Synthesis of enantiopure 1,3-oxazolidin-2-ones from α-dibenzylamino esters

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Abstract
A new method to obtain enantiopure 5-substituted 1,3-oxazolidin-2-ones 1 from α-dibenzylamino esters 2 is reported. This methodology is based on the Lewis acid catalyzed stereoselective addition of trimethylsilyl cyanide to chiral α-dibenzylamino aldehydes 3. Magnesium chloride and zinc iodide were tested to catalyze the addition, obtaining higher stereoselectivity with zinc iodide than with magnesium chloride.

Keywords: Enantiopure, 1,3-oxazolidin-2-ones, stereoselective addition

Introduction
In 1981, 4-substituted 1,3-oxazolidin-2-ones were introduced into organic synthesis as chiral auxiliaries by Evans.\(^1\) Since then they have been used in many reactions. These compounds are mainly prepared from the cyclization of chiral amino alcohols derived from nonracemic amino acids. Usually, N-acyloxazolidinones participate in stereoselective processes as alkylations, α-substitution reactions, aldol reactions, conjugate additions and pericyclic reactions. The majority of these reactions are performed in the presence of a metal ion.\(^2\)

Meanwhile, a group of 5-substituted 1,3-oxazolidin-2-ones, typified by linezolid (4) and eperozolid (5), represent a new class of synthetic antibacterial agents with potent activity against clinically important susceptible and resistant Gram-positive and anaerobic pathogens.\(^3\) This class of compounds has a novel mechanism of action that shows selective and unique binding to 50S ribosomal subunit, inhibiting bacterial translation at the initiation phase of protein synthesis.\(^4\) Due to its protein synthesis inhibitory activity these compounds are used against methicillin or vancomycin-resistant staphylococci, streptococci and enterococci bacteria that causes skin and soft tissue infections and pneumonia.\(^5\) Moreover, there are many reports for the synthesis of new...
compounds structurally related to linezolid that avoid bacterial resistance against these new antibiotics.  

\[
\begin{align*}
\text{6: } & \quad R_1 = \text{OMe} \quad R_2 = R_3 = \text{H} \\
\text{7: } & \quad R_1 = \text{H} \quad R_2 = R_3 = \text{Me}
\end{align*}
\]

Mephenoxalone (6) and metaxalone (7) are 5-aryloxymethyl-1,3-oxazolidin-2-one type compounds, which have shown activity as interneuron blocking agents or depressants of central synaptic transmission. They are generally antagonists of strychnine convulsions and have been used as skeletal muscle relaxants, anticonvulsants, and tranquilizers. These products are prescribed to rest, physical therapy, and for the relief of discomfort associated with acute, painful musculoskeletal conditions. Also, there are 5-substituted 1,3-oxazolidin-2-ones, which are a new class of reversible and selective third-generation of potent and selective monoamine oxidase type A (MAO) inhibitors as toloxatone (8; Humoryl®), cimoxatone (9) and befloxatone (10) which are indicated in the treatment of several neurological diseases. Therefore, the synthesis of chiral 1,3-oxazolidin-2-ones is an important field of research due to the potential as chiral inductors or biological active substances.

Reetz and coworkers reported the stereoselective cyanosilylation of non-racemic \(\alpha\)-dibenzyllamino aldehydes 3 by the addition of trimethylsilyl cyanide with different inorganic salts as Lewis acid catalysts. The application of some organometallic compounds have also been reported. These silylated intermediates are important building blocks in the synthesis of pharmacologically active compounds, but to the best of our knowledge, the synthesis of 1,3-oxazolidin-2-ones from these silylated intermediates has yet to be reported. Only the \(N\)-benzoyl-1,3-oxazolidin-2-one derivative from L-phenylalanine has been synthesized from a ring-closure reaction of \(\beta\)-hydroxyalkyl phenyl selenides through intramolecular displacement of the phenylselenoyl group with nitrogen nucleophiles. Previously, we have explored the construction of 1,3-oxazolidin-2-one ring from a silylated intermediate, as well as the stereoselective synthesis of new compounds with potential biological activity by transformation of chiral \(\alpha\)-amino esters. In this work, we have developed a new methodology for the synthesis
of enantiopure 5-substituted 1,3-oxazolidin-2-ones from chiral silylated intermediates prepared from enantiopure α-dibenzylamino esters.

Results and Discussion

N,N-Dibenzylamino esters 2 were prepared from L-phenylalanine, L-alanine, L-valine, L-leucine and L-isoleucine under standard procedures to generate 2a-e, respectively,\(^{17}\) and then reduced with lithium borohydride at reflux temperature in THF, to obtain amino alcohols 11a-e in 44% to 99% yield (Scheme 1). α-Dibenzylamino aldehydes 3a-e were obtained in very good yields (83% to 98%) by oxidation of compounds 11a-e, respectively, in Swern oxidation conditions. The stereoselective anti addition of trimethylsilyl cyanide to the α-dibenzylamino aldehydes 3 was achieved using zinc iodide (ZnI\(_2\)) or magnesium chloride (MgCl\(_2\)) in dichloromethane at 0 °C to give the corresponding trimethylsilylcyanohydrins 12a-e in 72% to 99% yield. When MgCl\(_2\) was used, two molar equivalents of TMSCN were required to complete the reaction.

\[
\begin{align*}
R & \quad \text{dibenzylamino ester} \\
\text{OCH}_3 & \quad \text{LiBH}_4 \\
\text{THF} & \quad \text{H} \\
R & \quad \text{dibenzylamino alcohol} \\
\text{N} & \quad \text{LiAlH}_4 \\
\text{TEA} & \quad \text{TMSCN} \\
\text{CH}_2\text{Cl}_2 & \quad \text{Catalyst} \\
\text{BTC} & \quad \text{DMSO, TEA} \\
\text{CH}_2\text{Cl}_2 & \quad \text{CH}_2\text{Cl}_2 \\
\end{align*}
\]

Scheme 1. Synthesis of 5-substituted 1,3-oxazolidin-2-ones 1.

