Asymmetric synthesis of \(N\)-tosyl amino acids from \(N\)-sulfinyl \(\alpha\)-amino-1,3-dithioketals

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This paper is dedicated to Cynthia A. Maryanoff and Bruce E. Maryanoff to honor their outstanding contributions to science and service to the profession

Abstract

Hydrolysis of diastereomERICALLY pure \(N\)-sulfinyl \(\alpha\)-amino-1,3-dithianes with 1,3-dibromo-5,5-dimethylhydantoin gives \(N\)-tosyl \(\alpha\)-amino aldehydes which when subjected to a Pinnick-type oxidation gave \(N\)-tosyl \(\alpha\)-amino acids without epimerization.

Keywords: Sulfinimine (\(N\)-sulfinyl imine); asymmetric synthesis; \(N\)-tosyl \(\alpha\)-amino acids; \(N\)-sulfinyl \(\alpha\)-amino-1,3-dithioketals.

Introduction

\(\alpha\)-Amino aldehydes and ketones are valuable chiral building blocks widely used in asymmetric synthesis.\(^1^,\,2\) They have been employed in the enantioselective synthesis of \(\alpha\)-amino alcohols, 1,2-diamines, allylic amines, heterocycles, and natural products. Most often \(\alpha\)-amino aldehydes and ketones are prepared from \(N\)-protected \(\alpha\)-amino acids and are limited by the availability of the starting material.\(^1\) Because these \(\alpha\)-amino carbonyl compounds are notoriously unstable, their formation and subsequent transformations require a suitable \(N\)-protecting group for stabilization to inhibit racemization and self-condensation.\(^1^,\,2^,\,3\)

\(N\)-Sulfinyl \(\alpha\)-amino-1,3-dithioketals \(2\) (\(R' = \text{alkyl aryl, H}\)), prepared by the addition of 2-lithio-1,3-dithianes to enantiopure sulfinimines (\(N\)-sulfinyl imines) \(1\), are new sulfinimine-derived chiral building blocks for the asymmetric synthesis of \(\alpha\)-amino aldehydes \(5\) and ketones \(6\) (Scheme 1).\(^4^,\,7\) Removal of the thioketal group in \(2b\) was selectively accomplished using the Stork reagent \(\text{PhI(O}_2\text{CCF}_3)_2\), affording the \(N\)-sulfinyl \(\alpha\)-amino ketone \((S,S)-6\) without epimerization.\(^4\) Similar treatment of \(2a\) resulted in decomposition, but with 1,3-dibromo-5,5-dimethylhydantoin (DBDMH, \(4\)) it gave the \(N\)-tosyl \(\alpha\)-amino aldehyde \((S)-5\), again without epimerization.\(^5\) The fact that acid hydrolysis of \(2\) gives the free amine \(3\) while leaving the carbonyl group protected offers unique opportunities for functional group manipulation.\(^4\) These
new chiral building blocks have been employed in asymmetric syntheses of hydroxyprolines such as (-)-3-hydroxy-3-methylproline, 1,2-amino alcohols, allylamines, the 2,3-disubstituted piperidine (L-733,060), and the amino ketone (-)-cathinone.

\[ \text{(S)-1} \quad R = \text{alkyl, aryl} \]

\[ \text{(S\textsubscript{S},S)-2a: } R' = \text{H} \]
\[ \text{(S\textsubscript{S},S)-2b: } R' = \text{alkyl, aryl} \]

\[ \text{(S)-3} \]

\[ \text{(S)-5} \]

\[ \text{(S\textsubscript{S},S)-6} \]

**Scheme 1.** Synthesis of α-amino-aldehydes and ketones.

Although the synthesis of α-amino acids from α-amino aldehydes has occasionally been described, this method has received little attention. Undoubtedly the reason for this is that α-amino aldehydes are usually prepared from α-amino acids. However, a procedure to prepare α-amino acids from α-amino-1,3-dithianes would have considerable merit because of the structural diversity of available sulfinimine-derived α-amino-1,3-dithianes. We describe here a simple method for the asymmetric synthesis of N-tosyl α-amino acids from N-tosyl α-amino aldehydes using a Pinnick-type oxidation.
Results and Discussion

