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A Straightforward Route to Homoallyl-Homocrotylamines Promoted by a Titanium Complex

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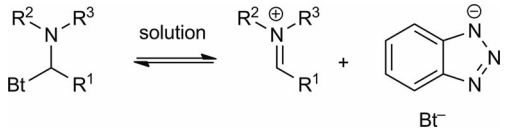
π-Allyltitanium complexes, generated in situ from 1,3-dienes and [Cp_2TiH], react with benzotriazole derivatives to give homoallylic amines in good yields. Under similar conditions, triple cascade reactions (allyltitanation followed by cationic 2-aza-Cope rearrangement followed by a second allyltitanation) occur from bis(benzotriazolyl) compounds affording a straightforward route to homoallyl-(*E*)-homocrotylamines. A theoretical study provides further insight into the factors that govern the selectivity of this sequence of reactions.

Introduction

Efficient syntheses of homoallylamines represent a major field of investigation in organic chemistry. This interest is mainly due to the important role that homoallylamines play as intermediates in the production of a large number of products[1] including amino acids,[2] drugs,[3] alkaloids,[4] and β-lactam derivatives.[5] Different synthetic methodologies have been developed, most frequently involving imines and allylating agents such as allylsilanes,[6] allylstannanes,[7] and allylboron species.[8] However, these syntheses often suffer from the poor electrophilic character of imines, which needs to be augmented by, for example, the presence of an electron-withdrawing group[9] or Lewis acid activation.[10] Compounds with a benzotriazolyl group (Bt) α to an amino functionality, developed mainly by Katritzky and collaborators,[11] represent a class of very interesting alternative substrates for this reaction. In solution, these adducts exist in equilibrium with a highly electrophilic imminium salt (Scheme 1). In addition, these compounds are readily accessible, inexpensive, and stable towards moisture. As part of our ongoing research on the potential of butadiene derivatives,[12] we recently started to explore the titanium-promoted reductive coupling of 1,3-dienes with benzotriazole compounds as an alternative approach to homallylic amines.[13,14]



Scheme 1. Equilibrium of benzotriazole adducts in solution.

Results and Discussion

We first synthesised several benzotriazole adducts **1**–**9** according to the procedures described in the literature (Figure 1).[15–17] The reaction of formaldehyde with *N*-methylaniline, dibenzylamine, *N*-methylbenzylamine, or diethylamine and one equivalent of benzotriazole produced substrates **1**–**4**, respectively.[15] Similarly, isobutyraldehyde and pyrrolidine gave product **5** in high yield.[15] Finally, the reaction of benzylamine, phenylethylamine, isopropylamine, or cyclohexylamine with two equivalents of formaldehyde and two equivalents of benzotriazole afforded bis(benzotriazolyl) compounds **6**–**9**. These are of special interest because they represent substrates containing two possible sites of reaction.[17]

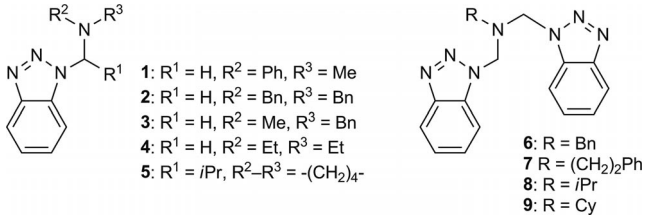


Figure 1. Benzotriazole derivatives synthesised in this study.

With the benzotriazole derivatives in hand, we explored the titanium-promoted reductive coupling of isoprene with substrate **1** (Scheme 2). The π-allyltitanium complex was

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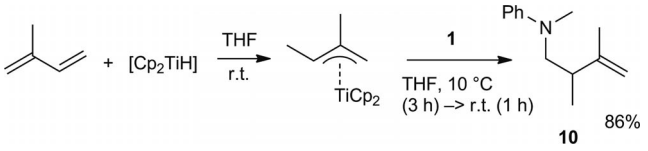
readily prepared by hydrotitanation of isoprene using [Cp_2TiH] generated in situ by the reaction of [Cp_2TiCl_2] with isopropylmagnesium chloride.[18] The resulting purple π-allyltitanium complex was added at 10 °C over three hours by means of a syringe pump to a solution of benzotriazole compound **1** in tetrahydrofuran (THF).[19] After the addition time, the solution was warmed to room temperature and stirred for one hour. Under these optimised conditions, allylation occurred smoothly, giving rise to the desired homoallylamine **10** in 86% yield. Notably, the analogous reaction with an unactivated imine required a much longer reaction time (12 h) at room temperature to go to completion.[20] The substrate scope was then evaluated by using benzotriazole compounds **2**–**9**; the results are summarised in Table 1. The reductive coupling of isoprene and benzotriazole adducts **2** and **3** gave **11** and **12**, respectively, in good yields (entries 2 and 3). We also demonstrated the feasibility of conducting the reaction with the more complex diene myrcene (entries 4 and 5).