Silylated cyanohydrins 12a-e were reduced with lithium aluminum hydride in diethyl ether at 0 °C to obtain the corresponding α-dibenzylamino alcohols 13a-e in 77% to 94% yield. Triphosgene (BTC) was used for the cyclization of amino alcohols 13a-e in dichloromethane at room temperature with yields of 35% to 73%. 1,3-Oxazolidin-2-ones 1a-e were obtained in moderate overall yields (15% to 64%, Table 1). Two reaction steps were critical in this synthesis; for the reduction of amino esters 2a-e different reaction times and yields were observed for each amino ester. Those with bulkier R substituent required longer reaction times and were obtained.
in lower yield in the order secbutyl < isopropyl < isobutyl. A similar effect was observed in the cyclization of amino alcohols 13a-e with BTC to form 1,3-oxazolidin-2-ones 1a-e.

**Table 1. Yields in the synthesis of 5-substituted 1,3-oxazolidin-2-ones**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bn</th>
<th>Me</th>
<th>isoPr</th>
<th>isoBu</th>
<th>secBu</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>99</td>
<td>94</td>
<td>60</td>
<td>76</td>
<td>44</td>
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<tr>
<td>3</td>
<td>95</td>
<td>83</td>
<td>97</td>
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<td>96</td>
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<td>12</td>
<td>99</td>
<td>97</td>
<td>82</td>
<td>94</td>
<td>72</td>
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<td>13</td>
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</tr>
<tr>
<td>1</td>
<td>73</td>
<td>67</td>
<td>35</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>Overall yield</td>
<td>64</td>
<td>41</td>
<td>15</td>
<td>39</td>
<td>16</td>
</tr>
</tbody>
</table>

The stereoselectivity in the synthesis of silylated cyanohydrins 12a-e was established by proton NMR chemical shifts and coupling constants. For the trimethylsilylcyanohydrin 12a synthesized using ZnI₂ as catalyst, a doublet signal at 4.46 ppm with \( J = 6.0 \) Hz was assigned to the hydrogen on the new chiral center. When the trimethylsilyl group was removed under mild acid conditions to afford the corresponding cyanohydrins compound,¹¹d the proton NMR signal for the same hydrogen was observed at 4.00 ppm with a \( J = 5.4 \) Hz. Comparing these values with those reported in literature, this compound was found to be the *anti* stereoisomer.¹²a When trimethylsilylcyanohydrin 12a was prepared using MgCl₂ as catalyst, in the proton NMR spectra was observed, in a minor proportion, a doublet signal at 4.34 ppm with \( J = 4.0 \) Hz, which was assigned to the hydrogen on the new chiral center for the *syn* stereoisomer. The addition was completely stereoselective with ZnI₂, but with MgCl₂ a mixture of stereoisomers was obtained (Table 2, entries 1 and 2). For compounds 12b-e only the *anti* stereoisomer was obtained when the addition was catalyzed with ZnI₂.

The stereoselectivity observed in the addition of trimethylsilyl cyanide to \( \alpha \)-dibenzylamino aldehydes 3 was explained in terms of a non-chelating control mechanism proposed by Reetz,¹¹a,¹¹d where the metal ion coordinates with the carbonyl group, but not with the \( \alpha \)-dibenzylamino. Also, the addition resulted to be in line with the Felkin-Ahn model (Figure 1), where the nucleophile approaches in an orthogonal position to the less hindered face of the carbonyl group and opposite to the dibenzylamino group resulting in an *anti* addition selectivity.
Table 2. Addition of trimethylsilyl cyanide to α-dibenzylamino aldehydes 3

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>R</th>
<th>Catalyst</th>
<th>Yield (%)</th>
<th>syn:anti</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12a</td>
<td>Bn</td>
<td>ZnI₂</td>
<td>99</td>
<td>1 : &gt;99</td>
</tr>
<tr>
<td>2</td>
<td>12a</td>
<td>Bn</td>
<td>MgCl₂</td>
<td>98</td>
<td>34 : 66</td>
</tr>
<tr>
<td>3</td>
<td>12b</td>
<td>Me</td>
<td>ZnI₂</td>
<td>97</td>
<td>1 : &gt;99</td>
</tr>
<tr>
<td>4</td>
<td>12c</td>
<td>iPr</td>
<td>ZnI₂</td>
<td>82</td>
<td>1 : &gt;99</td>
</tr>
<tr>
<td>5</td>
<td>12d</td>
<td>iBu</td>
<td>ZnI₂</td>
<td>94</td>
<td>1 : &gt;99</td>
</tr>
<tr>
<td>6</td>
<td>12e</td>
<td>sBu</td>
<td>ZnI₂</td>
<td>72</td>
<td>1 : &gt;99</td>
</tr>
</tbody>
</table>

Figure 1. Felkin-Ahn model for the addition of TMSCN to aldehydes 3.

Finally, the configuration of 1,3-oxazolidin-2-ones 1a-e was confirmed by the correlations of 

The H-5 hydrogen (4.83 ppm, J = 8.6 Hz for 1c) showed coupling with C4α-H (3.62 ppm, J = 8.6 Hz for 1c), C4β-H (3.23 ppm, J = 8.6 Hz for 1c) and with C1`-H (2.58 ppm, J = 8.6, 3.2 Hz for 1c). However, in NOESY experiments C5-H hydrogen showed only one correlation with C4α-H, which demonstrates the stereochemical anti relation between C5-H with C1`-H and with H C4β-H. Similar correlations were observed for the rest of the 1,3-oxazolidin-2-ones 1. Therefore, since the original asymmetric center in α-dibenzylamino ester 2 had an S absolute configuration and had not been involved in any epimerization-promoting processes, the absolute configuration of compounds 1a-e was established as 1`S, 5R.

