

## Communication

## Synthesis of (–)-coniine and (–)-pipecoline using ruthenium catalyzed ring closing metathesis

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Dedicated to Professor J.-F. Normant on the occasion of his 65th birthday

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Abstract

Ring closing metathesis employing the well-known Grubbs' ruthenium catalyst has been used as the key step in the synthesis of piperidine alkaloids, (–)-coniine and (–)-pipecoline, and the asymmetric induction has been performed by using (*R*)- $\alpha$ -methyl benzylamine as an auxiliary. © 2001 Elsevier Science B.V. All rights reserved.

**Keywords:** Grubbs' ruthenium catalyst; Ring closing metathesis; Synthesis; Piperidine alkaloids; (*R*)- $\alpha$ -methyl benzylamine

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## 1. Introduction

Recently ring closing metathesis (RCM) reaction using a ruthenium complex such as **1** (Scheme 1) has been shown [1] to be of great potential in organic synthesis. Several kinds of ring structures, including heterocycles, have been synthesized [2] by this approach. Coniine (**8**) belongs to a class of piperidine ring based alkaloids and numerous reports for its synthesis, in both the enantiomeric forms, have appeared in the recent past [3]. Strategies to form such a six-membered ring alkaloid include aza-Diels–Alder reaction [4], Mannich–Michael reaction [5], intramolecular cyclization through an appropriately attached nucleophilic nitrogen atom [6], condensation [7] of terminally bifunctionalized molecule with a nitrogen containing species and modifying an already available six membered nitrogen heterocycle [3,8]. The enantioselectivity has been induced mainly by starting with a chiral auxiliary containing substrate [5,6a–c,f,g,7,8], by enzymatic resolution [6d], using Sharpless asymmetric dihydroxylation [6e], fol-

lowing chiron approach (starting with properly functionalized allene) [6h,i], and by chiral catalysis [4].

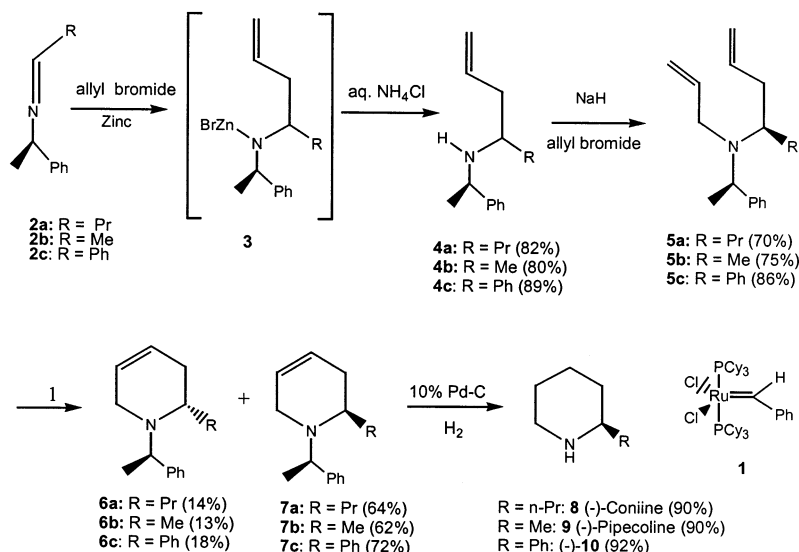
In this note we describe short syntheses of (–)-coniine (**8**) and (–)-pipecoline (**9**) starting from imines **2a** and **2b** which were, in turn, derived from butanal and acetaldehyde respectively using (*R*)- $\alpha$ -methyl benzylamine as a chiral auxiliary (Scheme 1). In the initial studies allylation of imine **2a** [4] was attempted using indium [9], magnesium [10], and zinc [11a], however, zinc based reaction in dry THF gave the best yield (82%) of the desired product **4a** whose reaction with allyl bromide in the presence of NaH and *n*-BuN<sup>+</sup>I<sup>–</sup> (catalytic amounts) in refluxing THF for 8 h led to the diene **5a**. The intermediate **3**, in all cases, could also be directly converted into the bis allylated products (**5a–5c**) by quenching the reactions with allyl bromide, thus saving one step in the synthetic operations. Yields of the dienes **5a–5c** obtained in this manner were comparable to the stepwise allylation.

