DOI: 10.1002/ejoc.200600944

# Regio- and Diastereoselective Three-Component Syntheses of Homoallylic Amines in Aqueous Media Catalyzed by Brønsted Acids

**Dong-Sheng Deng,[a] Ping Liu,[a] and Jiwen Cai*[a,b]**

**Keywords:** Aqueous media / Allylation / Multicomponent reactions /Amines

A systematic investigation into the three component allylation reaction of aldehydes, amines, and allyltributylstannanes catalyzed by Brønsted acids in aqueous media was reported. The reaction was effective and able to produce homoallylic amines in moderate to high yields under mild conditions, with a good scope of substrates. Moreover, the regioselectivity of the reaction favors the formation of the γ-product, and good diastereoselectivity in favor of the *syn* isomers when cinnamyltributylstannane was employed as the allylation reagent was observed.


## Introduction

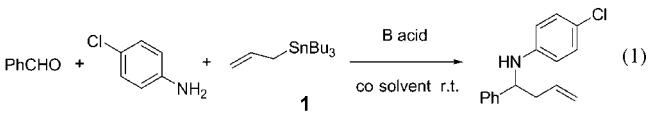
Homoallylic amines are important intermediates in the syntheses of nitrogen-containing compounds such as natural products and biologically active compounds.[1,2] The most useful methods for the synthesis of homoallylic amines are nucleophilic addition reactions of allylic organometallic species to imines and their derivatives, such as acylimines, acyliminium ions, and iminium ions.[3,4] Because any of the reagents including the imines, the Lewis acids employed as the catalysts, and the organotin reagents involved in the reactions could be hygroscopic and decompose in aqueous media,[5] the syntheses of homoallylic amines are generally carried out in organic solvents under strictly anhydrous conditions.[6]

Recently, organic reactions in aqueous media have attracted intensive attention[7] because water is a cheap and safe solvent in comparison with conventional organic solvents and has its inherent advantage as an environmental benign solvent. Consequently, three component syntheses of homoallylic amines in aqueous media becomes one of the most challenging projects in organic synthesis. Water-tolerant allylation of aldimines with allyltributylstannane and Barbier-type nucleophilic addition of allylic indium compounds to aldimine in water have been reported,[8] in which Lewis acids and zero-valent metals were used as catalysts. In comparison with Brønsted acids, zero-valent metals can be active and their use can lead to a significant amount of byproducts. Moreover, water-tolerant Lewis acids are expensive and toxic to the environment. Encouraged by the preliminary result showing that the Brønsted acid/surfactant *p*-dodecylbenzenesulfonic acid (DBSA) could catalyze allylation reactions,[9] as well as the facts that in aqueous media some imines could be stable[10] and organotin reagents could tolerate acidic media to some extent,[11] we carried out an investigation into the Brønsted acid catalyzed three component allylation reaction in aqueous media. The regio- and diastereoselectivities of the reactions were also explored for the first time.

[a] School of Chemistry & Chemical Engineering, Sun Yat-Sen University
Guangzhou 510275, China
[b] School of Pharmaceutical Sciences, Sun Yat-Sen University
Guangzhou 510080, China
Fax: +86-2087334718
E-mail: puscjw@mail.sysu.edu.cn

## Results and Discussion

The three component reaction of allyltributylstannane, benzaldehyde, and *p*-chloroaniline catalyzed by D-camphorsulfonic acid (CSA) was employed as the model reaction to explore the preliminary results [Equation (1)]. Reactions carried out in pure water, at room temperature for 24 h, afforded the products in 62–74% yield depending on the loading of the catalyst, with 20 mol-% as the optimal amount. When 10% (v) THF, acetonitrile, acetone, or ethanol was added as a cosolvent, the yield increased to 82–87%, with THF showing the best result. A series of Brønsted acids including carboxylic acids and sulfonic acids have been screened for their catalytic results and sulfonic acids are shown to be better promoters than carboxylic acids. Therefore, 20 mol-% CSA in THF/$H_2O$ (1:9) was chosen as the reaction media for further experiments.

