## A New Diastereoselective Synthetic Approach to the Enantiopure Peptidomimetic Scaffold 2-Oxo-1-azabicyclo[4.4.0]decane

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A general method for the synthesis of unsubstituted and C-7substituted azabicyclo[4.4.0]decane dipeptides (23, 30a, and 30b) that can serve as dipeptide mimetics has been developed. The key step of this new method involves the coupling

### Introduction

Over the past ten years the synthesis of enantiopure bicyclic dipeptides, and azabicycloalkanes in particular, has been extensively explored.<sup>[1,2]</sup> These structures, due to their constrained backbone and thus reinforced metabolic stability, have been proven to be useful for many studies on bindings of peptides to various receptors and have served as interesting probes for the understanding of the conformational requirements of the studied peptides.<sup>[3-7]</sup>

Most of the syntheses described in the literature have aimed at the preparation of the 5,6-fused<sup>[8-24]</sup> and 5,7fused<sup>[8,9,19,24-32]</sup> systems (Figure 1). Other research groups have focused on the 5,5-fused type,<sup>[19-33]</sup> while the 6,6-fused system has remained seldom explored. To the best of our knowledge, only one synthesis of an azabicyclo[4.4.0]decane dipeptide has been reported by Gosselin and Lubell.<sup>[30-34]</sup> This quinolizidinone-type dipeptide shows an excellent affinity for the opioid-like receptor (ORL1) in some recent studies,<sup>[3]</sup> and thus represents a target of choice for general synthetic methods. The possibility of incorporation of substituents on the backbone of such motifs could provide a



Figure 1. Some examples of azabicycloalkanes.

reaction of the oxazolidine aldehyde **5** and the sulfone **7**, both of which are derived from L-glutamic acid. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2005)

range of valuable constrained dipeptides. We now wish to report a new general method for the preparation of azabicy-clo[4.4.0]decane dipeptides.

### **Results and Discussion**

The strategy envisaged to synthesize the azabicyclo[4.4.0]decane scaffold is based on the condensation of two chiral units – an aldehyde and a newly prepared sulfone – both derived from L-glutamic acid. A C–C bond formation by the coupling of the  $\alpha$ -sulfonyl carbanion with this aldehyde, followed by the transformation of the adduct to a  $\beta$ -keto sulfone, would provide the backbone for constructing the desired bicyclic lactam with eventual alkylation at the C-7 position (Scheme 1).

Aldehyde **5** has been previously synthesized from L-glutamic acid,<sup>[35]</sup> albeit without any detailed protocols or full characterization of all the intermediate compounds. Thus, commercially available **1** was submitted to regioselective reduction of the  $\alpha$ -carboxylic acid moiety using the procedure described by Ohfune and co-workers<sup>[36]</sup> to afford **2** in 82% yield (Scheme 2). This alcohol was subsequently protected as the oxazolidine **3** in 92% yield according to a known protocol.<sup>[37]</sup> Compound **3** was reduced to **4** in 96% yield by treatment with LiAlH<sub>4</sub> in THF. The resulting alcohol was finally submitted to Swern oxidation to give the desired aldehyde **5** in 98% yield.

The chiral sulfone **7** was developed as a logical extension of our previous work,<sup>[38–41]</sup> and is a homologue of synthon **6**, derived from L-serine (Scheme 3). It was prepared as shown in Scheme 4: *N*-Cbz-protected L-glutamic acid **8** was converted in 98% yield into its dimethyl ester **9** using the procedure described by Watanabe and co-workers<sup>[42]</sup> (BF<sub>3</sub> etherate in MeOH). Compound **9** was reduced with LiBH<sub>4</sub> and three equivalents of methanol in THF to afford **10** in 79% yield. The diol **10** was then transformed into oxazolidine **11** in 88% yield by treatment with dimethoxypropane

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Scheme 1.





5

Scheme 2.



