3*H*-Pyrroles, Alkylidene-Pyrrolines and Functionalized Pyrrolidines by Radical Cyclization of β-Allenyliminyl Radicals

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In this work, we show that the tin hydride-mediated reaction of allene-tethered dithiosemicarbazides $\mathbf{4}$ is a convenient method for the preparation of five-membered unsaturated nitrogen heterocycles. The sulfur-directed intermolecular attack of the tin radical at the semicarbazide moiety leads to

an allene-tethered iminyl radical, which then undergoes a 5exo-dig cyclization leading to both the 3H-pyrroles **5** and the alkylidene pyrrolines **6**; thermal isomerization of **5** to **6** occurs in some cases.

Introduction

We have been interested in the free radical cyclization of functionalized β-allenic compounds for several years.^[1] Recently, we tried to obtain nitrogen heterocycles from the tin hydride-mediated free radical cyclization of allene-tethered benzoyloximes. As already reported,^[2] this pathway allowed us to produce highly unsaturated nitrogen heterocycles in fairly good yield but only with strongly hindered allenic precursors. In fact, in this case, six-membered heterocycles and five-membered heterocycles have been obtained as a mixture. The former result from the addition of the stannyl radical onto the sp carbon atom, followed by 6-endo cyclization of the so-formed allyl radical onto the N-atom of the C=N bond (Scheme 1, path A). The latter result from the addition of the stannyl radical onto the O-atom of the C=O bond followed by 5-exo cyclization of the so-formed iminyl radical onto the sp carbon atom (Scheme 1, path B). With allenic precursors that are not too strongly hindered, only five-membered carbocycles were obtained. These result from the addition of the stannyl radical onto the sp carbon atom followed by 5-exo cyclization of the so-formed allyl radical onto the C-atom of the C=N bond (Scheme 1, path A).

To produce only five-membered heterocycles, we decided to use more stannophilic precursors of the iminyl radical to avoid the competitive addition onto the allenyl moiety. Recently, using the high thiophilicity of stannyl radicals, Zard and co-workers have shown that dithiosemicarbazide derivatives can produce iminyl radicals.^[3]

Here, we describe the results obtained in the tin-mediated free radical cyclization of allene-tethered dithiosemicarbaz-



Scheme 1. Reaction of β-allenylbenzoyloximes

ides, and we show the efficiency of this method for building five-membered unsaturated nitrogen heterocycles.

Results and Discussion

Synthesis of the Radical Precursors 4

The β -allenylaldehydes **1** and β -allenylketones **2** were prepared according to our previous paper.^[2] The corresponding allene-tethered dithiosemicarbazides **4** were obtained in good to excellent yields by condensation of the hydrazine **3**^[4] onto **1** or **2** (Scheme 2). The bulkier R³ the higher the difficulty of condensation (see Experimental Section).

Reaction of *n*Bu₃SnH with the Radical Precursors 4

In all cases, the starting material disappeared after five hours when refluxed in cyclohexane with Bu_3SnH (1.2

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Scheme 2. Synthesis of radical precursors 4

equiv.) and AIBN (0.2 equiv.); only the products resulting from the formation of the iminyl radical were obtained (Scheme 3). These products were the 3H-pyrroles 5, the alkylidenepyrrolines 6 and, in some cases and in a very small quantity, the dimers 7. No product resulting from the addition of the stannyl radical onto the allenyl moiety was detected.



Scheme 3. Products of tin hydride reaction of radical precursors 4

Table 1 shows the efficiency of the method for the synthesis of unsaturated five-membered heterocycles, although the identification and the purification of the products obtained still need some comments. When $R^3 = H$ (4a-d), products 5, 6, and 7 were not isolated directly. For example, starting from 4b, after solvent removal, the NMR analysis of the crude mixture showed that the major product was **6b.** In fact, no signal of a vinylic proton corresponding to **5b** was detected by ¹H NMR spectroscopy. On the other hand, the ¹³C NMR spectrum shows two signals, one at $\delta = 174.5$ and the other at $\delta = 40.2$, both characteristic of the CH=N and CH_2 carbon atoms of compound **6b**, respectively. The purification of the crude mixture by silica gel chromatography was ineffective. Thus, we only obtained the dicarbonylated compound 8b resulting from hydrolysis of 6b (Scheme 4)

