,3). Finally, the sterically more demanding amines **1i** ($R^2=i$Pr) and **1j** ($R^2=R^3=Me$), and aryl-substituted amines **1d–g** exclusively led to homoallylamines **13d–i** (Table 2, entries 4–9). From these results, it seems that the bulkiness of groups R^2 and R^3 in amines **1** is directly related with the formation of homoallylamines **13** or amino ethers **14**. Thus, formation of **14** is favored when the starting amine **1** contains small R^2 and R^3 groups and, on the contrary, bigger R^2 and R^3 groups favor the formation of **13**.

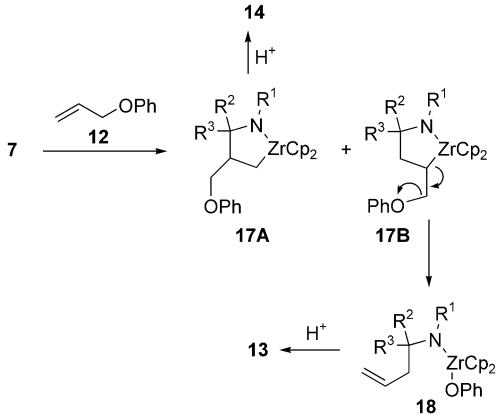
Finally, in Scheme 9 two examples are depicted that are intended to show that this zirconium-mediated coupling reaction might be useful to access more elaborate frameworks



Scheme 9. Synthesis of amino alcohols **16** from amines **1a**,**d** and ether **15**.

from simple starting materials.[13] Thus, the reaction of amines **1a**,**d** with the'symmetric allyl ether' 1,4-dihydro-1,4-epoxynaphthalene (**15**) led to amino alcohols **16a**,**b**, respectively, in high yield. Interestingly, compound **16a** was obtained as a single diastereoisomer while **16b** was isolated as a 1.6:1 mixture of two diastereiosomers.

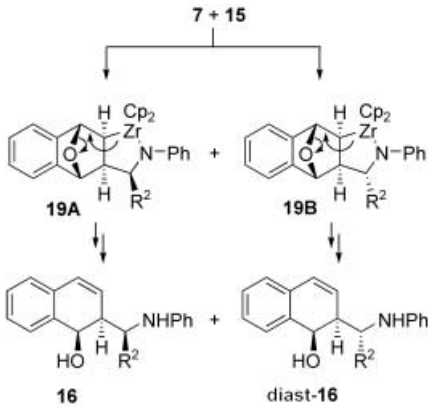
Mechanism of the insertion reaction of allyl ethers and imine–zirconocene complexes: In the first place, we must consider the η^2-imine complex **7** as described before (see Scheme 6). Insertion of the double bond of allyl ether **12** leads to the two regioisomers **17A** and **17B** depending on the orientation of **12** during the insertion step (Scheme 10).



Scheme 10. Proposed mechanism for the formation of homoallylamines **13** and amino ethers **14**.

Thus, when $R^2=R^3=H$, approach of the allyl ether to **7** takes place with the alkoxy group oriented far from the zirconocene moiety to avoid steric interactions with the Cp groups; this gives intermediate **17A** as the main product. On the other hand, when the bulkiness of R^2 increases or R^2 and $R^3\neq H$, intermediate **17B** is formed as the major or exclusive regioisomer. Presumably, in these cases the steric interactions between the alkoxy and R^2/R^3 groups are more important than the interaction between the alkoxy and the Cp groups. Intermediate **17A** is stable and its hydrolysis generates amino ether **14**. On the other hand, intermediate **17B** can evolve through a process of β elimination of the alkoxy group to give zirconocene derivative **18**, which after hydrolysis gives homoallylamine **13** (Scheme 10).

Formation of compounds **16** from amines **1a**,**d** and **15** follows the same mechanism. As indicated before, this reaction gives a single product when **1a** is used as the starting material, but a mixture of two diastereiosomers is observed from amine **1d**. This fact can be explained as depicted in Scheme 11. Thus, we propose that the insertion reaction of



Scheme 11. Proposed mechanism for the formation of amino alcohols **16**.

the double bond of **15** into **7** takes place from the less-hindered face of **15**. Moreover, an initial coordination of the oxygen atom of **15** to the zirconium atom can also be in-

voked to justify the coordination of the double bond of **15** from the face where the oxygen atom is placed. However, two different orientations of **7** are possible and two intermediates **19A** and **19B** can be formed. Each of these intermediates undergoes β elimination of the alkoxy group to finally generate a mixture of compounds **16** and *diast*-**16**. For **1a**, R^2 is H, in which case **16** and *diast*-**16** are the same product. Only if $R^2 \neq H$, can the two diastereiosomers be observed (for example, with **1d**).

Conclusions

We have described a new, easy, and efficient strategy to generate allylamines from simple amines and enol ethers through the formation of a η^2-imine–zirconocene complex. The use of 2,3-dihydrofuran as the enol ether counterpart allowed access to new amino alcohol derivatives containing a *Z* double bond in their structure. Further conventional modification of these amino alcohols permitted the synthesis of piperidine derivatives closely related with the structure of many alkaloids and other biologically active products. As an example, a three-step formal total synthesis of coniine from PMP-protected butylamine was achieved. Moreover, a study of the zirconium-mediated coupling reactions of amines and allyl ethers was carried out. Thus, it was observed that this reaction could generate homoallylamines or amino ethers depending on the structure of the starting amine. The zirconium-promoted reactions of amines with both enol and allyl ethers can be formally considered as a sequential C_α–H activation of the amine followed by a nucleophilic substitution of the alkoxy group. Moreover, all the products obtained following the strategies described here are of high interest in organic chemistry. Investigations directed toward the development of asymmetric, and also catalytic, versions of these processes are in progress.