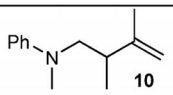
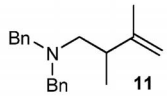
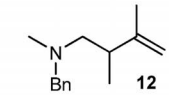
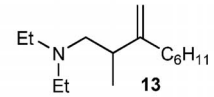
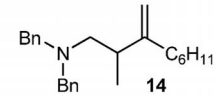
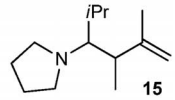
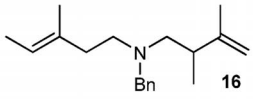
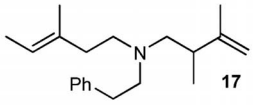
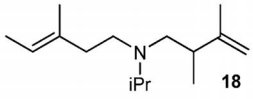
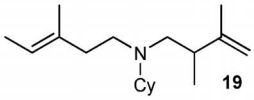
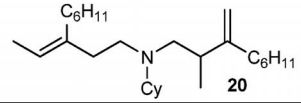


Scheme 2. Reductive coupling of benzotriazole derivative **1** with isoprene.

The reductive coupling of benzotriazole compound derived from aliphatic aldehyde **5** with isoprene led to formation of homoallylamine **15** in moderate yield and low diastereoselectivity (Table 1, entry 6).[21] We then investigated the double allyltitanation of bis(benzotriazolyl) compound **6**. Surprisingly, a tertiary amine **16** with both homoallyl- and homocrotyl fragments was formed as the major product (entry 7) and the expected bis(homoallyl)amine **21** could only be detected in trace amounts (<5%; Figure 2). Compound **16** was obtained as a single diastereoisomer and the configuration of the crotyl fragment was determined to be (*E*) according to NOE measurements. This reaction could be extended to other bis(benzotriazolyl) derivatives **7**–**9** and could be also performed with myrcene in place of isoprene (entries 8–11). In all cases, the homoallyl- (*E*)-homocrotylamines were isolated as single products. The formation of these products might be explained by two concomitant allylations, each with different yet defined regioselectivity, on the iminium and CH_2Bt groups (Figure 2).

However, this mechanism seems unlikely and, thus, we prefer to explain the reactivity by invoking a mechanism involving a triple cascade reaction as illustrated in Scheme 3. The allyltitanation of the iminium benzotriazole intermediate **B** leads first to the expected homoallylamine **C**. Due to the presence of the second benzotriazolyl fragment, a second iminium **D** is generated directly after allylation. This creates a species perfectly set up for a cationic 2-aza-Cope rearrangement. This [3+3] sigmatropic reaction, originally described by Geissman in 1950,[22] and beautifully applied by Overman to natural products synthe-

Table 1. Reductive coupling of benzotriazole derivative **1**–**9** with 1,3-dienes promoted by [Cp_2TiH].[a]

Entry	Bt deriv.	Diene	Product	Yield
1	**1**	isoprene	 **10**	86%
2	**2**	isoprene	 **11**	92%
3	**3**	isoprene	 **12**	75%
4	**4**	myrcene	 **13**	68%
5	**2**	myrcene	 **14**	70%
6	**5**	isoprene	 **15**	58%[b]
7	**6**	isoprene	 **16**	66%[c]
8	**7**	isoprene	 **17**	60%[c]
9	**8**	isoprene	 **18**	60%[c]
10	**9**	isoprene	 **19**	80%[c]
11	**9**	myrcene	 **20**	84%[c]

[a] Reaction conditions: THF (20 mL), benzotriazole derivative (1.2 mmol), diene (2.4 mmol), [Cp_2TiH] (1.2 mmol). [b] *syn/anti* ratio 40:60. [c] [Cp_2TiH] (2 equiv.), diene (4 equiv.) and bis(benzotriazolyl) derivative (1 equiv.) were used.

