[Ind_2TiMe_2]: A General Catalyst for the Intermolecular Hydroamination of Alkynes

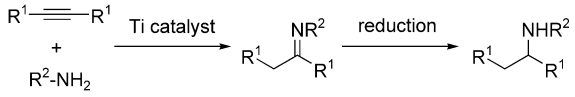
Andreas Heutling, Frauke Pohlki, and Sven Doye*[a]

Abstract: [Ind_2TiMe_2] (Ind = indenyl) is a highly active and general catalyst for the intermolecular hydroamination of alkynes. It catalyzes the reaction of primary aryl-, *tert*-alkyl-, *sec*-alkyl-, and *n*-alkylamines with internal and terminal alkynes. In the case of unsymmetrically substituted 1-phenyl-2-alkylalkynes, the reactions occur with modest to excellent regioselectivities, whereby formation of the anti-Markovnikov regioisomers is favored. While the major product of hydroamination reactions of terminal arylalkynes is always the anti-Markovnikov isomer, alkylalkynes react with arylamines to preferably give the Markovnikov products. To achieve reasonable rates for the addition of sterically less hindered *n*-alkyl- and benzylamines to alkynes, these amines must be added slowly to the reaction mixtures. This behavior is explained by the fact that the catalytic cycle proposed on the basis of an initial kinetic investigation includes the possibility that the rate of the reaction increases with decreasing concentration of the employed amine. Furthermore, no dimerization of the catalytically active imido complex is observed in the hydroamination of 1-phenylpropyne with 4-methylaniline in the presence of [Ind_2TiMe_2] as catalyst. In general, a combination of [Ind_2TiMe_2]-catalyzed hydroamination of alkynes with subsequent reduction leads to the formation of secondary amines with good to excellent yields. Particularly impressive is that [Ind_2TiMe_2] makes it possible for the first time to perform the reactions of *n*-alkyl- and benzylamines with 1-phenylpropyne in a highly regioselective fashion.

Keywords: alkynes · amination · homogeneous catalysis · metallocenes · titanium

Introduction

The development of catalytic methods for the hydroamination of unsaturated organic compounds can be regarded as one of the most challenging goals in synthetic organic chemistry.[1] While corresponding hydroamination methods for alkenes are still limited to activated substrates, more general catalytic hydroamination procedures have been developed for alkynes.[2] Among the steadily growing class of Group 4 metal catalysts for the hydroamination of alkynes,[3,4] the well-known reagent [Cp_2TiMe_2][5] has been used most extensively in the last few years.[6] In the presence of this catalyst, primary aryl-, *tert*-alkyl-, and *sec*-alkylamines react with symmetrically and unsymmetrically substituted internal and terminal alkynes. In the case of unsymmetrically substituted 1-aryl-2-alkylalkynes, the reactions occur with high regioselectivity to give the anti-Markovnikov isomers as major products.[6,7] However, reactions with sterically less demanding *n*-alkyl- and benzylamines are extremely slow and therefore useless from a synthetic point of view. As a result, the term "general" seems to be inappropriate for describing the performance of [Cp_2TiMe_2] as a hydroamination catalyst. Later, it was found that transformations employing sterically less demanding *n*-alkyl- and benzylamines are better performed in the presence of catalytic amounts of [$Cp^*_2TiMe_2$] ($Cp^* = \eta^5$-C_5Me_5).[8] Unfortunately, the regioselectivities observed for corresponding additions to unsymmetrically substituted alkynes such as 1-phenylpropyne are poor when [$Cp^*_2TiMe_2$] is used as catalyst. Furthermore, this catalyst cannot be used for the hydroamination of terminal alkynes.[8] Therefore, [$Cp^*_2TiMe_2$] cannot be regarded as a "general" catalyst either. However, inspired by the great success achieved with [Cp_2TiMe_2], many other titanium complexes have been identified as catalysts for the hydroamination of alkynes by us[9] and others.[10–14] These catalysts allow alkynes to be converted to secondary amines in efficient one-pot hydroamination/reduction sequences[8] (Scheme 1). A few other examples of efficient hydroamina-



Scheme 1. Hydroamination/reduction sequence for the synthesis of secondary amines.

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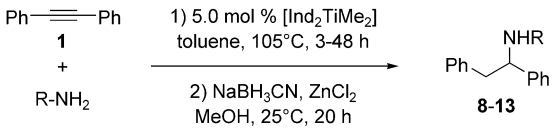
tion reactions of sterically less hindered amines have been reported,[11b,12c,14] but these experiments were only performed with terminal alkynes.

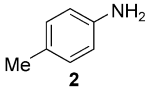
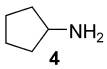
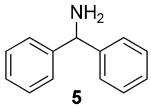
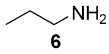
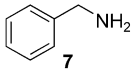
Although the scope and limitations are not well documented for most Ti catalysts, we recognized that the catalytic activities of the titanium complexes usually strongly depend on the properties of the employed substrates.[9] Recently, we compared 13 titanium complexes in two selected hydroamination/reduction test reaction sequences.[9] We found that, in contrast to other catalysts, the known complex [Ind_2TiMe_2] (Ind = indenyl)[15] gave good results in both test reactions. Therefore, we decided to investigate the catalytic performance of this catalyst in more detail, and we present the results here.

Results and Discussion

To get an impression of the activity of [Ind_2TiMe_2] as a hydroamination catalyst we first performed hydroamination reactions of diphenylacetylene (**1**) with various amines at 105 °C in toluene in the presence of 5.0 mol % of the catalyst. After subsequent reduction with $NaBH_3CN$ in the presence of $ZnCl_2$,[8] the desired secondary amines were isolated in pure form by chromatography (Table 1).

Table 1. [Ind_2TiMe_2]-catalyzed hydroamination of diphenylacetylene (**1**) with various amines and subsequent reduction.[a]



Entry	Amine	t [h]	Yield[a,b] [%]
1	 **2**	24	98 (**8**)
2	 **3**	5	84 (**9**)
3	 **4**	3	91 (**10**)
4	 **5**	5	90 (**11**)
5	 **6**	3	89 (**12**)
6	 **7**	48	30[c] (**13**)

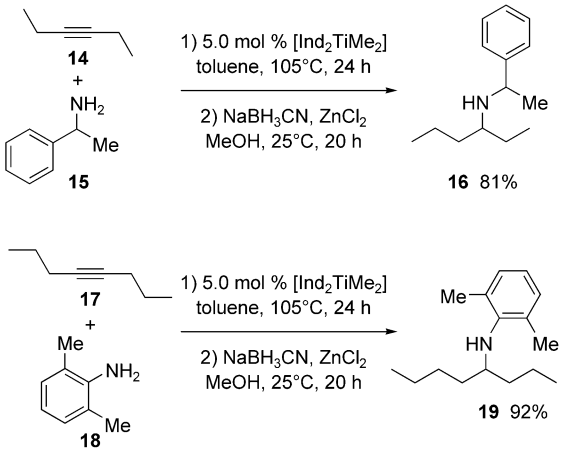
[a] Reaction conditions: 1) Alkyne **1** (2.40 mmol), amine (2.64 mmol), [Ind_2TiMe_2] (0.12 mmol, 5.0 mol %), toluene (1.0 mL), 105 °C, 3–48 h; 2) $NaBH_3CN$ (4.80 mmol), $ZnCl_2$ (2.40 mmol), MeOH (10 mL), 25 °C, 20 h. [b] Yields refer to isolated pure compounds. [c] 62 % of **1** was recovered.

While the hydroamination reaction between **1** and the aromatic amine 4-methylaniline (**2**) needed 24 h to reach 100 % conversion (entry 1, Table 1), corresponding reactions with *tert*-butylamine (**3**), cyclopentylamine (**4**), benzhydrylamine (**5**), and *n*-propylamine (**6**) went to completion within 3–5 h (entries 2–5, Table 1). The yields of the secondary amines **8**–**12** obtained after subsequent reduction were good to excellent (84–98 %) for all reactions (entries 1–5, Table 1). While the result obtained with 4-methylaniline (**2**) is comparable to earlier results obtained with [Cp_2TiMe_2],[16] the short reaction times for reactions of the alkylamines **3**–**6** indicate that [Ind_2TiMe_2] is a far more reactive catalyst than [Cp_2TiMe_2] for these substrates. This conclusion is illustrated most impressively by the fact that, after reduction, the yield of **12** was only 10 % when [Cp_2TiMe_2] (6.0 mol %) was used at 114 °C in toluene to convert diphenylacetylene (**1**) and *n*-propylamine (**6**) to **12**.[8] The results presented in Table 1 show that [Ind_2TiMe_2] is clearly a suitable catalyst for the addition of aromatic amines as well as *tert*-, *sec*-, and *n*-alkylamines to diphenylacetylene (**1**). The result obtained with benzhydrylamine (**5**) shows that [Ind_2TiMe_2] also seems to be suitable for the conversion of alkynes to primary amines, because **5** has already been used as an ammonia equivalent for Ti-catalyzed hydroamination reactions.[7a]

Abstract in German: *Die vorliegende Studie zeigt, dass der kommerziell erhältliche Komplex [Ind_2TiMe_2] ein hoch aktiver und generell einsetzbarer Katalysator für die intermolekulare Hydroaminierung von Alkinen ist. Mit diesem Katalysator können primäre Aryl-,* tert-*Alkyl-,* sec-*Alkyl- und* n-*Alkylamine erfolgreich an interne und terminale Alkine addiert werden. Im Fall von unsymmetrisch substituierten 1-Phenyl-2-alkylalkinen verlaufen die Reaktionen mit guten bis exzellenten Regioselektivitäten, wobei sich bevorzugt die Anti-Markovnikov-Regioisomere bilden. Während terminale Arylalkine mit allen Aminen bevorzugt zu den entsprechenden Anti-Markovnikov-Produkten reagieren, stellen bei Umsetzungen von terminalen Alkylalkinen mit Arylaminen die Markovnikov-Produkte die Hauptprodukte der Reaktionen dar. Um akzeptable Reaktionsgeschwindigkeiten für die Addition von sterisch wenig gehinderten Aminen wie* n-*Alkyl- und Benzylaminen an Alkine zu erreichen, müssen diese Amine langsam zur Reaktionsmischung zugetropft werden. Diese Tatsache kann dadurch erklärt werden, dass der in einer ersten kinetischen Studie ermittelte Katalysezyklus die Möglichkeit beinhaltet, dass die Reaktionsgeschwindigkeit minus erster Ordnung bezüglich des Amins ist. Darüber hinaus wurde festgestellt, dass es bei der Verwendung von [Ind_2TiMe_2] als Katalysator für die Umsetzung von 1-Phenylpropin mit 4-Methylanilin zu keiner reversiblen Dimerisierung der unter den Reaktionsbedingungen gebildeten katalytisch aktiven Spezies kommt. Insgesamt liefern die durchgeführten Sequenzen aus [Ind_2TiMe_2]-katalysierter Hydroaminierung von Alkinen und nachfolgender Reduktion sekundäre Amine in guten bis exzellenten Ausbeuten. Besonders vorteilhaft ist die Tatsache, dass es unter Verwendung von [Ind_2TiMe_2] als Katalysator erstmals gelingt, sterisch wenig gehinderte* n-*Alkyl- und Benzylamine mit hoher Regioselektivität an 1-Phenylpropin zu addieren.*

However, a disappointing result was obtained for the hydroamination of **1** with benzylamine (**7**). The reaction did not reach 100% conversion over 48 h. After subsequent reduction, only 30% of the desired product **13** was isolated, and 62% of unconverted starting material **1** was recovered (entry 6, Table 1). Since benzylamines are already known to be poor substrates for $[Cp_2TiMe_2]$-catalyzed hydroaminations we were not totally surprised by this finding. Hence, we initially continued our study without performing further experiments with other benzylamine derivatives. However, later on in this paper, we present a reinvestigation of the behavior of benzylamine derivatives in $[Ind_2TiMe_2]$-catalyzed hydroamination reactions.

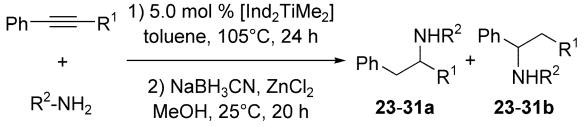
We converted the dialkylalkynes 3-hexyne (**14**) and 4-octyne (**17**) to secondary amines by hydroamination/reduction sequences (Scheme 2). The hydroamination reactions of **14** and **17** were performed in the presence of 5.0 mol% $[Ind_2TiMe_2]$ under standard conditions with (±)-1-phenylethylamine (**15**) and 2,6-dimethylaniline (**18**), respectively. After reaction times of 24 h for the hydroamination step (not minimized) and subsequent reduction the yields of **16** and **19** were 81 and 92%, respectively. These results in combination with the study employing **1** clearly indicate that $[Ind_2TiMe_2]$ is a suitable catalyst for the intermolecular hydroamination of symmetrical diaryl- and dialkylalkynes.

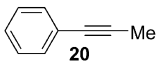
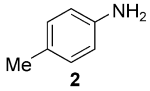
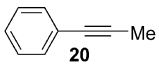
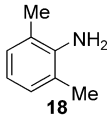
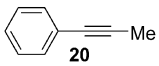
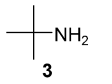
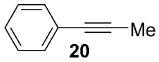
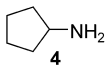
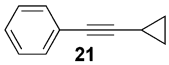
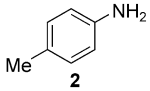
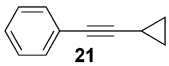
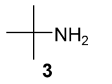
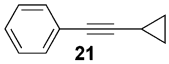
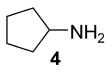
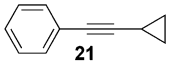
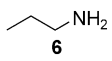
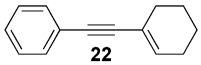
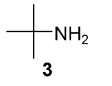


Scheme 2. $[Ind_2TiMe_2]$-catalyzed hydroamination of dialkylalkynes and subsequent reduction.