Table 1. Tin hydride reaction of radical precursors 4

4	Yield	5	Ratio 6	7
a	-		not isolated	
D	-		bb mainly formed ^{ray}	
d	-		not isolated	
e	85% ^[b]	70 ^[c]	30 ^[d]	0
f	71% ^[b]	39 ^[c]	54 ^[d]	7[c]
g	79% ^[b]	45 ^[c]	55 ^[d]	0
h	85% ^[b]	53 ^[c]	47 ^[d]	0
i	70% ^[d]	66	34	0
i	83% ^[d]	41 ^[c]	56	3[c]
k	75% ^[d]	58	42	0
1	71% ^[d]	58	42	0

^[a] On the basis of ¹H and ¹³C NMR spectroscopy of the crude reaction mixture. - ^[b] Yield obtained by Sammes' method (see main text). - ^[c] Determined on the basis of integration of the signals in the ¹H NMR spectrum. - ^[d] Yield obtained by chromatography through silica gel (see main text).



Scheme 4. Hydrolysis of 3*H*-pyrroles 5 and alkylidenepyrrolines 6

Sammes and co-workers have already reported a similar behaviour for 3*H*-pyrroles and alkylidenepyrrolines.^[5] To avoid this hydrolysis, they extracted the reaction mixture with an aqueous solution of hydrochloric acid. Then, they basified the aqueous layer and extracted it with diethyl ether to finally obtain pure 3H-pyrroles. In our case, this method gave a mixture of **6b** and the hydroxypyrroline **9b** resulting from partial hydrolysis of 6b. When this mixture was refluxed in CH₂Cl₂ with SiO₂ and few drops of water, compound 8b was formed. Since we were unable to isolate product 6b, we did not attempt to isolate directly the products resulting from the cyclization of precursors 4a-d. Consequently, to show the formation of nitrogen heterocycles, we decided to reduce the products of cyclization in situ and to protect the pyrrolidines so-obtained by benzoyl chloride. This method will be described later in this paper.

When $R^3 = Me(4e-h)$ we were also unable to separate the products of the reaction by silica gel or alumina chromatography. Thus, starting from 4f, the silica gel purification of the reaction mixture gave the corresponding diketone 8f. But, unlike the precursors 4a-d, the products of the reaction were stable enough to be separated from the organotin residues using Sammes' method. So, a mixture of 5, 6 and 7 was obtained as a ratio depending on R^1 and R^2 . This ratio was determined on the basis of the integration of the ¹H NMR spectrum of the mixture. Starting from 4e and 4g, the products 6e and 6g were obtained as a 1:1 mixture of Z and E isomers. On the other hand, we observed that under heating, the 3H-pyrroles 5e-h were prone to isomerize into their corresponding alkylidenepyrrolines 6e-h. In fact, when the mixtures of 5e-h, 6e-h, and 7e-h were refluxed in cyclohexane under argon for 48 hours, the sole products 6e-h and 7e-h were obtained. As in the case of precursors 4a-d, all the compounds formed by cyclization of precursors 4e-h were also reduced into their corresponding pyrrolidines and then protected by benzoyl chloride to permit characterization.

When $\mathbb{R}^3 = \mathbb{Ph} (4\mathbf{i}-\mathbf{l})$, the products of the reaction were stable enough to be separated by silica gel chromatography. Starting from the precursor $4\mathbf{j}$, separation of $6\mathbf{j}$ and $7\mathbf{j}$ was unsuccessful, so their relative population was determined by NMR spectroscopy. Compounds $6\mathbf{i}$ and $6\mathbf{k}$ were also obtained as a 1:1 mixture of Z and E isomers. Unlike in the case of $5\mathbf{e}-\mathbf{h} (\mathbb{R}^3 = \mathbf{Me})$, the 3H-pyrroles $5\mathbf{i}-\mathbf{l} (\mathbb{R}^3 = \mathbf{Ph})$ were not prone to thermal isomerization.

Finally, compounds 4a-1 are good precursors of the highly unsaturated nitrogen heterocycles 5 and 6, which have been obtained in high yield via β -allenyliminyl radicals. Nevertheless, starting from the precursors 4a-h (R³ = H, Me), the facile hydrolysis of the cyclized compounds led us to keep them as reduced products.