Scheme 3.

in the presence of a catalytic amount of *p*-toluenesulfonic acid in dichloromethane. Alcohol **11** was mesylated and readily converted to sulfone **12** in a novel one-pot procedure: the mesylate was first converted to its phenyl sulfide by treatment with sodium thiophenolate in THF followed by addition of magnesium monoperoxy phthalate (MMPP) to afford **12**. Cleavage of the oxazolidine ring of crude **12** and subsequent treatment of the resulting alcohol **13** with *tert*-butyldiphenylsilyl chloride (TBDPSCI) provided *tert*-butyldiphenylsilyloxy derivative **7** (in 87% yield from **11**).

As the synthesis of aldehyde 5 and sulfone 7 involves the borohydride reductions of an activated ester and a diester,

respectively, the possibility of epimerization of a potential  $\alpha$ -amino aldehyde intermediate must be taken into account. In previous work, the  $\alpha$ -carboxylic function of a number of  $\alpha$ -amino acids has been converted into a hydroxy function by this method. In those cases, these reductions were considered as racemization-free. However, no studies have been reported on the enantiomeric purity of these particular potentially valuable aldehyde  $5^{[43]}$  or alcohol 11.<sup>[44]</sup> Therefore, we decided to determine their optical purity by the following method: the pairs of Mosher esters of 4 and 11 [(2*S*,8*R*)-14 and (2*S*,8*S*)-15 and (2*S*,8*R*)-16 and (2*S*,8*S*)-17, respectively], were synthesized (Figure 2).<sup>[45]</sup> Unfortunately, the



Scheme 4.

determination of the diastereomeric excess could not be achieved by HPLC due to the fact that the mixture of diastereomers was inseparable on every achiral column we had in our possession.<sup>[46]</sup> As was to be expected in the case of such compounds, the <sup>1</sup>H NMR spectra of each pair of diastereomers presented a rather poor resolution in several solvents,<sup>[47]</sup> in particular around the methoxy chemical shift area. This observation is mainly due to the existence of two conformers (a well-known phenomenon, especially in the case of five-membered rings),<sup>[48,49]</sup> which arise from the strong steric hindrance between the Boc (or Cbz) and the oxazolidine dimethyl groups. Indeed, a fast rotation of the carbamate is hardly possible and thus engenders the existence of two distinct rotamers. As a consequence, the NMR spectra of this kind of compound, in general, will feature signal overlapping, splitting and broadening. The <sup>19</sup>F NMR spectrum finally allowed us to shed light on the excellent enantiomeric purity of both compounds. In the case of 14 and 15, each compound shows a set of two signals at  $\delta$  = -72.00 and -72.12 ppm, and at  $\delta = -72.04$  and -72.15 ppm, respectively.<sup>[50]</sup> The spectrum of the mixture of 14 and 15 displays the two sets of signals at exactly the same chemical shifts corresponding to the four rotamers. In the case of 16 and 17, overlapping of the signals gave rise to some difficulties, but the choice of deuterated acetonitrile as the solvent finally allowed us to overcome this problem and get rid of the splitting of the signals generated by the rotamers. We were pleased to observe that 16 and 17 both appear as a single peak (at  $\delta = -72.71$  and -72.78 ppm, respectively), and the spectrum of their mixture exhibits these two distinct

signals. Based on the results of the above experiments, we can now assume that the enantiomeric purity of aldehyde 5 and sulfone 7 is more than 95%.<sup>[51]</sup>



Figure 2. Mosher esters synthesized for the determination of the enantiomeric purity of alcohols 4 and 11.

The coupling of **5** and **7** was achieved under classical anionic reaction conditions: formation of the dianion by treatment with butyllithium in THF at -78 °C was followed by the addition of aldehyde **5** to provide the desired hydroxysulfone **18** in 85% yield (Scheme 5). Both oxidative cleavage of the oxazolidine and oxidation of the secondary alcohol could be smoothly achieved in a single step using



Scheme 5.