With these results in hand, we focused on $[Ind_2TiMe_2]$-catalyzed hydroaminiation reactions of unsymmetrically substituted 1-phenyl-2-alkylalkynes with various amines (Table 2). The corresponding hydroamination/reduction sequences were all performed under standard conditions with 5.0 mol% $[Ind_2TiMe_2]$. The reaction time of the hydroamination step was always 24 h (not minimized). All reaction sequences gave the desired secondary amines in good to excellent yields (76–99%). Interestingly, the anti-Markovnikov regioisomer (**23**–**31a**) is the major product in all cases. However, the regioselectivity is influenced by the nature of the alkyl substituent of the 1-phenyl-2-alkylalkyne and the bulkiness of the primary amine. Increasing regioselectivity is observed with increasing size of the amine (entries 1–4, Table 2). Furthermore, 1-phenyl-2-alkylalkynes with small alkyl substituents such as **20** are hydroaminated much more regioselectively than substrates with a bulky substituent, such as **22** (entries 3 and 9, Table 2). However,

Table 2. $[Ind_2TiMe_2]$-catalyzed hydroamination of unsymmetrically substituted 1-phenyl-2-alkylalkynes with various amines and subsequent reduction.



Entry	Alkyne	Amine	Yield [%][a]	Ratio **a**:**b**
1	 **20**	 **2**	99 (**23a/b**)	49:1
2	 **20**	 **18**	90 (**24a/b**)	>99:1
3	 **20**	 **3**	80 (**25a/b**)	>99:1
4	 **20**	 **4**	89 (**26a/b**)	18:1
5	 **21**	 **2**	84 (**27a/b**)	11:1
6	 **21**	 **3**	76 (**28a/b**)	6:1
7	 **21**	 **4**	92 (**29a/b**)	11:1
8	 **21**	 **6**	80 (**30a/b**)	3:1
9	 **22**	 **3**	87 (**31a/b**)	3:1

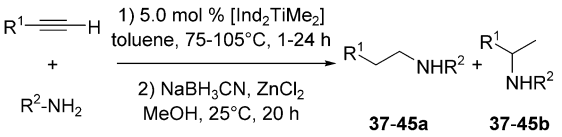
[a] Reaction conditions: 1) Alkyne (2.40 mmol), amine (2.64 mmol), $[Ind_2TiMe_2]$ (0.12 mmol, 5.0 mol%), toluene (1.0 mL), 105°C, 24 h; 2) $NaBH_3CN$ (4.80 mmol), $ZnCl_2$ (2.40 mmol), MeOH (10 mL), 25°C, 20 h. Yields refer to isolated compounds. Reaction times have not been minimized.

in **22** the phenyl and the 1-cyclohexenyl substituents can be regarded as sterically and electronically comparable. As expected, a medium-sized alkyl substituent like the cyclopropyl group in **21** results in modest to good regioselectivities (entries 5–8, Table 2). Correspondingly, the reaction between the bulky amine 4-methylaniline (**2**) and **20** gave a mixture of **23a** and **23b** in an excellent ratio of 49:1 (entry 1, Table 2), while the regioselectivity for the addition of sterically less demanding *n*-propylamine (**6**) to **21** is only 3:1 (entry 8, Table 2).

To complete the investigation of the behaviour of various alkynes in [Ind_2TiMe_2]-catalyzed hydroamination reactions, we focused on transformations of terminal alkyl- and arylalkynes with various amines (Table 3). All reactions were performed under standard conditions in the presence of 5.0 mol% catalyst. Although reactions were fast at 105°C, better yields and regioselectivities were obtained at 75°C (entries 2 and 3, Table 3). An explanation for this observation is that the formation of alkyne polymers decreases with decreasing temperature. In general, Table 3 shows that alkyl- (**32**, **33**) and arylalkynes (**34**–**36**) are suitable substrates for [Ind_2TiMe_2]-catalyzed hydroamination reactions. Particularly interesting are the good yields (71–77%) of the hydroamination/reduction sequences with arylalkynes **34**–**36**, because in the past only a few Ti-catalyzed hydroamination reactions of phenylacetylene (**34**) have been reported.[7b,11,13a] As observed before,[7b,11,12] the regioselectivity of amine addition to alkylalkynes such as 1-octyne (**32**) and 1-dodecyne (**33**) is strongly influenced by the nature of the amine. While reactions employing arylamine **2** (entries 1–3, Table 3) favor the formation of the Markovnikov regioisomers **37b** and **38b**, the anti-Markovnikov products **39a** and **40a** are the major products in reactions employing the alkylamines **3** and **4** (entries 4 and 5, Table 3). In contrast, reactions employing the arylalkynes **34**–**36** always favor formation of the anti-Markovnikov regioisomers **41**–**45a** (entries 6–10). The best anti-Markovnikov regioselectivities (>99:1) are generally observed with the sterically demanding amine *tert*-butylamine (**3**) (entries 4, 7, and 8, Table 3), which is in agreement with reports by Beller et al.[12] However, lower regioselectivities (1.5–4.5:1) were observed with arylamine **2** or the sterically less demanding alkylamine **4**. Comparison of the 4-methoxy- and 4-chloro-substituted phenylacetylenes **35** and **36** indicates that these substituents do not significantly change the behavior of the alkynes.

Since at this stage of the study benzylamine (**7**) was the only poor substrate for [Ind_2TiMe_2]-catalyzed hydroamination reactions we decided to reinvestigate the behavior of sterically less hindered benzylamines and related compounds in more detail (Table 4). After reproducing the result obtained with diphenylacetylene (**1**) and **7** (entry 1, Table 4), we obtained an even worse result with **1** and 4-methoxybenzylamine (**46**). Under standard conditions, after 48 h reaction time in the hydroamination step and subsequent reduction, the yield was only 22% (entry 2, Table 4). Since our initial result obtained with the sterically

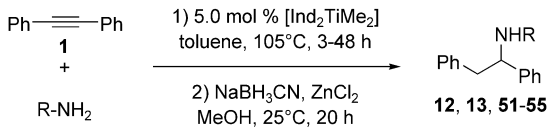
Table 3. [Ind_2TiMe_2]-catalyzed hydroamination of terminal alkynes with various amines and subsequent reduction.

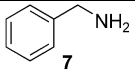
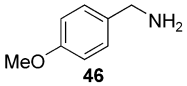
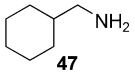
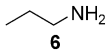
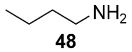
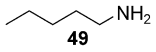
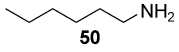


Entry	Alkyne	Amine	T [°C]	t [h]	Yield [%][a]	Ratio **a**:**b**
1	nC_6H_{13}—≡—H **32**	NH2, Me **2**	105	1	95 (**37a/b**)	1:4
2	$nC_{10}H_{21}$—≡—H **33**	NH2, Me **2**	105	2	87 (**38a/b**)	1:2.5
3	$nC_{10}H_{21}$—≡—H **33**	NH2, Me **2**	75	8	99 (**38a/b**)	1:3.8
4	$nC_{10}H_{21}$—≡—H **33**	NH2 **3**	105	2	75 (**39a/b**)	>99:1
5	$nC_{10}H_{21}$—≡—H **33**	NH2 **4**	105	24[b]	81 (**40a/b**)	1.5:1
6	H **34**	NH2, Me **2**	75	6	77 (**41a/b**)	4.5:1
7	MeO, H **35**	NH2 **3**	75	8	77 (**42a/b**)	>99:1
8	Cl, H **36**	NH2 **3**	75	8	71 (**43a/b**)	>99:1
9	MeO, H **35**	NH2 **4**	75	12	75 (**44a/b**)	2.7:1
10	Cl, H **36**	NH2 **4**	75	12	73 (**45a/b**)	2.6:1

[a] Reaction conditions: 1) Alkyne (2.40 mmol), amine (2.64 mmol), [Ind_2TiMe_2] (0.12 mmol, 5.0 mol%), toluene (1.0 mL), 75–105°C, 1–24 h; 2) $NaBH_3CN$ (4.80 mmol), $ZnCl_2$ (2.40 mmol), MeOH (10 mL), 25°C, 20 h. Yields refer to isolated compounds. [b] Reaction time has not been minimized.

Table 4. [Ind_2TiMe_2]-catalyzed hydroamination of diphenylacetylene (**1**) with benzyl- and *n*-alkylamines and subsequent reduction.



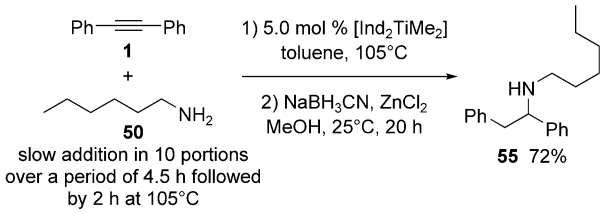
Entry	Amine	t [h]	Recovered **1** [%]	Yield [%][a]
1	 **7**	48	62	30 (**13**)
2	 **46**	48	58	22 (**51**)
3	 **47**	48	69	22 (**52**)
4	 **6**	3	–	89 (**12**)
5	 **48**	24	56	41 (**53**)
6	 **49**	24	80	19 (**54**)
7	 **50**	24	74	20 (**55**)

[a] Reaction conditions: 1) Alkyne **1** (2.40 mmol), amine (2.64 mmol), [Ind_2TiMe_2] (0.12 mmol, 5.0 mol %), toluene (1.0 mL), 105 °C, 3–48 h; 2) $NaBH_3CN$ (4.80 mmol), $ZnCl_2$ (2.40 mmol), MeOH (10 mL), 25 °C, 20 h. Yields refer to isolated pure compounds.

less hindered *n*-propylamine (**6**) was much better (89 %, 3 h reaction time for the hydroamination step), we thought that the benzylic position of the amino group might be responsible for the lack of reactivity of benzylamine derivatives. To verify this idea, we performed a comparable hydroamination reaction with **1** and cyclohexylmethylamine (**47**, entry 3, Table 4). To our surprise, the result was as poor (22 %) as that obtained with benzylamine derivative **46**. Since there is no obvious difference between the alkylamines **47** and **6** we additionally performed hydroamination/reduction sequences with **1** and *n*-butyl- (**48**), *n*-pentyl- (**49**), and *n*-hexylamine (**50**). Surprisingly, all these reactions were significantly slower than the reaction of *n*-propylamine (**6**). After performing the hydroaminations of **1** with **48**, **49**, and **50** for 24 h, the products **53**, **54**, and **55** were isolated after subsequent reduction in only 41, 19, and 20 % yield, respectively (entries 5–7, Table 4). In all cases, large amounts of unconverted alkyne **1** were recovered. While the results obtained with *n*-pentyl- (**49**) and *n*-hexylamine (**50**) are similar to those obtained with benzylamines **7** and **46** and cyclohexylmethyl derivative **47**, the 41 % yield of the reaction between **1** and *n*-butylamine (**48**) is remarkable. Since the structural differences of the *n*-alkylamines **6**, **48**, **49**, and **50** are remote from the reactive NH_2 group and therefore should not be responsible for significant changes in the reactivity of these substrates, we sought an alternative explanation for the strange behavior of the sterically unhindered *n*-alkylamines in [Ind_2TiMe_2]-catalyzed hydroamination reactions.

One difference between **6**, **48**, **49**, and **50** is the boiling point: *n*-propylamine (**6**), 48 °C; *n*-butylamine (**48**), 78 °C; *n*-pentylamine (**49**), 104 °C; *n*-hexylamine (**50**), 131 °C. Since the reactions are performed in sealed Schlenk tubes at 105 °C one can assume that under the reaction conditions the majority of *n*-propylamine (**6**) is in the gas phase rather than in the liquid phase. Therefore, the concentration of **6** in the liquid phase, where the reaction takes place, is low. Since the concentration of the amine in the liquid phase increases with increasing boiling point of the amine, the concentration of *n*-butylamine (**48**) in the liquid phase is higher under the reaction conditions than that of *n*-propylamine (**6**). The highest amine concentrations in the liquid phase are expected for *n*-pentylamine (**49**) and *n*-hexylamine (**50**), because the boiling points of these amines are above or in the range of the reaction temperature. Furthermore, the boiling points of the other sterically less hindered amines **7** (184 °C), **46** (236 °C), and **47** (159 °C) are also above 105 °C. Therefore, their behavior is comparable to those of **49** and **50**. Since the best results in hydroamination/reduction sequences employing sterically less hindered amines such as *n*-alkyl- and benzylamines are obtained with low-boiling amines it is conceivable that the rates of [Ind_2TiMe_2]-catalyzed hydroamination reactions employing these substrates increase with decreasing amine concentration in the liquid phase. Bergman et al. reported in 1992 that the zirconium bisamide-catalyzed hydroamination reaction between diphenylacetylene (**1**) and 2,6-dimethylaniline (**18**) is inverse first order with respect to the concentration of the amine.[4b] Accordingly, fast, high-yield [Ind_2TiMe_2]-catalyzed hydroamination of *n*-alkyl- and benzylamines should be possible if the concentration of the amine is kept low during the entire reaction.

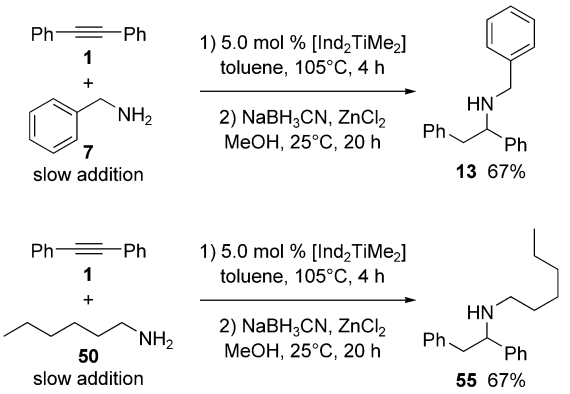
To verify this idea, we performed a slightly modified reaction between **1** and **50** in the presence of 5.0 mol % of [Ind_2TiMe_2] at 105 °C (Scheme 3). At the beginning of the



Scheme 3. [Ind_2TiMe_2]-catalyzed hydroamination of diphenylacetylene (**1**) with *n*-hexylamine (**50**) and subsequent reduction.