The addition of 1.5 equivalents of a preformed solution of 2-lithio-1,3-dithiane at -78 °C to (S)-(+) -N-(benzylidene)-p-toluenesulfinamid e 7a, (S)-(+) -N-(trifluoromethyl-benzylidene)-p- toluenesulfinamide 7b, (S)-(+) -N-(isobutylidene)-p-toluenesulfinamide 7c, or (S)-(+) -(2,2-dimethylpropylidene)-p-toluenesulfinamide 7d, readily gave the corresponding N-sulfinyl α-amino-1,3-dithianes (SS)-(+) -8a and (SS)-(+) -8b, (SS)-(+) -8c, and (SS)-(+) -8d (Scheme 2). The diastereoselectivities, determined by 1H-NMR on the crude reaction mixtures, were good to excellent (72-96% de) and the yields of the major diastereoisomers, isolated by flash chromatography, were good (Table 1). It is interesting to note that the highest de’s were found for addition of the 2-lithio-1,3-dithiane to the bulky tert-butyl sulfinimine (S)-(+) -7d and lowest for the smaller iso-propyl sulfinimine (S)-(+) -7c (Table 1, compare entries 3 and 4).

\[
\text{Scheme 2. Synthesis of } N\text{-sulfinyl } \alpha\text{-amino-1,3-dithianes.}
\]

\[
\text{Table 1. Synthesis of } N\text{-sulfinyl } \alpha\text{-amino-1,3-dithianes } (SS)-(+) -8
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sulfinimine 7 (R =)</th>
<th>% de\textsuperscript{a}</th>
<th>(+)-8, % yield\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7a (R = Ph)</td>
<td>82</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>7b (R = p-CF\textsubscript{3}Ph)</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>7c (R = i-Pr)</td>
<td>72</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>7d (R = CMe\textsubscript{3})</td>
<td>96</td>
<td>72</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Determined by 1H- NMR on the crude reaction mixture.

\textsuperscript{b} Isolated yield of pure major diastereoisomer.

The N-sulfinyl α-amino-1,3-dithianes 8 were hydrolyzed by treatment with 2 equivalents of DBDMH 4 in 80% acetone at -20 °C. The solution quickly turned red and then faded to yellow-
orange after a few minutes. The reaction was quenched after about 10 min by addition of aqueous sodium sulfite to afford the crude \(N\)-tosyl aldehydes \((S)\)-9 as colorless oils. Since the aldehydes were unstable to chromatographic purification they were used in crude form for the next reactions.

The enantiomeric purity of the crude \(N\)-tosyl amino aldehydes 9 were determined by reduction with 5 equiv. of \(\text{NaBH}_4\) to give the known 1,2-amino alcohols \((S)\)-\((+)-10\), which were transformed into their Mosher esters (Scheme 3). The enantiomeric purity of amino alcohol \((S)\)-\((+)-10a\) is estimated to be >97% ee based on its Mosher ester and by comparison its specific rotation to a literature value for this amino alcohol.\(^{10}\) Therefore the enantiomeric purity of the corresponding \(\alpha\)-amino aldehyde \(9a\), must be at least 97% ee. Similar results were found for 9c and 9d. These results confirm earlier studies that demonstrated that the \(N\)-tosyl group is an excellent protecting group for inhibiting base catalyzed epimerization in \(\alpha\)-amino aldehydes, because it stabilizes anions at nitrogen.\(^{7}\)

\[
\begin{align*}
\text{(S,S)-(+)-8} & \quad \xrightarrow{\text{1) 2 equiv DBDMH 4, 2) \text{Na}_2\text{SO}_3, acetone, H}_2\text{O, -20 °C}} \quad \text{(S)-9} \\
\text{NaBH}_4 & \quad \text{ (> 97% ee)} \\
\text{(S)-(+)10a: R = Ph (70%)} & \quad \text{(S)-(+)10c: R = i-Pr (58%)} \\
\text{(S)-(+)10d: R = t-Bu (42%)}
\end{align*}
\]

Scheme 3. Reduction of \(N\)-tosyl \(\alpha\)-amino aldehydes.