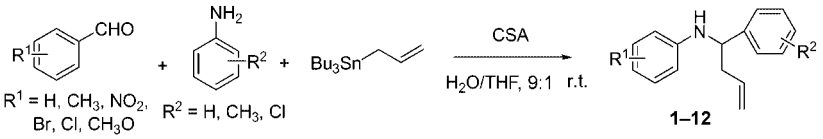


(1)

Allylation of various imines by allyltributylstannane was investigated and the results are summarized in Table 1. It is noted that the reactions can proceed smoothly and generate

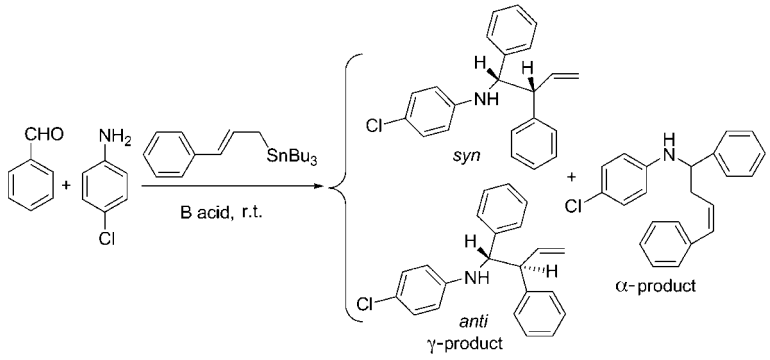
Table 1. The catalytic results of CSA on the three component allylation reaction.




| Entry | Aldehyde | Amine | Product | Yield [%][a] |
|---|---|---|---|---|
| 1 | $C_6H_5CHO$ | $C_6H_5NH_2$ | **1** | 80 |
| 2 | $C_6H_5CHO$ | *p*-$CH_3C_6H_4NH_2$ | **2** | 86 |
| 3 | $C_6H_5CHO$ | *p*-$ClC_6H_4NH_2$ | **3** | 87 |
| 4 | *p*-$CH_3C_6H_4CHO$ | $C_6H_5NH_2$ | **4** | 83 |
| 5 | *p*-$CH_3C_6H_4CHO$ | *p*-$ClC_6H_4NH_2$ | **5** | 86 |
| 6 | *p*-$ClC_6H_4CHO$ | *p*-$ClC_6H_4NH_2$ | **6** | 80 |
| 7 | *p*-$CH_3C_6H_4CHO$ | *p*-$CH_3C_6H_4NH_2$ | **7** | 82 |
| 8 | *p*-$NO_2C_6H_4CHO$ | $C_6H_5NH_2$ | **8** | 88 |
| 9 | *p*-$CH_3OC_6H_4CHO$ | *p*-$ClC_6H_4NH_2$ | **9** | 82 |
| 10 | $C_6H_5CHO$ | *o*-$ClC_6H_4NH_2$ | **10** | 79 |
| 11 | *p*-$CH_3C_6H_4CHO$ | *o*-$ClC_6H_4NH_2$ | **11** | 80 |
| 12 | *p*-$BrC_6H_4CHO$ | *p*-$ClC_6H_4NH_2$ | **12** | 80 |
| 13 | $C_6H_4CHO$ | 2-$C_{10}H_7CH_2NH_2$ | | trace |
| 14 | $C_6H_4CHO$ | $CH_3CH_2CH_2NH_2$ | | trace |
| 15 | $CH_3CH_2CHO$ | $C_6H_5NH_2$ | | trace |

[a] Isolated yield. All reactions were run for 24 h.

Table 2. The regio- and diastereoselectivity of the allylation reactions.