Conclusions

In this work a new methodology has been developed for the synthesis of enantiopure 5-substituted 1,3-oxazolidin-2-ones with potential biological activity from non-racemic α-dibenzylamino esters in moderate yields and high stereoselectivity. Magnesium chloride and zinc iodide were tested as catalysts in the addition of trimethylsilyl cyanide to α-dibenzylamino
aldehydes showing higher stereo selectivity with zinc iodide in comparison with magnesium chloride or other catalysts reported previously.\textsuperscript{11}

**Experimental Section**

**General Procedures.** All reagents were purchased in the higher quality available and were used without further purification. The solvents used in column chromatography were obtained from commercial suppliers and used without further distillation. Infrared spectra (FTIR) were recorded on a Perkin Elmer FT-IR 1600 spectrophotometer. Nuclear magnetic resonance $^1$H (at 200 MHz) and $^{13}$C (at 50 MHz) spectra were recorded on a Varian Mercury 200 MHz Spectrometer in CDCl$_3$ with TMS as internal standard. Liquid chromatograms were obtained on an Agilent 1100 Series LC with a reverse phase ZORBAX sβ-C18 column (5 mm, 3 x 150 mm) and MSD Trap. Electrospray ionization mass spectra (ESI-MS) were obtained with an ion trap, and the intensities are reported as a percentage relative to the base peak after the corresponding $m/z$ value. HR-MS were obtained in an Agilent LC-TOF (2006), a high resolution TOF analyzer with Windows XP based OS and APCI/ESI ionization. Melting points were obtained on an Electrothermal 88629 apparatus and are uncorrected. Optical rotations were determined using an Autopol III polarimeter.

**General procedure for the synthesis of $\alpha$-dibenzylamino alcohols 11**

To a solution of the $\alpha$-dibenzylamino ester 2 in dry THF was added LiBH$_4$ (2.0 equiv.) at 25°C under argon atmosphere. Then, the reaction mixture was refluxed for 8 h. A saturated NH$_4$Cl solution was added and the mixture stirred for 30 min and then filtered. The liquid phase was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The organic layer was separated and dried over Na$_2$SO$_4$, filtered, and the solvent was evaporated under reduced pressure to give a crude product that was purified by flash chromatography when was necessary.

**(S)-2-Dibenzy lamino-3-phenylpropan-1-ol (11a).** White solid. 99% yield. FTIR (KBr): 3426, 3026, 2958, 1601, 1029 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 200 MHz): δ 7.28 (m, 15H), 4.64 (br s, 1H), 3.91 (d, $J = 13.2$ Hz, 2H), 3.47 (d, $J = 13.2$ Hz, 2H), 3.32 (dd, $J = 10.6$, 4.5 Hz, 1H), 3.10 (m, 3H), 2.42 (dd, $J = 14.0$, 10.6 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 50 MHz): δ 138.8 (C), 138.7 (2 x C), 128.7 (6 x CH), 128.2 (6 x CH), 127.0 (2 x CH), 125.9 (CH), 60.7 (CH), 60.1 (CH$_2$), 53.2 (2 x CH$_2$), 31.7 (CH$_2$). ESI-MS $m/z$: 332 [M+H]$^+$; MS/MS $m/z$ (rel. int.): 240(75), 224(96), 181(100), 117(30). ESI-MS $m/z$: 354 [M+Na]$^+$

**(S)-2-Dibenzylaminopropan-1-ol (11b).** Colorless oil. 94% yield. FTIR (neat): 3421, 3060, 2929, 1601, 1364, 1035 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 200 MHz): δ 7.30 (m, 10H), 4.63 (br s, 1H), 3.81 (d, $J = 13.4$ Hz, 2H), 3.45 (t, $J = 10.6$ Hz, 1H), 3.35 (d, $J = 13.4$ Hz, 2H), 3.34 (dt, $J = 10.6$, 5.6 Hz, 1H), 2.98 (m, 1H), 0.97 (d, $J = 6.6$ Hz, 3H). $^{13}$C NMR (CDCl$_3$, 50 MHz): δ 138.8 (2 x C), 128.7 (4 x CH), 128.2 (4 x CH), 126.9 (2 x CH), 62.5 (CH), 56.0 (CH$_2$), 52.7 (2 x CH$_2$), 8.6
ESI-MS $m/z$: 256 [M+H]$^+$; MS/MS $m/z$ (rel. int.): 181(96), 164(35), 148(60), 91(100). ESI-MS $m/z$: 278 [M+Na]$^+$.

(5S)-2-Dibenzylamo-4-methylpentan-1-ol (11c). Colorless oil. 76% yield. FTIR (neat): 3430, 3027, 2955, 1601, 1364 1068 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 7.27 (m, 10H), 3.88 (d, $J = 13.2$ Hz, 2H), 3.67 (d, $J = 13.2$ Hz, 2H), 3.62 (br s, 1H), 3.57 (dd, $J = 10.6, 4.8$ Hz, 1H), 1.13 (d, $J = 6.6$ Hz, 3H), 0.88 (d, $J = 6.6$ Hz, 3H). $^{13}$C NMR (CDCl$_3$, 50 MHz): $\delta$ 139.7 (2 × C), 128.8 (4 × CH), 128.4 (4 × CH), 127.2 (2 × CH), 64.7 (CH), 59.2 (CH$_2$), 54.2 (2 × CH$_2$), 27.6 (CH), 22.7 (CH$_3$), 22.1 (CH$_3$). ESI-MS $m/z$: 284 [M+H]$^+$; MS/MS $m/z$ (rel. int.): 192(35), 181(90), 120(90), 91(100). ESI-MS $m/z$: 306 [M+Na]$^+$.

General procedure for the synthesis of $\alpha$-dibenzylamo aldehydes 3

To a solution of oxalyl chloride (1.1 equiv.) in dry CH$_2$Cl$_2$ was added dropwise a solution of DMSO (2.2 equiv.) in dry CH$_2$Cl$_2$ at -78 ºC under argon atmosphere and the mixture was stirred for 10 min. Then, a solution of the dibenzylamo alcohol 11 in dry CH$_2$Cl$_2$ was added dropwise and the reaction mixture was stirred for 30 min at the same temperature. After this time, a solution of triethylamine (5 equiv.) in CH$_2$Cl$_2$ was added dropwise and the mixture was stirred for 1 h and allowed to reach room temperature. The organic layer was washed with brine, separated, dried over Na$_2$SO$_4$, and filtered. The solvent was evaporated under reduced pressure to give a crude product that was used in the next reaction without further purification.