A Pinnick-type oxidation was used to oxidize the crude aldehydes \((S)\)-9 to the corresponding \(N\)-tosyl amine acids, which were isolated as their methyl esters 12 (Scheme 4).\(^{11}\) The crude \(N\)-tosylamino aldehydes 9 were converted into the amino acids 11 under standard conditions, \(i.e.\) \(\text{NaClO}_2\), \(\text{NaH}_2\text{PO}_4\) and 2-methyl-2-butene in \(\text{THF: t-BuOH: H}_2\text{O}\) at 0 °C. The crude amino acids were treated with (trimethylsilyl)diazomethane solution to give the amino acid methyl esters 12 in good yield for the four-step sequence (Scheme 4). The enantiomeric purities of the amino-acid methyl esters were excellent, as determined by comparison with literature values and conversion of the acids into the diastereomeric amides with \((R)\)-(+)\-\(\alpha\)-methylbenzylamine – and the other diastereomeric amide was not detected by \(^{1}\text{H-NMR.}\)

Conclusions

Hydrolysis of N-sulfinyl α-amino-1,3-thianes 8 with 1,3-dibromo-5,5-dimethylhydantoin 4 affords N-tosyl α-amino aldehydes 9 which were oxidized to N-tosyl α-amino acids 11 which were isolated as their methyl esters 12. The overall yield for the four-step sequence, 8 to 12 is very good, and epimerization was not detected. This protocol represents a valuable new method for the asymmetric synthesis of structurally diverse α-amino acids because of the great structural diversity of available sulfinimines. Furthermore, Rapoport has demonstrated the utility of N-arylsulfonyl protecting groups in many transformations of amino acids, including modifications of the carboxyl group to give α-amino ketones. Removal of the N-tosyl group is easily effected without epimerization, via reduction with sodium naphthalide or cleavage with HBr in HOAc. In our studies we have found that Na/NH₃ (liq.) is particularly effective for removal of the N-p-toluenesulfonyl protecting group.

Experimental Section

**General.** Chromatography was performed on silica gel, Merck grade 60 (230-400 mesh). TLC plates were visualized with UV, in an iodine chamber, or with phosphomolybdic acid, unless otherwise noted. $^1$H- and $^{13}$C- NMR spectra were recorded at 400 and 100 MHz, respectively. Unless stated otherwise, all reagents were purchased from commercial sources and used without additional purification. The sulfinimines $^7$a, $^7$b, $^7$c, $^7$d were prepared as previously described. RT denotes room temperature.

**General procedure for addition of 2-lithio-1,3-dithiane to sulfinimines ($S_S,S$)-(+)-$N(p$-toluenesulfinyl)-2-phenylaminomethyl-1,3-dithiane 8a**

In a 50 mL, oven dried, two-neck, round-bottomed flask equipped with a magnetic stirring bar, a rubber septum and an argon- filled balloon was placed 1,3-dithiane (0.37 g, 3.08 mmol, Aldrich) in THF (20 mL). The solution was cooled to -20 °C and n-BuLi (1.64 mL, 4.11 mmol, 2.5 M in hexane) was added slowly. After 1.5 h, the resulting solution was cooled to -78 °C and added via cannula to a -78 °C solution of sulfinimine (+)-$^7$a (0.5 g, 2.05 mmol) in THF (20 mL). The reaction was stirred for 20 min. and quenched at -78 °C by addition of sat. NH$_4$Cl solution (3 mL). To the reaction mixture was added EtOAc (25 mL), the aqueous phase was washed with brine (10 mL), dried (Na$_2$SO$_4$), and concentrated. Flash chromatography (EtOAc/hexane, 2:8) afforded 0.545 g (73%) of a white crystalline solid, mp 172-174 °C (dec.); [α]$_{20}^D$ +69.8 (c 1.0, CHCl$_3$); IR (KBr) 3260, 3040, 2941, 1418 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 7.40 (d, $J$ = 8.0 Hz, 2 H), 7.07 (m, 7 H), 5.05 (d, $J$ = 5.5 Hz, 1 H), 4.65 (t, $J$ = 6.5 Hz, 1 H), 4.25 (d, $J$ = 6.5 Hz, 1 H), 2.80-2.76 (m, 2 H), 2.72 (m, 2 H), 2.23 (s, 3 H), 2.11 (m, 1 H), 1.92-1.83 (m, 1 H); $^{13}$C NMR (CDCl$_3$) δ 141.1, 140.2, 129.5, 129.0, 128.4, 127.7, 125.9, 125.3, 58.0, 53.6, 29.5, 28.4, 25.6, 21.6. HRMS Calcd for C$_{18}$H$_{21}$NOS$_3$Na (M + Na) 386.0682. Found 386.0685.