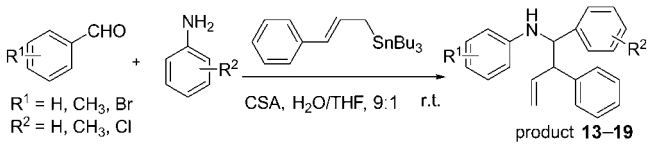



| Entry | Catalysis | Solvent | γ-Product [%][a] | *syn*/*anti*[b] | *de* [%] |
|---|---|---|---|---|---|
| 1 | CSA | $H_2O$ | 70 | 83:17 | 66 |
| 2 | CSA | THF | 84 | 72:28 | 44 |
| 3 | CSA | $CH_3CN$ | 83 | 71:29 | 42 |
| 4 | CSA | $CH_3CH_2OH$ | 83 | 75:25 | 50 |
| 5 | CSA | $H_2O$/THF (9:1) | 82 | 82:18 | 64 |
| 6 | DBSA | $H_2O$/THF (9:1) | 80 | 90:10 | 80 |
| 7 | 1,5-Nds[c] | $H_2O$/THF (9:1) | 46 | 82:18 | 64 |
| 8 | $CF_3SO_3H$ | $H_2O$/THF (9:1) | 80 | 82:18 | 64 |
| 9 | *p*-$NO_2C_6H_4CO_2H$ | $H_2O$/THF (9:1) | 62 | 77:23 | 54 |
| 10 | L-(+)-tartaric acid | $H_2O$/THF (9:1) | 52 | 77:23 | 54 |
| 11 | malonic acid | $H_2O$/THF (9:1) | 64 | 77:23 | 54 |
| 12 | maleic acid | $H_2O$/THF (9:1) | 62 | 77:23 | 54 |
| 13 | lauric acid | $H_2O$/THF (9:1) | trace | – | – |
| 14 | $SnCl_2{\cdot}2H_2O$ | $H_2O$/THF (9:1) | 85 | 88:12 | 76 |
| 15 | $AlCl_3{\cdot}6H_2O$ | $H_2O$/THF (9:1) | 80 | 88:12 | 76 |

[a] Isolated yield. The reactions of Entries 1–12 were run for 24 h and Entries 14 and 15 were run for 8 h. [b] *syn*/*anti* Ratio determined by 300 MHz $^1$H NMR spectroscopic analysis.[13] *syn*/*anti* Isomer is determined by the coupling constant value. Compare $\delta$ = 4.58 ppm ($J$ = 6.9 Hz) with $\delta$ = 4.48 ppm ($J$ = 8.1 Hz), the lower coupling constant ($J$ = 6.9 Hz) indicates that the two adjacent H atoms are located on the same side belonging to the *syn* isomer. In contrast to the *syn* isomer, $\delta$ = 4.48 ppm ($J$ = 8.1 Hz) is contributed by the *anti* isomer. [c] 1,5-Nds = 1,5-naphthalenedisulfonate.

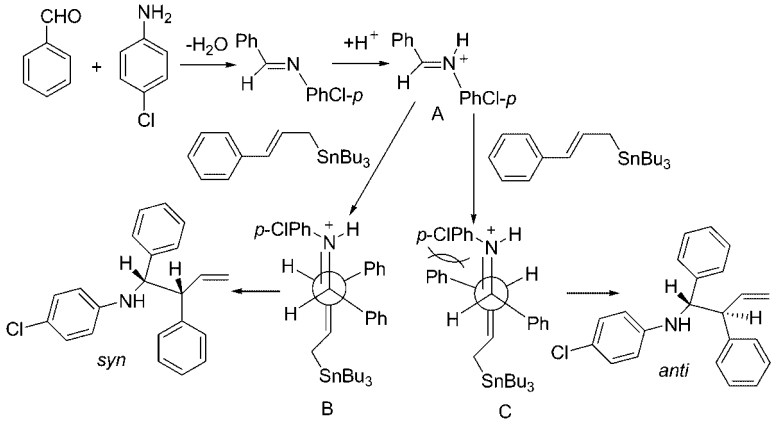
  

Table 3. The diastereoselectivity of the allylation reactions catalyzed by CSA.




| Entry | Aldehyde | Amine | Product | Yield[a] [%] | *syn*/*anti*[b] | *de* [%] |
|---|---|---|---|---|---|---|
| 1 | $C_6H_5CHO$ | *p*-$CH_3C_6H_4NH_2$ | **13** | 80 | 81:19 | 62 |
| 2 | $C_6H_5CHO$ | *p*-$ClC_6H_4NH_2$ | **14** | 82 | 82:18 | 64 |
| 3 | *p*-$CH_3C_6H_4CHO$ | *p*-$ClC_6H_4NH_2$ | **15** | 80 | 84:16 | 68 |
| 4 | *p*-$BrC_6H_4CHO$ | *p*-$CH_3C_6H_4NH_2$ | **16** | 76 | 89:11 | 78 |
| 5 | *p*-$CH_3C_6H_4CHO$ | *p*-$CH_3C_6H_4NH_2$ | **17** | 81 | 88:12 | 76 |
| 6 | *p*-$CH_3C_6H_4CHO$ | $C_6H_5NH_2$ | **18** | 79 | 88:12 | 76 |
| 7 | *p*-$CH_3C_6H_4CHO$ | *o*-$ClC_6H_4NH_2$ | **19** | 78 | 76:24 | 52 |