Reduction and Protection of 3H-Pyrroles 5a-h and Alkylidenepyrrolines 6a-h

Due to the lack of direct and precise characterization of products 5a-h and 6a-h, we developed an indirect method to validate our results. For this purpose, we chose to reduce the cyclization products in situ and then to protect the obtained pyrrolidines with benzoyl chloride, the compounds so-formed being stable enough to be purified. To this end, a reduction method was required that can reduce both imine and enamine in nonnucleophilic solvents to permit their subsequent protection by benzoyl chloride. On one hand, imine and iminium salts can be easily reduced by metallic hydrides such as LiAlH₄ or NaBH₄ and derivatives of NaBH₄.^[6] On the other hand, enamines are normally resistant to reduction by metal hydrides. However, the fast and reversible protonation of the carbon atom in acidic media permits the generation of an iminium salt that can be attacked by an hydride that supports acidic conditions.^[7] Thus, in our case, the reduction was performed with NaBH₄ and benzoic acid. Starting from precursors 4a-h, we obtained directly, in a one-pot reaction, compounds 10a-h with excellent yields (Scheme 5), except in the case of 10a.

Product 10c was obtained as an equimolar mixture of two diastereoisomers. In the case of precursors 4e-g, the reduction gave only the corresponding products 10e-g of *cis* relative configuration. The product 10g was obtained as an equimolar mixture of two diastereoisomers. For compound 10h, we obtained a mixture of two stereoisomers (*cis* and *trans*) in an approximate 9:1 ratio determined on the basis of ¹³C NMR integration.



Scheme 5. In situ reduction and protection of 5a-h and 6a-h

Discussion

Cyclisation of β-Allenyliminyl Radicals

Starting from the precursors 4a-l, the tributyltin hydride reduction selectively leads to an iminyl radical which then undergoes an intramolecular addition to the allenyl moiety. We now consider the mechanism of this cyclization. As only five-membered heterocycles were obtained, this means that the radical attacked the sp carbon atom of the allene. Starting from here, two cyclization modes are possible to explain the formation of 5 and 6: a 5-exo-dig cyclization or a 5endo-dig cyclization. Following Baldwin's rules^[8] on cyclization onto sp carbon atoms, both these modes of cyclization are stereoelectronically favoured. An EPR study of iminyl radicals has already been reported.^[9] The results are consistent with a radical in which the unpaired electron occupies a 2p orbital on nitrogen orthogonal to the C=N π system. If we consider the particular geometry of our allenic compounds, the best overlap of the orbital containing the unpaired electron is obtained with the π^* orbital of the distal double bond of the allenyl moiety (Scheme 6).



Scheme 6. Radical cyclization of β-allenyliminyl radicals

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Consequently, the 5-*exo-dig* cyclization process is strongly favoured over the 5-*endo-dig* one. The allylic radical **11** so formed then induces the formation of **5** and **6** by hydrogen atom abstraction from Bu_3SnH and the formation of **7** by a radical dimerisation.

Thermal Isomerization of 3H-Pyrroles 5

In our conditions, only the 3*H*-pyrroles 5e-h ($R^3 = Me$) isomerize to alkylidenepyrrolines 6e-h. Hydrogen migration is obviously implied in such a transformation. Since isomerization has not been observed when $R^3 = Ph$ (5e-h), it seems that a hydrogen from the methyl group is also involved in the process. Since a 1,5-sigmatropic hydrogen shift is unlikely in such a structure,^[10] we assume that a sequence of imine-enamine tautomer equilibrium is present in this isomerization.^[11]

Preparation of Amides 10a-h by Reduction and Benzoylation from 5a-h and 6a-h

With respect to the amides **10b-d**, the excellent yields obtained by this method allowed us to confirm that the products resulting from the 5-*exo* cyclization of the iminyl radical onto the allenyl moiety are formed *quasi*-quantitatively. We have no explanation concerning the low yield of product **10a**. In the case of products **10e-h**, the yield is also very high, but the higher steric hindrance makes the ¹H NMR and ¹³C NMR signals broader at 298 K due to the higher barrier of rotation for the aromatic amides **10e-h** than for the amides **10a-d**.^[12]