($S_S,S$)-(+)-$N(p$-Toluenesulfinyl)-2-(4-trifluoromethylphenylaminomethyl)-1,3-dithiane 8b.

Flash chromatography using EtOAc/hexane (3:7) gave 75% of a white solid, mp 139-140 °C; [α]$_{20}^D$ +70.4 (c 0.33, CHCl$_3$) IR (KBr) 3207, 2941, 1418 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 7.40 (d, $J$ = 8.0 Hz, 2 H), 7.07 (m, 7 H), 5.05 (d, $J$ = 5.5 Hz, 1 H), 4.65 (t, $J$ = 6.5 Hz, 1 H), 4.25 (d, $J$ = 6.5 Hz, 1 H), 2.80-2.76 (m, 2 H), 2.72 (m, 2 H), 2.23 (s, 3 H), 2.11 (m, 1 H), 1.92-1.83 (m, 1 H); $^{13}$C NMR (CDCl$_3$) δ 141.1, 140.2, 129.5, 129.0, 128.4, 127.7, 125.9, 125.3, 58.0, 53.6, 29.5, 28.4, 25.6, 21.6. HRMS Calcd for C$_{19}$H$_{21}$F$_3$NOS$_3$ (M + H) 432.0737. Found 432.0747.

($S_S,S$)-(+)-$N(p$-Toluenesulfinyl)-2-(1-amino-2-methylpropyl)-1,3-dithiane 8c.

Flash chromatography with EtOAc/hexane (3:7) gave 70% of a white solid, mp 94-96 °C; [α]$_{20}^D$ +51.8 (c 0.33, CHCl$_3$) IR (KBr) 3207, 2931, 1429, 1037 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 7.83 (d, $J$ = 7.5 Hz, 2 H), 7.30 (d, $J$ = 7.5 Hz, 2 H), 4.38 (d, $J$ = 4.5 Hz, 1 H), 4.13 (d, $J$ = 9.5 Hz, 1 H), 3.43-3.33 (m, 1 H), 2.97-2.83 (m, 4 H), 2.24 (s, 3 H), 2.17-2.10 (m, 1 H), 2.07-2.00 (m, 1 H), 1.94-1.84 (m, 1 H), 0.99 (d, $J$ = 3.0 Hz, 3 H), 0.98 (d, $J$ = 2.5 Hz, 3 H); $^{13}$C NMR (CDCl$_3$) δ 142.8, 141.2, 129.3, 139.5, 141.4, 143.7. HRMS Calcd for C$_{19}$H$_{21}$F$_3$NOS$_3$ (M + H) 432.0737. Found 432.0747.
126.2, 64.9, 54.4, 30.7, 30.4, 30.2, 26.2, 21.3, 20.5, 18.5. Anal. Calcd for C₁₅H₂₃NOS₃: C, 54.67; H, 7.03; N, 4.25. Found: C, 54.65; H, 7.06; N, 4.29%.

(S₈,S)-(+)–N-(p-Tolunesulfinyl)-2-(1-amino-2,2-dimethylpropyl)-1,3-dithiane 8d. Flash chromatography with EtOAc/hexane (3:7) gave 72% of a colorless oil, [α]²⁰_D +15.4 (c 1.91, CHCl₃); IR (KBr) 3219, 3040, 2955, 2899, 1473 cm⁻¹; ¹H NMR (CDCl₃) δ 7.91 (d, J = 8.0 Hz, 2 H), 7.26 (d, J = 8.0 Hz, 2 H), 4.49 (s, 1 H), 4.20 (d, J = 9.3, 1 H), 3.29 (d, J = 9.3 Hz, 1 H), 2.88 (m, 4 H), 2.36 (s, 3 H), 1.92 (m, 2 H), 1.03 (s, 9 H); ¹³C NMR (CDCl₃) δ 143.8, 141.6, 129.7, 126.8, 70.4, 53.8, 36.1, 32.3, 31.1, 28.1, 26.3, 21.7. HRMS Calcd for C₁₆H₂₅NOS₃ (M + H) 344.1176. Found 344.1181.