[a] Isolated yield. All reactions were run for 24 h. [b] *syn*/*anti* Ratio determined by 300 MHz $^1$H NMR spectroscopic analysis.[13]




Scheme 1. A plausible mechanism for the Brønsted acid catalyzed imine allylation reaction.

good yields with substrates bearing both electron-withdrawing and electron-donating groups on the phenyl rings of benzaldehyde and aniline (Table 1, Entries 1–12). As for aliphatic amines or aldehydes, the allylation reaction did not proceed (Table 1, Entries 13–15).

With the use of cinnamyltributylstannane as the allylation reagent, the regio- and diastereoselectivities were studied and the results are summarized in Table 2. The reactions produced only the γ-isomers. When sulfonic acids were used as the catalysts, moderate to good diastereoselectivity for the *syn* isomer was obtained (Table 2, Entries 5–8), with DBSA showing the best result (Table 2, Entry 6). In the case of the CSA-catalyzed reactions in different media (Table 2, Entries 1–5), the best selectivity was observed in pure water. When Lewis acids were used as the promoters (Table 2, Entries 14, 15), good diastereoselectivity for the *syn* isomer was obtained. However, 50 mol-% of the catalyst was needed to achieve effective results.

Finally, the diastereoselectivity of the allylation of varied imines by cinnamyltributylstannane, catalyzed by CSA, was investigated and the results are summarized in Table 3. The reactions afforded 100% γ-products with the *syn* isomers as the major isomers. A plausible mechanism for the Brønsted acid catalyzed imine allylation reaction is illustrated in Scheme 1. The γ-*syn* addition probably occurs via acyclic antiperiplanar transition state B, which results from the interaction of cinnamyltributylstannane with A, because of the steric hindrance between the *p*-chlorobenzyl group and the phenyl group in antiperiplanar transition state C, as shown in Scheme 1.[12]

## Conclusions

In summary, we present here the first systematic investigation into three component allylation reactions catalyzed by Brønsted acids in aqueous media. The reaction proved to be effective to produce homoallylic amines in moderate to high yields under mild conditions, with good substrate scopes. Moreover, the reactions have regioselectivity favoring the γ-products, as well as good diastereoselectivity favoring the *syn* isomers when cinnamyltributylstannane was employed as the allylation reagent.

## Experimental Section

**General Remarks:** All reagents are commercially available and used as received. $^1$H-NMR and $^{13}$C-NMR spectra were recorded with a

Varian UNITY/NOVA 300 MHz spectrometer with $CDCl_3$ as the solvent at room temperature. Chemical shifts were given in $\delta$ relative to tetramethylsilane, and expressed in ppm. Coupling constants ($J$) are given in Hz. Mass spectra were measured with a SHIMADZU LCMS-2010A.

**Typical Experimental Procedure for the Allylation Reactions of Imines:** The aromatic aldehyde (123 μL, 1.2 mmol) and aromatic amine (127 mg, 1 mmol) were mixed in degassed water (4.5 mL) for 30 min at room temperature. CSA (46 mg, 0.2 mmol), THF (0.5 mL), and allyltributylstannane (466 μL, 1.5 mmol) were added into the mixture, and the reaction was left to stir for 24 h, monitoring by TLC. The mixture was then quenched with saturated $NaHCO_3$ solution and extracted into ethyl acetate ($3 \times 20$ mL). The combined organic layers were treated by KF. The resulting solution was filtered to remove the resin and the filtrate was washed with brine, dried with anhydrous $MgSO_4$, and the solvent removed in vacuo to yield the crude product. Purification by silica gel chromatography 100–200 mesh ZCX II (typical eluent: hexane/ethyl acetate, 12:1, v/v) gave the homoallylic amine. The spectroscopic characteristics of known products **1**–**6**, **8**–**10**, and **14** are in agreement with the published data.[13,14] Spectral data of some selected compounds is given below.