Experimental Section

General: All reactions involving organometallic species were carried out under an atmosphere of dry N_2 with oven-dried glassware and syringes. THF, hexane and Et_2O were distilled over sodium benzophenone ketyl under N_2 immediately prior to use, and CH_2Cl_2 was distilled over P_2O_5. The solvents used in column chromatography, hexane and EtOAc, were distilled before use. TLC was performed on aluminum-backed plates coated with silica gel 60 with F_{254} indicator (Scharlau). Flash column chromatography was carried out on silica gel 60, 230–240 mesh. ^{1}H NMR (200, 300, 400 MHz) and ^{13}C NMR (50.5, 75.5, 100 MHz) spectra were measured at room temperature on Bruker AC-200, AC-300 and AMX-400 instruments, respectively, with tetramethylsilane ($\delta = 0.0$, ^{1}H NMR) or $CDCl_3$ ($\delta = 77.00$, ^{13}C NMR) as the internal standard. Carbon multiplicities were assigned by DEPT techniques. High-resolution mass spectra (HRMS) were determined on a Finnigan MAT 95 spectrometer. Elemental analyses were carried out on a Perkin–Elmer 2400 microanalyzer.

General procedure for the preparation of compounds 3: Butyllithium (1.2 mmol) was added to a stirred solution of the required amine **1** (1 mmol) in dry THF (10 mL) at −40 °C. After stirring at this temperature for 30 min, the solution was added dropwise through a cannula to a stirred solution of bis(cyclopentadienyl)zirconium methyl chloride (1.2 mmol) in dry THF (10 mL) in a sealed tube at −50 °C. After 30 min at this temperature the mixture was allowed to warm to room temperature and an excess of the appropriate enol ether **2** (10 mmol) was added. The sealed tube containing the reaction mixture was heated to 80 °C for 18 h. The reaction was cooled to room temperature, worked up by addition of water (20 mL) and then extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over anhydrous sodium sulphate and concentrated, and the residue was purified by column chromatography to give compounds **3**. Compound **3a** is commercially available and its analytical data were compared with those of an authentic sample. Analytical data for compounds **3b**,[14] **3d**,[15] **3e**,[16] and **3h**[17] were in complete accordance with literature values.

***N*-(1-Propyl-2-propenyl)aniline (3c)**: Amine **1c** (0.15 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and $[Cp_2Zr(Me)Cl]$ (0.34 g, 1.2 mmol). This was followed by addition of butyl vinyl ether (**2a**; 0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (10:1)) to give **3c** as a pale yellow oil. $R_f = 0.57$ (hexane/ethyl acetate (5:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.38$–7.20, 6.88–6.62 (2 × m, 5 H; ArH), 5.87 (ddd, $J = 16.4$, 10.8, 6.5 Hz, 1 H; C*H*=CH$_2$), 5.34 (d, $J = 16.4$ Hz, 1 H; CH=C*H*H), 5.24 (d, $J = 10.1$ Hz, 1 H; CH=CH*H*), 3.95 (q, $J = 6.2$ Hz, 1 H; NHC*H*), 3.72 (br s, 1 H; NH), 1.80–1.45 (m, 4 H; (C*H*$_2$)$_2$CH$_3$), 1.08 (t, $J = 7.0$ Hz, 3 H; CH$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.4$, 140.0, 128.9, 116.8, 114.7, 113.1, 55.4, 37.8, 18.9, 13.8 ppm; HRMS (EI): calcd for $C_{12}H_{17}N$: 175.1361; found: 175.1364; elemental analysis: calcd (%) for $C_{12}H_{17}N$: C 82.23, H 9.78, N 7.99; found: C 82.34, H 9.69, N 7.96.

***N*-[1-(4-Methoxyphenyl)-2-propenyl]aniline (3f)**: Amine **1f** (0.23 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and $[Cp_2Zr(Me)Cl]$ (0.34 g, 1.2 mmol). This was followed by addition of butyl vinyl ether (**2a**; 0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (7:1)) to give **3f** as a pale yellow oil. $R_f = 0.32$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–6.60 (m, 9 H; ArH), 6.08 (ddd, $J = 16.2$, 10.2, 5.8 Hz, 1 H; C*H*=CH$_2$), 5.33 (d, $J = 16.2$ Hz, 1 H; CH=C*H*H), 5.27 (d, $J = 10.2$ Hz, 1 H; CH=CH*H*), 4.95 (d, $J = 5.8$ Hz, 1 H; NHC*H*), 4.05 (br s, 1 H; NH), 3.84 (s, 3 H; OCH$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.7$, 147.1, 139.0, 133.8, 128.9, 128.1, 117.3, 115.6, 113.9, 113.4, 60.0, 55.1 ppm; HRMS (EI): calcd for $C_{16}H_{17}NO$: 239.1310; found: 239.1310; elemental analysis: calcd (%) for $C_{16}H_{17}NO$: C 80.30, H 7.16, N 5.85; found: C 80.41, H 7.07, N 5.93.

***N*-[1-(4-Bromophenyl)-2-propenyl]aniline (3g)**: Amine **1g** (0.28 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and $[Cp_2Zr(Me)Cl]$ (0.34 g, 1.2 mmol). This was followed by addition of butyl vinyl ether (**2a**; 0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (7:1)) to give **3g** as a pale yellow oil. $R_f = 0.37$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.60$–6.50 (m, 9 H; ArH), 6.06 (ddd, $J = 16.4$, 10.6, 6.0 Hz, 1 H; C*H*=CH$_2$), 5.29 (d, $J = 16.4$ Hz, 1 H; CH=C*H*H), 5.28 (d, $J = 10.6$ Hz, 1 H; CH=CH*H*), 4.95 (d, $J = 6.0$ Hz, 1 H; NHC*H*), 4.08 (br s, 1 H; NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 146.7, 140.7, 138.5, 131.7, 129.0, 128.7, 121.0, 117.8, 116.5, 113.4, 60.1 ppm; HRMS (EI): calcd for $C_{15}H_{14}BrN$: 287.0304; found: 287.0301; elemental analysis: calcd (%) for $C_{15}H_{14}BrN$: C 62.52, H 4.90, N 4.86; found: C 62.62, H 4.80, N 4.79.