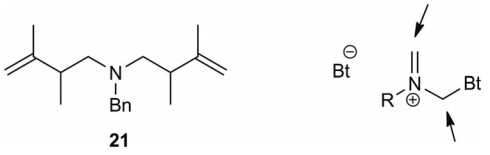
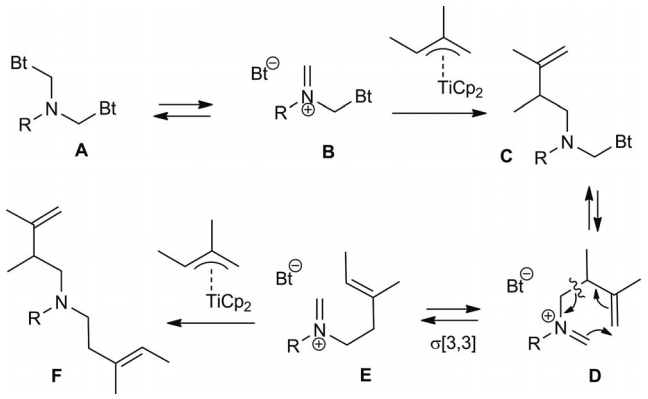


Figure 2. Left: Bis(homoallyl)amine **21**, expected product from the reductive coupling of isoprene and the bis(benzotriazolyl) compound **6**. Right: Iminium benzotriazole intermediate with two different potentially reactive sites toward allyltitanium complexes.

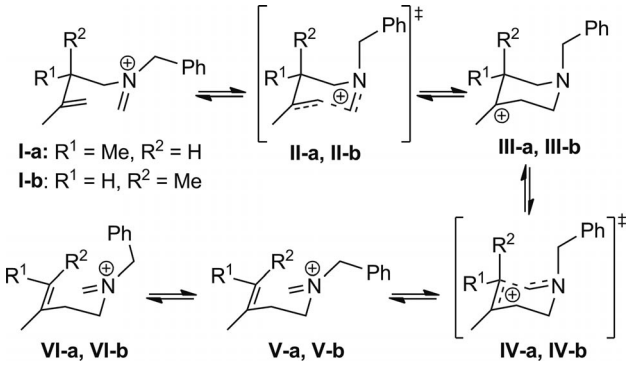
sis,[23,24] leads, in our case, to homocrotyl iminium salt **E**. Finally, a second allyltitanation occurs affording, after hydrolysis, the homoallyl- homocrotylamine **F**.



Scheme 3. Proposed mechanism for the formation of the homoallyl-homocrotylamines.

The proposed mechanism would seem to suggest a variety of possible products and it is, therefore, notable that we detect mainly one. Because the 2-aza-Cope rearrangement is reversible, species **E** and **D** will exist in equilibrium. Allyltitanation should be possible on either species, however, we detected mainly the product corresponding to allylation of species **E**, implying that allyltitanation takes place after rearrangement. Furthermore, we observed only the (*E*)-homocrotylamine, suggesting that the 2-aza-Cope rearrangement is highly selective. The detection of a single product, despite the multitude of pathways available, intrigued us and we therefore performed a theoretical study to gain insight into the factors that govern the selectivity of this sequence of reactions.

We first investigated the potential energy surface with the semiempirical RM1 Hamiltonian to find the most likely reaction pathways. These pathways were then investigated in detail by performing DFT B3LYP/6-31G** level calculations.[25–28] The model chosen for this study was the *N*-benzyliminium cation (species **D** in Scheme 3 and species **I** in Scheme 4). The results of the calculations suggest the most stable conformation is the chair-like structure (**I-a**) in which the methyl group in the β-position with respect to the N-atom is located in a pseudoequatorial position. The conformation with the same methyl group in the pseudoaxial position (**I-b**) is 2.4 kcal mol^{-1} higher in energy (Table 2).[29] The orientation of this methyl group is indeed crucial because it will define the final configuration (*E* or *Z*) of the homocrotylamine. Both reaction paths ("**a**" and "**b**") exhibit the same features, proceeding via a short-lived intermediate carbocation (**III-a**, **III-b**), which is probably stabilised by hyperconjugation, and two transition states (**II-a**, **II-b** and **IV-a**, **IV-b**) with geometries close to that of the intermediate. Similar energy profiles have previously been proposed for aza-Cope rearrangements involving vinylsilanes.[30]



Scheme 4. Calculated mechanism for the cationic 2-aza-Cope rearrangement (**I** and **VI** match compounds **D** and **E**, respectively, in Scheme 3).

Table 2. DFT free-energies relative to **V-a**, in kcal mol^{-1} (RM1 free-energies are reported in parentheses).