**4-Methyl-*N*-(4-methylphenyl)-α-2-propenylbenzenemethanamine (7):** Light yellow liquid. Yield: 206 mg (82%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.26 (d, $J$ = 7.8 Hz, 2 H, ArH), 7.20 (d, $J$ = 8.1 Hz, 2 H, ArH), 6.90 (d, $J$ = 8.1 Hz, 2 H, ArH), 6.44 (d, $J$ = 8.4 Hz, 2 H, ArH), 5.72–5.85 (m, 1 H, CH), 5.13–5.22 (m, 2 H, $CH_2$), 4.34 (q, $J$ = 5.1 Hz, 1 H, CH), 2.45–2.64 (m, 2 H, $CH_2$), 2.35 (s, 3 H, $CH_3$), 2.21 (s, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = = 145.1, 140.7, 136.6, 135.0, 129.7 129.4, 126.8, 126.4, 118.3, 113.9, 57.6, 43.6, 21.4, 20.7 ppm. MS (ESI): $m/z$ = 252 $[M + H]^+$.

**4-Methyl-*N*-(2-chlorophenyl)-α-2-propenylbenzenemethanamine (11):** Light yellow liquid. Yield: 217 mg (80%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.20 (d, $J$ = 8.1 Hz, 3 H, ArH), 7.11 (d, $J$ = 8.1 Hz, 2 H, ArH), 6.94–7.03 (m, 1 H, ArH), 6.61 (d, $J$ = 0.9 Hz, 1 H, ArH), 6.50 (s, 1 H, ArH), 6.34–6.37 (m, 1 H, ArH), 5.66–5.83 (m, 1 H, CH), 5.12–5.20 (m, 2 H, $CH_2$), 4.33 (q, $J$ = 5.7 Hz, 1 H, CH), 2.45–2.66 (m, 2 H, $CH_2$), 2.33 (s, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 143.3, 140.0, 136.8, 134.4, 129.5, 129.1, 127.7, 126.3, 119.5, 118.7, 117.3, 112.8, 57.1, 43.6, 21.4 ppm. MS (ESI): $m/z$ = 272 $[M + H]^+$.

**4-Bromo-*N*-(4-chlorophenyl)-α-2-propenylbenzenemethanamine (12):** Light yellow liquid. Yield: 268 mg (80%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.44 (d, $J$ = 8.4 Hz, 2 H, ArH), 7.20 (d, $J$ = 8.4 Hz, 2 H, ArH), 7.02 (d, $J$ = 8.7 Hz, 2 H, ArH), 6.37 (d, $J$ = 8.7 Hz, 2 H, ArH), 5.66–5.79 (m, 1 H, CH), 5.16–5.22 (m, 2 H, $CH_2$), 4.31 (q, $J$ = 5.1 Hz, 1 H, CH), 2.42–2.64 (m, 2 H, $CH_2$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 145.4, 142.0, 134.0, 131.9, 129.1, 128.2, 122.7, 121.1, 119.1, 114.9, 57.2, 43.3 ppm. MS (ESI): $m/z$ = 336 $[M + H]^+$.

***N*-(4-Methylphenyl)-α-2-phenyl-2-propenyl-benzenemethanamine (13):** Light yellow liquid. Yield: 250 mg (80%) (*syn*/*anti* = 81:19). *syn* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.31–6.98 (m, 10 H, ArH), 6.82 (d, $J$ = 7.8 Hz, 2 H, ArH), 6.33 (d, $J$ = 8.4 Hz, 2 H, ArH), 6.03–5.91 (m, 1 H, CH), 5.06 (d, $J$ = 10.2 Hz, 1 H, CH), 4.95 (d, $J$ = 16.8 Hz, 1 H, CH), 4.56 (d, $J$ = 7.2 Hz, 1 H, CH), 3.70 (t, $J$ = 7.8 Hz, 1 H, CH), 2.15 (s, 3 H, $CH_3$) ppm. *anti* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.31–6.98 (m, 2 H, ArH), 6.86 (d, $J$ = 8.7 Hz, 0.4 H, ArH), 6.41 (d, $J$ = 8.4 Hz, 0.4 H, ArH), 6.23–6.12 (m, 0.2 H, CH), 5.27–5.18 (m, 0.4 H, $CH_2$), 4.46 (d, $J$ = 8.1 Hz, 0.2 H, CH), 3.58–3.51 (m, 0.2 H, CH), 2.17 (s, 3 H, $CH_3$) ppm.