Jones' reagent, yielding 76% of 19. Desulfonylation was then undertaken; it was our speculation that the presence of an epimerizable center such as the  $\alpha$ -carbon of the carboxylic acid could cause some problems during this step considering the basic reaction conditions commonly employed. Indeed, when desulfonylation was carried out using sodium amalgam in methanol, a 50:50 mixture of two diastereomers was obtained. While searching for milder conditions, we determined that, under rather vigorous hydrogenolysis conditions, although neutral from an acidobasic point of view, the sulforyl and the benzyloxycarbonyl groups could be simultaneously removed to allow reductive amination to take place. Thus, keto sulfone 19 was treated with Raney nickel in refluxing ethanol to provide the desired cyclic dipeptide 20 in 85% yield. The lactam formation was accomplished using the common reagents EDCI and HOBt in DMF and 21 was isolated as a single isomer in 77% yield. Finally, the alcohol deprotection to afford 22 followed by TEMPO/NaOCl oxidation<sup>[52]</sup> furnished the carboxylic acid which was, in turn, converted to methyl ester 23 in 84% yield (two steps).

Incorporation of substituents on the scaffold backbone is quite a demanding task, especially because of the problems in terms of stereoselectivity. As an application of the method described above for the synthesis of such peptidomimetic scaffolds, we decided to append a methyl group at the C-7 position to mimic an Ala-Nle (physiological equivalent of Ala-Met<sup>[53]</sup>) dipeptide unit (Scheme 6). Intermediate **18** was oxidized with *o*-iodoxybenzoic acid (IBX) to give keto sulfone **24**. Treatment with K<sub>2</sub>CO<sub>3</sub> and methyl iodide in DMF gave rise to the desired product **25** methylated at the  $\alpha$ -sulfonyl carbon position in an excellent 97% yield. Approximately the same sequence as the one discussed above for the unsubstituted azabicyclo[4.4.0]decane dipeptide was then effected. An oxidative cleavage of oxazolidine 25 provided 26, and the desulfonylation-deprotection-reductive amination sequence yielded 27 in 82%. After cyclization by intramolecular peptide-bond formation, a 5:1 mixture of two diastereomers was obtained. This mixture was easily separated by column chromatography on silica gel to afford 28a and 28b in 78% yield. Deprotection was then carried out on each of the two isomers with TBAF in THF. The final oxidation step under either Jones or TEMPO/NaOCl conditions failed and gave unidentifiable and inseparable mixtures. To our delight, this difficulty was surmounted by using NaIO<sub>4</sub>/RuCl<sub>3</sub> hydrate as the oxidising agent<sup>[54]</sup> to provide the carboxylic acid. The obtained acid was directly esterified with (trimethylsilyl)diazomethane to provide 30a and 30b in 69% yield.

The configuration at the ring-fusion center of **23** was tentatively determined by NOESY experiments.<sup>[55]</sup> Molecular modeling of the two possible diastereomers indicated that, in the case of the (6*S*)-isomer, the hydrogen atom H<sup>6</sup> is too distant from H<sup>3</sup> or H<sup>10</sup> to exhibit any NOE (Figure 3). However, NOEs were observed between H<sup>6</sup> ( $\delta$  = 3.46 ppm) and H<sup>3</sup> and/or H<sup>10</sup> (overlapped at  $\delta$  = 4.10 ppm). This allowed us to assign the (3*S*,6*R*,10*S*) configuration to this compound.

The configuration of the new stereogenic centers of **30a** and **30b** was determined in the same manner (Figure 3). The experiments were conducted with the silyloxy derivatives **28a** and **28b**, for which the <sup>1</sup>H NMR spectra present no overlapping for most of the signals. Out of the four diastereomers that were studied by molecular modeling, **31** and **32** were readily discarded as, for both compounds, NOEs were observed between H<sup>3</sup>, H<sup>6</sup> and H<sup>10</sup>, whereas **31** and **32** 



Figure 3. NOE-assisted determination of the absolute configuration of the C-6 and C-7 stereocenters of the azabicyclo[4.4.0]decanes 23, 30a, and 30b.

Scheme 6.

clearly cannot exhibit any NOE for those hydrogen atoms ( $\delta = 4.16$ , 3.58 and 4.00 ppm and  $\delta = 4.03$ , 3.05 and 3.73 ppm for **28a** and **28b**, respectively), as confirmed by the average values of the hydrogen–hydrogen distances (around 4 Å) according to molecular modeling. Moreover, the major compound shows a very strong NOE between H<sup>6</sup> ( $\delta = 3.58$  ppm) and H<sup>7</sup> ( $\delta = 1.96$  ppm), and no detectable NOE between H<sup>6</sup> and the methyl group at C-7 ( $\delta = 0.90$  ppm). On the contrary, the minor isomer displays a strong NOE between H<sup>6</sup> ( $\delta = 3.05$  ppm) and the methyl group at C-7 ( $\delta = 0.87$  ppm), and no signal is detected between H<sup>6</sup> and H<sup>7</sup> ( $\delta = 1.64$  ppm). As these observations are in agreement with the values obtained from the molecular modeling calculations, a (3S, 6S, 7S, 10S) configuration to **28b**.