	I	II	III	IV	V	VI
a	**2.7** (2.7)	**8.8** (14.2)	**7.8** (11.9)	**8.0** (13.2)	**0** (0)	**–0.9** (–1.6)
b	**5.1** (3.0)	**12.0** (15.9)	**11.2** (14.9)	**11.4** (16.9)	**1.3** (0.3)	**0.6** (–0.6)

As shown in Table 2, path "**a**" is consistently favoured over path "**b**". This is in agreement with the fact that only the (*E*) isomer of the homocrotyl fragment is experimentally observed and is consistent with chair-like conformers generally preferring substituents to be in the pseudoequatorial position.

The results of the calculations predict the product **V-a** is more stable than the reactant **I-a** (ΔG = –2.7 kcal mol^{-1}). A further simple reorientation of the benzyl group leads to a more stable conformation **VI-a**, further increasing the predicted ΔG between products and reactants to –3.6 kcal mol^{-1}. This would lead to an equilibrium ratio of about 1000:2 in favour of **VI** (species **E**, Scheme 3) at the reaction temperature (10 °C). The stabilisation obtained through the rearrangement is likely due to the formation of a more substituted alkene. Furthermore the low activation energy of 6.1 kcal mol^{-1} is in the range of other cationic 2-aza-Cope rearrangements previously reported[30] and suggests a fast process. Thus, once species **D** is formed it rapidly enters into an equilibrium heavily favouring species **E** before the second equivalent of π-allyltitanium complex has the chance to attack. Once it does attack, the π-allyltitanium complex meets a 1000:2 mixture of **E**/**D**, producing the homoallyl-homocrotylamine **F** as the predominant species.

Conclusions

We have described the titanium-promoted synthesis of tertiary homoallylamines from 1,3-dienes and benzotriazole derivatives. The reaction occurred within three hours at 10 °C and led to the target homoallylamines in moderate to good yields. The addition of two equivalents of allyltitanium complexes to bis(benzotriazolyl) compounds led se-

lectively to homoallyl-homocrotylamines. This unpredicted reactivity was interpreted as a triple cascade reaction (allyltitanation – cationic 2-aza-Cope rearrangement – allyltitanation). A theoretical study provided insight into the thermodynamic and kinetic factors that govern the cationic 2-aza-Cope rearrangement and accounted for the exclusive formation of the homoallyl-(*E*)-homocrotylamines.

Experimental Section

General: Column chromatography was performed using alumina gel (Merck, aluminium oxide 90 standardised). ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX 300 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual $CHCl_3$ (δ = 7.26 ppm). Chemical shifts for ^{13}C are reported in parts per million downfield of TMS and are referenced to the carbon resonance of the solvent ($CDCl_3$: δ = 77.0 ppm). Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants in Hertz (Hz), and integration. Gas chromatography mass spectroscopy (GC–MS) spectra were collected with a Finnigan Trace GC ultra gas chromatograph (column Thermo TR 5MS; capillary 30 m × 0.25 ID × 0.25 μm film) and Trace DSC mass detector. Electrospray ionisation (ESI) mass spectrometry experiments were performed with a MicrOTOF Q. Elementary analysis were obtained with an EA 1108 CHNS-O FISONS detector.

Materials: All solvents were distilled before use from sodium/benzophenone complex under an atmosphere of argon. Deuterated solvents were purchased from euriso-top and were used without further purification. Benzotriazole compounds **1**–**9** were prepared according to previously reported procedures.[15–17]

General Procedure for the Synthesis of Amines 10–15: Diene (2.4 mmol) was added to a solution of $[Cp_2TiCl_2]$ (1.2 mmol) in THF (20 mL). The reaction was stirred at room temperature for 15 min and cooled to 0 °C and then a solution of *i*PrMgCl (2 M in THF, 0.6 mL, 1.2 mmol) was added dropwise by using a syringe. The resulting purple solution was stirred for 5 min at 0 °C followed by 30 min at room temperature. The allyltitanocene generated in situ was added over 3 h by using a syringe pump to a solution of benzotriazole compound (1.2 mmol) in THF (4 mL) at 10 °C. After the addition, the resulting green solution was warmed and was stirred at room temperature for 1 h. After hydrolysis by the addition of 2 M NaOH (20 mL) and extraction with Et_2O (4 × 30 mL), the combined organic layers were washed with water (3 × 50 mL) until neutral pH. The solution was dried with $MgSO_4$, filtered, and concentrated in vacuo to yield an oil. The compounds were purified by alumina column chromatography.