(5S)-2-Dibenzylamo-3-methylbutan-1-ol (11d). Colorless oil. 60% yield. FTIR (neat): 3440, 3060, 2952, 1600, 1151, 1030 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 7.27 (m, 10H), 3.80 (d, $J = 13.2$ Hz, 2H), 3.44 (m, 2H), 3.36 (d, $J = 13.2$ Hz, 2H), 3.25 (br s, 1H), 2.84 (m, 1H), 1.51 (m, 2H), 1.15 (m, 1H), 0.91 (d, $J = 6.2$ Hz, 3H), 0.85 (d, $J = 6.4$ Hz, 3H). $^{13}$C NMR (CDCl$_3$, 50 MHz): $\delta$ 139.0 (2 × C), 128.7 (4 × CH), 128.1 (4 × CH), 126.9 (2 × CH), 67.7 (CH), 56.7 (CH$_2$), 52.9 (2 × CH$_2$), 33.9 (CH$_2$), 25.4 (CH), 23.9 (CH$_3$), 22.0 (CH$_3$). ESI-MS $m/z$: 298 [M+H]$^+$; MS/MS $m/z$ (rel. int.): 206(50), 190(96), 181(90), 91(100). ESI-MS $m/z$: 320 [M+Na]$^+$.

(2S,3S)-2-Dibenzylamo-3-methylpentan-1-ol (11e). Colorless oil. 44% yield. FTIR (neat): 3376, 3060, 2962, 1601, 1377, 1070, 1027 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 7.26 (m, 10H), 4.67 (br s, 1H), 3.88 (d, $J = 13.2$ Hz, 2H), 3.59 (d, $J = 13.2$ Hz, 2H), 3.53 (d, $J = 7.2$ Hz, 2H), 2.64 (q, $J = 7.0$ Hz, 1H), 1.87 (m, 1H), 1.60 (m, 1H), 1.25 (m, 1H), 0.90 (d, $J = 4.4$ Hz, 3H), 0.87 (t, $J = 6.6$ Hz, 3H). $^{13}$C NMR (CDCl$_3$, 50 MHz): $\delta$ 139.4 (2 × C), 128.7 (4 × CH), 128.1 (4 × CH), 126.8 (2 × CH), 62.7 (CH), 58.6 (CH$_2$), 53.9 (2 × CH$_2$), 32.7 (CH), 28.3 (CH$_2$), 15.9 (CH$_3$), 11.5 (CH$_3$). ESI-MS $m/z$: 298 [M+H]$^+$; MS/MS $m/z$ (rel. int.): 206(35), 181(95), 120(85), 91(100). ESI-MS $m/z$: 320 [M+Na]$^+$.
C), 129.1 (2 × CH), 128.4 (4 × C), 128.1 (6 × CH), 127.0 (2 × CH), 125.9 (CH), 68.3 (CH), 54.7 (2 × CH2), 30.0 (CH2). ESI-MS \textit{m/z}: 362 [M+MeOH+H]+; MS/MS \textit{m/z} (rel. int.): 344(100), 330(35).

\textbf{(S)-2-Dibenzylaminopropanal (3b)}. Yellow oil. 83% yield. FTIR (neat): 3060, 2807, 2706, 1725, 1372, 1149, 1028 cm\textsuperscript{-1}. \textit{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 200 MHz):} \(\delta\) 9.71 (s, 1H), 7.28 (m, 10H), 3.73 (d, \(J = 13.6\) Hz, 2H), 3.55 (d, \(J = 13.6\) Hz, 2H), 2.77 (q, \(J = 6.6\) Hz, 1H), 1.17 (d, \(J = 6.6\) Hz, 3H). \textit{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 50 MHz):} \(\delta\) 204.0 (CH), 138.7 (2 × C), 128.5 (4 × CH), 128.1 (4 × CH), 127.0 (2 × CH), 62.7 (CH), 54.8 (2 × CH2), 30.0 (CH2). ESI-MS \textit{m/z}: 254 [M+H]+.

\textbf{(S)-2-Dibenzylamino-3-methylbutanal (3c)}. Yellow oil. 97% yield. FTIR (neat): 3060, 2961, 2723, 1728, 1198 cm\textsuperscript{-1}. \textit{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 200 MHz):} \(\delta\) 9.83 (d, \(J = 3.4\) Hz, 1H), 7.32 (m, 10H), 4.01 (d, \(J = 13.6\) Hz, 2H), 3.70 (d, \(J = 13.6\) Hz, 2H), 2.71 (dd, \(J = 10.0, 3.4\) Hz, 1H), 2.25 (m, 1H), 1.07 (d, \(J = 6.6\) Hz, 3H), 0.85 (d, \(J = 6.6\) Hz, 3H). \textit{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 50 MHz):} \(\delta\) 204.6 (CH), 138.8 (2 × C), 128.4 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 71.3 (CH), 54.4 (2 × CH2), 25.9 (CH), 20.1 (CH3), 19.7 (CH3). ESI-MS \textit{m/z}: 282 [M+H]+. ESI-MS \textit{m/z}: 314 [M+MeOH+H]+.

\textbf{(S)-2-Dibenzylamino-4-methylpentanal (3d)}. Yellow oil. 98% yield. FTIR (neat): 3061, 2954, 2706, 1727, 1370, 1145 cm\textsuperscript{-1}. \textit{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 200 MHz):} \(\delta\) 9.74 (s, 1H), 7.31 (m, 10H), 3.78 (d, \(J = 13.8\) Hz, 2H), 3.69 (d, \(J = 13.8\) Hz, 2H), 3.21 (t, \(J = 6.4\) Hz, 1H), 1.56 (m, 3H), 0.82 (d, \(J = 6.6\) Hz, 3H), 0.77 (d, \(J = 6.6\) Hz, 3H). \textit{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 50 MHz):} \(\delta\) 203.5 (CH), 138.9 (2 × C), 128.5 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 32.9 (CH2), 25.1 (CH), 22.6 (CH3), 22.4 (CH3). ESI-MS \textit{m/z}: 296 [M+H]+. ESI-MS \textit{m/z}: 328 [M+MeOH+H]+.