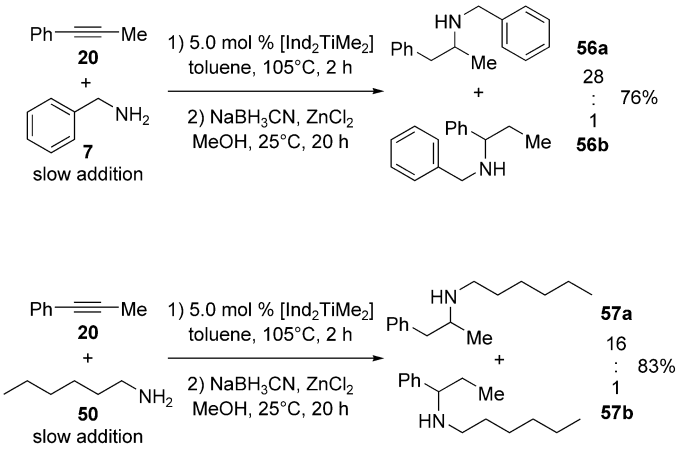
experiment we added only 15 mol % of amine **50** to the reaction mixture. After 30 min at 105 °C we added another 10 mol % of **50**. The remaining 80 mol % of **50** ($\Sigma =$ 105 mol %) was then added in eight portions of 10 mol % over a period of 4 h at 105 °C. Finally, the mixture was stirred for a further 2 h at 105 °C. Thus, the desired product **55** was obtained with 72 % yield after subsequent reduction. Compared to the same reaction performed without slow addition of the amine (20 % yield, 24 h reaction time for the hydroamination step) the yield is remarkably improved. Clearly, much higher yields of [Ind_2TiMe_2]-catalyzed hydroamination reactions of alkynes employing sterically less hindered amines are obtained when the amine is added slowly to the reaction mixture.

To determine whether slow addition of the amine can also improve the yields of other hydroaminations with sterically less hindered amines, we performed some additional reactions. In an initial set of experiments with alkyne **1**, addition of benzylamine (**7**) or *n*-hexylamine (**50**) to the reaction mixture over a period of 4 h by syringe pump was followed by reduction. The desired products **13** and **55** were both obtained in 67% yield (Scheme 4).



Scheme 4. $[Ind_2TiMe_2]$-catalyzed hydroamination of diphenylacetylene (**1**) with benzyl- and *n*-alkylamines and subsequent reduction.

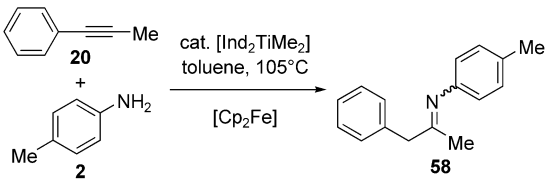
Finally, we focused on two reactions of the unsymmetrically substituted alkyne 1-phenylpropyne (**20**) with the sterically less hindered amines benzylamine (**7**) and *n*-hexylamine (**50**). In these experiments, the amines were added over 2 h by syringe pump. After subsequent reduction, regioisomeric mixtures of the products **56a/b** and **57a/b** were obtained in 76 and 83% yield, respectively (Scheme 5).



Scheme 5. $[Ind_2TiMe_2]$-catalyzed hydroamination of 1-phenylpropyne (**20**) with benzyl- and *n*-alkylamines and subsequent reduction.

Most impressively, the reactions which favor the formation of the anti-Markovnikov products take place with high regioselectivities ($\geq$16:1). In comparison, the same reactions take place with regioselectivities of less than 3:1 in the presence of $[Cp_2^*TiMe_2]$.[8] Therefore, the use of $[Ind_2TiMe_2]$ as hydroamination catalyst in combination with slow addition of the amine must be regarded as the first possibility for performing high-yield additions of sterically less demanding *n*-alkyl- and benzylamines to unsymmetrically substituted 1-aryl-2-alkylalkynes with high regioselectivity.

To compare the activities of $[Ind_2TiMe_2]$ and $[Cp_2TiMe_2]$ and to obtain some mechanistic insight, a kinetic investigation was carried out. For this purpose, we chose the addition of 4-methylaniline (**2**) to 1-phenylpropyne (**20**), which was already used for a detailed kinetic investigation of the $[Cp_2TiMe_2]$-catalyzed hydroamination of alkynes (Scheme 6).[7c]



Scheme 6. Kinetically investigated reaction of 1-phenylpropyne (**20**) and 4-methylaniline (**2**).

In the presence of ferrocene as internal standard, the changes in the concentrations of **2**, **20**, and **58** (two isomers) could be determined by ^{1}H NMR spectroscopy. The kinetic experiments were carried out with a ninefold excess of amine **2** at 105$\pm$0.1 °C, and the concentration of alkyne **20** was monitored as a function of time by ^{1}H NMR spectroscopy. All experiments in the presence of varying amounts of $[Ind_2TiMe_2]$ showed a first-order disappearance of alkyne **20**; hence, the rate law in Equation (1) (ν = reaction rate) describes the reaction.

$$\nu = -\frac{dc(\mathbf{20})}{dt} = k_{obs}c(\mathbf{20}) \quad (1)$$

A plot of the obtained k_{obs} for different concentrations of $[Ind_2TiMe_2]$ versus $c([Ind_2TiMe_2])$ is shown in Figure 1. A corresponding plot for $[Cp_2TiMe_2]$[7c] is also included. For all

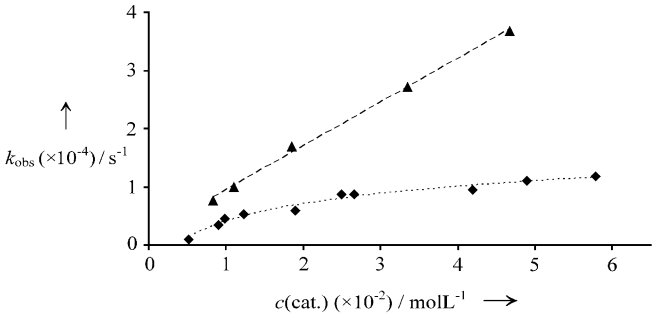
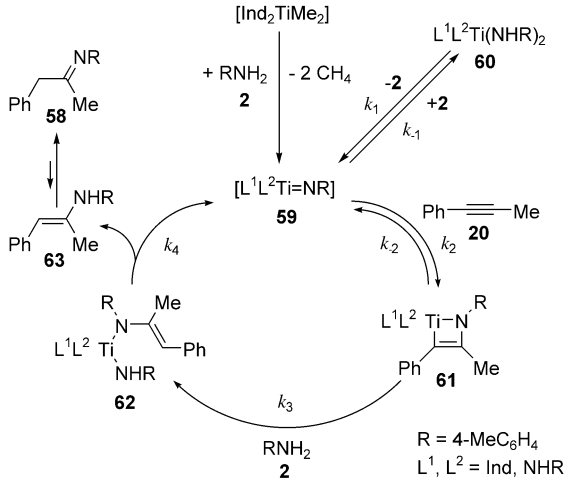


Figure 1. Plot of k_{obs} versus the concentrations of $[Ind_2TiMe_2]$ (▲) and $[Cp_2TiMe_2]$ (◆).

catalyst concentrations reactions in the presence of $[Ind_2TiMe_2]$ are much faster than reactions in the presence of $[Cp_2TiMe_2]$. Therefore, $[Ind_2TiMe_2]$ must be regarded as a more active catalyst than $[Cp_2TiMe_2]$, at least for the investigated transformation. Unfortunately, direct comparison

of the catalytic activities of $[Ind_2TiMe_2]$ and titanium dipyrrolylmethane catalysts is not possible at the moment, because for the latter catalysts, reaction rates were determined for a different reaction.[11d] The linear relationship between k_{obs} and the concentration of $[Ind_2TiMe_2]$ indicates that the reaction is first-order in the concentration of $[Ind_2TiMe_2]$. The small deviation from linearity for high catalyst concentrations can be explained by the fact that the hydroamination reactions are very fast in these cases. As a result, the hydroamination reactions already proceed significantly while $[Ind_2TiMe_2]$ is still being converted to the catalytically active species. Therefore, the obtained k_{obs} data are not as high as expected for these catalyst concentrations. Since the curve obtained for $[Cp_2TiMe_2]$ can only be explained by a reversible dimerization of the catalytically active species (a titanium imido complex), the $[Ind_2TiMe_2]$-catalyzed hydroamination obviously takes place without a corresponding dimerization of an imido complex. Given this result and other mechanistic investigations of Zr- and Ti-catalyzed hydroaminations,[4b,7c,10a,17] the catalytic cycle shown in Scheme 7



Scheme 7. Proposed mechanism of the $[Ind_2TiMe_2]$-catalyzed hydroamination of 1-phenylpropyne (**20**) with 4-methylaniline (**2**).

seems to be appropriate to describe the $[Ind_2TiMe_2]$-catalyzed addition of **2** to **20**. This catalytic cycle, which is essentially the same as that published by Bergman et al. for the Zr-catalyzed addition of 2,6-dimethylaniline (**18**) to diphenylacetylene (**1**),[4b] includes irreversible and quantitative transformation of $[Ind_2TiMe_2]$ into the catalytically active imido complex **59**, reversible addition of **2** to **59**, reversible [2+2] cycloaddition between **59** and alkyne **20**, irreversible protonation of the formed azametallacyclobutene **61**, and final α-elimination of the product, which regenerates **59**.

By applying a steady-state assumption to the mechanism shown in Scheme 7 with respect to all intermediates, the rate law given in Equation (2) can be derived.[4b]

$$v = \frac{k_1 k_2 k_3 c(\mathbf{20}) c([Ind_2TiMe_2])}{k_{-1}[k_{-2} + k_3 c(\mathbf{2})]} \quad (2)$$

Equation (2) is in good agreement with the experimentally observed facts that the reaction is first-order in the concentration of alkyne **20** and first-order in the concentration of $[Ind_2TiMe_2]$. With regard to the concentration of amine **2**, two possibilities exist. With the assumption $k_{-2} \gg k_3 c(\mathbf{2})$ the reaction rate is zero-order in the concentration of amine **2**. Therefore, the amine concentration does not influence the rate of the hydroamination. With the assumption $k_{-2} \ll k_3 c(\mathbf{2})$ the rate of the reaction is inverse-first-order in the concentration of amine **2**. Such a dependence has already been observed for the Zr-catalyzed addition of 2,6-dimethylaniline (**18**) to diphenylacetylene (**1**).[4b] As a result, the hydroamination is assumed to be fast for low amine concentrations and slow for high amine concentrations. Since the latter case was qualitatively observed for hydroamination reactions with sterically less hindered *n*-alkyl- and benzylamines, one can assume that for these amines the protonation of the azametallacyclobutene intermediate (k_3) is faster than its cleavage into the alkyne and the catalytically active titanium imido complex (k_{-2}). Note that with the assumption $k_{-2} \ll k_3 c(\mathbf{2})$ the rate of a corresponding hydroamination reaction that involves reversible dimerization of the catalytically active imido complex is also expected to increase with decreasing amine concentration.[7c] However, in this case, a more complex relationship between the rate and the amine concentration is expected. Thus, the behavior observed for *n*-alkyl- and benzylamines can easily be understood. To verify the observation that hydroamination reactions of sterically less demanding amines are indeed fast for low amine concentrations, an initial NMR experiment was performed. An NMR tube containing a mixture of 1.30 mmol diphenylacetylene (**1**), 0.14 mmol benzylamine (**7**) (ratio 9:1), 0.0013 mmol $[Ind_2TiMe_2]$ (9.3 mol%), 0.5 mL $[D_8]$toluene, and hydroquinone dimethyl ether as internal standard was heated to 105 °C. Unfortunately, the progress of the reaction could not be monitored exactly because the reaction went to completion within less than 5 min. However, this finding undoubtedly proves that the investigated reaction is indeed fast for low amine concentrations. The fact that a corresponding reaction is extremely slow for high amine concentrations was confirmed in an additional kinetic experiment. In this case, a Schlenk tube containing a mixture of benzylamine (**7**, $c(\mathbf{7}) = 2.42\ mol\,L^{-1}$), 1-phenylpropyne (**20**, $c_0(\mathbf{20}) = 0.27\ mol\,L^{-1}$, ratio 9:1), $[Ind_2TiMe_2]$ $[c([Ind_2TiMe_2]) = 1.72 \times 10^{-2}\ mol\,L^{-1}$ (6.4 mol%)], toluene, and hydroquinone dimethyl ether as internal standard was heated to 105 °C. As expected, the reaction did not reach 10% conversion after 40 h.