***N*-(2,3-Dimethyl-3-butenyl)-*N*-methylaniline (10):** Yellow oil (195 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24–7.30 (m, 2 H, Ar), 6.69–6.76 (m, 3 H, Ar), 4.80 (*pseudo* s, 2 H, =CH_2), 3.44 (dd, $^3J_{H,H}$ = 6.6, $^2J_{H,H}$ = 14.7 Hz, 1 H, CH_2N), 3.21 (dd, $^3J_{H,H}$ = 6.6, $^2J_{H,H}$ = 14.7 Hz, 1 H, CH_2N), 2.99 (s, 3 H, CH_3N), 2.69 (m, 1 H, C*H*), 1.80 (s, 3 H, CH_3), 1.08 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4 (=*C*), 148.4 (1 C, Ar), 129.2 (2 C, Ar), 115.8 (1 C, Ar), 112.0 (2 C, Ar), 110.8 (=*C*H_2), 58.2 (*C*H_2N), 39.7 (*C*H_3N), 39.5 (*C*H), 20.1 (*C*H_3), 17.5 (*C*H_3) ppm. MS (ESI): *m*/*z* calcd. for $C_{13}H_{19}N$ $[MH]^+$ 190.1590; found 190.1591. MS: *m*/*z* = 189 $[M]^+$, 120, 77. $C_{13}H_{19}N$ (189.3): calcd. C 82.48, H 10.12, N 7.40; found C 82.43, H 9.93, N 7.46.

***N*,*N*-Dibenzyl-2,3-dimethyl-3-butenylamine (11):** Pale-yellow oil (308 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.24 (m, 10 H, Ar), 4.71 (*pseudo* s, 1 H, =CH_2), 4.68 (*pseudo* s, 1 H, =CH_2), 3.56 (d, $^2J_{H,H}$ = 13.5 Hz, 2 H, CH_2N), 3.48 (d, $^2J_{H,H}$ = 13.5 Hz, 2 H, CH_2N), 2.54–2.39 (m, 2 H, C*H*, CH_2N), 2.23 (dd, $^2J_{H,H}$ = 12.3, $^3J_{H,H}$ = 7.2 Hz, 1 H, CH_2N), 1.52 (s, 3 H, CH_3), 0.97 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.3 (=*C*), 140.0 (2 C, Ar), 129.1 (4 C, Ar), 128.2 (4 C, Ar), 126.9 (2 C, Ar), 110.1 (=*C*H_2), 58.8 (2 C, *C*H_2N), 58.7 (*C*H_2N), 39.5 (CH), 19.1 (*C*H_3), 18.0 (*C*H_3) ppm. MS (ESI): *m*/*z* calcd. for $C_{20}H_{25}N$ $[MH]^+$ 280.2021; found 280.2023. MS: *m*/*z* = 279 $[M]^+$, 210, 91. $C_{20}H_{25}N$ (279.42): calcd. C 85.97, H 9.02, N 5.01; found C 85.45, H 8.53, N 5.07.

***N*-Benzyl-*N*,2,3-trimethyl-3-butenylamine (12):** Yellow oil (182 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.23 (m, 5 H, Ar), 4.74 (*pseudo* s, 1 H, =CH_2), 4.72 (*pseudo* s, 1 H, =CH_2), 3.50 (br. s, 2 H, CH_2N), 2.48–2.40 (m, 2 H, C*H*, CH_2N), 2.22 (m, 1 H, CH_2N), 2.19 (s, 3 H, CH_3N), 1.67 (s, 3 H, CH_3), 1.04 (d, $^3J_{H,H}$ = 7 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4 (=*C*), 139.8 (1 C, Ar), 129.2 (2 C, Ar), 128.3 (2 C, Ar), 127.0 (1 C, Ar), 110.0 (=*C*H_2), 62.9 (*C*H_2N), 62.7 (*C*H_2N), 42.6 (*C*H_3N), 39.5 (*C*H), 19.4 (*C*H_3), 18.2 (*C*H_3) ppm. MS (ESI): *m*/*z* calcd. for $C_{14}H_{21}N$ $[MH^+]$ 204.17468; found 204.17429. MS: *m*/*z* = 203.2 $[MH^+]$, 134.04 [M – isoprene]. $C_{14}H_{21}N$ (203.3): calcd. C 82.70, H 10.41, N 6.89; found C 82.89, H 10.30, N 6.88.