\textbf{(2S,3S)-2-Dibenzylamino-3-methylpentanal (3e)}. Yellow oil. 96% yield. FTIR (neat): 3061, 2964, 2730, 1723, 1207, 1028 cm\textsuperscript{-1}. \textit{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 200 MHz):} \(\delta\) 9.84 (d, \(J = 4.0\) Hz, 1H), 7.31 (m, 10H), 4.00 (d, \(J = 13.7\) Hz, 2H), 3.68 (d, \(J = 13.7\) Hz, 2H), 2.81 (dd, \(J = 9.6, 4.0\) Hz, 1H), 2.07 (m, 1H), 1.87 (m, 1H), 1.19 (m, 1H), 0.84 (d, \(J = 6.6\) Hz, 3H), 0.79 (t, \(J = 7.4\) Hz, 3H). \textit{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 50 MHz):} \(\delta\) 205.0 (CH), 138.8 (2 × C), 128.5 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 69.8 (CH), 54.4 (2 × CH2), 31.9 (CH), 25.4 (CH2), 15.8 (CH3), 10.4 (CH3). ESI-MS \textit{m/z}: 296 [M+H]+; MS/MS \textit{m/z} (rel. int.): 206(35), 181(95), 120(85), 91(100). ESI-MS \textit{m/z}: 328 [M+MeOH+H]+.

\textbf{General procedure for the synthesis of trimethylsilylcyanohydrins 12}

To a solution of aldehyde 3 (1.0 equiv.) in dry CH\textsubscript{2}Cl\textsubscript{2} was added ZnI\textsubscript{2} (1.0 equiv.) at 0°C under argon atmosphere and the mixture was stirred for 10 min. Then, trimethylsilyl cyanide (1.0 equiv.) was added dropwise and the reaction mixture was stirred for 2 h at the same temperature. After this time, water was added and the mixture was stirred for 5 min and allowed to reach room temperature. The organic layer was washed with brine, separated, dried over Na\textsubscript{2}SO\textsubscript{4}, and filtered. The solvent was evaporated under reduced pressure to give a pure crude product that was used in the next reaction without further purification.
(2S,3S)-3-Dibenzylamino-4-phenyl-2-(trimethylsilyloxy)butanenitrile (12a). Colorless oil. 99% yield. FTIR (neat): 3028, 2950, 2368, 1254, 1114, 850 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 200 MHz): \(\delta\) 7.22 (m, 15H), 4.46 (d, \(J = 6.2\) Hz, 1H), 3.72 (br s, 4H), 3.38 (dt, \(J = 8.0, 6.2\) Hz, 1H), 2.99 (m, 2H), 0.17 (s, 9H). \(^13\)C NMR (CDCl\(_3\), 50 MHz): \(\delta\) 138.9 (C), 138.6 (2 × C), 129.1 (2 × C), 128.5 (4 × CH), 128.0 (2 × CH), 127.9 (4 × CH), 126.8 (2 × CH), 126.0 (CH), 119.5 (C), 63.0 (CH), 62.7 (CH), 54.7 (2 × CH\(_2\)), 33.1 (CH\(_2\)), -0.4 (3 × CH\(_3\)). ESI-MS \(m/z\): 429 [M+H]\(^+\); MS/MS \(m/z\) (rel. int.): 311(100), 210(20). ESI-MS \(m/z\): 451 [M+Na]\(^+\).

(2S,3S)-3-Dibenzylamino-2-(trimethylsilyloxy)butanenitrile (12b). Colorless oil. 97% yield. FTIR (neat): 3061, 2959, 2212, 1253, 1092, 845 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 200 MHz): \(\delta\) 7.43 (m, 10H), 4.47 (d, \(J = 8.8\) Hz, 1H), 3.87 (d, \(J = 13.6\) Hz, 2H), 3.64 (d, \(J = 13.6\) Hz, 2H), 3.24 (m, 1H), 1.24 (d, \(J = 6.6\) Hz, 3H), 0.14 (s, 9H). \(^13\)C NMR (CDCl\(_3\), 50 MHz): \(\delta\) 139.0 (2 × C), 128.8 (4 × CH), 128.4 (4 × CH), 120.0 (C), 65.2 (CH), 57.6 (CH), 55.1 (2 × CH\(_2\)), 9.5 (CH\(_3\)), 0.08 (3 × CH\(_3\)). ESI-MS \(m/z\): 353 [M+H]\(^+\). ESI-MS \(m/z\): 375 [M+Na]\(^+\).

(2S,3S)-3-Dibenzylamino-4-methyl-2-(trimethylsilyloxy)pentanenitrile (12c). Colorless oil. 82% yield. FTIR (neat): 3062, 2957, 2218, 1250, 1085, 840 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 200 MHz): \(\delta\) 7.32 (m, 10H), 4.77 (d, \(J = 4.4\) Hz, 1H), 4.19 (d, \(J = 13.2\) Hz, 2H), 3.73 (d, \(J = 13.2\) Hz, 2H), 2.66 (dd, \(J = 10.6, 5.8\) Hz, 1H), 2.15 (m, 1H), 1.02 (d, \(J = 6.6\) Hz, 3H), 0.97 (d, \(J = 6.6\) Hz, 3H), 0.27 (s, 9H). \(^13\)C NMR (CDCl\(_3\), 50 MHz): \(\delta\) 138.9 (2 × C), 129.2 (4 × CH), 128.5 (4 × CH), 127.4 (2 × CH), 119.9 (C), 64.6 (CH), 59.3 (CH), 54.6 (2 × CH\(_2\)), 28.9 (CH), 22.4 (CH\(_3\)), 20.1 (CH\(_3\)), -0.2 (3 × CH\(_3\)). ESI-MS \(m/z\): 367 [M-Me+2H]\(^+\); MS/MS \(m/z\) (rel. int.): 325(95), 275(100), 199(10).