Now that the stereochemistry of **23**, **30a**, and **30b** has been assigned, the observed diastereoselectivity deserves some comments. The step involving the Raney nickel catalyst is quite remarkable in the sense that three steps are accomplished in one-pot: the cleavage of the *N*-benzylcarbamate, the reductive amination and the desulfonylation. It has been reported that reductive amination can be achieved easily at room temperature with the Raney nickel catalyst,<sup>[56,57]</sup> whereas the desulfonylation step requires the reaction mixture to be refluxed for several hours. Besides, it is to be assumed that the reductive amination takes place only after the carbamate group is cleaved. The question arises whether or not the desulfonylation process occurs prior to the amine deprotection. As the alkylation of the keto sulfone **24** afforded a 50:50 mixture of diastereomers,<sup>[58]</sup> this ratio should have been reflected in the final compounds **30a** and **30b**. However, the observed ratio was 5:1, which suggests that the desulfonylation proceeds after the cyclization,<sup>[59–61]</sup> and should be the last step of the sequence.

The stereochemical outcome observed for 23, 30a, and 30b can be explained by the following hypothesis. The iminium intermediate 33 leading to piperidine 20 can exist as two pairs of conformers<sup>[62]</sup> (34/35 and 40/41) as shown in Figure 4. Of the eight possible resulting products, 38, 39, 42, and 43 require boatlike transition states and are disfavored kinetically. Furthermore, 36 and 37 suffer from a severe 1,3-diaxial interaction between the bulky *tert*-butyldiphenylsilyloxymethyl substituent and the incoming hydrogen donor, therefore 44 and 45 are the more favored pos-



Figure 4. Reactive intermediates possibly involved in the reductive amination step.



Figure 5. The 1,3-diaxial interaction between the electronic lone pairs explaining the observed ratio of diastereomers.

sibilities and explain the stereochemistry of the resulting lactam **21**. It should be noted that the selectivity of the nucleophilic attack does not depend on the conformational position of the phenylsulfonyl group. Therefore, if the  $\alpha$ -sulfonyl hydrogen of **33** is replaced by a methyl group, the same conclusion accounts for the stereochemistry observed at C-6 of **28a** and **28b**.

On the other hand, the cause for the observed ratio of the C-7 isomers for 30a and 30b is not obvious. Although the mechanism of desulfonylation with Raney nickel has been investigated in the past,<sup>[63,64]</sup> unambiguous evidence about the nature of the reactive intermediate is still lacking.<sup>[65]</sup> The problem is to choose between a free radical, an anionic mechanism, or a concerted mechanism, while a cationic intermediate seems the least likely. In our case, a concerted mechanism cannot account for the observed ratio. A proposal explaining the formation of the major isomer would be a 1,3-diaxial electronic repulsion between the lone pair of the nitrogen and the anion generated by the cleavage of the phenylsulfone group (Figure 5). The more stable conformation would then be the one involving an axial position of the methyl group, and would lead to the major isomer.

#### Conclusions

In conclusion, we have developed a general method for the synthesis of enantiopure 6,6-fused 1-azabicyclo[4.4.0]decane dipeptides. We have also demonstrated the versatility of our new approach by synthesizing quinolizidinone dipeptides **30a** and **30b** substituted at the C-7 position. The incorporation of such substituted units could provide beneficial information on the prerequisites of biologically active peptides. The preparation of 5,7-fused systems is also under investigation, and could be possible from the orthogonally protected intermediate **18**.