General procedure for hydrolysis of α-amino 1,3-dithianes to N-tosyl α-amino aldehydes using 1,3-dibromo-5,5-dimethylhydantoin (DBDMH, 4)
In a 50 mL round-bottomed flask equipped with a magnetic stirring bar and a rubber septum was placed (+)–8a (0.5 g, 1.377 mmol) in acetone (20 mL) at 25 °C, and this solution was added with stirring to a solution of 1,3-dibromo-5,5-dimethylhydantion (DBDMH, 4) (0.787 g, 2.754 mmol) in 80% acetone (14 mL) at -20 °C. The solution quickly became red, but soon faded to yellow-orange, and was stirred for 10 min. The solution was then shaken with a mixture of saturated aq. sodium sulfite (10 mL) and 1:1 hexane-dichloromethane (10 mL). The organic phase was washed with aqueous sodium bicarbonate (12 mL), water (12 mL), then brine (12 mL), dried (Na₂SO₄), and concentrated to give a colorless oil that was used directly in the next step.

General procedure for the reduction of α-amino aldehydes using NaBH₄. (S)-(+)–N-(2-hydroxy-1-phenyl-ethyl)-4-methyl-benzenesulfonamide 10a
In a 25-mL, oven-dried, single-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon balloon, was placed the crude aldehyde 9a (0.08 g, 0.276 mmol) in EtOH (15 mL). The solution was cooled to 0 °C and NaBH₄ (0.125 g, 3.321 mmol) was added. After 10 min, the reaction mixture was quenched by addition of saturated aqueous NH₄Cl solution (10 mL) at 0 °C and diluted with EtOAc (10 mL). The aqueous phase was extracted with EtOAc (2 x 10 mL), and the combined organic phases were washed with brine (15 mL), dried (Na₂SO₄), and concentrated to give a colorless oil that was used directly in the next step.

(S)-(+)–N-(1-Hydroxymethyl-2-methylpropyl)-4-methylbenzenesulfonamide 10c. Flash chromatography with EtOAc/hexane (4:6) gave 0.0450 g (70%) of a white solid, mp 89-90 °C [lit.¹⁶ mp 88-89 °C]; [α]²⁰_D +30.7 (c 0.5, CHCl₃), [lit.¹⁶ [α]²⁵_D +29.4 (c, 0.837, CHCl₃); IR (KBr) 3531, 3302, 2972, 1162 cm⁻¹; ¹H- NMR (CDCl₃) δ 7.82 (d, J = 4.5 Hz, 2 H), 7.38 (d, J = 4.5 Hz,
2 H), 4.81 (d, J = 5.8 Hz, 1 H), 3.60-3.62 (m, 2 H), 3.08 (m, 1 H), 2.49 (s, 3 H), 1.82-1.92 (m, 1 H), 0.83 (d, J = 3.0 Hz, 3 H), 0.80 (d, J = 3.0 Hz, 3 H); $^{13}$C NMR (CDCl$_3$, δ143.5, 137.5, 129.7, 127.2, 63.1, 60.9, 29.4, 29.6, 21.5, 19.1, 18.4; Anal. Calcd for C$_{12}$H$_{19}$NO$_3$: C, 56.00; H, 7.44; N, 5.44. Found: C, 55.94; H, 7.47; N, 5.45%.

**General procedure for the formation of amino acids. (S)-(+) Methyl-2-(p-toluenesulfonyl)amino-2-phenyl acetate 12a.**

In a 50-mL, oven-dried, single-necked, round-bottomed flask equipped with a magnetic stirring bar and a glass stopper was placed the crude aldehyde 9a (0.225 g, 0.778 mmol) in THF: t-BuOH (1:1, 15 mL). The solution was cooled to 0 bar and a glass stopper was placed the crude aldehyde

In a 50-mL, oven-dried, single-necked, round-bottomed flask equipped with a magnetic stirring

toluenesulfonyl)amino-2-phenyl acetate 12a

Flash chromatography with EtOAc/hexane (3:7) gave 0.032 g (42%) of a light yellow solid, mp 111-112 °C; [α]$^{20}_D +10.3$ (c 1.45, CHCl$_3$); IR (KBr) 3471, 3292, 2958, 2924, 1325, 1154 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 7.85 (d, J = 6.0 Hz, 2 H), 7.37 (d, J = 6.0 Hz, 2 H), 4.96 (d, J = 6.0 Hz, 1 H), 3.67 (m, 2 H), 3.07 (m, 1 H), 2.49 (s, 3 H), 2.01 (s, 1 H), 0.86 (s, 9 H); $^{13}$C NMR (CDCl$_3$) δ 143.9, 138.0, 130.0, 127.7, 64.4, 62.7, 34.4, 27.3, 21.9. Anal. Calcd for C$_{13}$H$_{21}$NO$_3$: C, 57.54; H, 7.80; N, 5.16. Found: C, 57.52; H, 7.82; N, 5.19%.