**4-Methyl-*N*-(4-chlorophenyl)-α-2-phenyl-2-propenylbenzenemethanamine (15):** Light yellow liquid. Yield: 277 mg (80%) (*syn*/*anti* = 84:16). *syn* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.35–6.95 (m, 12 H, ArH), 6.38–6.33 (m, 2 H, ArH), 6.06–5.94 (m, 1 H, CH), 5.12 (d, $J$ = 10.2 Hz, 1 H, CH), 4.98 (d, $J$ = 16.8 Hz, 1 H, CH), 4.55 (d, $J$ = 7.2 Hz, 1 H, CH), 3.71 (t, $J$ = 7.8 Hz, 1 H, CH), 2.35 (s, 3 H, $CH_3$) ppm. *anti* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.35–6.95 (m, 2 H, ArH), 6.44–6.41 (m, 0.4 H, ArH), 6.25–6.13 (m, 0.2 H, CH), 5.30–5.25 (m, 0.4 H, $CH_2$), 4.46 (d, $J$ = 8.1 Hz, 0.2 H, CH), 3.61–3.55 (m, 0.2 H, CH), 2.28 (s, 0.6 H, $CH_3$) ppm.

**4-Bromo-*N*-(4-methylphenyl)-α-2-phenyl-2-propenylbenzenemethanamine (16):** Light yellow liquid. Yield: 305 mg (78%) (*syn*/*anti* = 89:11). *syn* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.37–6.94 (m, 9 H, ArH), 6.83 (d, $J$ = 7.8 Hz, 2 H, ArH), 6.30 (d, $J$ = 7.8 Hz, 2 H, ArH), 6.00–5.88 (m, 1 H, C*H*), 5.12 (d, $J$ = 10.2 Hz, 1 H, CH), 4.98 (d, $J$ = 16.8 Hz, 1 H, CH), 4.52 (d, $J$ = 6.9 Hz, 1 H, CH), 3.64 (t, $J$ = 7.8 Hz, 1 H, CH), 2.16 (s, 3 H, $CH_3$) ppm. *anti* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.37–6.94 (m, 1 H, Ar*H*), 6.86 (d, $J$ = 8.7 Hz, 0.2 H, Ar*H*), 6.38–6.34 (m, 0.2 H, ArH), 6.21–6.09 (m, 0.1 H, CH), 5.28–5.20 (m, 0.2 H, $CH_2$), 4.46 (d, $J$ = 8.1 Hz, 0.1 H, CH), 3.51–3.45 (m, 0.1 H, CH), 2.18 (s, 0.3 H, $CH_3$) ppm.

**4-Methyl-*N*-(4-methylphenyl)-α-2-phenyl-2-propenylbenzenemethanamine (17):** Light yellow liquid. Yield: 265 mg (81%) (*syn*/*anti* = 88:12). *syn* isomer:$^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.33–6.96 (m, 9 H, ArH), 6.83 (d, $J$ = 8.1 Hz, 2 H, ArH), 6.35 (d, $J$ = 8.4 Hz, 2 H, ArH), 6.04–5.91 (m, 1 H, CH), 5.08 (d, $J$ = 10.2 Hz, 1 H, CH), 4.96 (d, $J$ = 17.1 Hz, 1 H, CH), 4.54 (d, $J$ = 7.2 Hz, 1 H, CH), 3.71 (t, $J$ = 7.8 Hz, 1 H, CH), 2.32 (s, 3 H, $CH_3$), 2.16 (s, 3 H, $CH_3$) ppm. *anti* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.33–6.96 (m, 1 H, ArH), 6.87 (d, $J$ = 8.7 Hz, 0.2 H, ArH), 6.38–6.35 (m, 0.2 H, ArH), 6.21–6.09 (m, 0.1 H, CH), 5.28–5.20 (m, 2 H, $CH_2$), 4.40 (d, $J$ = 8.1 Hz, 0.1 H, CH), 3.51–3.45 (m, 0.1 H, CH), 3.35 (s, 0.3 H, $CH_3$), 2.18 (s, 0.3 H, $CH_3$) ppm.