***N*,*N*-Diethyl-2,7-dimethyl-3-methylene-6-octenylamine (13):** Colourless oil (182 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.12 (t, $^3J_{H,H}$ = 6.9 Hz, 1 H, =C*H*), 4.76 (*pseudo* s, 1 H, =CH_2), 4.74 (*pseudo* s, 1 H, =CH_2), 2.59–2.34 (m, 5 H, CH_2N), 2.32–1.85 (m, 6 H, CH_2N, C*H*, CH_2), 1.68 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.04 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3), 0.98 (t, $^3J_{H,H}$ = 7.2 Hz, 6 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.0 (=*C*), 131.6 (=*C*), 124.5 (=*C*H), 108.0 (=*C*H_2), 59.0 (*C*H_2N), 47.6 (2 C, *C*H_2N), 38.6 (*C*H), 34.5 (*C*H_2), 26.8 (*C*H_2), 25.8 (*C*H_3), 18.8 (*C*H_3), 17.8 (*C*H_3), 11.8 (2 C, *C*H_3) ppm. MS (ESI): *m*/*z* calcd. for $C_{15}H_{29}N$ $[MH]^+$ 224.2334; found 224.2379. MS: *m*/*z* = 223 $[M]^+$, 86, 58.

***N*,*N*-Dibenzyl-2,7-dimethyl-3-methylene-6-octenylamine (14):** Pale-yellow oil (291 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 10 H, Ar), 5.13 (m, 1 H, =C*H*), 4.77 (*pseudo* s, 1 H, =CH_2), 4.74 (*pseudo* s, 1 H, =CH_2), 3.62 (d, $^2J_{H,H}$ = 13.5 Hz, 2 H, CH_2N), 3.52 (d, $^2J_{H,H}$ = 13.5 Hz, 2 H, CH_2N), 2.48 (m, 2 H, CH_2N), 2.30 (m, 1 H, C*H*), 2.21–1.85 (m, 4 H, CH_2), 1.74 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.06 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.3 (=*C*), 140.0 (Ar), 131.5 (=*C*), 129.1 (Ar), 128.9 (Ar), 128.3 (Ar), 126.9 (Ar), 124.6 (=*C*H), 108.3 (=*C*H_2), 59.5 (*C*H_2N), 58.9 (*C*H_2N), 58.4 (*C*H_2N), 38.5 (*C*H), 33.7 (*C*H_2), 26.6 (*C*H_2), 25.8 (*C*H_3), 18.5 (*C*H_3), 17.8 (*C*H_3) ppm. MS (ESI): *m*/*z* calcd. for $C_{25}H_{33}N$ $[MH]^+$ 348.2685; found 348.2685. MS: *m*/*z* = 347 $[M]^+$, 209, 99. $C_{25}H_{33}N$ (347.54): calcd. C 86.40, H 9.57, N 4.03; found C 85.45, H 8.53, N 5.07.

1-(2,4,5-Trimethyl-5-hexen-3-yl)pyrrolidine (15): Orange oil (136 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer) = 4.74 (*pseudo* s, 1 H, =CH_2), 4.68 (*pseudo* s, 1 H, =CH_2), 2.84 (m, 4 H, CH_2), 2.53 (m, 1 H, C*H*), 2.46 (m, 1 H, NC*H*), 1.77 (m, 1 H, C*H*), 1.73 (m, 4 H, CH_2), 1.68 (s, 3 H, CH_3), 0.99 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3), 0.93 (d, $^3J_{HH}$ = 6.6 Hz, 3 H, CH_3), 0.83 (d, $^3J_{HH}$ = 6.9 Hz, 3 H, CH_3); δ (minor isomer) = 4.71 (*pseudo* s, 2 H, =CH_2), 2.67 (m, 4 H, CH_2), 2.51 (m, 1 H, C*H*), 2.46 (m, 1 H, NC*H*), 1.89 (m, 1 H, C*H*), 1.68 (s, 3 H, CH_3), 1.65 (m, 4 H, CH_2), 1.01 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 0.95 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 0.92 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer) = 149.0 (=*C*), 109.4 (=*C*H_2), 65.2 (*C*H), 50.0 (*C*H_2),

40.6 (*C*H), 29.9 (*C*H), 23.7 (*C*H$_2$), 19.7 (*C*H$_3$), 18.5 (*C*H$_3$), 17.6 (*C*H$_3$), 16.7 (*C*H$_3$); δ (minor isomer) = 149.2 (=*C*), 108.8 (=*C*H$_2$), 65.2 (*C*H), 49.5 (*C*H$_2$), 41.4 (*C*H), 27.4 (*C*H), 22.9 (*C*H$_2$), 21.3 (*C*H$_3$), 20.2 (*C*H$_3$), 18.2 (*C*H$_3$), 15.6 (*C*H$_3$) ppm. MS (ESI): *m*/*z* calcd. for $C_{13}H_{25}N$ [MH]$^+$ 196.2060; found 196.2074. MS: *m*/*z* = 195 [M]$^+$, 152, 126,70. $C_{13}H_{25}N$ (195.34): calcd. 79.93, H 12.90, N 7.17; found C 80.25, H12.76, N 7.32.