(*Z*)-5-Phenylamino-3-penten-1-ol (3i): Amine **1a** (0.11 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and $[Cp_2Zr(Me)Cl]$ (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3i** as a pale yellow oil. $R_f = 0.19$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–7.20, 6.90–6.55 (2 × m, 5 H; ArH), 5.76 (dt, $J = 10.8$, 6.5 Hz, 1 H; NHCHC*H*=CH), 5.65 (dt, $J = 10.8$, 6.7 Hz, 1 H; NHCHCH=C*H*), 3.79 (d, $J = 6.5$ Hz, 2 H; NHC*H*$_2$), 3.67 (t, $J = 6.7$ Hz, 2 H; C*H*$_2$OH), 3.40 (br s, 1 H; OH), 2.41 (q, $J = 6.7$ Hz, 2 H; CH=CHC*H*$_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.9$, 129.0, 128.9, 128.8, 117.5, 113.0, 61.4, 40.8, 30.7 ppm; HRMS (EI): calcd for $C_{11}H_{15}NO$: 177.1154; found: 177.1150; elemental analysis: calcd (%) for $C_{11}H_{15}NO$: C 74.54, H 8.53, N 7.90; found: C 74.66, H 8.46, N 7.96.

(*Z*)-5-Phenylamino-3-hexen-1-ol (3j): Amine **1b** (0.12 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and $[Cp_2Zr(Me)Cl]$ (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL,

10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3j** as a yellow oil. $R_f = 0.25$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.30$–7.18, 6.82–6.59 (2×m, 5H; ArH), 5.59–5.39 (m, 2H; C*H*=C*H*), 4.29 (quintet, $J = 6.6$ Hz, 1H; NHC*H*), 3.68 (t, $J = 6.4$ Hz, 2H; CH_2OH), 2.95 (br s, 2H; OH and NH), 2.55–2.35 (m, 2H; CH=CHCH_2), 1.31 (d, $J = 6.6$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.1$, 136.6, 129.0, 126.5, 117.5, 113.6, 61.8, 46.4, 31.1, 21.8 ppm; HRMS (EI): calcd for $C_{12}H_{17}NO$: 191.1310; found: 191.1307; elemental analysis: calcd (%) for $C_{12}H_{17}NO$: C 75.35, H 8.96, N 7.32; found: C 75.41, H 8.88, N 7.41.

(*Z*)-5-Phenyl-5-phenylamino-3-penten-1-ol (3k): Amine **1d** (0.18 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [Cp_2Zr(Me)Cl] (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3k** as a pale yellow oil. $R_f = 0.25$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.50$–6.55 (m, 10H; ArH), 5.73 (dd, $J = 10.7$, 8.6 Hz, 1H; NHCHC*H*=CH), 5.60 (dt, $J = 10.7$, 7.6 Hz, 1H; NHCHCH=C*H*), 5.21 (d, $J = 8.6$ Hz, 1H; NHC*H*), 3.71 (t, $J = 6.4$ Hz, 2H; CH_2OH), 2.80 (br s, 2H; OH and NH), 2.60–2.40 (m, 2H; CH=CHCH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.1$, 142.9, 134.3, 129.0, 128.6, 127.7, 127.0, 126.4, 117.6, 113.6, 61.6, 55.5, 31.3 ppm; HRMS (EI): calcd for $C_{17}H_{19}NO$: 253.1467; found: 253.1466; elemental analysis: calcd (%) for $C_{17}H_{19}NO$: C 80.60, H 7.56, N 5.53; found: C 80.74, H 7.47, N 5.60.

(*Z*)-5-Benzylamino-5-phenyl-3-penten-1-ol (3l): Amine **1e** (0.20 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [Cp_2Zr(Me)Cl] (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3l** as a pale yellow oil. $R_f = 0.35$ (hexane/ethyl acetate (1:2)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.35$–6.25 (m, 10H; ArH), 5.79 (dd, $J = 10.7$, 8.7 Hz, 1H; NHCHC*H*=CH), 5.62 (dt, $J = 10.7$, 7.4 Hz, 1H; NHCHCH=C*H*), 4.61 (d, $J = 8.7$ Hz, 1H; NHC*H*), 3.75 (s, 2H; CH_2Ph), 3.75–3.55 (m, 2H; CH_2OH), 2.78 (br s, 2H; OH and NH), 2.52 (dq, $J = 14.4$, 7.4 Hz, 1H; CH=CHC*H*H), 2.38 (dq, $J = 14.4$, 7.4 Hz, 1H; CH=CHCH*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 142.4$, 139.1, 134.1, 128.3, 128.1, 127.6, 126.9, 126.8, 126.7, 60.8, 58.1, 50.5, 31.3 ppm; HRMS (EI): calcd for $C_{18}H_{21}NO$: 267.1618; found: 267.1608; elemental analysis: calcd (%) for $C_{18}H_{21}NO$: C 80.86, H 7.92, N 5.24; found: C 80.93, H 7.82, N 5.17.

(*Z*)-5-(4-Methoxyphenyl)-5-phenylamino-3-penten-1-ol (3m): Amine **1f** (0.23 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [Cp_2Zr(Me)Cl] (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3m** as a pale yellow oil. $R_f = 0.65$ (hexane/ethyl acetate (1:2)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–6.55 (m, 9H; ArH), 5.74 (dd, $J = 10.9$, 8.3 Hz, 1H; NHCHC*H*=CH), 5.59 (dt, $J = 10.9$, 7.1 Hz, 1H; NHCHCH=C*H*), 5.18 (d, $J = 8.3$ Hz, 1H; NHC*H*), 3.95–3.60 (m with s at 3.82, 5H; CH_2OH and OCH_3), 2.58–2.48 (m, 2H; CH=CHCH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.6$, 147.1, 134.8, 128.9, 127.5, 127.3, 117.6, 114.0, 113.6, 61.8, 55.1, 54.9, 31.3 ppm; HRMS (EI): calcd for $C_{18}H_{21}NO_2$: 283.1572; found: 283.1569; elemental analysis: calcd (%) for $C_{18}H_{21}NO_2$: C 76.29, H 7.47, N 4.94; found: C 76.41, H 7.41, N 5.01.