Conclusion

In summary, the investigation presented here undoubtedly proves that $[Ind_2TiMe_2]$ is a highly active and general catalyst for the intermolecular hydroamination of alkynes. With this catalyst, reactions of primary aryl-, *tert*-alkyl-, *sec*-alkyl-, and *n*-alkylamines can be performed with internal and terminal alkynes. In the case of unsymmetrically substituted 1-phenyl-2-alkylalkynes, the reactions take place with modest to excellent regioselectivities, and formation of the anti-Markovnikov regioisomers is favored. While the major product

of hydroamination reactions of terminal arylalkynes is always the anti-Markovnikov isomer, alkylalkynes react with arylamines to give the Markovnikov products preferably. However, to achieve reasonable rates for the addition of sterically less hindered *n*-alkyl- and benzylamines to alkynes these amines must be added slowly to the reaction mixtures. This behavior can be understood by the fact that the catalytic cycle proposed on the basis of an initial kinetic investigation includes the possibility that the rate of the reaction increases with decreasing concentration of the employed amine. Furthermore, the same kinetic study revealed that no dimerization of the catalytically active imido complex is observed for hydroamination reactions of alkyne **20** with 4-methylaniline (**2**) in the presence of [Ind_2TiMe_2] as catalyst. This finding is in contrast to results obtained for corresponding [Cp_2TiMe_2]-catalyzed reactions. In general, a one-pot combination of the [Ind_2TiMe_2]-catalyzed hydroamination of alkynes with a subsequent reduction leads to the formation of secondary amines with good to excellent yields. At 105 °C, in the presence of 5.0 mol % [Ind_2TiMe_2], typical reaction times for the hydroamination step are in the range of 1–24 h. Particularly impressive is the fact that using [Ind_2TiMe_2] makes it possible for the first time to perform reactions of *n*-alkyl- and benzylamines with 1-phenylpropyne (**20**) in a highly regioselective fashion. In our opinion, [Ind_2TiMe_2] is the first general catalyst with improved activity that can be used efficiently for all substrate combinations in intermolecular hydroamination reactions. Moreover, [Ind_2TiMe_2] is a stable crystalline compound that can be conveniently handled in air. It can be synthesized in one step from [Ind_2TiCl_2] and methyllithium.[15] [Ind_2TiMe_2] is also commercially available.[18]

Experimental Section

General: All reactions were performed under an inert atmosphere of argon in flame-dried Duran glassware (e.g., Schlenk tubes equipped with Teflon stopcocks). Toluene was distilled from molten sodium under argon. Methanol was dried with molecular sieves (3 Å). [Ind_2TiMe_2] was synthesized according to ref. [15]. Diphenylacetylene (**1**) was dissolved in CH_2Cl_2, dried with Na_2SO_4, and recovered by evaporation of the solvent. All other alkynes (except **20** and **33**) and amines (except **5**) were distilled and stored over molecular sieves (4 Å). All other reagents were purchased from commercial sources and were used without further purification. Unless otherwise noted, yields refer to isolated pure compounds, as gauged by TLC and ^1H and ^{13}C NMR. All products were characterized by ^1H NMR, ^{13}C NMR, and IR spectroscopy, and mass spectrometry (MS). Additional characteristic data were obtained by high-resolution MS (HRMS) and/or CHN elemental analysis. NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer. All ^1H NMR data are reported relative to TMS as internal standard. All ^{13}C NMR data are reported relative to the central line of the triplet for $CDCl_3$ at $\delta = 77.0$ ppm. IR spectra were recorded on a Bruker Vector 22 spectrometer by using an attenuated total reflection (ATR) method. Mass spectra were recorded on a Finnigan MAT 312 or a VG Autospec (EI) with an ionization potential of 70 eV or a Micromass LCT (ESI). Elemental analyses were carried out on an Elementar Vario EL machine. PE: light petroleum ether, b.p. 40–60 °C.

Hydroamination of alkynes: general procedure A: A Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with the alkyne (2.40 mmol), the amine (2.64 mmol), [Ind_2TiMe_2] (37 mg, 0.12 mmol, 5.0 mol %), and toluene (1.0 mL). The resulting mixture was heated to 105 °C (TLC control). Then, the mixture was cooled to room temperature and a mixture of $NaBH_3CN$ (302 mg, 4.80 mmol) and $ZnCl_2$ (326 mg, 2.40 mmol) in methanol (10 mL) was added. After this mixture had been stirred at 25 °C for 20 h, CH_2Cl_2 (50 mL) and saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (50 mL). After extraction, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (6×50 mL). The combined organic layers were dried with Na_2SO_4. After concentration under vacuum, the residue was purified by flash chromatography (SiO_2).

Hydroamination of diphenylacetylene (1) with *n*-hexylamine (50): A Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with diphenylacetylene (**1**, 428 mg, 2.40 mmol), *n*-hexylamine (**50**, 36 mg, 0.36 mmol), [Ind_2TiMe_2] (37 mg, 0.12 mmol, 5.0 mol %), and toluene (1.0 mL). The resulting mixture was heated to 105 °C. After 30 min at 105 °C another portion of **50** (24 mg, 0.24 mmol) was added to the reaction mixture. The remaining **50** (192 mg, 1.92 mmol) was added in eight portions (0.24 mmol every 30 min) over 4 h. Finally, the mixture was stirred for a further 2 h at 105 °C. Then, the mixture was cooled to room temperature, and a mixture of $NaBH_3CN$ (302 mg, 4.80 mmol) and $ZnCl_2$ (326 mg, 2.40 mmol) in methanol (10 mL) was added. After the resulting mixture had been stirred at 25 °C for 20 h, CH_2Cl_2 (50 mL) and saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (50 mL). After extraction, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (6×50 mL). The combined organic layers were dried with Na_2SO_4. After concentration under vacuum and purification by flash chromatography (PE/EtOAc, 5/1), **55** (487 mg, 1.73 mmol, 72 %) was isolated as a colorless oil. For characteristic data, see **Amine 55**.

Hydroamination of diphenylacetylene (1) with *n*-alkyl- and benzylamines: general procedure B: A Schlenk tube equipped with a rubber septum and a magnetic stirring bar was charged with diphenylacetylene (**1**, 428 mg, 2.40 mmol), [Ind_2TiMe_2] (37 mg, 0.12 mmol, 5.0 mol %), and toluene (1.0 mL). The resulting mixture was heated to 105 °C, and a solution of the amine (2.64 mmol) in toluene ($c = 2.64$ mol L^{-1}) was added by syringe pump over 4 h. Then, the mixture was cooled to room temperature, and a mixture of $NaBH_3CN$ (302 mg, 4.80 mmol) and $ZnCl_2$ (326 mg, 2.40 mmol) in methanol (10 mL) was added. After the resulting mixture had been stirred at 25 °C for 20 h, CH_2Cl_2 (50 mL) and saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (50 mL). After extraction, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (6×50 mL). The combined organic layers were dried with Na_2SO_4. After concentration under vacuum, the residue was purified by flash chromatography (SiO_2).

Hydroamination of 1-phenylpropyne (20) with *n*-alkyl- and benzylamines: general procedure C: A Schlenk tube equipped with a rubber septum and a magnetic stirring bar was charged with 1-phenylpropyne (**20**, 279 mg, 2.40 mmol), [Ind_2TiMe_2] (37 mg, 0.12 mmol, 5.0 mol %), and toluene (1.0 mL). The resulting mixture was heated to 105 °C, and a solution of the amine (2.64 mmol) in toluene ($c = 2.64$ mol L^{-1}) was added by syringe pump over 2 h. Then, the mixture was cooled to room temperature, and a mixture of $NaBH_3CN$ (302 mg, 4.80 mmol) and $ZnCl_2$ (326 mg, 2.40 mmol) in methanol (10 mL) was added. After this mixture had been stirred at 25 °C for 20 h, CH_2Cl_2 (50 mL) and saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (50 mL). After extraction, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (6×50 mL). The combined organic layers were dried with Na_2SO_4. After concentration under vacuum, the residue was purified by flash chromatography (SiO_2).

Amine 8: General procedure A was used to synthesize amine **8** from diphenylacetylene (**1**) and 4-methylaniline (**2**). The reaction time of the hydroamination step was 24 h. After purification by flash chromatography (PE/EtOAc, 40/1), **8** (675 mg, 2.35 mmol, 98 %) was isolated as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.17$–7.32 (m, 8H), 7.09–7.11 (m, 2H), 6.85 (d, $J = 8.0$ Hz, 2H), 6.37 (d, $J = 8.5$ Hz, 2H), 4.54 (dd, $J = 5.6$, 8.3 Hz, 1H), 4.02 (brs, 1H), 3.11 (dd, $J = 5.6$, 13.9 Hz, 1H), 2.98 (dd, $J = 8.3$, 14.1 Hz, 1H), 2.15 ppm (s, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 145.0$ (C), 143.6 (C), 137.8 (C), 129.5 (CH), 129.2 (CH), 128.5 (CH), 128.5 (CH), 127.0 (CH), 126.6 (CH), 126.6 (C), 126.4 (CH),

113.8 (CH), 59.5 (CH), 45.1 (CH_2), 20.3 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3407, 3026, 2917, 1617, 1519, 1494, 1453, 1301, 808, 757, 700 cm^{-1}; MS (25 °C): *m/z* (%): 287 (11) [M^+], 196 (100) [$M^+-C_7H_7$], 91 (29) [$C_7H_7^+$]; HRMS calcd for $C_{21}H_{21}N$: 287.1674; found: 287.1674; elemental analysis (%) calcd for $C_{21}H_{21}N$: C 87.76, H 7.37, N 4.87; found: C 87.63, H 7.44, N 4.83.

Amine 9: General procedure A was used to synthesize amine **9** from diphenylacetylene (**1**) and *tert*-butylamine (**3**). The reaction time of the hydroamination step was 5 h. After purification by flash chromatography (PE/EtOAc, 10/1), **9** (511 mg, 2.02 mmol, 84%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.4 Hz, 2H), 7.24–7.29 (m, 4H), 7.17–7.21 (m, 2H), 7.12 (d, *J* = 7.0 Hz, 2H), 3.98 (dd, *J* = 5.6, 9.0 Hz, 1H), 2.92 (dd, *J* = 5.6, 12.0 Hz, 1H), 2.72 (dd, *J* = 9.0, 12.0 Hz, 1H), 1.20 (br s, 1H), 0.84 ppm (s, 9H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 147.6 (C), 139.3 (C), 129.3 (CH), 128.3 (CH), 128.0 (CH), 127.1 (CH), 126.4 (CH), 126.3 (CH), 59.2 (CH), 51.1 (C), 47.2 (CH_2), 29.9 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2958, 1601, 1493, 1453, 1364, 1228, 1096, 1069, 1027, 757, 697 cm^{-1}; MS (25 °C): *m/z* (%): 238 (4) [M^+-CH_3], 162 (32) [$M^+-C_7H_7$], 106 (100) [$C_7H_8N^+$], 91 (9) [$C_7H_7^+$]; HRMS calcd for $C_{17}H_{20}N$: 238.1596; found: 238.1593; elemental analysis (%) calcd for $C_{18}H_{23}N$: C 85.32, H 9.15, N 5.53; found: C 85.11, H 8.87, N 5.78.

Amine 10: General procedure A was used to synthesize amine **10** from diphenylacetylene (**1**) and cyclopentylamine (**4**). The reaction time of the hydroamination step was 3 h. After purification by flash chromatography (PE/EtOAc, 5/1), **10** (579 mg, 2.18 mmol, 91%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10–7.30 (m, 10H), 3.92 (dd, *J* = 6.0, 8.0 Hz, 1H), 2.82–2.92 (m, 3H), 1.67–1.73 (m, 2H), 1.47–1.53 (m, 3H), 1.35–1.39 (m, 2H), 1.11–1.18 ppm (m, 2H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 144.2 (C), 139.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 127.3 (CH), 126.9 (CH), 126.2 (CH), 63.2 (CH), 57.3 (CH), 45.4 (CH_2), 33.7 (CH_2), 32.3 (CH_2), 23.5 (CH_2), 23.5 ppm (CH_2); IR (neat): $\tilde{\nu}$ = 2948, 1946, 1602, 1493, 1453, 756, 699 cm^{-1}; MS (25 °C): *m/z* (%): 264 (2) [M^+], 174 (100) [$M^+-C_7H_7$], 106 (59) [$C_7H_8N^+$], 91 (27) [$C_7H_7^+$]; elemental analysis (%) calcd for $C_{19}H_{23}N$: C 85.99, H 8.74, N 5.28; found: C 85.82; H 8.76; N 5.24.

Amine 11: General procedure A was used to synthesize amine **11** from diphenylacetylene (**1**) and benzhydrylamine (**5**). The reaction time of the hydroamination step was 5 h. After purification by flash chromatography (PE/EtOAc, 40/1), **11** (781 mg, 2.15 mmol, 90%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13–7.34 (m, 16H), 7.05–7.07 (m, 2H), 6.91–6.93 (m, 2H), 4.56 (s, 1H), 3.74 (dd, *J* = 5.4, 8.7 Hz, 1H), 2.86–2.97 (m, 2H), 2.01 ppm (br s, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 144.6 (C), 143.8 (C), 143.0 (C), 138.9 (C), 129.4 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 127.6 (CH), 127.3 (CH), 127.3 (CH), 127.0 (CH), 126.8 (CH), 126.7 (CH), 126.3 (CH), 63.2 (CH), 61.3 (CH), 45.2 ppm (CH_2); IR (neat): $\tilde{\nu}$ = 3025, 1600, 1492, 1452, 1028, 744, 694 cm^{-1}; MS (140 °C): *m/z* (%): 272 (31) [$M^+-C_7H_7$], 167 (100) [$C_{13}H_{11}^+$], 91 (8) [$C_7H_7^+$]; elemental analysis (%) calcd for $C_{20}H_{27}N$: C 85.35, H 9.67, N 4.98; found: C 85.15, H 9.61, N 5.19.

Amine 12: General procedure A was used to synthesize amine **12** from diphenylacetylene (**1**) and *n*-propylamine (**6**). The reaction time of the hydroamination step was 3 h. After purification by flash chromatography (PE/EtOAc, 3/1), compound **12** (511 mg, 2.14 mmol, 89%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10–7.35 (m, 10H), 3.83 (dd, *J* = 5.9, 8.0 Hz, 1H), 2.93 (dd, *J* = 5.9, 13.4 Hz, 1H), 2.88 (dd, *J* = 8.2, 13.4 Hz, 1H), 2.28–2.41 (m, 2H), 1.51 (br s, 1H), 1.37 (sext, *J* = 7.3 Hz, 2H), 0.76 ppm (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 144.1 (C), 139.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 127.3 (CH), 126.9 (CH), 126.3 (CH), 64.8 (CH), 49.6 (CH_2), 45.3 (CH_2), 23.1 (CH_2), 11.6 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2957, 2928, 1602, 1494, 1453, 756, 696 cm^{-1}; MS (25 °C): *m/z* (%): 239 (2) [M^+], 148 (100) [$M^+-C_7H_7$]; elemental analysis (%) calcd for $C_{17}H_{21}N$: C 85.31, H 8.84, N 5.85; found: C 84.91, H 8.82, N 5.88.