General Procedure for the Synthesis of Homoallyl-(*E*)-homocrotylamines 16–20: Produced as described for the synthesis of **10**–**15** except that two equivalents of allyltitanium complex were used.

(*E*)-*N*-Benzyl-*N*-(2,3-dimethyl-3-butenyl)-3-methyl-3-pentenylamine (16): Orange oil (215 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.21 (m, 5 H, Ar), 5.19 (q, $^3J_{H,H}$ = 7 Hz, 1 H, =C*H*), 4.71 (*pseudo* s, 1 H, =CH_2), 4.69 (*pseudo* s, 1 H, =CH_2), 3.59 (d, $^2J_{H,H}$ = 13.8 Hz, 1 H, CH_2N), 3.53 (d, $^2J_{H,H}$ = 13.8 Hz, 1 H, CH_2N), 2.55–2.10 (m, 7 H, CH_2N, CH_2, C*H*), 1.64 (s, 3 H, CH_3), 1.56 (d, $^3J_{H,H}$ = 7 Hz, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 1.01 (d, $^3J_{H,H}$ = 7 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.6 (=*C*), 140.4 (=*C*), 134.5 (1 C, Ar), 129.1 (2 C, Ar), 128.1 (2 C, Ar), 126.8 (1 C, Ar), 119.5 (=*C*H), 109.9 (=*C*H$_2$), 59.2 (*C*H$_2$N), 58.9 (*C*H$_2$N), 53.0 (*C*H$_2$N), 39.6 (*C*H), 36.9 (*C*H$_2$), 19.6 (*C*H$_3$), 18.1 (*C*H$_3$), 16.0 (*C*H$_3$), 13.5 (*C*H$_3$) ppm. MS (ESI): *m*/*z* calcd. for $C_{19}H_{29}N$ [MH]$^+$ 272.2372; found 272.2361. MS: *m*/*z* = 271 [M]$^+$, 209, 91. $C_{19}H_{29}N$ (271.44): calcd. C 84.07, H 10.77, N 5.16; found C 83.73, H 10.67, N 5.07.

(*E*)-*N*-(2,3-Dimethyl-3-butenyl)-3-methyl-*N*-phenylethyl-3-pentenylamine (17): Yellow oil (205 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.16 (m, 5 H, Ar), 5.21 (q, $^3J_{H,H}$ = 7 Hz, 1 H, =C*H*), 4.71 (*pseudo* s, 2 H, =CH_2), 2.70 (s, 4 H, CH_2), 2.56 (m, 2 H, CH_2), 2.49 (m, 2 H, CH_2), 2.31 (m, 1 H, C*H*), 2.11 (m, 2 H, CH_2), 1.69 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 1.55 (d, $^3J_{H,H}$ = 7 Hz, 3 H, CH_3), 1.00 (*pseudo* s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4 (=*C*), 128.9 (Ar), 128.5 (Ar), 126.1 (Ar), 119.9 (br., =*C*H), 110.2 (=*C*H$_2$), 59.1 (*C*H$_2$N), 56.3 (*C*H$_2$N), 53.4 (*C*H$_2$N), 39.6 (*C*H), 36.7 (*C*H$_2$), 33.3 (*C*H$_2$), 19.7 (*C*H$_3$), 18.3 (*C*H$_3$), 16.1 (*C*H$_3$), 13.5 (*C*H$_3$) ppm. MS (ESI): *m*/*z* calcd. for $C_{20}H_{31}N$ [MH$^+$] 286.2529; found 286.2543. MS: *m*/*z* = 286 [MH]$^+$, 216.12 [M – isoprene]. $C_{20}H_{31}N$ (285.4): calcd. C 84.15, H 10.95, N 4.91; found C 81.74, H 11.12, N 5.08.