Ring closing metathesis using ruthenium catalyst **1** gave the expected heterocycle **7a** which on treatment with 10% Pd–C/H<sub>2</sub> at room temperature for 8 h gave (–)-coniine (**8**). For comparison purpose, coniine was isolated as its HCl salt by reacting it with dry HCl gas in ether which showed a melting point of 209°C and its

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Scheme 1.

$^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectral data were comparable with the literature [8a] values. It may be noted that although the two diastereomers were inseparable at the stage of the diene **5a** they could be separated after the cyclization and the major product **7a** was further transformed into (–)-coniine. The diastereomeric ratio was determined to be 85:15 which was also confirmed by finding out the enantiomeric excess of **8** [12]<sup>1</sup> from its Mosher's ester. Since the substitution at two-position is dependent on the initial imine we have also synthesized pipercoline **9** [13] in 71% ee from the imine **2b** following the same strategy which permitted incorporation of methyl side chain readily. Likewise, two chromatographically separable diastereomers **6c** and **7c** (ratio 17:83) were synthesized from benzaldehyde derived imine **2c** and the major isomer **7c** was converted into 2-phenyl piperidine (**10**) [14].

In summary, the present approach of imine allylation followed by *N*-allylation either stepwise or in-situ and further followed sequentially by ring closing metathesis and hydrogenolysis/hydrogenation is flexible and we expect it to be useful in the synthesis of two-substituted based piperidine alkaloids.

## 2. Experimental

### 2.1. General

$^1\text{H}$ -NMR spectra (400 MHz) were recorded on JEOL JNM LA-400 FT NMR spectrometers with  $\text{Me}_4\text{Si}$  as

<sup>1</sup> Optical purity of (–)-coniine was determined from the analysis of the  $^1\text{H}$ -NMR (400 MHz) spectrum of the amide prepared by treatment of **7** with (*R*)-(+)- $\alpha$ -methoxy- $\alpha$ -(trifluoromethyl) phenylacetyl chloride.

internal standard. The  $^{13}\text{C}$ -NMR spectra were recorded on JNM LA-400 spectrometers at 100 Hz. IR spectra were recorded on Perkin–Elmer 1320 spectrophotometer. Mass spectra were recorded on GC-MS (FINNIGAN VOYAGER). Optical rotations were measured using Autopol II Rudolph polarimeter. All the experiments were performed under an atmosphere of dry argon unless otherwise specified. The products were purified by column chromatography on silica gel (100–200 mesh). Melting points were determined in a Fischer John melting point apparatus.

Compound **2** was prepared according to a literature procedure [4].

### 2.2. Preparation of secondary amines (4a–c)

A mixture of imine **2** (5 mmol), allyl bromide (6 mmol), activated zinc powder (6 mmol) and  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$  (0.5 mmol) in 5 ml of THF was stirred at room temperature (r.t.) for 1 h. Usually the exothermal reaction proceeded readily and the metal disappeared within 10–20 min. The reaction mixture was extracted with ethyl acetate and the organic layer was worked up as usual. Purification of the crude product by column chromatography gave secondary amines **4a–c**.