Amine 13: General procedure B was used to synthesize amine **13** from diphenylacetylene (**1**) and benzylamine (**7**). After purification by flash chromatography (PE/EtOAc, 5/1), **13** (462 mg, 1.61 mmol, 67%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.37 (m, 4H), 7.17–7.28 (m, 7H), 7.09–7.11 (m, 4H), 3.87 (dd, *J* = 5.5, 8.7 Hz, 1H), 3.65 (d, *J* = 13.6 Hz, 1H), 3.45 (d, *J* = 13.6 Hz, 1H), 2.86–2.98 (m, 2H), 1.72 ppm (br s, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 143.7 (C), 140.5 (C), 138.8 (C), 129.2 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 127.1 (CH), 126.7 (CH), 126.3 (CH), 63.6 (CH), 51.3 (CH_2), 45.3 ppm (CH_2); IR (neat): $\tilde{\nu}$ = 3026, 1601, 1494, 1453, 1113, 1028, 756, 694 cm^{-1}; MS (100 °C): *m/z* (%): 196 (91) [$M^+-C_7H_7$], 91 (100) [$C_7H_7^+$]; HRMS calcd for $C_{14}H_{14}N$: 196.1126; found: 196.1127; elemental analysis (%) calcd for $C_{21}H_{21}N$: C 87.76, H 7.36, N 4.87; found: C 87.52, H 7.38, N 4.91.

Amine 16: General procedure A was used to synthesize amine **16** from 3-hexyne (**14**) and (±)-1-phenylethylamine (**15**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 10/1), **16** (399 mg, 1.95 mmol, 81%) was isolated as a colorless oil. The two diastereomers (ratio 1:1 (GC)) could not be separated by flash chromatography. The data refer to the mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.31 (m, 5H), 3.86 (dq, *J* = 2.5, 6.7 Hz, 1H), 2.25–2.30 (m, 1H), 1.12–1.50 (m, 7H), 1.32 (d, *J* = 6.7 Hz, 3H), 0.78–0.91 ppm (m, 6H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 146.5 (C), 146.4 (C), 128.2 (CH), 126.6 (CH), 55.4 (CH), 55.1 (CH), 54.9 (CH), 54.7 (CH), 36.5 (CH_2), 35.7 (CH_2), 27.1 (CH_2), 25.7 (CH_2), 24.9 (CH_3), 24.8 (CH_3), 19.0 (CH_2), 18.5 (CH_2), 14.5 (CH_3), 14.2 (CH_3), 10.1 (CH_3), 9.1 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2957, 2925, 2871, 1452, 1368, 1120, 760, 699 cm^{-1}; MS (25 °C): *m/z* (%): 190 (24) [M^+-CH_3], 176 (53) [$M^+-C_2H_5$], 161 (42) [$M^+-C_3H_8$], 105 (100) [$C_7H_7N^+$], 106 (37) [$M^+-C_7H_7N$]; elemental analysis (%) calcd for $C_{14}H_{23}N$: C 81.89, H 11.29, N 6.82; found: C 82.18, H 11.19, N 6.91.

Amine 19: General procedure A was used to synthesize amine **19** from 4-octyne (**17**) and 2,6-dimethylaniline (**18**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 40/1), compound **19** (513 mg, 2.20 mmol, 92%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (d, *J* = 7.4 Hz, 2H), 6.75 (t, *J* = 7.4 Hz, 1H), 3.19–3.20 (m, 1H), 2.84 (br s, 1H), 2.24 (s, 6H), 1.23–1.47 (m, 10H), 0.85–0.89 ppm (m, 6H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 145.3 (C), 128.9 (CH), 128.3 (C), 120.6 (CH), 55.9 (CH), 37.9 (CH_2), 35.2 (CH_2), 28.2 (CH_2), 23.0 (CH_2), 19.2 (CH_2), 14.3 (CH_3), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2955, 2929, 2859, 1995, 1473, 1257, 1221, 1099, 760, 711 cm^{-1}; MS (25 °C): *m/z* (%): 233 (28) [M^+], 190 (100) [$M^+-C_3H_7$], 176 (78) [$M^+-C_4H_9$]; HRMS calcd for $C_{16}H_{27}N$: 233.2144; found: 233.2140; elemental analysis (%) calcd for $C_{16}H_{27}N$: C 82.34, H 11.66, N 6.00; found: C 82.21, H 11.38, N 6.11.

Amines 23a/23b: General procedure A was used to synthesize amines **23a/23b** from 1-phenylpropyne (**20**) and 4-methylaniline (**2**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 40/1), **23a** (522 mg, 2.33 mmol, 97%) and **23b** (11 mg, 0.05 mmol, 2%) were isolated as colorless oils. **23a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.32 (m, 2H), 7.15–7.23 (m, 3H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 3.66–3.77 (m, 1H), 2.93 (dd, *J* = 4.7, 13.4 Hz, 1H), 2.67 (dd, *J* = 7.3, 13.3 Hz, 1H), 2.24 (s, 3H), 1.13 ppm (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 145.0 (C), 138.7 (C), 129.9 (CH), 129.5 (CH), 128.3 (CH), 126.4 (C), 126.2 (CH), 113.7 (CH), 49.7 (CH), 42.4 (CH_2), 20.4 (CH_3), 20.2 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2920, 1617, 1517, 1452, 1250, 1150, 805, 743, 699 cm^{-1}; MS (25 °C): *m/z* (%): 225 (34) [M^+], 134 (100) [$M^+-C_7H_7$], 91 (34) [$C_7H_7^+$]; HRMS calcd for $C_{16}H_{19}N$: 225.1518; found: 225.1514; elemental analysis (%) calcd for $C_{16}H_{19}N$: C 85.29, H 8.50, N 6.22; found: C 85.64, H 8.65, N 6.35. **23b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.34 (m, 4H), 7.17–7.23 (m, 1H), 6.88 (d, *J* = 6.5 Hz, 2H), 6.43 (d, *J* = 6.7 Hz, 2H), 4.19 (t, *J* = 6.6 Hz, 1H), 2.17 (s, 3H), 1.74–1.87 (m, 2H), 0.94 ppm (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 145.3 (C), 144.1 (C), 129.6 (CH), 128.4 (CH), 126.8 (CH), 126.5 (CH), 126.2 (C), 113.4 (CH), 60.0 (CH), 31.7 (CH_2), 20.3 (CH_3), 10.8 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2963, 2921, 1618, 1518, 1452, 1301, 805, 749, 700 cm^{-1}; MS (25 °C): *m/z* (%): 225 (46) [M^+], 196 (100) [$M^+-C_2H_5$], 91 (49) [$C_7H_7^+$]; HRMS calcd for $C_{16}H_{19}N$: 225.1518; found: 225.1518; elemental analysis (%) calcd for $C_{16}H_{19}N$: C 85.29, H 8.50, N 6.22; found: C 85.24, H 8.40, N 6.14.

Amine 24a: General procedure A was used to synthesize amine **24a** from 1-phenylpropyne (**20**) and 2,6-dimethylaniline (**18**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 40/1), **24a** (515 mg, 2.15 mmol, 90%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.29 (m, 2H), 7.15–7.22 (m, 3H), 6.98 (d, *J* = 7.5 Hz,

2H), 6.79 (t, J=7.4 Hz, 1H), 3.45–3.53 (m, 1H), 2.90–2.94 (m, 2H), 2.54 (dd, J=8.5, 13.0 Hz, 1H), 2.22 (s, 6H), 1.03 ppm (d, J=6.2 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=144.8 (C), 139.4 (C), 129.4 (CH), 129.2 (C), 128.9 (CH), 128.2 (CH), 126.1 (CH), 121.4 (CH), 54.0 (CH), 44.4 (CH_2), 20.8 (CH_3), 19.0 ppm (CH_3); IR (neat): $\tilde{\nu}$=2962, 1594, 1473, 1453, 1259, 1220, 1099, 761, 737, 698; MS (25 °C): m/z (%): 239 (9) [M^+], 148 (100) [$M^+-C_7H_7$]; HRMS calcd for $C_{17}H_{21}N$: 239.1674; found: 239.1667; elemental analysis (%) calcd for $C_{17}H_{21}N$: C 85.31, H 8.84, N 5.85; found: C 85.12, H 8.58, N 6.53.

Amine 25a: General procedure A was used to synthesize amine **25a** from 1-phenylpropyne (**20**) and *tert*-butylamine (**3**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 10/1), **25a** (368 mg, 1.92 mmol, 80%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26–7.30 (m, 2H), 7.17–7.21 (m, 3H), 2.97 (sext, J=6.6 Hz, 1H), 2.68 (dd, J=6.7, 13.2 Hz, 1H), 2.57 (dd, J=7.3, 13.2 Hz, 1H), 1.17 (br s, 1H), 1.06 (d, J=6.3 Hz, 3H), 1.01 ppm (s, 9H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=140.1 (C), 129.2 (CH), 128.2 (CH), 126.0 (CH), 50.9 (C), 49.1 (CH), 46.3 (CH_2), 29.8 (CH_3), 23.8 ppm (CH_3); IR (neat): $\tilde{\nu}$=2959, 1494, 1453, 1362, 1228, 743, 698; MS (25 °C): m/z (%): 191 (22) [M^+], 176 (48) [M^+-CH_3], 105 (71) [$C_8H_9^+$], 100 (80) [$M^+-C_7H_7$], 91 (100) [$C_7H_7^+$]; due to the low boiling point of **25a**, no elemental analysis and no HRMS could be obtained.

Amines 26a/26b: General procedure A was used to synthesize amines **26a**/**26b** from 1-phenylpropyne (**20**) and cyclopentylamine (**4**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 5/1→1/1), **26a** (408 mg, 2.01 mmol, 84%) and **26b** (23 mg, 0.11 mmol, 5%) were isolated as colorless oils. **26a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26–7.30 (m, 2H), 7.18–7.22 (m, 3H), 3.18 (quint, J=7.1 Hz, 1H), 2.96 (sext, J=6.5 Hz, 1H), 2.74 (dd, J=6.8, 13.2 Hz, 1H), 2.58 (dd, J=6.8, 13.3 Hz, 1H), 1.76–1.93 (m, 2H), 1.44–1.65 (m, 4H), 1.09–1.28 (m, 3H), 1.05 ppm (d, J=6.3 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=139.6 (C), 129.2 (CH), 128.3 (CH), 126.0 (CH), 56.9 (CH), 52.8 (CH), 43.9 (CH_2), 33.8 (CH_2), 33.0 (CH_2), 23.7 (CH_2), 23.6 (CH_2), 20.6 ppm (CH_3); IR (neat): $\tilde{\nu}$=2953, 2865, 1452, 1372, 1140, 752, 698 cm^{-1}; MS (25 °C): m/z (%): 188 (6) [M^+-CH_3], 112 (100) [$M^+-C_7H_7$], 91 (19) [$C_7H_7^+$]; HRMS calcd for $C_{13}H_{18}N$: 188.1439; found: 188.1439; elemental analysis (%) calcd for $C_{14}H_{21}N$: C 82.70, H 10.41, N 6.89; found: C 82.43, H 10.47, N 7.04. **26b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.14–7.26 (m, 5H), 3.45 (dd, J=5.8, 8.0 Hz, 1H), 2.77 (quint, J=7.0 Hz, 1H), 1.08–1.76 (m, 11H), 0.71 ppm (t, J=7.4 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=144.6 (C), 128.1 (CH), 127.3 (CH), 126.7 (CH), 63.5 (CH), 57.1 (CH), 33.9 (CH_2), 32.7 (CH_2), 31.2 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 10.9 ppm (CH_3); IR (neat): $\tilde{\nu}$=2950, 2865, 1453, 1015, 753, 699 cm^{-1}; MS (25 °C): m/z (%): 203 (2) [M^+], 174 (100) [$M^+-C_2H_5$], 106 (76) [$C_7H_8N^+$], 91 (70) [$C_7H_7^+$]; HRMS calcd for $C_{14}H_{20}N$: 202.1596; found: 202.1598.

Amines 27a/27b: General procedure A was used to synthesize amines **27a**/**27b** from alkyne **21** and 4-methylaniline (**2**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 40/1), **27a** (465 mg, 1.85 mmol, 77%) and **27b** (42 mg, 0.17 mmol, 7%) were isolated as colorless oils. **27a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.19–7.28 (m, 5H), 6.98 (d, J=8.0 Hz, 2H), 6.52 (d, J=8.4 Hz, 2H), 3.52 (br s, 1H), 2.98–3.02 (m, 1H), 2.92 (d, J=5.4 Hz, 2H), 2.23 (s, 3H), 0.72–0.80 (m, 1H), 0.39–0.50 (m, 2H), 0.23–0.29 (m, 1H), 0.11–0.17 ppm (m, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=145.4 (C), 138.5 (C), 129.8 (CH), 129.7 (CH), 128.1 (CH), 126.3 (C), 126.1 (CH), 113.5 (CH), 58.3 (CH), 40.6 (CH_2), 20.3 (CH_3), 15.7 (CH), 3.7 (CH_2), 3.0 ppm (CH_2); IR (neat): $\tilde{\nu}$=3001, 2918, 1616, 1516, 1494, 1453, 1317, 1300, 1248, 805, 699 cm^{-1}; MS (25 °C): m/z (%): 251 (13) [M^+], 210 (5) [$M^+-C_3H_5$], 160 (100) [$M^+-C_7H_7$], 91 (23) [$C_7H_7^+$]; HRMS calcd for $C_{18}H_{21}N$: 251.1674; found: 251.1673; elemental analysis (%) calcd for $C_{18}H_{21}N$: C 86.01, H 8.42, N 5.57; found: C 85.98, H 8.21, N 5.89. **27b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.36 (d, J=7.3 Hz, 2H), 7.29 (t, J=7.5 Hz, 2H), 7.20 (t, J=7.2 Hz, 1H), 6.89 (d, J=8.3 Hz, 2H), 6.44 (d, J=8.4 Hz, 2H), 4.38 (t, J=6.7, 1H), 4.16 (br s, 1H), 2.17 (s, 3H), 1.61–1.75 (m, 2H), 0.64–0.74 (m, 1H), 0.40–0.53 (m, 2H), 0.03–0.15 ppm (m, 2H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=145.3 (C), 144.4 (C), 129.5 (CH), 128.4 (CH), 126.7 (CH), 126.4 (CH), 126.3 (C), 113.4 (CH), 59.2 (CH), 43.9 (CH_2), 20.3 (CH_3), 8.1 (CH), 4.7 (CH_2), 4.4 ppm (CH_2); IR (neat): $\tilde{\nu}$=2999, 2917, 1617, 1517, 1453, 1300, 1017, 805, 750, 698 cm^{-1}; MS (60 °C): m/z (%): 251 (11) [M^+], 196 (100) [$M^+-C_4H_7$], 119 (19) [$C_8H_9N^+$], 91 (42) [$C_7H_7^+$]; HRMS calcd for $C_{18}H_{21}N$: 251.1674; found: 251.1674; elemental analysis (%) calcd for $C_{18}H_{21}N$: C 86.01, H 8.42, N 5.57; found: C 85.67, H 8.20, N 6.03.