(*Z*)-5-(4-Bromophenyl)-5-phenylamino-3-penten-1-ol (3n): Amine **1g** (0.28 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [Cp_2Zr(Me)Cl] (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3n** as a pale yellow oil. $R_f = 0.70$ (hexane/ethyl acetate (1:2)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.60$–6.50 (m, 9H; ArH), 5.85–5.55 (m, 2H; C*H*=C*H*), 5.21 (d, $J = 7.6$ Hz, 1H; NHC*H*), 3.70 (t, $J = 6.4$ Hz, 2H; CH_2OH), 2.62–2.36 (m, 2H; CH=CHCH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 146.7$, 141.9, 133.4, 131.5, 128.9, 128.0, 120.5, 117.7, 113.5, 61.3, 54.8, 31.1 ppm; HRMS (EI): calcd for $C_{17}H_{18}BrNO$: 331.0566; found: 331.0559; elemental analysis: calcd (%) for $C_{17}H_{18}BrNO$: C 61.46, H 5.46, N 4.22; found: C 61.56, H 5.37, N 4.30.

(*Z*)-5-(4-Methoxyphenylamino)-3-octen-1-ol (3o): Amine **1h** (0.18 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [Cp_2Zr(Me)Cl] (0.34 g, 1.2 mmol). This was followed by addition of enol ether **2c** (0.76 mL, 10 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (2:1)) to give **3o** as a pale yellow oil. $R_f = 0.30$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.75$ (d, $J = 9.0$ Hz, 2H; ArH), 6.58 (d, $J = 9.0$ Hz, 2H; ArH), 5.47 (dt, $J = 10.4$, 7.2 Hz, 1H; NHCHCH=C*H*), 5.29 (t, $J = 10.4$ Hz, 1H; NHCHC*H*=CH), 4.05–3.85 (m, 1H; NHC*H*), 3.71 (s, 3H; OCH_3), 3.70–3.50 (m, 2H; CH_2OH), 3.05 (br s, 2H; OH and NH), 2.50–2.20 (m, 2H; CH=CHCH_2), 1.70–1.20 (m, 4H; $(CH_2)_2CH_3$), 0.91 (t, $J = 6.7$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 152.0$, 141.2, 135.1, 127.2, 115.3, 114.4, 61.6, 55.3, 51.6, 37.7, 31.2, 18.8, 13.8 ppm; HRMS (EI): calcd for $C_{15}H_{23}NO_2$: 249.1729; found: 249.1733; elemental analysis: calcd (%) for $C_{15}H_{23}NO_2$: C 72.25, H 9.30, N 5.62; found: C 72.33, H 9.19, N 5.53.

General procedure for the preparation of compounds 4: Tosyl chloride (1.2 mmol), Et_3N (1.5 mmol), and a catalytic amount of DMAP were added to a solution of the appropriate amino alcohol **3** (1 mmol) in dichloromethane (10 mL). After stirring for 6 h the reaction was quenched by addition of water (10 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were dried over anhydrous sodium sulphate and concentrated, and the residue was purified by column chromatography to give compounds **4**.

1,2,3,6-Tetrahydro-1,6-diphenylpyridine (4a): Amino alcohol **3k** (0.25 g, 1 mmol) was treated with TsCl (0.23 g, 1.2 mmol), Et_3N (0.21 mL, 1.5 mmol), and a catalytic amount of DMAP. After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (5:1)) to give **4a** as a pale yellow oil. $R_f = 0.55$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.42$–7.18, 6.97–6.75 (2×m, 10H; ArH), 6.11–5.95 (m, 2H; C*H*=C*H*), 5.19 (s, 1H; PhC*H*), 3.69 (dt, $J = 12.9$, 5.0, 1H; NC*H*H), 3.46 (ddd, $J = 12.9$, 9.2, 4.2 Hz, 1H; NCH*H*), 2.46 (ddd, $J = 14.5$, 9.2, 5.0, 1H; C*H*HCH=CH), 2.29–2.15 (m, 1H; CH*H*CH=CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 149.9$, 141.8, 129.2, 128.9, 128.3, 126.9, 126.7, 125.6, 117.9, 115.4, 59.8, 42.0, 24.3 ppm; HRMS (EI): calcd for $C_{17}H_{17}N$: 235.1355; found: 235.1351; elemental analysis: calcd (%) for $C_{17}H_{17}N$: C 86.77, H 7.28, N 5.95; found: C 86.84, H 7.21, N 5.90.

1-Benzyl-1,2,3,6-tetrahydro-6-phenylpyridine (4b): Amino alcohol **3l** (0.30 g, 1 mmol) was treated with TsCl (0.23 g, 1.2 mmol), Et_3N (0.21 mL, 1.5 mmol), and a catalytic amount of DMAP. After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (5:1)) to give **4b** as a pale yellow oil. $R_f = 0.50$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.70$–7.10 (m, 10H; ArH), 5.92–5.80 (m, 1H; CH_2CH=CH), 5.67 (dd, $J = 9.8$, 1.2 Hz, 1H; CH_2CH=C*H*), 4.05 (s, 1H; PhC*H*), 3.88 (d, $J = 13.6$ Hz, 1H; PhC*H*H), 3.21 (d, $J = 13.6$ Hz, 1H; PhCH*H*), 3.09–2.93 (m, 1H; C*H*HCH=CH), 2.51–2.34 (m, 2H; NCH_2), 2.17–2.01 (m, 1H; CH*H*CH=CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 143.5$, 139.4, 130.4, 128.5, 128.3, 127.9, 127.0, 126.6, 124.2, 66.2, 58.8, 47.2, 25.8 ppm; HRMS (EI): calcd for $C_{18}H_{19}N$: 249.1517; found: 249.1522; elemental analysis: calcd (%) for $C_{18}H_{19}N$: C 86.70, H 7.68, N 5.62; found: C 86.84, H 7.58, N 5.56.