Consequently, in the case of **10e-h**, the NMR experiments were performed in deuterated benzene at 325 K with a 100 MHz apparatus. For **10e-g**, NOESY experiments showed that the only stereoisomers formed were of a *cis* relative configuration. For **10h**, a 1:9 mixture of *trans* and *cis* isomers was obtained. Indeed, it is known that the steric hindrance of acyloxiboranes often makes the reduction of cyclic enamines stereoselective, the hydride approach taking place from the less-hindered side of the molecule.^[13]

Conclusion

In summary, we have shown in this work that upon treatment with tributyltin hydride, a wide range of allenetethered dithiosemicarbazides selectively lead to highly unsaturated five-membered nitrogen heterocycles in good yields. Depending on the substitution pattern of these allenyldithiosemicarbazides, the 3*H*-pyrroles **5** and the alkylidenepyrrolines **6** so obtained are either stable enough to be separated or are hydrolyzed. In this latter case the heterocycle can be preserved by reduction to the pyrrolidines **10**. The behaviour of these allene-tethered dithiosemicarbazides towards the tributyltin radical contrasts with that of the allenylbenzoyloximes which we had early studied.^[2]

Experimental Section

We present only selected data here. A complete Experimental Section is available as Supporting Information.

General Remarks: Melting points are uncorrected. $- {}^{1}$ H and 13 C NMR spectra were performed in CDCl₃ or C₆D₆ with tetramethylsilane as internal reference, and recorded with Bruker AC 100, Bruker AC 200 and AMX 400 spectrometers. - Merk silica gel 60 (230–400 mesh) was used for column chromatography. - Solvents and reagents were purified according to standard laboratory techniques. - Abbreviation used: AIBN = 2,2'-azobis(2-methylpropionitrile).

Preparation of Precursors 4a-d: β -Allenylaldehyde 1 (10 mmol) and the hydrazine 3 (10 mmol) were dissolved in 20 mL of methanol with 1 g of anhydrous Na₂SO₄. The mixture was refluxed for six hours under argon. After cooling, the mixture was filtered and the solvent concentrated under reduced pressure giving crude precursors **4a-d**. Compound **4a** was purified by silica-gel column chromatography (eluent: Et₂O/pentane) whereas compounds **4b-d** were recrystallized from pentane.

Methyl 2-(2,2,5-Trimethyl-3,4-hexadienylidene)-1-methylhydrazinecarbodithioate (4b): 87% yield, white crystals, m.p. 66–68 °C. – ¹H NMR (CDCl₃, 200 MHz): δ = 1.26 [s, 6 H, C(CH₃)₂], 1.70 [d, *J* = 2.9 Hz, 6 H, (CH₃)₂C=C], 2.52 (s, 3 H, SCH₃), 3.78 (s, 3 H, NCH₃), 5.01 (m, *J* = 2.9 Hz, 1 H, C*H*=C), 7.12 (s, 1 H, CHN) – ¹³C NMR (CDCl₃, 50 MHz): δ = 19.6 (CH₃), 20.7 (CH₃), 25.8 (CH₃), 35.3 (CH₃), 40.1 [C(CH₃)₂], 96.4 (C=C=*C*H), 97.9 (*C*=C= CH), 151.9 (CHN), 200.5 (C), 202.6 (C). – C₁₂H₂₀N₂S₂ (256.4): calcd. C 56.21, H 7.86, N 10.92; found C 55.69, H 7.86, N 10.88.

Preparation of precursors 4e–l: Ketone **2** (10 mmol) and hydrazine **3** (15 mmol) were dissolved in 30 mL of anhydrous toluene with 1 mmol of *para*-toluenesulfonic acid and three grams of 4 Å molecular sieves. The mixture was refluxed for 16 hours under argon. After cooling, the mixture was filtered over celite and the solvent concentrated under reduced pressure. The precursors **4e–l** were purified by silica-gel column chromatography (eluent: Et₂O/pent-ane).