#### 2.2.1. (*R*)-(+)–*N*-[(*R*)- $\alpha$ -Methylbenzyl]-hept-1-ene-4-amine (4a)

Yield, 82%.  $[\alpha]_{\text{D}} = +24^\circ$  (*c* 1.05,  $\text{CHCl}_3$ ), IR( $\text{CH}_2\text{Cl}_2$ ):  $1635\text{ cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ):  $\delta$  0.78 (t,  $J = 8.6\text{ Hz}$ , 3H,  $-\text{CH}_2\text{CH}_3$ ), 1.27–1.50 (m, 5H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $-\text{NCH}-$ ), 1.33 (d,  $J = 7\text{ Hz}$ , 3H,  $-\text{CHCH}_3$ ), 2.15–2.42 (m, 3H,  $-\text{NH}$ ,  $-\text{CH}_2\text{CH}:\text{CH}_2$ ), 3.87–3.92 (m, 1H,  $\text{PhCH}-$ ), 5.02–5.18 (m, 2H,  $-\text{CH}_2\text{CH}:\text{CH}_2$ ), 5.6–5.9 (m, 1H,  $-\text{CH}_2\text{CH}:\text{CH}_2$ ),

7.2–7.33 (m, 5H, aromatic).  $^{13}\text{C-NMR}(\text{CDCl}_3)$ :  $\delta$  13.88, 19.05, 24.89, 37.05, 37.66, 53.43, 54.90, 116.93, 126.43, 126.48, 126.7, 127.62, 128, 128.33, 135.48. Mass  $m/z$  (%): 218 (3)  $[\text{M}^+ + 1]$ , 217 (12)  $[\text{M}^+]$ . Anal. Calc. for  $\text{C}_{15}\text{H}_{23}\text{N}$ : C, 82.89; H, 10.66; N, 6.44. Found: C, 82.79; H, 10.50; N, 6.40%.

### 2.2.2. (R)-(+)-N-[(R)- $\alpha$ -Methylbenzyl]-pent-1-ene-4-amine (**4b**)

Yield, 80%.  $[\alpha]_{\text{D}} = +18$  (c 0.65,  $\text{CH}_2\text{Cl}_2$ ), IR( $\text{CH}_2\text{Cl}_2$ ): 1632  $\text{cm}^{-1}$ .  $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  0.95 (d,  $J = 6.6$  Hz, 3H,  $-\text{CHCH}_3$ ), 1.32 (d,  $J = 8.52$  Hz, 3H,  $\text{PhCHCH}_3$ ), 1.5 (br s, 1H,  $-\text{NH}$ ), 2.05–2.64 (m, 3H,  $-\text{CHCH}_2\text{CH:CH}_2$ ), 3.89 (q,  $J = 2.68$  Hz, 1H,  $\text{PhCH-}$ ), 5.03–5.1, 5.6–5.81 (m, 3H,  $-\text{CH}_2\text{CH:CH}_2$ ), 7.18–7.34 (m, 5H, aromatic).  $^{13}\text{C-NMR}(\text{CDCl}_3)$ :  $\delta$  21.08, 24.58, 40.27, 49.66, 55.09, 117.02, 126.38–128.33 (6C) 135.47. Mass  $m/z$  (%): 189 (10)  $[\text{M}^+]$ . Anal. Calc. for  $\text{C}_{13}\text{H}_{19}\text{N}$ : C, 82.48; H, 10.12; N, 7.39. Found: C, 82.28; H, 10.16; N, 7.28%.

### 2.2.3. (R)-(+)-N-[(R)- $\alpha$ -Methylbenzyl]-4-phenyl-but-1-ene-4-amine (**4c**)

Yield, 89%.  $[\alpha]_{\text{D}} = +35.6$  (c 3.15,  $\text{CH}_2\text{Cl}_2$ ); IR( $\text{CH}_2\text{Cl}_2$ ): 1620  $\text{cm}^{-1}$ .  $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  1.26 (d,  $J = 6.84$  Hz, 3H,  $\text{PhCHCH}_3$ ), 1.74 (brs, 1H,  $-\text{NH}$ ), 2.25–2.55 (m, 2H,  $-\text{CH}_2\text{CH:CH}_2$ ), 3.30–3.50 (m, 1H,  $\text{PhCH-}$ ), 3.72 (q,  $J = 6.8$  Hz, 1H,  $\text{PhCHCH}_3$ ), 4.98–5.05 (m, 2H,  $-\text{CH}_2\text{CH:CH}_2$ ), 5.60–5.72 (m, 1H,  $-\text{CH}_2\text{CH:CH}_2$ ), 7.11–7.32 (m, 10H, aromatic).  $^{13}\text{C-NMR}(\text{CDCl}_3)$ :  $\delta$  24.82, 43.26, 54.80, 58.98, 117.27, 126.53, 128.29 (12C), 135.65. Mass  $m/z$  (%): 252 (5)  $[\text{M}^+ + 1]$ , 251 (10)  $[\text{M}^+]$ . Anal. Calc. for  $\text{C}_{18}\text{H}_{21}\text{N}$ : C, 86.0; H, 8.42; N, 5.57. Found: C, 86.03; H, 8.40; N, 5.42%.