6-(4-Bromophenyl)-1,2,3,6-tetrahydro-1-phenylpyridine (4c): Amino alcohol **3n** (0.33 g, 1 mmol) was treated with TsCl (0.23 g, 1.2 mmol), Et_3N (0.21 mL, 1.5 mmol), and a catalytic amount of DMAP. After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (5:1)) to give **4c** as a pale yellow oil. $R_f = 0.58$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.50$–7.15, 6.98–6.75 (2×m, 9H; ArH), 6.12–5.92 (m, 2H; C*H*=C*H*), 5.13 (s, 1H, BrC_6H_4CH), 3.65 (dt, $J = 12.5$, 4.5 Hz, 1H; NC*H*H), 3.42 (ddd, $J = 12.5$, 8.9, 4.5 Hz, 1H; NCH*H*), 2.55–2.38 (m, 1H; C*H*HCH=CH), 2.31–2.17 (m, 1H; CH*H*CH=CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 149.8$, 141.0, 131.3, 129.0, 128.8, 128.6, 126.1, 120.5, 118.5, 115.9, 59.4, 42.3, 24.4 ppm; HRMS (EI): calcd for $C_{17}H_{16}BrN$: 313.0466; found: 313.0471; elemental analysis: calcd (%) for $C_{17}H_{16}BrN$: C 64.98, H 5.13, N 4.46; found: C 65.06, H 5.08, N 4.40.

1,2,3,6-Tetrahydro-1-(4-methoxyphenyl)-6-propylpyridine (4d): Amino alcohol **3o** (0.23 g, 1 mmol) was treated with TsCl (0.23 g, 1.2 mmol), Et_3N (0.21 mL, 1.5 mmol), and a catalytic amount of DMAP. After the extractive work-up, the resulting crude product was purified by silica gel

column chromatography (hexane/ethyl acetate (7:1)) to give **4d** as a pale yellow oil. $R_f = 0.75$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.93$ (d, $J = 9.0$ Hz, 2H; ArH), 6.85 (d, $J = 9.0$ Hz, 2H; ArH), 6.95–6.78 (m, 2H; C*H*=C*H*), 3.98–3.85 (m, 1H; $CH_3(CH_2)_2CH$), 3.78 (s, 3H; OCH_3), 3.39 (ddd, $J = 12.6$, 5.5, 3.5 Hz, 1H; NC*H*H), 3.21 (ddd, $J = 12.6$, 8.9, 4.3 Hz, 1H; NCH*H*), 2.39–2.19 (m, 1H; C*H*HCH=CH), 2.14–1.97 (m, 1H; CH*H*CH=CH), 1.50–1.20 (m, 4H; $CH_3(CH_2)_2$), 0.91 (t, $J = 6.7$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 152.9$, 144.9, 129.8, 125.1, 118.9, 114.3, 56.8, 55.4, 43.1, 34.7, 24.4, 19.3, 14.1 ppm; HRMS (EI): calcd for $C_{15}H_{21}NO$: 231.1618; found: 231.1610; elemental analysis: calcd (%) for $C_{15}H_{21}NO$: C 77.88, H 9.15, N 6.05; found: C 78.00, H 9.09, N 5.97.

1-(4-Methoxyphenyl)-2-propylpiperidine (5): Amine **4d** (0.23 g, 1 mmol) was added to a suspension of palladium (10 wt% on carbon, 0.70 g) in ethyl acetate (10 mL). The suspension was stirred under hydrogen (1 atm) for 1 h and then filtered through a plug of silica gel to give, after removal of the solvents, pure compound **5** as a colorless oil. $R_f = 0.75$ (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.94$ (d, $J = 9.0$ Hz, 2H; ArH), 6.85 (d, $J = 9.0$ Hz, 2H; ArH), 3.79 (s, 3H; OCH_3), 3.47–3.31 (m, 1H; $CH_3(CH_2)_2CH$), 3.12–2.90 (m, 2H; NCH_2), 1.90–0.90 (m, 10H; $CH_3(CH_2)_2$ and aliphatic ring), 0.88 (t, $J = 6.7$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.4$, 145.7, 120.3, 114.1, 57.7, 55.3, 47.9, 30.4, 28.7, 25.9, 20.5, 19.7, 14.1 ppm; HRMS (EI): calcd for $C_{15}H_{23}NO$: 233.1780; found: 233.1781; elemental analysis: calcd (%) for $C_{15}H_{23}NO$: C 77.21, H 9.93, N 6.00; found: C 77.26, H 9.88, N 5.97.

General procedure for the preparation of compounds 13 and 14: The procedure is analogous to that described before for the synthesis of compounds **3**. Instead of addition of the appropriate enol ether, in these cases allyl phenyl ether (**12**; 2 mmol) was used. Analytical data for compounds **13e**,[18] **13f**,[19] **13g**,[20] and **13h**[21] were in complete accordance with literature values.