### **Experimental Section**

**General Remarks:** Tetrahydrofuran was distilled from sodium benzophenone ketyl, and dichloromethane from  $P_2O_5$  immediately prior to use. All reagents obtained from commercial sources were used without purification, unless otherwise specified. All reactions were conducted under argon. Flash column chromatography was performed using Kieselgel 60 (230–400 mesh, E. Merck). Optical rotations were recorded on a JASCO P-1010 polarimeter, and IR spectra on a Perkin–Elmer Spectrum BX spectrometer. High resolution mass spectra (HRMS) were run on a Waters Micromass LCT with an electrospray source (ZQ) in positive mode ionization (ESI). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AM-300 with chemical shifts reported in ppm relative to the central line of the solvent residual peak:  $\delta = 7.26$  ppm in CDCl<sub>3</sub>,  $\delta = 1.94$  ppm in CD<sub>3</sub>CN, and  $\delta$  = 3.31 ppm in MeOD for <sup>1</sup>H, and  $\delta$  = 77.16 ppm in CDCl<sub>3</sub>,  $\delta$  = 1.32 in CD<sub>3</sub>CN, and  $\delta$  = 49.00 in MeOD for <sup>13</sup>C. Some spectra were recorded preferentially in CD<sub>3</sub>CN because of the significant improvement of their readability in that solvent (presence of rotamers).

General Procedure A. Oxazolidine Oxidative Deprotection: Freshly prepared Jones' reagent (3 equiv., 2.67 M) was added at 0 °C to a solution of the oxazolidine in acetone (0.1 M). The reaction mixture was stirred for 6 h at 0 °C. A saturated solution of NaHCO<sub>3</sub> was added to obtain a pH value of 5–6. The aqueous phase was then extracted with EtOAc, and the combined organic extracts were washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and concentrated in vacuo to give the crude carboxylic acid.

General Procedure B. Piperidine Formation: Raney nickel<sup>[66]</sup> (around 1000 wt.-%) was added to a solution of the  $\beta$ -keto sulfone in ethanol (0.05 M). The mixture was refluxed until complete conversion of the starting material into a single product (monitored by TLC: 10% MeOH in dichloromethane). The mixture was cooled to room temp. and filtered through a pad of Celite and Na<sub>2</sub>SO<sub>4</sub>. The solid was well rinsed with ethanol, the filtrates were combined, and the solvents evaporated in vacuo to afford the crude piperidine.

General Procedure C. Amino Acid Cyclization: EDCI (1.2 equiv.) and HOBt (1.2 equiv.) were added at room temperature to a solution of the amino acid in DMF (0.2 M). The reaction mixture was stirred for 3 h. Water was added and the aqueous phase was extracted with EtOAc. The combined extracts were washed with 1 M HCl, H<sub>2</sub>O, saturated aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, and brine. The solution was dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and concentrated in vacuo to afford the crude lactam.

General Procedure D. OTBDPS Deprotection: TBAF (1.05 equiv., 1  $\mbox{m}$  in THF) was added at room temperature to a solution of the *tert*-butyldiphenylsilyl ether in THF (0.1  $\mbox{m}$ ). The reaction mixture was stirred for 1 h, then quenched by addition of saturated aqueous NaHCO<sub>3</sub>. After stirring for 10 min, the aqueous phase was extracted with EtOAc, and the combined organic extracts were washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and concentrated in vacuo to give the crude alcohol.

General procedure E. Ruthenium-Catalyzed Oxidation of Alcohol to Carboxylic Acid: NaIO<sub>4</sub> (4 equiv.) and a catalytic amount<sup>[54]</sup> of RuCl<sub>3</sub>·*n*H<sub>2</sub>O were added at room temperature to a solution of the alcohol in CCl<sub>4</sub>/CH<sub>3</sub>CN/H<sub>2</sub>O (0.15 M, 2:2:3). The reaction mixture was stirred for 1.5 h. Dichloromethane (2 mL) and water (2 mL) were added, and the aqueous phase was extracted with dichloromethane. The organic extracts were dried with MgSO<sub>4</sub>, filtered through a pad of Celite, and concentrated in vacuo to give a pale oil. The carboxylic acid obtained was dissolved in toluene/methanol (0.1 M, 4:1) and TMSCHN<sub>2</sub> (1.1 equiv., 2 M in hexanes) was added dropwise. The reaction mixture was stirred for 5 min and was quenched with acetic acid. The solvents were removed in vacuo to afford the crude methyl ester.