## 2.3. Preparation of dienes (**5a–c**):

To a suspension of NaH (2 mmol) in THF at  $0^\circ\text{C}$  was added secondary amine **4** (1 mmol) dropwise and stirred for 15 min. To this reaction mixture was added allyl bromide (1.2 mmol) and n-butyl ammonium iodide (0.2 mmol) and the reaction mixture refluxed for 8 h. It was quenched with satd.  $\text{NH}_4\text{Cl}$  solution and extracted with ether, washed with water and brine. The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The crude material after concentration was purified by column chromatography gave dienes (**5a–c**).

### 2.3.1. (R)-(+)-N-Allyl, N-[(R)- $\alpha$ -methylbenzyl]-hept-1-ene-4-amine (**5a**)

Yield, 70%. IR ( $\text{CH}_2\text{Cl}_2$ ): 1630  $\text{cm}^{-1}$ .  $[\alpha]_{\text{D}} = +24^\circ$  (c 1,  $\text{CHCl}_3$ ).  $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  0.83 (t,  $J = 9.2$  Hz, 3H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.23–1.49 (m, 5H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $-\text{NCH-}$ ), 1.34 (d,  $J = 6.84$  Hz, 3H,  $-\text{CHCH}_3$ ), 1.77–1.99 (m, 2H,  $-\text{CHCH}_2\text{CH:CH}_2$ ), 3.08–3.29 (m, 2H,

$-\text{NCH}_2\text{CH:CH}_2$ ), 3.95 (q,  $J = 10.5$  Hz, 1H,  $\text{PhCH-}$ ), 4.81–5.2 (m, 4H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 5.55–5.9 (m, 2H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 7.19–7.33 (m, 5H, aromatic).  $^{13}\text{C-NMR}(\text{CDCl}_3)$ :  $\delta$  14.08, 20.16, 20.69, 34.6, 35.71, 48.75, 57.2, 58.43, 114.74, 115.27, 126.4, 126.6, 127.72, 127.75, 127.9, 128.0, 137.82, 140.0. Mass  $m/z$  (%): 257 (10)  $[\text{M}^+]$ . Anal. Calc. for  $\text{C}_{18}\text{H}_{27}\text{N}$ : C, 83.99; H, 10.57; N, 5.44. Found: C, 83.0; H, 10.6; N, 5.42%.