***N*-(1-Methyl-3-butenyl)aniline (13b)**: Amine **1b** (0.12 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (10:1)) to give **13b** as a pale yellow oil. $R_f = 0.26$ (hexane/ethyl acetate (20:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–7.11, 6.85–6.52 (2×m, 5H; ArH), 5.85–5.70 (m, 1H; C*H*=CH_2), 5.14 (d, $J = 17.0$ Hz, 1H; CH=C*H*H), 5.12 (d, $J = 10.0$ Hz, 1H; CH=CH*H*), 3.65–3.49 (m, 1H; NHC*H*), 2.48–2.26 (m, 2H; NHCHCH_2), 1.22 (d, $J = 6.4$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 147.2, 134.8, 129.2, 117.4, 116.9, 113.2, 47.8, 40.7, 20.2 ppm; HRMS (EI): calcd for $C_{11}H_{15}N$: 161.1204; found: 161.1205; elemental analysis: calcd (%) for $C_{11}H_{15}N$: C 81.94, H 9.38, N 8.69; found: C 82.05, H 9.28, N 8.63.

***N*-(1-Propyl-3-butenyl)aniline (13c)**: Amine **1c** (0.15 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (10:1)) to give **13c** as a pale yellow oil. $R_f = 0.50$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.25$–7.10, 6.73–6.54 (2×m, 5H; ArH), 5.88–5.70 (m, 1H; C*H*=CH_2), 5.18–5.05 (m, 2H; CH=CH_2), 3.60–3.35 (m, 2H; NH and NHC*H*), 2.38–2.25 (m, 2H; NHCHCH_2), 1.65–1.25 (m, 4H; $CH_3(CH_2)_2$), 0.93 (t, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 147.7, 134.9, 129.1, 117.4, 116.7, 113.0, 52.0, 38.4, 36.5, 19.1, 14.0 ppm; HRMS (EI): calcd for $C_{13}H_{19}N$: 189.1517; found: 189.1517; elemental analysis: calcd (%) for $C_{13}H_{19}N$: C 82.48, H 10.12, N 7.40; found: C 82.53, H 10.02, N 7.41.

***N*-(1-Isopropyl-3-butenyl)aniline (13d)**: Amine **1i** (0.15 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (10:1)) to give **13d** as a pale yellow oil. $R_f = 0.50$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–7.10, 6.80–6.55 (2×m, 5H; ArH), 5.96–5.80 (m, 1H; C*H*=CH_2), 5.21–5.07 (m, 2H; CH=CH_2), 3.58 (brs, 1H; NH), 3.33 (dt, $J = 7.4$, 5.1 Hz, 1H; NHC*H*), 2.46–1.88 (m, 3H; NHCHCH_2 and C$H(CH_3)_2$), 1.03 (d, $J = 7.4$ Hz, 3H; CH_3), 1.01 (d, $J = 7.4$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 148.1, 135.5, 129.1, 116.9, 116.5, 113.0, 57.7, 35.5, 30.7, 18.5, 18.3 ppm; HRMS (EI): calcd for $C_{13}H_{19}N$: 189.1517; found: 189.1519; elemental analysis: calcd (%) for $C_{13}H_{19}N$: C 82.48, H 10.12, N 7.40; found: C 82.55, H 10.01, N 7.36.

***N*-[1-(4-Bromophenyl)-3-butenyl]aniline (13i)**: Amine **1g** (0.28 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (7:1)) to give **13i** as a pale yellow oil. $R_f = 0.40$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.57$ (d, J = 8.4 Hz, 2H; 4-BrC_6H_4), 7.35 (d, J = 8.4 Hz, 2H; 4-BrC_6H_4), 7.29–6.55 (m, 5H; ArH), 5.86 (ddt, $J = 17.0$, 10.0, 6.7 Hz, 1H; C*H*=CH_2), 5.30 (d, $J = 17.0$ Hz, 1H; CH=C*H*H), 5.28 (d, $J = 10.0$ Hz, 1H; CH=CH*H*), 4.46 (dd, $J = 7.7$, 5.2 Hz, 1H; NHC*H*), 4.28 (brs, 1H; NH), 2.80–2.45 (m, 2H; NHCHCH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 146.6$, 142.3, 133.8, 131.3, 128.8, 127.8, 120.3, 118.3, 117.3, 113.2, 56.2, 42.7 ppm; HRMS (EI): calcd for $C_{16}H_{16}BrN$: 301.0461; found: 301.0456; elemental analysis: calcd (%) for $C_{16}H_{16}BrN$: C 63.59, H 5.34, N 4.63; found: C 63.63, H 5.28, N 4.68.

***N*-(2-Methyl-3-phenoxypropyl)aniline (14a)**: Amine **1a** (0.11 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (7:1)) to give **14a** as a yellow oil. $R_f = 0.40$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.55$–6.66 (m, 10H; ArH), 4.06 (dd, $J = 9.0$, 5.2 Hz, 1H; PhOC*H*H), 4.00 (dd, $J = 9.0$, 6.3 Hz, 1H; PhOCH*H*), 3.41 (dd, $J = 12.5$, 7.0 Hz, 1H; PhNHC*H*H), 3.25 (dd, $J = 12.5$, 6.3 Hz, 1H; PhNHCH*H*), 2.90 (brs, 1H; NH), 2.55–2.30 (m, 1H; C*H*CH_3), 1.24 (d, $J = 6.6$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.7$, 148.2, 129.4, 129.1, 120.7, 117.4, 114.4, 112.6, 71.0, 47.4, 33.0, 15.3 ppm; HRMS (EI): calcd for $C_{16}H_{19}NO$: 241.1467; found: 241.1467; elemental analysis: calcd (%) for $C_{16}H_{19}NO$: C 79.63, H 7.94, N 5.80; found: C 79.78, H 7.79, N 5.71.