Amines 28a/28b: General procedure A was used to synthesize amines **28a**/**28b** from alkyne **21** and *tert*-butylamine (**3**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 5/1), **28a** (338 mg, 1.56 mmol, 65%) was isolated as a colorless oil. **28b** (56 mg, 0.26 mmol, 11%) could not be obtained in pure form. **28a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.19–7.31 (m, 5H), 2.88 (dd, J=5.8, 13.3 Hz, 1H), 2.80 (dd, J=7.2, 13.3 Hz, 1H), 2.18–2.23 (m, 1H), 1.38 (br s, 1H), 1.09 (s, 9H), 0.71–0.80 (m, 1H), 0.38–0.47 (m, 2H), 0.13–0.18 (m, 1H), (−0.03)–0.02 ppm (m, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=139.9 (C), 129.6 (CH), 128.0 (CH), 125.9 (CH), 58.1 (CH), 50.4 (C), 44.9 (CH_2), 30.2 (CH_3), 18.1 (CH), 4.7 (CH_2), 4.1 ppm (CH_2); IR (neat): $\tilde{\nu}$=2959, 1494, 1454, 1361, 1227, 1017, 743, 698 cm^{-1}; MS (25 °C): m/z (%): 202 (5) [M^+-CH_3], 126 (82) [$M^+-C_7H_7$], 91 (32) [$C_7H_7^+$]; HRMS calcd for $C_{14}H_{20}N$: 202.1596; found: 202.1596; elemental analysis (%) calcd for $C_{15}H_{23}N$: C 82.89, H 10.67, N 6.44, found: C 82.28, H 10.78, N 6.33.

Amines 29a/29b: General procedure A was used to synthesize amines **29a**/**29b** from alkyne **21** and cyclopentylamine (**4**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 5/1→1/1), **29a** (467 mg, 2.04 mmol, 85%) and **29b** (41 mg, 0.18 mmol, 7%) were isolated as colorless oils. **29a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26–7.29 (m, 2H), 7.18–7.21 (m, 3H), 3.33 (quint, J=7.0 Hz, 1H), 2.89 (dd, J=5.5, 13.4 Hz, 1H), 2.78 (dd, J=7.5, 13.4 Hz, 1H), 1.99–2.05 (m, 1H), 1.40–1.91 (m, 7H), 1.15–1.25 (m, 1H), 1.03–1.11 (m, 1H), 0.67–0.76 (m, 1H), 0.50–0.57 (m, 1H), 0.36–0.43 (m, 1H), 0.18–0.24 (m, 1H), (−0.07)–(−0.01) ppm (m, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=139.5 (C), 129.3 (CH), 128.2 (CH), 126.0 (CH), 62.9 (CH), 56.9 (CH), 42.1 (CH_2), 33.7 (CH_2), 32.9 (CH_2), 23.8 (CH_2), 23.7 (CH_2), 16.4 (CH), 4.6 (CH_2), 2.4 ppm (CH_2); IR (neat): $\tilde{\nu}$=2949, 2865, 1603, 1494, 1454, 1017, 742, 697 cm^{-1}; MS (25 °C): m/z (%): 228 (3) [M^+-H], 138 (100) [$M^+-C_7H_7$], 106 (66) [$C_7H_8N^+$], 91 (68) [$C_7H_7^+$]; HRMS calcd for $C_{16}H_{22}N$: 228.1752; found: 228.1747. **29b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.29–7.32 (m, 4H), 7.21–7.26 (m, 1H), 3.75 (t, J=7.0 Hz, 1H), 2.87 (quint, J=7.1 Hz, 1H), 1.57–1.86 (m, 6H), 1.17–1.51 (m, 5H), 0.48–0.58 (m, 1H), 0.38–0.43 (m, 1H), 0.29–0.35 (m, 1H), 0.05–0.10 (m, 1H), (−0.08)–(−0.02) ppm (m, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=144.9 (C), 128.1 (CH), 127.3 (CH), 126.7 (CH), 62.4 (CH), 57.2 (CH), 43.6 (CH_2), 33.9 (CH_2), 32.7 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 8.3 (CH), 4.6 (CH_2), 4.1 ppm (CH_2); IR (neat): $\tilde{\nu}$=2950, 2858, 1453, 1015, 753, 699 cm^{-1}; MS (25 °C): m/z (%): 228 (2) [M^+-H], 174 (100) [$M^+-C_4H_7$], 106 (85) [$C_7H_8N^+$], 91 (30) [$C_7H_7^+$]; HRMS calcd for $C_{16}H_{22}N$: 228.1752; found: 228.1744.

Amines 30a/30b: General procedure A was used to synthesize amines **30a**/**30b** from alkyne **21** and *n*-propylamine (**6**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 5/1→1/1), **30a** (290 mg, 1.43 mmol, 60%) and **30b** (95 mg, 0.47 mmol, 20%) were isolated as colorless oils. **30a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.28–7.32 (m, 2H), 7.21–7.23 (m, 3H), 2.92 (dd, J=5.1, 13.4 Hz, 1H), 2.74–2.81 (m, 2H), 2.48–2.55 (m, 1H), 1.92–1.98 (m, 1H), 1.28–1.53 (m, 3H), 0.85 (t, J=7.4 Hz, 3H), 0.69–0.78 (m, 1H), 0.53–0.60 (m, 1H), 0.39–0.45 (m, 1H), 0.21–0.27 (m, 1H), (−0.04)–0.02 ppm (m, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=139.5 (C), 129.3 (CH), 128.2 (CH), 126.0 (CH), 64.8 (CH), 49.8 (CH_2), 42.0 (CH_2), 23.3 (CH_2), 16.1 (CH), 11.7 (CH_3), 4.7 (CH_2), 2.0 ppm (CH_2); IR (neat): $\tilde{\nu}$=2957, 2924, 1494, 1454, 1126, 1018, 741, 697 cm^{-1}; MS (25 °C): m/z (%): 162 (30) [$M^+-C_3H_5$], 112 (100) [$M^+-C_7H_7$]; elemental analysis (%) calcd for $C_{14}H_{21}N$: C 82.70, H 10.41, N 6.89; found: C 82.41, H 10.50, N 6.87. **30b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.22–7.32 (m, 5H), 3.68 (t, J=7.0 Hz, 1H), 2.35–2.46 (m, 2H), 1.65–1.72 (m, 2H), 1.41–1.52 (m, 3H), 0.87 (t, J=7.3 Hz, 3H), 0.51–0.59 (m, 1H), 0.39–0.46 (m, 1H), 0.30–0.37 (m, 1H), 0.06–0.11 (m, 1H), (−0.07)–(−0.01) ppm (m, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ=144.7 (C), 128.2 (CH), 127.2 (CH), 126.7 (CH), 64.0 (CH), 49.7 (CH_2), 43.4 (CH_2), 23.3 (CH_2), 11.8 (CH_3), 8.3 (CH), 4.6 (CH_2), 4.1 (CH_2); IR (neat): $\tilde{\nu}$=2958, 2921, 1454, 1126, 1016, 752, 699 cm^{-1}.

Amines 31a/31b: General procedure A was used to synthesize amines **31a**/**31b** from alkyne **22** and *tert*-butylamine (**3**). The reaction time of the

hydroamination step was 24 h (not minimized). After purification by flash chromatography (PE/EtOAc, 10/1), a mixture of **31a** and **31b** (538 mg, 2.10 mmol, 87 %, **31a**/**31b** 3/1) was isolated as a colorless oil. Only the minor product **31b** (105 mg, 0.45 mmol, 19 %) could be obtained in pure form after a second chromatographic purification step. **31b**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.32$ (d, $J = 7.2$ Hz, 2H), 7.19 (t, $J = 7.5$ Hz, 2H), 7.08–7.11 (m, 1H), 5.42 (s, 1H), 3.77 (dd, $J = 4.2$, 10.0 Hz, 1H), 1.80–2.07 (m, 6H), 1.44–1.57 (m, 4H), 1.21 (brs, 1H), 0.87 ppm (s, 9H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 148.7$ (C), 135.1 (C), 127.9 (CH), 126.9 (CH), 126.1 (CH), 125.2 (CH), 54.6 (CH), 50.8 (C), 49.9 (CH_2), 30.1 (CH_3), 28.0 (CH_2), 25.3 (CH_2), 22.9 (CH_2), 22.4 ppm (CH_2); IR (neat): $\tilde{\nu} = 2923$, 2855, 1494, 1454, 1361, 1227, 754, 798 cm^{-1}; MS (25 °C): *m/z* (%): 242 (4) [$M^+ - CH_3$], 162 (79) [$M^+ - C_7H_{11}$], 106 (100) [$C_7H_8N^+$], 91 (13) [$C_7H_7^+$]; elemental analysis (%) calcd for $C_{18}H_{27}N$: C 83.99, H 10.57, N 5.44; found: C 83.71, H 10.50, N 5.30.

Amines 37a/37b: General procedure A was used to synthesize amines **37a**/**37b** from 1-octyne (**32**) and 4-methylaniline (**2**). The reaction time of the hydroamination step was 1 h. After purification by flash chromatography (PE/EtOAc, 40/1), **37a** (100 mg, 0.46 mmol, 19 %) and **37b** (399 mg, 1.82 mmol, 76 %) were isolated as colorless oils. **37a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.97$ (d, $J = 8.2$ Hz, 2H), 6.52 (d, $J = 8.4$ Hz, 2H), 3.42 (brs, 1H), 3.06 (t, $J = 7.1$ Hz, 2H), 2.23 (s, 3H), 1.59 (quint, $J = 7.2$ Hz, 2H), 1.28–1.39 (m, 10H), 0.88 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 146.3$ (C), 129.7 (CH), 126.2 (C), 112.9 (CH), 44.4 (CH_2), 31.8 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 27.2 (CH_2), 22.6 (CH_2), 20.3 (CH_3), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu} = 2920$, 2851, 1620, 1522, 1468, 1306, 1246, 1182, 807 cm^{-1}; MS (25 °C): *m/z* (%): 219 (48) [M^+], 134 (29) [$M^+ - C_6H_{13}$], 120 (100) [$M^+ - C_7H_{15}$], 91 (28) [$C_7H_7^+$]; HRMS calcd for $C_{15}H_{25}N$: 219.1987; found: 219.1986; elemental analysis (%) calcd for $C_{15}H_{25}N$: C 82.13, H 11.49, N 6.39; found: C 82.20, H 11.65, N 6.34. **37b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.99$ (d, $J = 8.2$ Hz, 2H), 6.53 (d, $J = 8.4$ Hz, 2H), 3.43 (sext, $J = 6.1$ Hz, 1H), 3.29 (brs, 1H), 2.25 (s, 3H), 1.55–1.61 (m, 1H), 1.30–1.40 (m, 9H), 1.18 (d, $J = 6.3$ Hz, 3H), 0.91 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 145.5$ (C), 129.7 (CH), 125.9 (C), 113.3 (CH), 48.8 (CH), 37.3 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 26.1 (CH_2), 22.6 (CH_2), 20.8 (CH_3), 20.3 (CH_3), 14.0 ppm (CH_3); IR (neat): $\tilde{\nu} = 2924$, 2855, 1618, 1518, 1455, 1316, 1300, 1249, 804 cm^{-1}; MS (25 °C): *m/z* (%): 219 (36) [M^+], 204 (29) [$M^+ - CH_3$], 134 (100) [$M^+ - C_6H_{13}$], 91 (19) [$C_7H_7^+$]; HRMS calcd for $C_{15}H_{25}N$: 219.1987; found: 219.1987; elemental analysis (%) calcd for $C_{15}H_{25}N$: C 82.13, H 11.49, N 6.39; found: C 82.07, H 11.71, N 6.69.