### 2.3.2. (R)-(+)-N-Allyl, N-[(R)- $\alpha$ -methylbenzyl]-pent-1-ene-4-amine (**5b**)

Yield, 75%. IR ( $\text{CH}_2\text{Cl}_2$ ): 1630  $\text{cm}^{-1}$ .  $[\alpha]_{\text{D}} = +10^\circ$  (c 0.95,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  0.99 (d,  $J = 6.6$  Hz, 3H,  $-\text{CHCH}_3$ ), 1.34 (d,  $J = 6.84$  Hz, 3H,  $\text{PhCHCH}_3$ ), 1.80–2.33 (m, 2H,  $-\text{CH}_2\text{CH:CH}_2$ ), 2.88 (q,  $J = 6.56$  Hz, 1H,  $-\text{NCHCH}_3$ ), 3.06–3.28 (m, 2H,  $-\text{NCH}_2\text{CH:CH}_2$ ), 4.0 (q,  $J = 6.6$  Hz, 1H,  $\text{PhCHCH}_3$ ), 4.80–5.21 (m, 4H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 5.58–5.90 (m, 2H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 7.18–7.39 (m, 5H, aromatic).  $^{13}\text{C-NMR}(\text{CDCl}_3)$ :  $\delta$  17.19, 18.63, 39.32, 48.70, 52.94, 57.36, 115.04, 115.26, 126.36, 126.44, 127.48, 127.62, 127.91, 128.0, 137.5, 139.63. Mass  $m/z$  (%): 230 (5)  $[\text{M}^+ + 1]$ , 229 (20)  $[\text{M}^+]$ . Anal. Calc. for  $\text{C}_{16}\text{H}_{23}\text{N}$ : C, 83.79; H, 10.11; N, 6.11. Found: C, 83.82; H, 10.18; N, 6.30%.

### 2.3.3. (R)-(+)-N-Allyl, N-[(R)- $\alpha$ -methylbenzyl]-4-phenyl-but-1-ene-4-amine (**5c**)

Yield, 86%. IR ( $\text{CH}_2\text{Cl}_2$ ): 1625  $\text{cm}^{-1}$ .  $[\alpha]_{\text{D}} = +13.8^\circ$  (c 2.65,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  1.11 (d,  $J = 6.84$  Hz, 3H,  $\text{PhCHCH}_3$ ), 2.40–3.43 (m, 4H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 3.86–4.10 (m, 2H,  $\text{PhCHCH}_3$ ,  $\text{PhCHCH}_2$ ), 4.84–5.15 (m, 4H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 5.55–5.86 (m, 2H,  $2 \times -\text{CH}_2\text{CH:CH}_2$ ), 7.15–7.45 (m, 10H, aromatic).  $^{13}\text{C-NMR}(\text{CDCl}_3)$ :  $\delta$  20.15, 36.83, 49.56, 56.05, 62.73, 115.38, 115.94, 126.40, 126.47, 126.74, 126.79, 127.56, 127.69, 127.86, 127.96, 128.04, 128.07, 128.42, 128.79, 136.70, 141.39. Mass  $m/z$  (%): 292 (6)  $[\text{M}^+ + 1]$ , 291 (10)  $[\text{M}^+]$ . Anal. Calc. for  $\text{C}_{21}\text{H}_{25}\text{N}$ : C, 86.55; H, 8.65; N, 4.81. Found: C, 86.6; H, 8.75; N, 4.75%.

## 2.4. Ring closing metathesis: preparation of cyclic olefins (**7a–c**)

To a solution of diene **5** (1 mmol) in  $\text{CH}_2\text{Cl}_2$  was added the Grubb's catalyst **1** (10 mol%) under nitrogen and stirred at room temperature for 24 h. The reaction mixture was filtered through Celite and washed with  $\text{CH}_2\text{Cl}_2$  and evaporation of solvent to give a crude products (**7a–c**) which were purified by column chromatography.

### 2.4.1. 2R-(+)-4,5-Didehydro-N-[(R)- $\alpha$ -methylbenzyl]-2-propyl-piperidine (**7a**)

Yield, 64%. IR ( $\text{CH}_2\text{Cl}_2$ ): 1632  $\text{cm}^{-1}$ .  $[\alpha]_{\text{D}} = +6^\circ$  (c 1.25,  $\text{CHCl}_3$ ). IR ( $\text{CH}_2\text{Cl}_2$ ): 1630  $\text{cm}^{-1}$ ,  $^1\text{H-NMR}$