***N*-(1,2-Dimethyl-3-phenoxypropyl)aniline (14b)**: Amine **1b** (0.12 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (7:1)) to give **14b** as a pale yellow oil. $R_f = 0.18$ (hexane/ethyl acetate (20:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.51$–6.65 (m, 10H; ArH), 4.10 (dd, $J = 9.1$, 7.4 Hz, 1H; PhOC*H*H), 3.98 (dd, $J = 9.1$, 5.5 Hz, 1H; PhOCH*H*), 3.95–3.85 (m, 1H; PhNHC*H*), 3.75 (brs, 1H; NH), 2.45–2.30 (m, 1H; $PhOCH_2CH$), 1.33 (d, $J = 5.4$ Hz, 3H; CH_3), 1.20 (d, $J = 7.1$ Hz, 3H; CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.6$, 147.6, 129.2, 129.1, 120.5, 116.7, 114.3, 112.5, 69.9, 50.1, 37.4, 17.1, 12.7 ppm; HRMS (EI): calcd for $C_{17}H_{21}NO$: 255.1623; found: 255.1628; elemental analysis: calcd (%) for $C_{17}H_{21}NO$: C 79.96, H 8.29, N 5.49; found: C 80.08, H 8.23, N 5.39.

***N*-[1-(1-Methyl-2-phenoxyethyl)butyl]aniline (14c)**: Amine **1c** (0.15 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of allyl phenyl ether (**12**; 0.27 mL, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (7:1)) to give **14c** as a pale yellow oil. $R_f = 0.41$ (hexane/ethyl acetate (10:1)); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.49$–6.65 (m, 10H; ArH), 4.02 (t, $J = 9.0$ Hz, 1H; PhOC*H*H), 3.88 (dd, $J = 9.0$, 5.6 Hz, 1H; PhOCH*H*), 3.77 (brs, 1H; NH), 3.68–3.46 (m, 1h; PhNHC*H*), 2.42–2.39 (m, 1H; C*H*CH_3), 1.70–1.30 (m, 4H; $(CH_2)_2CH_3$), 1.10 (d, $J = 6.5$ Hz, 3H; $CHCH_3$), 1.00 (t, $J = 6.9$ Hz, 3H; $(CH_2)_2CH_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.7$, 148.6, 129.2, 129.1, 120.4, 116.5, 114.4, 112.8, 70.2, 53.9, 36.5, 35.2, 19.9, 14.0, 11.7 ppm; HRMS (EI): calcd for $C_{19}H_{25}NO$: 283.1936; found: 283.1937; elemental analysis: calcd (%) for $C_{19}H_{25}NO$: C 80.52, H 8.89, N 4.94; found: C 80.61, H 8.86, N 5.04.

General procedure for the preparation of compounds 16: The procedure is analogous to that described before for the synthesis of compounds **3**. Instead of addition of the appropriate enol ether, in these cases 1,4-dihydro-1,4-epoxynaphthalene (**15**; 2 mmol) was used.

(1*R,2*S**)-1,2-Dihydro-2-phenylaminomethyl-1-naphthol (16a)**: Amine **1a** (0.11 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of 1,4-dihydro-1,4-epoxynaphthalene (**15**; 0.29 g, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (5:1)) to give **16a** as a colorless oil. R_f=0.55 (hexane/ethyl acetate (2:1)); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.50–6.70 (m, 9H; ArH), 6.65 (d, J=9.5 Hz, 1H; ArC*H*=CH), 5.93 (dd, J=9.5, 3.2 Hz, 1H; ArCH=C*H*), 4.85 (d, J=4.9 Hz, 1H; C*H*OH), 3.58 (dd, J=12.8, 8.9 Hz, 1H; NHC*H*H), 3.45 (dd, J=12.8, 5.8 Hz, 1H; NHCH*H*), 3.22 (brs, 2H; OH and NH), 2.98–2.84 (m, 1H; CH=CHC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=147.8, 136.0, 132.4, 129.1, 128.1, 128.0, 127.4, 127.0, 126.1, 117.6, 113.2, 69.7, 43.7, 39.3 ppm; HRMS (EI): calcd for $C_{17}H_{17}NO$: 251.1309; found: 251.1305; elemental analysis: calcd (%) for $C_{17}H_{17}NO$: C 81.24, H 6.82, N 5.57; found: C 81.31, H 6.78, N 5.49.

(1*R,2*S**)-1,2-Dihydro-2-(1-phenyl-1-phenylaminoethyl)-1-naphthol (16b):** Amine **1d** (0.18 g, 1 mmol) was treated with BuLi (0.75 mL, 1.2 mmol) and [$Cp_2Zr(Me)Cl$] (0.34 g, 1.2 mmol). This was followed by addition of 1,4-dihydro-1,4-epoxynaphthalene (**15**; 0.29 g, 2 mmol). After the extractive work-up, the resulting crude product was purified by silica gel column chromatography (hexane/ethyl acetate (5:1)) to give **16b** as a colorless oil and as mixture of two diastereoisomers. R_f=0.60 (hexane/ethyl acetate (2:1)); major diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.50–6.60 (m, 15H; ArH and ArC*H*=CH), 6.15 (dd, J=9.7, 2.2 Hz, 1H; ArCH=C*H*), 5.00–4.92 (m, 1H; C*H*OH), 4.64–4.51 (m, 1H; NHC*H*), 2.93–2.84 (m, 1H; CH=CHC*H*) ppm; minor diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.50–6.60 (m, 15H; ArH and ArC*H*=CH), 5.92 (dd, J=9.6, 2.9 Hz, 1H; ArCH=C*H*), 4.88 (d, J=7.1 Hz, 1H; C*H*OH), 4.71 (d, J=3.8 Hz, 1H; NHC*H*), 3.04–2.95 (m, 1H; CH=CHC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=147.0 (maj), 146.9 (min), 141.7 (maj), 141.1 (min), 136.2 (maj), 136.0 (min), 132.6 (min), 132.2 (maj), 129.3, 128.5, 128.4, 127.7, 127.6, 127.4, 127.0, 126.7, 126.5, 126.4, 117.5 (maj), 117.4 (min), 113.9 (min), 113.6 (maj), 69.6 (maj), 59.5 (min), 57.5 (maj), 47.4 (maj), 45.8 (min) ppm (maj=major diastereoisomer, min=minor diastereoisomer); HRMS (EI): calcd for $C_{23}H_{21}NO$: 327.1633; found: 327.1618; elemental analysis: calcd (%) for $C_{23}H_{21}NO$: C 84.37, H 6.46, N 4.28; found: C 84.46, H 6.35, N 4.18.