(2S,3S)-3-Dibenzylamino-5-methyl-2-(trimethylsilyloxy)hexanenitrile (12d). Colorless oil. 94% yield. FTIR (neat): 3061, 2957, 2212, 1250, 1085, 840 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 200 MHz): \(\delta\) 7.34 (m, 10H), 4.45 (d, \(J = 4.8\) Hz, 1H), 4.19 (d, \(J = 13.2\) Hz, 2H), 3.73 (d, \(J = 13.2\) Hz, 2H), 2.66 (dd, \(J = 10.6, 5.8\) Hz, 1H), 2.15 (m, 1H), 1.02 (d, \(J = 6.6\) Hz, 3H), 0.97 (d, \(J = 6.6\) Hz, 3H), 0.27 (s, 9H). \(^13\)C NMR (CDCl\(_3\), 50 MHz): \(\delta\) 139.0 (2 × C), 128.6 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 119.8 (C), 63.2 (CH), 58.8 (CH), 54.6 (2 × CH\(_2\)), 36.4 (CH\(_2\)), 25.0 (CH), 23.3 (CH\(_3\)), 22.0 (CH\(_3\)), -0.4 (3 × CH\(_3\)). ESI-MS \(m/z\): 395 [M+H]\(^+\). ESI-MS \(m/z\): 417 [M+Na]\(^+\). ESI-MS \(m/z\): 381 [M-Me+2H]\(^+\); MS/MS \(m/z\) (rel. int.): 290(100), 248(10), 213(12), 157(10).

(2S,3S,4S)-3-Dibenzylamino-4-methyl-2-(trimethylsilyloxy)hexanenitrile (12e). Colorless oil. 94% yield. FTIR (neat): 3061, 2955, 2228, 1255, 1106, 848 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 200 MHz): \(\delta\) 7.33 (m, 10H), 4.78 (d, \(J = 4.8\) Hz, 1H), 3.87 (d, \(J = 13.6\) Hz, 2H), 3.65 (d, \(J = 13.6\) Hz, 2H), 3.65 (s, 9H), 3.00 (m, 1H), 1.75 (m, 2H), 1.25 (m, 1H), 0.90 (d, \(J = 6.6\) Hz, 3H), 0.70 (d, \(J = 6.6\) Hz, 3H), 0.20 (s, 9H). \(^13\)C NMR (CDCl\(_3\), 50 MHz): \(\delta\) 139.1 (2 × C), 128.6 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 119.8 (C), 63.2 (CH), 58.8 (CH), 54.6 (2 × CH\(_2\)), 36.4 (CH\(_2\)), 25.0 (CH), 23.3 (CH\(_3\)), 22.0 (CH\(_3\)), -0.4 (3 × CH\(_3\)). ESI-MS \(m/z\): 395 [M+H]\(^+\). ESI-MS \(m/z\): 417 [M+Na]\(^+\). ESI-MS \(m/z\): 381 [M-Me+2H]\(^+\); MS/MS \(m/z\) (rel. int.): 290(100), 248(10), 213(12), 157(10).

General procedure for the synthesis of α-dibenzylamino amino alcohols 13

To a solution of trimethylsilylcyanohydrins 12 (1.0 equiv.) in dry THF was added drop wise a solution of LiAlH\(_4\) (2.0 equiv.) in dry diethyl ether at 0°C under argon atmosphere and stirred for 5 h at same temperature. Then, a 5% KOH solution was added drop wise until a white solid was
form and the reaction mixture was filtered. The organic layer was dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure to give a crude product that was used in the next reaction without further purification.

**(**2R,3S)-1-Amino-3-dibenzylamino-4-phenylbutan-2-ol (13a).** Colorless oil. 94% yield. FTIR (neat): 3365, 3299, 2926, 1600, 1251, 1110 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.21 (m, 15H), 4.63 (s, 1H), 3.93 (dd, J = 13.4, 9.4 Hz, 1H), 3.70 (d, J = 13.6 Hz, 2H), 3.57 (d, J = 13.6 Hz, 2H), 3.43 (dd, J = 15.0, 13.4 Hz, 1H), 2.82 (m, 4H), 1.96 (br s, 2H). ¹³C NMR (CDCl₃, 50 MHz): δ 141.1 (C), 139.5 (2 × C), 129.1 (2 × CH), 128.5 (4 × CH), 128.2 (2 × CH), 127.9 (4 × CH), 126.6 (2 × CH), 125.5 (CH), 72.0 (CH), 61.4 (CH), 54.4 (2 × CH₂), 44.6 (CH₂), 32.5 (CH₂). ESI-MS m/z: 361 [M+H]+; MS/MS m/z (rel. int.): 344(98), 300(20), 210 (100).

**(**2R,3S)-1-Amino-3-dibenzylaminobutan-2-ol (13b).** Colorless oil. 81% yield. FTIR (neat): 3363, 3284, 3027, 2958, 1578, 1076 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.25 (m, 10H), 4.59 (s, 1H), 3.65 (d, J = 13.6 Hz, 2H), 3.62 (dd, J = 11.0, 5.8 Hz, 1H), 3.43 (m, 1H), 3.31 (d, J = 13.6 Hz, 2H), 2.76 (dd, J = 11.0, 6.4 Hz, 1H), 2.55 (q, J = 6.6 Hz, 1H), 1.76 (br s, 2H), 1.10 (d, J = 6.6 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 140.3 (2 × C), 129.1 (4 × CH), 128.5 (4 × CH), 127.2 (2 × CH), 73.5 (CH), 65.6 (CH), 54.7 (2 × CH₂), 44.6 (CH₂), 12.1 (CH₃). ESI-MS m/z: 286 [M+H]+; MS/MS m/z (rel. int.): 268(100), 199(5), 91(10).