(*E*)-*N*-(2,3-Dimethyl-3-butenyl)-*N*-isopropyl-3-methyl-3-pentenylamine (18): Yellow oil (160 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.21 (q, $^3J_{H,H}$ = 6.7 Hz, 1 H, =C*H*), 4.70 (*pseudo* s, 1 H, =CH_2), 4.69 (*pseudo* s, 1 H, =CH_2), 2.91 (sept, $^3J_{H,H}$ = 6.7 Hz, C*H*), 2.42 (m, 2 H, CH_2N), 2.37 (m, 1 H, CH_2N), 2.21 (m, 1 H, C*H*), 2.17 (m, 1 H, CH_2N), 2.07 (m, 2 H, CH_2), 1.70 (s, 3 H, CH_3), 1.61 (br. s, 3 H, CH_3), 1.56 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3), 1.00 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3), 0.96 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3), 0.92 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1 (=*C*), 134.9 (=*C*), 119.2 (=*C*H), 109.4 (=*C*H$_2$), 55.5 (*C*H$_2$N), 50.3 (*C*HN), 49.8 (*C*H$_2$N), 40.4 (*C*H), 39.7 (*C*H$_2$), 20.2 (*C*H$_3$), 19.0 (*C*H$_3$), 17.9 (*C*H$_3$), 17.4 (*C*H$_3$), 16.2 (*C*H$_3$), 13.5 (*C*H$_3$) ppm. MS (ESI): *m*/*z* calcd. for $C_{15}H_{29}N$ [MH$^+$] 224.2372; found 224.2364. MS: *m*/*z* = 224.4 [MH$^+$], 154.12, 112.06.

(*E*)-*N*-(2,3-Dimethyl-3-butenyl)-*N*-(3-methyl-3-pentenyl)cyclohexylamine (19): Yellow oil (252 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.22 (q, $^3J_{H,H}$ = 6.5 Hz, 1 H, =C*H*), 4.70 (*pseudo* s, 2 H, =CH_2), 2.50–2.47 (m, 4 H, Cy, C*H*, CH_2N), 2.25 (m, 2 H, CH_2N), 2.09 (m, 2 H, CH_2), 1.76–1.72 (m, 4 H, Cy), 1.70 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.57 (d, $^3J_{H,H}$ = 7 Hz, 3 H, CH_3), 1.30–1.20 (m, 6 H, Cy), 1.02 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1 (=*C*), 134.9 (=*C*), 119.2 (=*C*H), 109.4 (=*C*H$_2$), 60.3 (*C*H, Cy), 56.1 (*C*H$_2$N), 50.3 (*C*H$_2$N), 40.5 (*C*H), 39.7 (*C*H$_2$), 29.8 (*C*H$_2$, 1 C, Cy), 28.5 (*C*H$_2$, 1 C, Cy), 26.5 (*C*H$_2$, 3 C, Cy), 20.2 (*C*H$_3$), 18.0 (*C*H$_3$), 16.2 (*C*H$_3$), 13.5 (*C*H$_3$) ppm. MS (ESI): *m*/*z* calcd. for $C_{18}H_{33}N$ [MH$^+$] 264.2686; found 264.2701. MS: *m*/*z* = 263 [M]$^+$, 194, 111, 55. $C_{18}H_{33}N$ (263.46): calcd. C 82.06, H 12.63, N 5.32; found C 82.33, H 12.67, N 5.14.

(*E*)-*N*-(2,7-Dimethyl-3-methylene-6-octenyl)-*N*-(3-ethylidene-7-methyl-6-octenyl)cyclohexylamine (20): Yellow oil (402 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.23 (q, $^3J_{H,H}$ = 6.6 Hz, 1 H, =C*H*), 5.14 (m, 2 H, =C*H*), 4.74 (m, 2 H, =CH_2), 2.54–2.34 (m, 4 H, Cy, C*H*, CH_2N), 2.16–2.02 (m, 12 H, CH_2N, CH_2), 1.82–1.72 (m, 4 H, Cy), 1.68 (s, 6 H, CH_3), 1.62 (s, 6 H, CH_3), 1.58 (d, $^3J_{H,H}$ = 7 Hz, 3 H, CH_3), 1.30–1.20 (m, 6 H, Cy), 1.04 (d, *J* = 6.6 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3 (=*C*), 139.1 (=*C*), 131.6 (=*C*), 131.5 (=*C*), 124.6 (2 C, =*C*H), 124.3 (=*C*H), 107.7 (=*C*H$_2$), 60.3 (*C*HN), 57.1 (*C*H$_2$N), 50.9, 39.7, 39.6, 37.9, 35.0, 30.4, 30.2, 27.2, 27.0, 26.9, 26.6 (*C*H$_3$), 25.8 (*C*H$_3$), 18.4 (*C*H$_3$), 17.8 (*C*H$_3$), 13.4 (*C*H$_3$) ppm. MS (ESI): *m*/*z* calcd. for $C_{28}H_{49}N$ [MH]$^+$ 400.3943; found 400.4008. MS: *m*/*z* = 399 [M]$^+$, 262. $C_{28}H_{49}N$ (399.69): calcd. C 84.14, H 12.36, N 3.50; found C 84.32, H 12.12, N 3.68.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of **10**–**20**.

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