(CDCl<sub>3</sub>):  $\delta$  0.92 (t,  $J = 7.08$  Hz, 3H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.23–1.51 (m, 4H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.31 (d,  $J = 6.56$ , 3H,  $-\text{CHCH}_3$ ), 1.77–1.99 (m, 1H,  $-\text{NCH}-$ ), 2.27–3.1 (m, 4H,  $-\text{NCH}_2\text{CH:CH}-$ ,  $-\text{NCHCH}_2\text{CH:CH}-$ ), 3.68 (q,  $J = 6.84$  Hz, 1H,  $\text{PhCH}-$ ), 5.54–5.70 (m, 2H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 7.18–7.37 (m, 5H, aromatic). <sup>13</sup>C-NMR(CDCl<sub>3</sub>):  $\delta$  14.41, 20.1, 20.79, 27.84, 28.42, 45.17, 51.18, 60.29, 123.48, 125.42, 126.59, 127.36, 127.40, 128.19, 128.2, 146.313. Mass  $m/z$  (%): 230 (5) [ $\text{M}^+ + 1$ ], 229 (10) [ $\text{M}^+$ ]. Anal. Calc. for C<sub>16</sub>H<sub>23</sub>N: C, 83.79; H, 10.11; N, 6.11. Found: C, 83.7; H, 10.14; N, 6.13%.

**2.4.2. 2R-(–)-4,5-Didehydro-N-[(R)- $\alpha$ -methylbenzyl]-2-propyl-piperidine (6a)**

Yield, 14%. IR (CH<sub>2</sub>Cl<sub>2</sub>): 1630 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = –6° (c 1.25, CHCl<sub>3</sub>). IR (CH<sub>2</sub>Cl<sub>2</sub>): 1630 cm<sup>–1</sup>, <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  0.82 (t,  $J = 7.08$  Hz, 3H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.16–1.55 (m, 4H,  $-\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.33 (d,  $J = 6.6$  Hz, 3H,  $\text{PhCHCH}_3$ ), 1.7–1.83 (m, 1H,  $-\text{NCH}-$ ), 2.20–3.30 (m, 4H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 3.7 (q,  $J = 6.32$  Hz, 1H,  $\text{PhCH}-$ ), 5.64–5.72 (m, 2H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 7.19–7.36 (m, 5H, aromatic). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  14.30, 20.19, 22.38, 26.92, 28.18, 44.76, 51.38, 60.49, 123.93, 125.49, 126.68, 127.24, 127.24, 128.30, 128.3 146.39. Mass  $m/z$  (%): 230 (3) [ $\text{M}^+ + 1$ ], 229 (8) [ $\text{M}^+$ ]. Anal. Calc. for C<sub>16</sub>H<sub>23</sub>N: C, 83.79; H, 10.11; N, 6.11. Found: C, 83.74; H, 10.18; N, 6.0%.

**2.4.3. 2R-(+)-4,5-Didehydro-N-[(R)- $\alpha$ -methylbenzyl]-2-methyl-piperidine (7b)**

Yield, 62%. IR (CH<sub>2</sub>Cl<sub>2</sub>): 1605 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = +5.6° (c 0.45, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  1.02 (d,  $J = 6.8$  Hz, 3H,  $-\text{CHCH}_3$ ), 1.32 (d,  $J = 6.8$  Hz, 3H,  $\text{PhCHCH}_3$ ), 1.82–2.91 (m, 4H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 3.3–3.9 (m, 1H,  $-\text{CHCH}_3$ ), 3.65 (q,  $J = 6.8$  Hz, 1H,  $\text{PhCHCH}_3$ ), 5.48–5.63 (m, 2H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 7.19–7.38 (m, 5H, aromatic). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  11.75, 19.22, 32.98, 45.28, 46.54, 60.37, 123.17, 123.17, 125.13, 126.64, 127.49, 127.49, 128.23, 128.23. Mass  $m/z$  (%): 202 (10) [ $\text{M}^+ + 1$ ], 201 (45) [ $\text{M}^+$ ], 186 (80) [ $\text{M}^+ - 15$ ], 96 (25) [ $\text{M}^+ - 105$ ]. Anal. Calc. for C<sub>14</sub>H<sub>19</sub>N: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.74; H, 9.42; N, 6.90%.