Methyl 2-(1,2,2,5-Tetramethyl-3,4-hexadienylidene)-1-methylhydrazinecarbodithioate (4f): 81% yield, yellow oil. – ¹H NMR (CDCl₃, 200 MHz): δ = 1.33 [s, 6 H, C(CH₃)₂], 1.73 [d, *J* = 2.9 Hz, 6 H, (CH₃)₂C=C], 1.89 (s, 3 H, CH₃C=N), 2.55 (s, 3 H, SCH₃), 3.58 (s, 3 H, NCH₃), 5.03 (m, *J* = 2.9 Hz, 1 H, CH=C). – ¹³C NMR (CDCl₃, 50 MHz): δ = 15.5 (CH₃), 19.2 (CH₃), 20.4 (CH₃), 25.6 (CH₃), 42.3 (CH₃), 44.0 [*C*(CH₃)₂], 96.0 (C=C=*C*H), 98.6 (*C*=C= CH), 185.5 (C=N), 192.1 (C), 200.9 (C). – C₁₃H₂₂N₂S₂ (270.4): calcd. C 57.73, H 8.20, N 10.36; found C 57.64, H 8.16, N 10.26.

Methyl 2-(2,2,5-Trimethyl-1-phenyl-3,4-hexadienylidene)-1-methylhydrazinecarbodithioate (4j): 87% yield, pale yellow oil. – ¹H NMR (CDCl₃, 200 MHz): δ = 1.37 [s, 6 H, C(CH₃)₂], 1.67 [d, *J* = 2.8 Hz, 6 H, (CH₃)₂C=C], 2.62 (s, 3 H, SCH₃), 3.13 (s, 3 H, NCH₃), 5.16 (m, *J* = 2.8 Hz, 1 H, *CH*=C). 7.19–7.23 (m, 2 H, Ph), 7.36–7.41 (m, 3 H, Ph). – ¹³C NMR (CDCl₃, 50 MHz): δ = 19.4 (CH₃), 20.2 (CH₃), 26.5 (CH₃), 43.4 (CH₃), 44.3 [*C*(CH₃)₂], 96.5 (C=C=*C*H), 98.8 (*C*=C=CH), 126.6 128.2 and 129.2 (CH, Ph), 135.0 (C, Ph), 181.1 (C=N), 194.8 (C), 201.3 (C). – C₁₈H₂₄N₂S₂ (332.5): calcd. C 65.02, H 7.28, N 8.42; found C 64.95, H 7.27, N 8.34.

General Procedure for the Cyclization of Precursors 4a-l: Bu₃SnH (1.2 equiv.) and AIBN (0.2 equiv.) were added to a cyclohexane solution (0.02 M) of the compounds 4a-l. After this solution was degassed with a stream of argon, the mixture was heated under reflux and monitored by TLC until the starting material had disappeared (approximately five hours). Then, the mixture was worked-up differently according to the nature of the precursors 4a-l (see main text).

General Procedure for the Extraction of Nitrogen Heterocycles: The mixture previously obtained was extracted twice with 5 mL of a 3.5% aqueous solution of HCl. The acidic aqueous layer was then basified with an aqueous saturated Na₂CO₃ solution and extracted with Et₂O. The organic layer was dried with MgSO₄ and concentrated under reduced pressure giving a mixture of **5**, **6**, and **7**.

Extraction of the mixture obtained from **4b** gave a mixture of **6b** (in a very small quantity, compound not described) and **9b**.

3,4-Dihydro-5-hydroxy-2-isopropyl-4,4-dimethyl-2*H***-pyrrole (9b): ¹H NMR (CDCl₃, 200 MHz): \delta = 0.94 (s, 3 H, CH₃), 1.07 [d, J = 7.0 Hz, 6 H, (C***H***₃)₂CH], 1.08 (s, 3 H, CH₃), 2.20 and 2.38 (syst. AB, J_{\text{HH}} = 16.9 Hz, 2 H), 2.53 [sept, J = 7.0 Hz, 1 H, (CH₃)₂C***H***], 5.01 (s, 1 H, CHOH). – ¹³C NMR (CDCl₃, 50 MHz): \delta = 19.6 and 21.4 [C(CH₃)₂], 25.9 and 26.2 [(CH₃)₂CH], 32.8 [(CH₃)₂CH], 41.9 [***C***(CH₃)₂], 48.8 (CH₂), 99.9 (CHOH), 183.9 (C=N).**

Hydrolysis of the Mixture of 6b and 9b: The mixture of 6b and 9b, silica (0.5 g), and three drops of water were refluxed for 16 hours in 10 mL of CH_2Cl_2 . After filtration, the solvent was dried with MgSO₄ and concentrated under reduced pressure giving 8b.