Amines 38a/38b: General procedure A was used to synthesize amines **38a**/**38b** from 1-dodecyne (**33**) and 4-methylaniline (**2**). The reaction time of the hydroamination step was 8 h. The temperature was 75 °C. After purification by flash chromatography (PE/EtOAc, 40/1), **38a** (137 mg, 0.50 mmol, 21 %) and **38b** (515 mg, 1.87 mmol, 78 %) were isolated as colorless oils. **38a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.98$ (d, $J = 8.2$ Hz, 2H), 6.53 (d, $J = 8.4$ Hz, 2H), 3.42 (brs, 1H), 3.07 (t, $J = 7.2$ Hz, 2H), 2.23 (s, 3H), 1.60 (quint, $J = 7.2$ Hz, 2H), 1.26–1.40 (m, 18H), 0.88 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 146.3$ (C), 129.7 (CH), 126.3 (C), 112.9 (CH), 44.4 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 27.2 (CH_2), 22.7 (CH_2), 20.3 (CH_3), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu} = 2921$, 2852, 1619, 1519, 1300, 805, 720 cm^{-1}; MS (70 °C): *m/z* (%): 275 (51) [M^+], 260 (3) [$M^+ - CH_3$], 232 (2) [$M^+ - C_3H_7$], 120 (100) [$M^+ - C_8H_{10}N$], 91 (4) [$C_7H_7^+$]; HRMS calcd for $C_{19}H_{33}N$: 275.2613; found: 275.2612; elemental analysis (%) calcd for $C_{19}H_{33}N$: C 82.84, H 12.07, N 5.08; found: C 82.76, H 12.23, N 5.04. **38b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.96$ (d, $J = 8.2$ Hz, 2H), 6.49 (d, $J = 8.4$ Hz, 2H), 3.40 (sext, $J = 6.1$ Hz, 1H), 3.26 (brs, 1H), 2.22 (s, 3H), 1.52–1.59 (m, 1H), 1.26–1.43 (m, 17H), 1.14 (d, $J = 6.3$ Hz, 3H), 0.88 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 145.5$ (C), 129.7 (CH), 125.9 (C), 113.3 (CH), 48.8 (CH), 37.2 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 20.8 (CH_3), 20.3 (CH_3), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu} = 2923$, 2853, 1620, 1520, 1465, 1317, 1301, 806 cm^{-1}; MS (25 °C): *m/z* (%): 275 (12) [M^+], 134 (100) [$C_9H_{12}N^+$]; HRMS calcd for $C_{19}H_{33}N$: 275.2613; found: 275.2613; elemental analysis (%) calcd for $C_{19}H_{33}N$: C 82.84, H 12.07, N 5.08; found: C 82.73, H 12.02, N 5.24.

Amine 39a: General procedure A was used to synthesize amine **39a** from 1-dodecyne (**33**) and *tert*-butylamine (**3**). The reaction time of the hydroamination step was 2 h. After purification by flash chromatography (MeOH/EtOAc, 1/2), compound **39a** (437 mg, 1.81 mmol, 75 %) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.53$ (t, $J = 7.3$ Hz, 2H), 1.41–1.48 (m, 2H), 1.26–1.33 (m, 18H), 1.10 (s, 9H), 0.88 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 50.2$ (C), 42.6 (CH_2), 31.9 (CH_2), 31.1 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.0 (CH_3), 27.6 (CH_2), 22.7 (CH_2), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu} = 2922$, 2853, 1464, 1359, 1231, 692 cm^{-1}; MS (25 °C): *m/z* (%): 241 (7) [M^+], 226 (100) [$M^+ - CH_3$]; HRMS calcd for $C_{15}H_{32}N$: 226.2535; found: 226.2535.

Amines 40a/40b: General procedure A was used to synthesize amines **40a**/**40b** from 1-dodecyne (**33**) and cyclopentylamine (**4**). The reaction time of the hydroamination step was 24 h (not minimized). After purification by flash chromatography (MeOH/EtOAc, 1/2), **40a** (297 mg, 1.17 mmol, 49 %) and **40b** (198 mg, 0.78 mmol, 32 %) were isolated as colorless oils. **40a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.06$ (quint, $J = 6.9$ Hz, 1H), 2.58 (t, $J = 7.4$ Hz, 2H), 2.05 (brs, 1H), 1.82–1.90 (m, 2H), 1.64–1.72 (m, 2H), 1.48–1.56 (m, 2H), 1.26–1.38 (m, 20H), 0.88 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 59.9$ (CH), 48.7 (CH_2), 33.0 (CH_2), 31.9 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 27.5 (CH_2), 24.1 (CH_2), 24.1 (CH_2), 22.7 (CH_2), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu} = 2921$, 2852, 1456, 1375, 721 cm^{-1}; MS (25 °C): *m/z* (%): 253 (13) [M^+], 113 (58) [$C_8H_{17}^+$]; HRMS calcd for $C_{17}H_{35}N$: 253.2770; found: 253.2765. **40b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.23$ (quint, $J = 7.2$ Hz, 1H), 2.71–2.77 (m, 1H), 1.89–1.92 (m, 2H), 1.70–1.73 (m, 2H), 1.52–1.56 (m, 4H), 1.26–1.45 (m, 19H), 1.11 (d, $J = 6.3$ Hz, 3H), 0.88 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 56.8$ (CH), 51.9 (CH), 36.6 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 27.4 (CH_2), 26.1 (CH_2), 24.0 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 22.7 (CH_2), 19.8 (CH_3), 14.1 ppm (CH_3); IR (neat): $\tilde{\nu} = 2920$, 2852, 1456, 1376, 1056, 721 cm^{-1}; MS (25 °C): *m/z* (%): 253 (3) [M^+], 238 (7) [$M^+ - CH_3$], 113 (100) [$C_8H_{17}^+$]; HRMS calcd for $C_{17}H_{35}N$: 253.2770; found: 253.2766.

Amines 41a/41b: General procedure A was used to synthesize amines **41a**/**41b** from phenylacetylene (**34**) and 4-methylaniline (**2**). The reaction time of the hydroamination step was 6 h. The temperature was 75 °C. After purification by flash chromatography (PE/EtOAc, 40/1), compounds **41a** (319 mg, 1.51 mmol, 63 %) and **41b** (72 mg, 0.34 mmol, 14 %) were isolated as colorless oils. **41a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.29$–7.32 (m, 2H), 7.20–7.24 (m, 3H), 6.98 (d, $J = 8.0$ Hz, 2H), 6.53 (d, $J = 8.4$ Hz, 2H), 3.52 (brs, 1H), 3.36 (t, $J = 7.0$ Hz, 2H), 2.89 (t, $J = 7.0$ Hz, 2H), 2.23 ppm (s, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 145.7$ (C), 139.4 (C), 129.7 (CH), 128.8 (CH), 128.5 (CH), 126.6 (C), 126.3 (CH), 113.2 (CH), 45.4 (CH_2), 35.5 (CH_2), 20.3 ppm (CH_3); IR (neat): $\tilde{\nu} = 3404$, 3024, 2917, 1615, 1518, 1257, 806, 747, 698 cm^{-1}; MS (25 °C): *m/z* (%): 211 (65) [M^+], 120 (100) [$M^+ - C_7H_7$], 91 (66) [$C_7H_7^+$]; HRMS calcd for $C_{15}H_{17}N$: 211.1361; found: 211.1362; elemental analysis (%) calcd for $C_{15}H_{17}N$: C 85.26, H 8.11, N 6.63; found: C 85.08, H 7.96, N 6.53. **41b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.19$–7.34 (m, 5H), 6.89 (d, $J = 8.0$ Hz, 2H), 6.42 (d, $J = 8.4$ Hz, 2H), 4.44 (q, $J = 6.7$ Hz, 1H), 3.89 (brs, 1H), 2.18 (s, 3H), 1.49 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 145.4$ (C), 145.0 (C), 129.6 (CH), 128.6 (CH), 126.8 (CH), 126.3 (C), 125.8 (CH), 113.4 (CH), 53.7 (CH), 25.0 (CH_3), 20.3 ppm (CH_3); IR (neat): $\tilde{\nu} = 3408$, 2955, 2916, 1616, 1519, 1299, 1256, 808, 755, 700 cm^{-1}; MS (25 °C): *m/z* (%): 211 (82) [M^+], 196 (77) [$M^+ - CH_3$], 120 (100) [$M^+ - C_7H_7$], 107 (87) [$C_7H_8N^+$], 91 (62) [$C_7H_7^+$]; HRMS calcd for $C_{15}H_{17}N$: 211.1361; found: 211.1360; elemental analysis (%) calcd for $C_{15}H_{17}N$: C 85.26, H 8.11, N 6.63; found: C 85.30, H 7.76, N 6.55.

Amine 42a: General procedure A was used to synthesize amine **42a** from 4-methoxyphenylacetylene (**35**) and *tert*-butylamine (**3**). The reaction time of the hydroamination step was 8 h. The temperature was 75 °C. After purification by flash chromatography (MeOH/EtOAc, 1/2), **42a** (380 mg, 1.84 mmol, 77 %) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.14$ (d, $J = 8.7$ Hz, 2H), 6.84 (d, $J = 8.5$ Hz, 2H), 3.79 (s, 3H), 2.77–2.81 (m, 2H), 2.70–2.74 (m, 2H), 1.07 ppm (s, 9H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 158.0$ (C), 132.2 (C), 129.5 (CH), 113.8 (CH), 55.2 (CH_3), 50.2 (C), 44.2 (CH_2), 36.2 (CH_2), 28.9 ppm (CH_3); IR (neat): $\tilde{\nu} = 2956$, 1612, 1243, 1176, 1109, 1035, 821, 700 cm^{-1};

MS (25 °C): *m/z* (%): 207 (2) [M^+], 192 (25) [M^+-CH_3], 135 (88) [$C_9H_{11}O^+$], 121 (37) [$C_8H_9O^+$]; HRMS calcd for $C_{12}H_{18}NO$: 192.1388; found: 192.1388; elemental analysis (%) calcd for $C_{13}H_{21}NO$: C 68.07, H 8.57, N 6.62; found: C 67.78, H 8.67, N 6.54.

Amine 43a: General procedure A was used to synthesize amine **43a** from 4-chlorophenylacetylene (**36**) and *tert*-butylamine (**3**). The reaction time of the hydroamination step was 8 h. The temperature was 75 °C. After purification by flash chromatography (MeOH/EtOAc, 1/2), compound **43a** (359 mg, 1.70 mmol, 71%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.26$ (d, $J = 8.4$ Hz, 2H), 7.15 (d, $J = 8.4$ Hz, 2H), 2.73–2.83 (m, 4H), 1.32 (br s, 1H), 1.08 ppm (s, 9H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 138.6$ (C), 131.9 (C), 130.0 (CH), 128.5 (CH), 50.4 (C), 43.8 (CH_2), 36.5 (CH_2), 28.9 ppm (CH_3); IR (neat): $\tilde{\nu} = 2961$, 2863, 1492, 1360, 1229, 1091, 1015, 809, 706 cm^{-1}; MS (25 °C): *m/z* (%): 198 (19) [$M^+(^{37}Cl)-CH_3$], 141 (27) [$M^+(^{37}Cl)-C_4H_{10}N$], 139 (37) [$M^+(^{35}Cl)-C_4H_{10}N$], 106 (76) [$C_7H_8N^+$], 91 (70) [$C_7H_7^+$], 86 (100) [$M^+-C_5H_{12}N$]; HRMS calcd for $C_{11}H_{15}NCl$: 196.0893; found: 196.0890; elemental analysis (%) calcd for $C_{12}H_{18}NCl$: C 68.07, H 8.57, N 6.62; found: C 67.78, H 8.67, N 6.54.

Amines 44a/44b: General procedure A was used to synthesize amines **44a/44b** from 4-methoxyphenylacetylene (**35**) and cyclopentylamine (**4**). The reaction time of the hydroamination step was 12 h. The temperature was 75 °C. After purification by flash chromatography (MeOH/EtOAc, 1/3→1/1), **44a** (290 mg, 1.32 mmol, 55%) and **44b** (107 mg, 0.49 mmol, 20%) were isolated as colorless oils. **44a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.13$ (d, $J = 8.7$ Hz, 2H), 6.84 (d, $J = 8.7$ Hz, 2H), 3.79 (s, 3H), 3.09 (quint, $J = 7.0$ Hz, 1H), 2.76–2.87 (m, 5H), 1.81–1.89 (m, 2H), 1.63–1.71 (m, 2H), 1.50–1.57 (m, 2H), 1.30–1.38 ppm (m, 2H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 158.0$ (C), 131.8 (C), 129.6 (CH), 113.9 (CH), 59.6 (CH), 55.2 (CH_3), 49.9 (CH_2), 35.1 (CH_2), 32.7 (CH_2), 32.7 (CH_2), 24.0 (CH_2), 24.0 ppm (CH_2); IR (neat): $\tilde{\nu} = 2949$, 1612, 1511, 1454, 1243, 1176, 1034, 821 cm^{-1}; MS (25 °C): *m/z* (%): 204 (12) [M^+-CH_3], 98 (100) [$M^+-C_8H_9O$], 121 (14) [$C_8H_9O^+$]; elemental analysis (%) calcd for $C_{14}H_{21}NO$: C 76.67, H 9.65, N 6.39; found: C 75.93, H 9.43, N 6.22. **44b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.23$ (d, $J = 8.5$ Hz, 2H), 6.87 (d, $J = 8.7$ Hz, 2H), 3.80 (s, 3H), 2.87 (q, $J = 7.2$ Hz, 1H), 1.58–1.87 (m, 5H), 1.37–1.51 (m, 2H), 1.33 (d, $J = 6.5$ Hz, 3H), 1.19–1.30 ppm (m, 2H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 158.4$ (C), 137.9 (C), 127.6 (CH), 113.7 (CH), 57.1 (CH), 55.9 (CH), 55.2 (CH_3), 33.6 (CH_2), 32.7 (CH_2), 24.5 (CH_3), 23.9 (CH_2), 23.8 ppm (CH_2); IR (neat): $\tilde{\nu} = 2952$, 1610, 1510, 1462, 1240, 1174, 1036, 829, 809 cm^{-1}; MS (25 °C): *m/z* (%): 204 (32) [M^+-CH_3], 135 (44) [$M^+-C_5H_{10}ON$], 112 (100) [$M^+-C_7H_7O$], 91 (28) [$C_7H_7^+$]; elemental analysis (%) calcd for $C_{14}H_{21}NO$: C 76.67, H 9.65, N 6.39; found: C 76.47, H 9.66, N 6.18.