**(**2R,3S)-1-Amino-3-dibenzylamino-5-methylhexan-2-ol (13c).** Colorless oil. 92% yield. FTIR (neat): 3342, 3283, 3061, 2955, 1601, 1361, 1068 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.24 (m, 10H), 3.87 (d, J = 13.2 Hz, 2H), 3.76 (s, 1H), 3.66 (d, J = 13.2 Hz, 2H), 3.56 (dd, J = 10.6, 4.8 Hz, 1H), 3.42 (t, J = 10.6 Hz, 1H), 3.19 (br s, 2H), 2.52 (m, 1H), 2.06 (m, 1H), 1.12 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 139.7 (2 × C), 128.9 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 70.5 (CH), 64.0 (CH), 55.1 (2 × CH₂), 44.7 (CH₂), 26.3 (CH), 23.6 (CH₃), 20.1 (CH₃). ESI-MS m/z: 313 [M+H]+; MS/MS m/z (rel. int.): 296(100), 278(5), 199(10), 91(7).

**(**2R,3S)-1-Amino-3-dibenzylamino-5-methylhexan-2-ol (13d).** Colorless oil. 89% yield. FTIR (neat): 3345, 3289, 3060, 2955, 1601, 1376, 1061, 1027 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.24 (m, 10H), 3.76 (m, 1H), 3.63 (s, 1H), 3.62 (br s, 4H), 3.38 (dd, J = 13.2, 11.8 Hz, 1H), 2.76 (dd, J = 12.6, 3.8 Hz, 1H) 2.66 (m, 3H), 1.60 (m, 1H), 1.83 (br s, 2H), 0.91 (d, J = 6.6 Hz, 3H), 0.73 (d, J = 6.4 Hz, 2H), 0.73 (d, J = 6.4 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 139.7 (2 × C), 128.7 (4 × CH), 127.9 (4 × CH), 126.6 (2 × CH), 71.4 (CH), 56.8 (CH), 54.6 (2 × CH₂), 44.9 (CH₂), 35.5 (CH₂), 25.2 (CH), 23.2 (CH₃), 22.7 (CH₃). ESI-MS m/z: 327 [M+H]+; MS/MS m/z (rel. int.): 327(100), 310(45), 198(30).

**(**2R,3S,4S)-1-Amino-3-dibenzylamino-4-methylhexan-2-ol (13e).** Colorless oil. 77% yield. FTIR (neat): 3345, 3289, 3060, 2955, 1601, 1376, 1061, 1027 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.24 (m, 10H), 3.75 (d, J = 13.2 Hz, 2H), 3.73 (m 2H), 3.63 (s, 1H), 3.54 (d, J = 13.2 Hz, 2H), 2.65 (dd, J = 13.6, 7.0 Hz, 1H), 2.44 (dd, J = 7.6, 4.6 Hz, 1H), 2.24 (m, 1H), 2.03 (br s, 2H), 1.90 (m, 1H), 1.65 (m, 1H), 1.08 (d, J = 6.6 Hz, 3H), 0.95 (t, J = 7.6 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 139.7 (2 × C), 128.8 (4 × CH), 128.0 (4 × CH), 126.8 (2 × CH), 70.1 (CH), 62.5 (CH), 54.8 (2 × CH₂), 44.6 (CH₂), 32.4 (CH), 29.8 (CH₂), 16.1 (CH₃), 12.2 (CH₃). ESI-MS m/z: 327 [M+H]+; MS/MS m/z (rel. int.): 309(100), 292(10), 198(35), 91(5).
General procedure for the synthesis of 1,3-oxazolidin-2-ones 1

To a solution of amino alcohol 13 in dry CH₂Cl₂ was added dropwise a solution of triphosgene (1.0 equivalent) in dry CH₂Cl₂ at 0 °C. Then, the reaction mixture was stirred at room temperature for 8 h. A saturated NaHCO₃ solution was added and the mixture was stirred for 30 min and then was extracted with dichloromethane (3 × 20 mL). The organic layer was separated, dried over Na₂SO₄, and filtered. The solvent was evaporated under reduced pressure to give a crude product that was purified by flash chromatography.

(R)-5-((S)-1-Dibenzylamino-2-phenylethyl)-1,3-oxazolidin-2-one (1a). White solid. 73% yield. Mp 102 °C. *R* 0.50 (ethyl acetate/petroleum ether 1/1); [α]D²⁰ = +8.0° (c 1.00, CHCl₃). FTIR (KBr): 3283, 3026, 2931, 1754, 1368, 1240 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.21 (m, 15H), 5.91 (br s, 1H), 4.80 (m, 1H), 3.62 (br s, 4H), 3.52 (t, *J* = 8.8 Hz, 1H), 3.08 (t, *J* = 8.8 Hz, 1H), 3.06 (br s, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 159.6 (C), 139.5 (C), 138.8 (2 × C), 129.3 (2 × CH), 128.4 (4 × CH), 128.1 (2 × CH), 127.9 (4 × CH), 126.8 (2 × CH), 126.0 (CH), 76.8 (CH), 62.4 (CH), 54.4 (2 × CH₂), 44.8 (CH₂), 32.4 (CH₂). ESI-MS m/z: 387 [M+H]+; MS/MS m/z (rel. int.): 326(75), 295(100), 181(40). HPLC: 0.8 mL/min; 70:30 MeOH/H₂O; *t*ₕ: 6.3 min. HRMS calculated for [C₂₅H₂₆N₂O₂ + H]⁺ 387.2073. Found 387.2075.

(R)-5-((S)-1-Dibenzylaminoethyl)oxazolidin-2-one (1b). White solid. 67% yield. Mp 95 °C. *R* 0.48 (ethyl acetate/petroleum ether 1/1); [α]D²⁰ +21.2° (c 1.00, CHCl₃). FTIR (KBr): 3254, 2826, 1748, 1239 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.25 (m, 10H), 5.84 (br s, 1H), 4.46 (q, *J* = 8.6 Hz, 1H), 3.70 (d, *J* = 13.6 Hz, 2H), 3.54 (t, *J* = 8.6 Hz, 1H), 3.43 (d, *J* = 13.6 Hz, 2H), 3.23 (t, *J* = 8.6 Hz, 1H), 2.82 (dd, *J* = 8.6, 6.6 Hz, 1H), 1.22 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 159.7 (C), 138.8 (2 × C), 128.7 (4 × CH), 128.1 (4 × CH), 127.0 (2 × CH), 78.3 (CH), 56.5 (CH), 54.4 (2 × CH₂), 44.7 (CH₂), 8.6 (CH₃). ESI-MS m/z: 311 [M+H]+; MS/MS m/z (rel. int.): 250(50), 219(100), 181(93), 91(60). HPLC: 0.8 mL/min; 70:30 MeOH/H₂O; *t*ₕ: 5.8 min. HRMS calculated for [C₁₉H₂₂N₂O₂ + H]⁺ 311.1760. Found 311.1758.