3,3,5-Trimethyl-4-oxohexanal (8b): Colourless oil. $-{}^{1}$ H NMR (CDCl₃, 200 MHz): $\delta = 1.07$ [d, J = 7.0 Hz, 6 H, (CH₃)₂CH], 1.11 [s, 6 H, (CH₃)₂], 2.56 [sept, J = 7.0 Hz, 1 H, (CH₃)₂CH], 2.76 (s, 2 H, CH₂), 9.58 (s, 1 H, CHO). $-{}^{13}$ C NMR (CDCl₃, 50 MHz): $\delta = 17.9$ (CH₃), 22.1 (CH₃), 40.8 (CH), 43.6 [*C*(CH₃)₂], 48.8 (CH₂), 204.8 (CHO), 212.4 (C=O).

Extraction of the Mixture Obtained from 4e-h: The proportions of products were estimated by ¹H NMR spectroscopy. Compound **4f** gave a 39:54:7 mixture of **5f**, **6f**, and **7f** as a pale yellow oil with an overall yield of 71%.

5-Isopropyl-2,3,3-trimethyl-3*H***-pyrrole (5f):** ¹H NMR (CDCl₃, 400 MHz): $\delta = 1.00$ [s, 6 H, (CH₃)₂], 1.05 [d, J = 6.9 Hz, 6 H, (CH₃)₂CH], 1.98 (s, 3 H, CH₃), 2.56 [d sept, J = 6.9 Hz and 1.4 Hz, 1 H, (CH₃)₂C*H*], 5.48 (d, J = 1.4 Hz, 1 H, CH). $- {}^{13}$ C NMR (CDCl₃, 100 MHz): $\delta = 14.8$ (CH₃), 21.0 (CH₃), 21.8 (CH₃), 29.4 (CH), 55.8 [*C*(CH₃)₂], 125.3 (CH=C), 160.1 (C–N), 187.7 (C=N).

3,4-Dihydro-2-isopropylidene-4,4,5-trimethyl-*2H***-pyrrole** (**6f**): ¹H NMR (CDCl₃, 400 MHz): $\delta = 1.02$ [s, 6 H, (CH₃)₂], 1.55 (m, 3 H, CH₃C=C), 1.85 (m, 3 H, CH₃C=C), 1.91 (s, 3 H, CH₃C=N), 2.26 (m, 2 H, CH₂). - ¹³C NMR (CDCl₃, 100 MHz): $\delta = 15.1$ (CH₃), 19.1 (CH₃), 20.5 (CH₃), 26.2 (CH₃), 42.1 (CH₂), 48.8 [*C*(CH₃)₂], 119.4 (*C*=C-N), 147.4 (C-N), 182.0 (C=N).

2,3,3-Trimethyl-5-[1,1,2-trimethyl-2-(2,3,3-trimethyl-3*H***-pyrrol-5yl)propyl]-3***H***-pyrrole (7f): ¹H NMR (CDCl₃, 400 MHz): \delta = 0.97 [s, 12 H, (CH₃)₂], 1.11 [s, 12 H, (CH₃)₂], 1.95 (s, 6 H, CH₃C=N), 5.47 (s, 1 H, CH=C). - ¹³C NMR (CDCl₃, 100 MHz): \delta = 14.7 (CH₃), 21.6 (CH₃), 24.3 (CH₃), 41.0 (C), 55.2 [***C***(CH₃)₂], 129.1 (CH=C), 160.5 (C-N), 184.8 (C=N).**

Hydrolysis of the Mixture of 5f, 6f, and 7f: The mixture of 5f, 6f and 7f, silica (0.5 g), and three drops of water were refluxed for 16 hours in 10 mL of CH_2Cl_2 . After filtration, the solvent was dried with MgSO₄ and concentrated under reduced pressure giving 8f.