(S)-(+) Methyl-2-(p-toluenesulfonyl)amino-2-phenyl acetate 12b.

Flash chromatography (EtOAc/hexane, 3:5:6.5) afforded 0.137 g (52%) of 12a as a white solid, mp 132 °C [lit.$^{17}$ mp 131-133 °C]; [α]$^{20}_D +101.6$ (c, 0.52, CHCl$_3$), [lit.$^{17}$ [α]$^{25}_D +102.0$ (c, 1.12, CHCl$_3$); IR (KBr) 3255, 1742, 1084 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 7.4 (d, J = 8.1 Hz, 2 H), 7.38-7.21 (m, 7 H), 5.72 (d, J = 7.8 Hz, 1 H), 5.13 (d, J = 7.8 Hz, 1 H), 3.61 (s, 3 H), 2.42 (s, 3 H); $^{13}$C NMR (CDCl$_3$) δ 172.1, 143.9, 136.4, 135.1, 130.1, 129.7, 128.8, 128.5, 127.1, 59.6, 53.2, 21.2. HRMS Calcd for C$_{16}$H$_{17}$NO$_4$SNa (M + Na)$^+$ 342.0775. Found 342.0773.

(S)-(+) Methyl-2-(p-toluenesulfonyl)amino-2-(4-trifluoromethyl-phenyl)-acetate 12c.

Flash chromatography EtOAc/hexane (4:6) gave 44% of a white solid, mp 78 °C [lit.$^{17}$ mp 77-78 °C]; [α]$^{20}_D +15.2$ (c, 0.91, CHCl$_3$), [lit.$^{17}$ [α]$^{25}_D +15.6$ (c, 0.89, CHCl$_3$); IR (KBr) 3247, 1723, 1092 cm$^{-1}$; $^1$H NMR
(CDCl$_3$) δ 7.65 (d, $J = 8.0$ Hz, 2 H), 7.21 (d, $J = 8.0$ Hz, 2 H), 4.98 (d, $J = 8.4$ Hz, 1 H), 3.69 (d, $J = 8.4$ Hz, 1 H), 3.39 (s, 3 H), 2.38 (s, 3 H), 2.02-1.93 (m, 1 H), 0.94 (d, $J = 6.7$ Hz, 3 H), 0.87 (d, $J = 6.7$ Hz, 3 H); $^{13}$C NMR (CDCl$_3$) δ 171.0, 142.9, 136.8, 129.8, 126.1, 61.2, 52.1, 32.1, 21.8, 19.4, 18.6. Anal. Calcd for C$_{13}$H$_{19}$NO$_4$: C, 54.72; H, 6.71; N, 4.91. Found: C, 54.69; H, 6.88; N, 4.89%.

(S)-(+)–Methyl-3,3-dimethyl-2-(p-toluenesulfonyl)-amino-butyrate 12d. Flash chromatography EtOAc/hexane (4:6) gave 40% of a white solid, mp 108-110°C; [α]$_{20}^D$ +42.1 (c, 0.7, CHCl$_3$); IR (KBr) 3250, 1732, 1449, 1088 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 7.69 (d, $J = 8.0$ Hz, 2 H), 7.23 (d, $J = 8.0$ Hz, 2 H), 5.08 (d, $J = 12$ Hz, 1 H), 3.57 (d, $J = 12$ Hz, 1 H), 3.33 (s, 3 H), 2.41 (s, 3 H), 0.94 (m, 9 H); $^{13}$C NMR (CDCl$_3$) δ 171.1, 144.1, 136.8, 129.9, 127.8, 64.6, 52.1, 34.9, 26.6, 21.9. Anal. Calcd for C$_{14}$H$_{21}$NO$_4$: C, 56.16; H, 7.07; N, 4.68. Found: C, 56.14; H, 7.12; N, 4.71%.

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References