**4-Methyl-*N*-phenyl-α-2-phenyl-2-propenylbenzenemethanamine (18):** Light yellow liquid. Yield: 247 mg (79%) (*syn*/*anti* = 84:16). *syn* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.32–6.97 (m, 11 H, ArH), 6.63–6.57 (m, 1 H, ArH), 6.42 (d, $J$ = 8.4 Hz, 2 H, ArH), 6.05–5.93 (m, 1 H, CH), 5.09 (d, $J$ = 10.2 Hz, 1 H, CH), 4.98 (d, $J$ = 16.8 Hz, 1 H, CH), 4.57 (d, $J$ = 6.9 Hz, 1 H, CH), 3.70 (t, $J$ = 7.8 Hz, 1 H, CH), 2.32 (s, 3 H, $CH_3$) ppm. *anti* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.32–6.97 (m, 2 H, ArH), 6.65–6.62 (m, 0.2 H, ArH), 6.49 (d, $J$ = 7.8 Hz, 0.4 H, ArH), 6.26–6.12 (m, 0.2 H, CH), 5.28–5.18 (m, 0.4 H, $CH_2$), 4.46 (d, $J$ = 8.1 Hz, 0.2 H, CH), 3.59–3.51 (m, 0.2 H, CH), 2.26 (s, 0.6 H, $CH_3$) ppm.

**4-Methyl-*N*-(2-chlorophenyl)-α-2-phenyl-2-propenylbenzenemethanamine (19):** Light yellow liquid. Yield: 270 mg (78%) (*syn*/*anti* = 76:24). *syn* isomer: $\delta$ = 7.36–6.96 (m, 7 H, ArH), 6.92–6.87 (m, 2 H, ArH), 6.57–6.49 (m, 2 H, ArH), 6.48–6.31 (m, 2 H, ArH), 6.14–6.01 (m, 1 H, CH), 5.16 (d, $J$ = 10.2 Hz, 1 H, CH), 5.09 (d, $J$ = 16.8 Hz, 1 H, CH), 4.61 (d, $J$ = 6.6 Hz, 1 H, CH), 3.79 (t, $J$ = 7.8 Hz, 1 H, CH), 2.32 (s, 3 H, $CH_3$) ppm. *anti* isomer: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.36–6.96 (m, 2 H, ArH), 6.92–6.87 (m, 0.5 H, ArH), 6.57–6.49 (m, 0.5 H, ArH), 6.42–6.31 (m, 0.5 H, ArH), 6.28–6.17 (m, 0.2 H, CH), 5.32–5.23 (m, 0.5 H, $CH_2$), 4.52 (d, $J$ = 7.8 Hz, 0.2 H, CH), 3.65 (t, $J$ = 8.4 Hz, 0.2 H, CH), 2.27 (s, 0.7 H, $CH_3$) ppm.

## Acknowledgments

We are grateful for the financial support of the Natural Science Foundation of Guangdong (Grant No. 04105493).