(R)-5-((S)-1-Dibenzylamino-2-methylpropyl)oxazolidin-2-one (1c). White solid. 35% yield. Mp 45 °C. *R* 0.55 (ethyl acetate/petroleum ether 1/1); [α]D²⁰ = -9.0° (c 1.00, CHCl₃). FTIR (KBr): 3284, 2958, 1752, 1239 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.25 (m, 10H), 5.73 (br s, 1H), 4.83 (q, *J* = 8.6 Hz, 1H), 3.67 (d, *J* = 13.4 Hz, 2H), 3.62 (t, *J* = 8.6 Hz, 1H), 3.55 (d, *J* = 13.4 Hz, 2H), 3.23 (t, *J* = 8.6 Hz, 1H), 2.58 (dd, *J* = 8.6, 3.2 Hz, 1H), 2.33 (m, 1H), 1.13 (d, *J* = 7.4 Hz, 3H), 1.09 (d, *J* = 7.4 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 159.7 (C), 138.8 (2 × C), 128.7 (4 × CH), 128.1 (4 × CH), 127.0 (2 × CH), 78.3 (CH), 56.5 (CH), 54.4 (2 × CH₂), 44.7 (CH₂), 8.6 (CH₃), 64.1 (CH), 54.6 (2 × CH₂), 45.5 (CH₂), 25.1 (CH₂), 23.3 (CH₃), 19.0 (CH₃). ESI-MS m/z: 339 [M+H]+; MS/MS m/z (rel. int.): 283(100), 247(40), 188(45). HPLC: 0.8 mL/min; 70:30 MeOH/H₂O; *t*ₕ: 5.8 min. HRMS calculated for [C₂₁H₂₆N₂O₂ + H]⁺ 339.2073. Found 339.2071.

(R)-5-((S)-1-Dibenzylamino-3-methylbutyl)-1,3-oxazolidin-2-one (1d). White solid. 62% yield. Mp 43 °C. *R* 0.52 (ethyl acetate/petroleum ether 1/1); [α]D²⁰ = -30.9° (c 1.00, CHCl₃). FTIR (KBr): 3277, 3028, 1753, 1240, 1080 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz): δ 7.27 (m, 10H), 6.09
(br s, 1H), 4.75 (m, 1H), 3.72 (d, $J = 13.8$ Hz, 2H), 3.58 (t, $J = 8.4$ Hz, 1H), 3.55 (d, $J = 13.8$ Hz, 2H), 3.12 (t, $J = 8.4$ Hz, 1H), 2.67 (q, $J = 7.0$ Hz, 1H), 1.96 (hpt, $J = 6.6$ Hz, 1H), 1.73 (q, $J = 7.0$ Hz, 1H), 1.27 (m, 1H), 0.92 (d, $J = 6.6$ Hz, 3H), 0.73 (d, $J = 6.2$ Hz, 3H).

$^{13}$C NMR (CDCl$_3$, 50 MHz): $\delta$ 159.9 (C), 139.2 (2 × C), 128.6 (4 × CH), 128.0 (4 × CH), 126.9 (2 × CH), 76.8 (CH), 58.2 (CH), 54.4 (2 × CH$_2$), 44.9 (CH$_2$), 35.1 (CH$_2$), 24.7 (CH), 23.3 (CH$_3$), 22.4 (CH$_3$). ESI-MS m/z: 353 [M+H]$^+$; MS/MS m/z (rel. int.): 261(100), 202(75), 181(80).

HPLC: 0.8 mL/min; 70:30 MeOH/H$_2$O; $t_R$: 6.8 min. HRMS calculated for [C$_{22}$H$_{28}$N$_2$O$_2$ + H]$^+$ 353.2229. Found 353.2226.

(R)-5-((1S,2S)-1-Dibenzylamino-2-methylbutyl)oxazolidin-2-one (1e). White solid. 66% yield. Mp 42 °C. $R_f$ 0.62 (ethyl acetate/petroleum ether 1/1); $\left[\alpha\right]_{D}^{20} = +11.5^\circ$ (c 1.00, CHCl$_3$).

FTIR (KBr): 3277, 2961, 1752, 1237, 1077 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 7.27 (m, 10H), 5.49 (br s, 1H), 4.86 (q, $J = 8.4$ Hz, 1H), 3.73 (d, $J = 13.6$ Hz, 2H), 3.66 (t, $J = 8.4$ Hz, 1H), 3.48 (d, $J = 13.6$ Hz, 2H), 3.26 (t, $J = 8.4$ Hz, 1H), 2.66 (dd, $J = 9.0$, 1.6 Hz, 1H), 2.03 (m, 1H), 1.44 (m, 2H), 1.14 (d, $J = 7.0$ Hz, 3H), 0.93 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (CDCl$_3$, 50 MHz): $\delta$ 159.9 (C), 139.2 (2 × C), 129.0 (4 × CH), 128.4 (4 × CH), 127.3 (2 × CH), 75.4 (CH), 63.6 (CH), 54.7 (2 × CH$_2$), 45.7 (CH$_2$), 31.7 (CH), 30.0 (CH), 15.6 (CH$_3$), 12.4 (CH$_3$). ESI-MS m/z: 353 [M+H]$^+$; MS/MS m/z (rel. int.): 283(100), 202(45). HPLC: 0.8 mL/min; 70:30 MeOH/H$_2$O; $t_R$: 8.4 min. HRMS calculated for [C$_{22}$H$_{28}$N$_2$O$_2$ + H]$^+$ 353.2229. Found 353.2225.

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References