3,3,6-Trimethylheptan-2,5-dione (8f): Colourless oil. $- {}^{1}$ H NMR (CDCl₃, 200 MHz): $\delta = 1.09$ [d, J = 6.9 Hz, 6 H, (CH₃)₂CH], 1.20 [s, 6 H, (CH₃)₂], 2.21 (s, 3 H, CH₃CO), 2.57 [sept, J = 6.9 Hz, 1 H, (CH₃)₂C*H*], 2.80 (s, 2 H, CH₂). $- {}^{13}$ C NMR (CDCl₃, 50 MHz): $\delta = 18.0$ (CH₃), 23.3 (CH₃), 25.0 (CH₃), 40.7 (CH), 45.2 [C(CH₃)₂], 50.8 (CH₂), 212.8 (C=O), 213.3 (C=O). $- C_{10}H_{18}O_2$ (170.2): calcd. C 70.55, H 10.66; found C 70.36, H 10.60.

Isolation of Nitrogen Heterocycles Obtained from 4i–1: The nitrogen heterocycles obtained from 4i-1 were purified by silica-gel chromatography (eluent: Et₂O/pentane). Products 5j-1 and 6j-1have already been described in our preceding paper.^[2] Compound 4i gave a mixture of 5i and 6i.

5-Ethyl-3,3-dimethyl-2-phenyl-3*H***-pyrrole (5i):** 46% yield, colourless oil. $^{-1}$ H NMR (CDCl₃, 200 MHz): $\delta = 1.23$ (t, J = 7.4 Hz, 3 H, CH₃CH₂), 1.40 [s, 6 H, (CH₃)₂], 2.57 (qd, J = 7.4 Hz and 1.7 Hz, 2 H, CH₃CH₂), 5.76 (t, J = 1.7 Hz, 1 H, CH), 7.39–7.43 (m, 3 H, Ph), 7.95–8.00 (m, 2 H, Ph). $^{-13}$ C NMR (CDCl₃, 50 MHz): $\delta = 12.0$ (CH₃), 22.9 (CH₃), 23.8 (CH₂), 56.0 [*C*(CH₃)₂], 127.8 128.4 129.8 and 130.3 (CH, Ph and CH=C), 133.4 (C, Ph), 155.3 (C–N), 183.3 (C=N). $^{-13}$ H₁₇N (199.2): calcd. C 84.37, H 8.60, N 7.03; found C 83.97, H 8.48, N 6.87.

2-Ethylidene-3,4-dihydro-4,4-dimethyl-5-phenyl-2*H***-pyrrole (6i): 24% yield, colourless oil. - ¹H NMR and ¹³C NMR spectra of the 1:1 mixture of** *Z* **and** *E* **isomers. ¹H NMR (CDCl₃, 200 MHz): \delta = 1.43 [s, 6 H, (CH₃)₂], 1.73 and 1.77 (2m, 3 H, CH₃), 2.59 (m, 2 H, CH₂), 5.87 and 5.91 (2m, 1 H, CH), 7.36–7.40 (m, 3 H, Ph), 7.85–7.90 (m, 2 H, Ph). - ¹³C NMR (CDCl₃, 50 MHz): \delta = 14.3 (CH₃), 27.5 (CH₃), 44.0 (CH₂), 49.1 [***C***(CH₃)₂], 115.5 (CH=C–N), 128.3 and 129.9 (CH, Ph), 134.2 (C, Ph), 154.5 (C–N), 180.1 (C=N).**

Compound 4j gave a mixture of 5j, 6j, and 7j.

3,3-Dimethyl-2-phenyl-5-[1,1,2-trimethyl-2-(3,3-dimethyl-2-phenyl-*3H*-pyrrol-5-yl)propyl]-*3H*-pyrrole (7j): 2.5% yield, obtained as colourless oil in mixture with 5j. - ¹H NMR (CDCl₃, 200 MHz): $\delta =$ 1.38 [s, 12 H, (CH₃)₂], 1.39 [s, 12 H, (CH₃)₂], 5.77 (s, 1 H, CH= C), 7.25-7.44 (m, 3 H, Ph), 7.90-8.00 (m, 2 H, Ph). - ¹³C NMR (CDCl₃, 50 MHz): $\delta =$ 22.8 (CH₃), 24.4 (CH₃), 41.2 (C), 55.2 [C(CH₃)₂], 129.3 and 132.2 (CH, Ph and CH=C), 160.3 (C-N), 180.2 (C=N).