Amines 45a/45b: General procedure A was used to synthesize amines **45a/45b** from 4-chlorophenylacetylene (**36**) and cyclopentylamine (**4**). The reaction time of the hydroamination step was 12 h. The temperature was 75 °C. After purification by flash chromatography (MeOH/EtOAc, 1/3→1/1), **45a** (286 mg, 1.28 mmol, 53%) and **45b** (110 mg, 0.49 mmol, 20%) were isolated as colorless oils. **45a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.26$ (d, $J = 9.0$ Hz, 2H), 7.14 (d, $J = 8.5$ Hz, 2H), 3.06 (quint, $J = 6.8$ Hz, 1H), 2.75–2.86 (m, 4H), 1.79–1.87 (m, 2H), 1.61–1.71 (m, 2H), 1.46–1.57 (m, 2H), 1.23–1.32 ppm (m, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 138.7$ (C), 131.8 (C), 130.0 (CH), 128.5 (CH), 59.8 (CH), 49.8 (CH_2), 36.0 (CH_2), 33.1 (CH_2), 33.1 (CH_2), 24.0 (CH_2), 24.0 ppm (CH_2); IR (neat): $\tilde{\nu} = 2948$, 2862, 1893, 1492, 1453, 1090, 1015, 808 cm^{-1}; MS (25 °C): *m/z* (%): 223 (2) [M^+], 139 (18) [$C_8H_8Cl^+$], 125 (9) [$C_7H_6Cl^+$], 98 (100) [$M^+-C_7H_6Cl$]; elemental analysis (%) calcd for $C_{13}H_{18}NCl$: C 69.79, H 8.11, N 6.26; found: C 69.36, H 7.85, N 6.46. **45b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.23$–7.30 (m, 4H), 3.81 (q, $J = 6.6$ Hz, 1H), 2.85 (quint, $J = 7.1$ Hz, 1H), 2.74 (br s, 1H), 1.19–1.83 (m, 8H), 1.32 ppm (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 144.5$ (C), 132.3 (C), 128.5 (CH), 128.0 (CH), 57.3 (CH), 56.1 (CH), 33.7 (CH_2), 32.8 (CH_2), 24.6 (CH_3), 23.9 (CH_2), 23.8 ppm (CH_2); IR (neat): $\tilde{\nu} = 2954$, 2865, 1897, 1489, 1090, 1013, 8278 cm^{-1}; MS (25 °C): *m/z* (%): 208 (72) [M^+-CH_3], 139 (100) [$C_8H_8Cl^+$]; elemental analysis (%) calcd for $C_{13}H_{18}NCl$: C 69.79, H 8.11, N 6.26; found: C 69.72, H 8.01, N 5.95.

Amine 51: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.29$–7.37 (m, 4H), 7.15–7.28 (m, 4H), 7.08 (d, $J = 6.7$ Hz, 2H), 7.01 (d, $J = 8.5$ Hz, 2H), 6.78 (d, $J = 8.7$ Hz, 2H), 3.86 (dd, $J = 5.7$, 8.4 Hz, 1H), 3.76 (s, 3H), 3.58 (d, $J = 13.2$ Hz, 1H), 3.39 (d, $J = 13.3$ Hz, 1H), 2.94 (dd, $J = 5.7$, 13.6 Hz, 1H), 2.88 (dd, $J = 8.5$, 13.6 Hz, 1H), 1.84 ppm (br s, 1H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 158.5$ (C), 143.7 (C), 138.8 (C), 132.5 (C), 129.2 (CH), 129.1 (CH), 128.3 (CH), 128.3 (CH), 127.4 (CH), 127.0 (CH), 126.3 (CH), 113.6 (CH), 63.5 (CH), 55.2 (CH_3), 50.7 (CH_2), 45.2 ppm (CH_2); IR (neat): $\tilde{\nu} = 2833$, 1610, 1510, 1494, 1453, 1243, 1173, 1104, 1033, 821, 754, 697 cm^{-1}; MS (70 °C): *m/z* (%): 316 (1) [M^+-H], 226 (64) [$M^+-C_7H_7$], 121 (100) [$C_8H_9O^+$].

Amine 52: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.17$–7.30 (m, 8H), 7.12–7.14 (m, 2H), 3.80 (dd, $J = 5.7$, 8.4 Hz, 1H), 2.85 (dd, $J = 8.4$, 13.4 Hz, 1H), 2.93 (dd, $J = 5.7$, 13.6 Hz, 1H), 2.16–2.24 (m, 2H), 1.47–1.61 (m, 6H), 1.26–1.37 (m, 1H), 1.01–1.22 (m, 3H), 0.68–0.80 ppm (m, 2H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 144.2$ (C), 139.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 127.2 (CH), 126.9 (CH), 126.2 (CH), 64.8 (CH), 54.5 (CH_2), 45.4 (CH_2), 37.9 (CH), 31.3 (CH_2), 31.2 (CH_2), 26.7 (CH_2), 26.0 (CH_2), 26.0 ppm (CH_2); IR (neat): $\tilde{\nu} = 2919$, 2849, 1602, 1494, 1451, 1121, 756, 697 cm^{-1}; MS (60 °C): *m/z* (%): 292 (2) [M^+], 202 (100) [$M^+-C_7H_7$].

Amine 53: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.17$–7.30 (m, 8H), 7.11–7.13 (m, 2H), 3.83 (dd, $J = 5.9$, 8.2 Hz, 1H), 2.85–2.96 (m, 2H), 2.31–2.43 (m, 2H), 1.13–1.39 (m, 5H), 0.80 ppm (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 144.1$ (C), 139.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 127.2 (CH), 126.9 (CH), 126.2 (CH), 64.9 (CH), 47.5 (CH_2), 45.3 (CH_2), 32.2 (CH_2), 20.3 (CH_2), 13.9 ppm (CH_3); IR (neat): $\tilde{\nu} = 2925$, 2858, 1494, 1453, 756, 697 cm^{-1}; MS (50 °C): *m/z* (%): 252 (1) [M^+-H], 162 (100) [$M^+-C_7H_7$].

Amine 54: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.27$–7.30 (m, 8H), 7.13 (m, 2H), 3.83 (dd, $J = 5.9$, 8.2 Hz, 1H), 2.85–2.96 (m, 2H), 2.30–2.42 (m, 2H), 1.08–1.41 (m, 7H), 0.81 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta ? = 144.1$ (C), 139.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 127.2 (CH), 126.9 (CH), 126.3 (CH), 64.8 (CH), 47.7 (CH_2), 45.3 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 22.5 (CH_2), 14.0 ppm (CH_3); IR (neat): $\tilde{\nu} = 2924$, 1946, 1602, 1494, 1453, 756, 697 cm^{-1}; MS (50 °C): *m/z* (%): 266 (1) [M^+-H], 176 (100) [$M^+-C_7H_7$].

Amine 55: General procedure B was used to synthesize amine **55** from diphenylacetylene (**1**) and *n*-hexylamine (**50**). After purification by flash chromatography (PE/EtOAc, 5/1), **55** (451 mg, 1.61 mmol, 67%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.16$–7.33 (m, 8H), 7.12 (d, $J = 6.9$ Hz, 2H), 3.83 (dd, $J = 5.9$, 8.2 Hz, 1H), 2.93 (dd, $J = 5.9$, 13.4 Hz, 1H), 2.88 (dd, $J = 8.3$, 13.5 Hz, 1H), 2.30–2.43 (m, 2H), 1.45 (br s, 1H), 1.30–1.38 (m, 2H), 1.12–1.27 (m, 6H), 0.82 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 144.0$ (C), 139.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 127.3 (CH), 126.9 (CH), 126.3 (CH), 64.8 (CH), 47.7 (CH_2), 45.3 (CH_2), 31.6 (CH_2), 29.9 (CH_2), 26.8 (CH_2), 22.5 (CH_2), 14.0 ppm (CH_3); IR (neat): $\tilde{\nu} = 2923$, 2853, 1602, 1494, 1453, 756, 697 cm^{-1}; MS (25 °C): *m/z* (%): 281 (1) [M^+], 190 (100) [$M^+-C_7H_7$]; elemental analysis (%) calcd for $C_{20}H_{27}N$: C 85.35, H 9.67, N 4.98; found: C 85.15, H 9.61, N 5.19.

Amines 56a/56b: General procedure C was used to synthesize amines **56a/56b** from 1-phenylpropyne (**20**) and benzylamine (**7**). After purification by flash chromatography (PE/EtOAc, 5/1→1/1), compounds **56a** (394 mg, 1.75 mmol, 73%) and **56b** (14 mg, 0.06 mmol, 3%) were isolated as colorless oils. **56a:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.10$–7.30 (m, 10H), 3.84 (d, $J = 13.3$ Hz, 1H), 3.73 (d, $J = 13.3$ Hz, 1H), 2.93 (sext, $J = 6.4$ Hz, 1H), 2.76 (dd, $J = 7.0$, 13.4 Hz, 1H), 2.64 (dd, $J = 6.4$, 13.3 Hz, 1H), 1.54 (br s, 1H), 1.09 ppm (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 140.5$ (C), 139.4 (C), 129.2 (CH), 128.3 (CH), 128.3 (CH), 127.9 (CH), 126.7 (CH), 126.1 (CH), 53.7 (CH), 51.2 (CH_2), 43.6 (CH_2), 20.2 ppm (CH_3); IR (neat): $\tilde{\nu} = 2957$, 2927, 1454, 1100, 747, 697 cm^{-1}; MS (25 °C): *m/z* (%): 225 (2) [M^+], 134 (100) [$M^+-C_7H_7$], 91 (100) [$C_7H_7^+$]; elemental analysis (%) calcd for $C_{16}H_{19}N$: C 85.29, H 8.50, N 6.22; found: C 85.05, H 8.65, N 6.49. **56b:** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.13$–7.35 (m, 10H), 3.65 (d, $J = 13.2$ Hz, 1H), 3.48–3.56 (m, 2H), 1.59–1.80 (m, 3H), 0.80 (t, $J = 7.4$ Hz, 3H) ppm; ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): $\delta = 144.1$ (C), 140.8 (C), 128.3 (CH), 128.3 (CH), 128.1 (CH), 127.4 (CH), 126.9 (CH), 126.8 (CH), 64.2 (CH), 51.5 (CH_2), 31.1 (CH_2), 10.7 ppm (CH_3); IR (neat): $\tilde{\nu} = 2961$, 2926, 1492, 1452, 1117, 1027, 741, 696 cm^{-1}; MS (25 °C): *m/z* (%): 225 (3) [M^+], 196 (99) [$M^+-C_2H_5$], 91 (100) [$C_7H_7^+$].

Amines 57a/57b: General procedure C was used to synthesize amines **57a/57b** from 1-phenylpropyne (**20**) and *n*-hexylamine (**50**). After purification by flash chromatography (PE/EtOAc, 3/1→1/1), **57a** (411 mg,

1.88 mmol, 78%) and **57b** (25 mg, 0.11 mmol, 5%) were isolated as colorless oils. **57a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.32 (m, 2H), 7.16–7.23 (m, 3H), 2.88 (sext, J = 6.5 Hz, 1H), 2.47–2.76 (m, 4H), 1.36–1.48 (m, 2H), 1.18–1.32 (m, 7H), 1.05 (d, J = 6.3 Hz, 3H), 0.86 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 139.6 (C), 129.2 (CH), 128.3 (CH), 126.0 (CH), 54.6 (CH), 47.4 (CH_2), 43.7 (CH_2), 31.7 (CH_2), 30.1 (CH_2), 27.0 (CH_2), 22.5 (CH_2), 20.2 (CH_3), 14.0 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2926, 2854, 1603, 1469, 1453, 1127, 742, 698 cm^{-1}; MS (25 °C): *m/z* (%) 219 (2) [M^+], 204 (5) [M^+-CH_3], 190 (96) [$M^+-C_2H_5$], 128 (100) [$M^+-C_7H_7$] 91 (55) [$C_7H_7^+$]; elemental analysis (%) calcd for $C_{15}H_{25}N$: C 82.13, H 11.49, N 6.38; found: C 81.84, H 11.87, N 6.34. **57b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.34 (m, 5H), 3.46 (dd, J = 5.8, 7.9 Hz, 1H), 2.33–2.49 (m, 2H), 1.70–1.82 (m, 1H), 1.56–1.69 (m, 1H), 1.36–1.50 (m, 2H), 1.18–1.33 (m, 7H), 0.86 (t, J = 6.7 Hz, 3H), 0.80 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 144.4 (C), 128.2 (CH), 127.3 (CH), 126.7 (CH), 65.2 (CH), 47.8 (CH_2), 31.7 (CH_2), 31.0 (CH_2), 30.3 (CH_2), 27.0 (CH_2), 22.6 (CH_2), 14.0 (CH_3), 10.8 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 2958, 2926, 2854, 1453, 1125, 751, 699 cm^{-1}; MS (25 °C): *m/z* (%): 219 (2) [M^+], 190 (100) [$M^+-C_2H_5$], 91 (46) [$C_7H_7^+$]; HRMS calcd for $C_{15}H_{24}N$: 218.1909; found: 218.1909.

Kinetic investigations: The kinetic investigation of the [Ind_2TiMe_2]-catalyzed reaction between **2** and **20** (Figure 1) was performed as described in ref. [7c] The obtained data for k_{obs} are: 7.66×10^{-5} s^{-1} (c([Ind_2TiMe_2]) = 8.36×10^{-3} mol L^{-1} (3.0 mol%), c(**2**) = 2.57 mol L^{-1}, c_0(**20**) = 0.28 mol L^{-1}); 9.85×10^{-5} s^{-1} (c([Ind_2TiMe_2]) = 1.11×10^{-2} mol L^{-1} (4.1 mol%), c(**2**) = 2.59 mol L^{-1}, c_0(**20**) = 0.27 mol L^{-1}); 1.69×10^{-4} s^{-1} (c([Ind_2TiMe_2]) = 1.85×10^{-2} mol L^{-1} (6.8 mol%), c(**2**) = 2.63 mol L^{-1}, c_0(**20**) = 0.27 mol L^{-1}); 2.71×10^{-4} s^{-1} (c([Ind_2TiMe_2]) = 3.35×10^{-2} mol L^{-1} (12.3 mol%), c(**2**) = 2.57 mol L^{-1}, c_0(**20**) = 0.27 mol L^{-1}); 3.67×10^{-4} s^{-1} (c([Ind_2TiMe_2]) = 4.67×10^{-2} mol L^{-1} (17.4 mol%), c(**2**) = 2.51 mol L^{-1}, c_0(**20**) = 0.27 mol L^{-1}).

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