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[1] *Bioorganic Chemistry: Peptides and Proteins* (Ed.: S. Hetch), Oxford University Press, Oxford, **1998**.
[2] M. Hesse, *Alkaloids: Nature's Curse or Blessing?*, Wiley-VCH, New York, **2000**.
[3] For some recent and selected examples of synthesis of allylamines, see: a) T. Ohmura, J. F. Hartwig, *J. Am. Chem. Soc.* **2002**, *124*, 15 164; b) P. A. Evans, J. E. Robinson, J. D. Nelson, *J. Am. Chem. Soc.* **1999**, *121*, 6761; c) Y. Donde, L. E. Overman, *J. Am. Chem. Soc.* **1999**, *121*, 2933; d) B. M. Trost, R. Radinov, *J. Am. Chem. Soc.* **1997**, *119*, 5962.
[4] S. Akutagawa, K. Tani, in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), 2nd ed., Wiley-VCH, Weinheim, Germany, **2000**, p. 145.
[5] a) S. L. Buchwald, B. T. Watson, M. W. Wannamaker, J. C. Dewan, *J. Am. Chem. Soc.* **1989**, *111*, 4486. For an enantioselective version, see: b) R. B. Grossman, W. M. Davis, S. L. Buchwald, *J. Am. Chem. Soc.* **1991**, *113*, 2321.
[6] For an excellent study on the formation of η^2-imine–zirconocene complexes from amines, see: N. Coles, M. C. J. Harris, R. J. Whitby, J. Blagg, *Organometallics* **1994**, *13*, 190.
[7] a) J. Barluenga, R. Sanz, F. J. Fañanás, *Chem. Eur. J.* **1997**, *3*, 1324; b) J. Barluenga, R. Sanz, F. J. Fañanás, *J. Org. Chem.* **1997**, *62*, 5953; c) J. Barluenga, R. Sanz, F. J. Fañanás, *J. Chem. Soc. Chem. Commun.* **1995**, 1009; d) J. Barluenga, R. Sanz, F. J. Fañanás, *Z. Naturforsch. Teil B* **1995**, *50*, 312; e) J. Barluenga, R. Sanz, R. González, F. J. Fañanás, *J. Chem. Soc. Chem. Commun.* **1994**, 989.
[8] The same behavior was observed in the reaction of η^2-alkyne–zirconocene complexes and enol ethers: T. Takahashi, D. Y. Kondakov, Z. Xi, N. Suzuki, *J. Am. Chem. Soc.* **1995**, *117*, 5871.
[9] 2-Substituted piperidine subunits are widely found in biologically active molecules and natural products: a) A. Numata, T. Ibuka, in *The Alkaloids, Vol. 31* (Ed.: A. Brossi), Academic Press, New York, **1987**. For some recent reviews, see: b) S. Laschat, T. Dickner, *Synthesis* **2000**, 1781; c) A. Mitchinson, A. Nadin, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2862.
[10] Coniine is a common synthetic target. For some selected examples, see: a) A. B. Charette, M. Grenon, A. Lemire, M. Pourasraf, J. Martel, *J. Am. Chem. Soc.* **2001**, *123*, 11 829; b) T. J. Wilkinson, N. W. Stehle, P. Beak, *Org. Lett.* **2000**, *2*, 155; c) M. T. Reding, S. L. Buchwald, *J. Org. Chem.* **1998**, *63*, 6344; d) A. R. Katritzky, G. Qiu, B. Yang, P. J. Steel, *J. Org. Chem.* **1998**, *63*, 6699; e) M. J. Munchhof, A. I. Meyers, *J. Org. Chem.* **1995**, *60*, 7084.
[11] The same electronic effects have been invoked to explain the results of the hydroboration reaction of enol ethers: E. Negishi, *Organometallics in Organic Synthesis*, John Wiley & Sons, New York, **1980**, p. 297.
[12] N. Coles, R. J. Whitby, J. Blagg, *Synlett* **1990**, 271.
[13] A large number of bioactive molecules possess a tetrahydronaphthalene core, for example, the antidepressant sertraline (M. Lautens, T. Rovis, *J. Org. Chem.* **1997**, *62*, 5246, and references therein) and the anticancer agent podophyllotoxin (A. Kamal, N. L. Gayatri, *Tetrahedron Lett.* **1996**, *37*, 3359, and references therein).
[14] F. Ozawa, H. Okamoto, S. Kawagishi, S. Yamamoto, T. Minami, M. Yoshifuji, *J. Am. Chem. Soc.* **2002**, *124*, 10 968.
[15] M. Johannsen, K. A. Joergensen, *J. Org. Chem.* **1994**, *59*, 214.
[16] R. Takeuchi, N. Ue, K. Tanabe, K. Yamashita, N. Shiga, *J. Am. Chem. Soc.* **2001**, *123*, 9525.
[17] Y. Yoshida, Y. Tanabe, *Synthesis* **1997**, 533.
[18] K. Maruoka, T. Miyazaki, M. Ando, Y. Matsumura, S. Sakane, K. Hattori, H. Yamamoto, *J. Am. Chem. Soc.* **1983**, *105*, 2831.
[19] S. Kobayashi, S. Nagayama, *J. Am. Chem. Soc.* **1997**, *119*, 10 049.
[20] P. G. M. Wuts, Y. W. Jung, *J. Org. Chem.* **1991**, *56*, 365.
[21] C. K. Z. Andrade, N. R. Azevedo, G. R. Oliveira, *Synthesis* **2002**, 928.

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