General Procedure for the Preparation of Amides 10a-h by Reduction and Benzoylation from 5a-h and 6a-h: Bu₃SnH (1.2 mmol) and AIBN (0.2 mmol) were added to a 0.02 M cyclohexane solution (50 mL) of the compounds 4a-h (1 mmol). After this solution was degassed with a stream of argon, the mixture was heated under reflux and monitored by TLC until the starting material had disappeared (approximately five hours). After cooling, the solvent was removed under reduced pressure at 25 °C. Then 5 mL of THF were added, the mixture was cooled at -20 °C and NaBH₄ (75 mg, 4 mmol) was added portionwise. After two hours of stirring at room temperature, PhCO₂H (0.92 g, 7.5 mmol) and 20 mL of CH₂Cl₂ were added to the mixture. After one hour of additional stirring, the mixture was diluted with 40 mL of Et₂O and 10 mL of pyridine, then 1 mL of PhCOCl was added dropwise. The mixture was stirred for three hours and then 10 mL of water was added. The mixture was diluted with 80 mL of Et₂O and the organic layer was extracted successively with a saturated aqueous solution of Na₂CO₃ to remove PhCO₂H and a 5% aqueous solution of CuSO₄ to remove pyridine. The solvent was dried with MgSO4 and concentrated under reduced pressure. The purification of the residue by silica-gel chromatography (eluent Et₂O/pentane) gave the amides 10a - h

1-Benzoyl-2-isopropyl-4,4-dimethylpyrrolidine (10b): 80% yield, white crystals, m.p. 85–86 °C (pentane). – ¹H NMR (CDCl₃, 200 MHz): $\delta = 0.85$ (s, 3 H, CH₃), 0.87 [d, J = 6.5 Hz, 6 H, (CH₃)₂CH], 1.00 (s, 3 H, CH₃), 1.51–1.61 (m, 2 H, CH₂), 2.52 [m, 1 H, (CH₃)₂CH], 3.10 (m, 2 H, CH₂N), 4.26–4.36 (m, 1 H, CHN), 7.33–7.52 (m, 5 H, Ph). – ¹³C NMR (CDCl₃, 50 MHz): $\delta = 15.6$

(CH₃), 19.1 (CH₃), 25.5 (CH₃), 25.6 (CH₃), 28.9 (*C*H(CH₃)₂], 38.1 [*C*(CH₃)₂], 39.0 (CH₂), 61.4 (CHN), 63.9 (CH₂N), 127.6 128.2 et 130.1 (CH, Ph), 137.3 (C, Ph), 170.7 (C=O). $-C_{16}H_{23}NO$ (245.3): calcd. C 78.32, H 9.45, N 5.71; found C 78.30, H 9.38, N 5.68.

1-Benzoyl-5-isopropyl-2,3,3-trimethylpyrrolidine (**10f**): 76% yield, colourless oil. – ¹H NMR (C₆D₆, 100 MHz, 325 K): δ = 0.67 (s, 3 H, CH₃), 0.78 (s, 3 H, CH₃), 0.84 (d, *J* = 6.8 Hz, 3 H, CH₃CHN), 0.93 [d, *J* = 6.8 Hz, 6 H, (CH₃)₂CH], 1.40 (d, *J* = 8.8 Hz, 2 H, CH₂CHN), 2.11 [oct, *J* = 6.8 Hz, 1 H, (CH₃)₂CH], 3.27 (q, *J* = 6.8 Hz, 1 H, CH₃CHN), 4.26 (td, *J* = 8.8 Hz and 6.8 Hz, CHN), 7.33–7.52 (m, 5 H, Ph). – ¹³C NMR (C₆D₆, 25 MHz, 325 K): δ = 17.4 (CH₃), 17.9 (CH₃), 19.8 (CH₃), 22.8 (CH₃), 27.3 (CH₃), 32.2 (CH(CH₃)₂], 39.0 (CH₂), 40.3 [*C*(CH₃)₂], 61.4 (CHN), 65.2 (CHN), 126.5 and 128.0 (CH, Ph), 139.5 (C, Ph), 172.0 (C=O). – C₁₇H₂₅NO (259.3): calcd. C 78.72, H 9.71, N 5.40; found C 78.66, H 9.52, N 4.97.

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