[1] C. E. Neipp, J. M. Humpherey, S. F. Martin, *J. Org. Chem.* **2001**, *66*, 531–537.
[2] Y. Gao, F. Sato, *J. Org. Chem.* **1995**, *60*, 8136–8137.
[3] a) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207–2293; b) R. Bloch, *Chem. Rev.* **1998**, *98*, 1407–1438; c) J.-I. Yoshida, S. Suga, S. Suzuki, N. Kinomura, A. Yamamoto, K. Fujiwara, *J. Am. Chem. Soc.* **1999**, *121*, 9546–9549.
[4] D. K. Wang, L. X. Dai, X. L. Hou, *Tetrahedron Lett.* **1996**, *37*, 4187–4188.
[5] a) P. A. Grieco, A. Bahsas, *J. Org. Chem.* **1987**, *52*, 1378–1380; b) H. Nakamura, H. Iwama, Y. Yamamoto, *J. Am. Chem. Soc.* **1996**, *118*, 6641–6647.
[6] a) C. Bellucci, P. G. Cozzi, A. U. Ronchi, *Tetrahedron Lett.* **1995**, *36*, 7289–7292; b) H. C. Aspinall, J. S. Bissett, N. Greeves, D. Levin, *Tetrahedron Lett.* **2002**, *43*, 323–325; c) M. Bao, H. Nakamura, Y. Yamamoto, *Tetrahedron Lett.* **2000**, *41*, 131–134; d) G. E. Keck, E. J. Enholm, *J. Org. Chem.* **1985**, *50*, 147–149; e) M. A. Ciufolini, G. O. Spencer, *J. Org. Chem.* **1989**, *54*, 4739–4741; f) M. Yasuda, Y. Sugawa, A. Yamamoto, I. Shibata, A. Baba, *Tetrahedron Lett.* **1996**, *37*, 5951–5954.
[7] a) C. J. Li, T. H. Chan, *Tetrahedron* **1999**, *55*, 11149–11176; b) S. Kobayashi, K. Manabe, *Acc. Chem. Res.* **2002**, *35*, 209–217; c) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751–2772; d) C. J. Li, *Chem. Rev.* **2005**, *105*, 3095–3165.
[8] a) S. Kobayashi, T. Wakabayashi, S. Nagayama, *Tetrahedron Lett.* **1997**, *38*, 4559–4562; b) S. Kobayashi, T. Busujima, S. Nagayama, *Chem. Commun.* **1998**, 19–20; c) I. H. S. Estevam, L. W. Bieber, *Tetrahedron Lett.* **2003**, *44*, 667–670; d) S. Kumar, P. Kaur, *Tetrahedron Lett.* **2004**, *45*, 3413–3416; e) H. M. S. Kumar, S. Anjaneyulu, E. J. Reddy, J. S. Yadav, *Tetrahedron Lett.* **2000**, *41*, 9311–9314; f) W. Lu, T. K. Chan, *J. Org. Chem.* **2000**, *65*, 8589–8594; g) L. Bernardi, V. Cere, C. Femoni, S. Pollicino, A. Ricci, *J. Org. Chem.* **2003**, *68*, 3348–3351.
[9] K. Manabe, Y. Mori, S. Kobayashi, *Tetrahedron* **2001**, *57*, 2537–2544.
[10] K. Tanaka, R. Shiraishi, *Green Chem.* **2000**, *2*, 272–273.
[11] a) H. C. Aspinall, N. Greeves, E. G. McIver, *Tetrahedron Lett.* **1998**, *39*, 9283–9286; b) K. Manabe, S. Kobayashi, *Tetrahedron Lett.* **1999**, *40*, 3773–3776; c) T. P. Loh, J. Xu, Q. Y. Hu, J. J. Vittal, *Tetrahedron: Asymmetry* **2000**, *11*, 1565–1569; d) G. L. Li, G. Zhao, *J. Org. Chem.* **2005**, *70*, 4272–4278; e) T. H. Chan, Y. Yang, C. J. Li, *J. Org. Chem.* **1999**, *64*, 4452–4455; f) A. Yanagisawa, M. Morodome, H. Nakashima, H. Yamamoto, *Synlett* **1997**, 1309–1311.
[12] a) Y. Masuyama, J. Tosa, Y. Kurusu, *Chem. Commun.* **1999**, 1075–1076; b) S. J. Veenstra, P. Schmid, *Tetrahedron Lett.* **1997**, *38*, 997–1000; c) T. H. Chan, W. Lu, *Tetrahedron Lett.* **1998**, *39*, 8605–8608; d) Y. Masuyama, K. Takeuchi, Y. Kurusu, *Tetrahedron Lett.* **2005**, *46*, 2861–2863.
[13] M. Shimizu, M. Kimura, T. Watanabe, Y. Tamaru, *Org. Lett.* **2005**, *7*, 637–640.
[14] a) T. Akiyama, Y. J. Onuma, *J. Chem. Soc., Perkin Trans. 1* **2002**, *9*, 1157–1158; b) B. H. Kim, R. Han, R. J. Park, K. H. Bai, Y. M. Jun, W. Baik, *Synth. Commun.* **2001**, *31*, 2297–2303; c) B. M. Choudary, S. Chidara, Ch. V. Raja Sekhar, *Synlett* **2002**, *10*, 1694–1696.

Received: October 30, 2006
Published Online: February 2, 2007