**2.4.4. 2R-(–)-4,5-Didehydro-N-[(R)- $\alpha$ -methylbenzyl]-2-methyl-piperidine (6b)**

Yield, 13%. IR (CH<sub>2</sub>Cl<sub>2</sub>): 1605 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = –5.6° (c 0.45, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  0.88 (d,  $J = 6.32$  Hz, 3H,  $-\text{CHCH}_3$ ), 1.35 (d,  $J = 6.56$  Hz, 3H,  $\text{PhCHCH}_3$ ), 1.63–1.9 (m, 1H,  $-\text{CHCH}_3$ ), 2.29–3.50 (m, 4H, 2  $\times$   $-\text{CH}_2\text{CH:CH}_2$ ), 3.60 (q,  $J = 6.56$  Hz, 1H,  $\text{PhCHCH}_3$ ), 5.7 (m, 2H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 7.20–7.38 (m, 5H, aromatic). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  9.67, 22.18, 29.68, 32.43, 44.54, 46.86, 61.13, 123.59, 124.79, 126.82, 127.24, 128.40. Mass  $m/z$  (%): 202 (5) [ $\text{M}^+ + 1$ ],

201 (30) [ $\text{M}^+$ ], 186 (95) [ $\text{M}^+ - 15$ ]. Anal. Calc. for C<sub>14</sub>H<sub>19</sub>N: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.54; H, 9.41; N, 6.80%.

**2.4.5. 2R-(+)-4,5-Didehydro-N-[(R)- $\alpha$ -methylbenzyl]-2-phenyl-piperidine (7c)**

Yield, 72%. IR (CH<sub>2</sub>Cl<sub>2</sub>): 1635 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = +67.3 (c 2.05, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  1.21 (d,  $J = 9$  Hz, 3H,  $\text{PhCHCH}_3$ ), 2.30–3.16 (m, 4H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 3.82 (dd,  $J = 5.12$ , 8 Hz, 1H,  $\text{PhCH}-$ ), 3.92, (q,  $J = 1.65$  Hz, 1H,  $\text{PhCHCH}_3$ ), 5.63–5.77 (m, 2H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 7.16–7.48 (m, 10H, aromatic). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  10.59, 35.26, 43.57, 55.87, 60.19, 124.32–128.5 (12C), 143.58, 144.27. Mass  $m/z$  (%): 264 (2) [ $\text{M}^+ + 1$ ], 265 (10) [ $\text{M}^+$ ]. Anal. Calc. for C<sub>19</sub>H<sub>21</sub>N: C, 86.65; H, 8.04; N, 5.32. Found: C, 83.76; H, 8.23; N, 5.45%.

**2.4.6. 2R-(–)-4,5-Didehydro-N-[(R)- $\alpha$ -methylbenzyl]-2-phenyl-piperidine (6c)**

Yield, 18%. IR (CH<sub>2</sub>Cl<sub>2</sub>): 1635 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = –67.3 (c 2.05, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  1.34 (d,  $J = 6.84$  Hz, 3H,  $\text{PhCHCH}_3$ ), 2.2–3.18 (m, 4H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 3.75 (t,  $J = 5.36$  Hz, 1H,  $\text{PhCH}-$ ), 3.80 (q,  $J = 6.8$  Hz, 1H,  $\text{PhCHCH}_3$ ), 5.77–5.86 (m, 2H,  $-\text{CH}_2\text{CH:CHCH}_2-$ ), 7.22–7.48 (m, 10H, aromatic). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  20.99, 29.67, 33.60, 44.01, 58.32, 124.49–128.38 (12C), 142.43, 142.94. Mass  $m/z$  (%): 264 (10) [ $\text{M}^+ + 1$ ], 263 (2) [ $\text{M}^+$ ]. Anal. Calc. for C<sub>19</sub>H<sub>21</sub>N: C, 86.65; H, 8.04; N, 5.32. Found: C, 83.77; H, 8.13; N, 5.55%.

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