**General Procedure F. Mosher Ester Formation:** The preparation of the Mosher esters from the alcohols was achieved according to the method described in the literature.<sup>[45]</sup> Commercially available (+)-and (–)-MTPA-Cl were used. The reactions were monitored by

TLC and were quenched after complete conversion of the starting material. Purification was performed by preparative TLC (EtOAc/ heptanes 1:1), and care was exercised that both isomers were completely collected. As these esters were prepared in very small amounts and were obtained as rotamers, no <sup>13</sup>C NMR spectra were recorded.

Hydroxy Ester 2: DCC (16.8 g, 80.6 mmol, 1.2 equiv.) was added at 0 °C to a solution of 1 (22.7 g, 67.1 mmol) and N-hydroxysuccinimide (9.5 g, 80.6 mmol, 1.2 equiv.) in EtOAc (220 mL, HPLC grade). The reaction mixture was warmed to room temperature and stirred overnight. The mixture was then filtered and the filtrate was washed successively with aqueous NaHCO3 and brine, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo to give 32 g of crude ester. NaBH<sub>4</sub> (2.8 g, 70.5 mmol, 1.05 equiv.) was added at 0 °C to a solution of the residue (32 g) in THF (180 mL). Absolute EtOH (60 mL) was then added and the suspension was stirred at 0 °C for 30 min. The reaction was quenched with saturated aqueous NH<sub>4</sub>Cl and the mixture was extracted with EtOAc. The combined organic extracts were dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated to give crude 2 (25.0 g), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 2:1) to yield pure 2 (17.7 g, 81%) as a white solid.  $[\alpha]_{D}^{25} = -10$  (c = 1.0, MeOH); m.p. 75–76 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.33 (m, 5 H), 5.10 (s, 2 H), 5.04 (br. d, J = 8.1 Hz, 1 H), 3.57 (m, 3 H), 3.26 (m, 1 H), 2.44 (t, J = 7.8 Hz, 2 H), 1.96-1.66 (m, 2 H), 1.41 (s, 9 H) ppm.  $^{13}\mathrm{C}$  NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$ = 173.6, 156.3, 135.8, 128.6, 128.3, 79.6, 66.5, 64.9, 52.1, 30.9, 28.4, 26.4 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3439$ , 3009, 2981, 2935, 1707, 1501, 1368, 1167 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>17</sub>H<sub>25</sub>NNaO<sub>5</sub> 346.1630; found 346.1620.

Ester 3: pTsOH (208 mg, 0.02 equiv.) was added at room temperature to a solution of 2 (17.7 g, 54.8 mmol) in dimethoxypropane (180 mL). The reaction mixture was stirred at room temperature for 48 h. Et<sub>3</sub>N (160  $\mu$ L, 0.02 equiv.) was added and the solvent was evaporated in vacuo. The residue was dissolved in EtOAc and washed with saturated aqueous NaHCO3, brine, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated to give the crude ester (18.7 g), which was purified by flash chromatography on silica gel (heptanes/ EtOAc, 5:1) to afford pure **3** (18.3 g, 92%) as a clear oil.  $[\alpha]_{D}^{25}$  = +20 (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.33$  (m, 5 H), 5.10 (m, 2 H), 4.03–3.78 (m, 2 H), 3.69 (d, J = 8.2 Hz, 1 H), 2.38 (m, 2 H), 2.12–1.82 (m, 2 H), 1.56 (two br. s, 3 H), 1.45 (s, 12 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 172.9, 152.4, 151.9, 136.0, 135.9, 128.6, 128.3, 93.9, 93.4, 80.1, 79.8, 66.9, 66.3, 56.7, 56.5, 31.0, 28.9, 28.5, 27.6, 26.8, 24.4, 23.1 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} =$ 2978, 2936, 2876, 1738, 1694, 1390, 1376, 1365, 1258, 1166 cm<sup>-1</sup>. HRMS (ESI)  $[M + Na]^+$ : *m*/*z* calcd. for C<sub>20</sub>H<sub>29</sub>NNaO<sub>5</sub> 386.1943; found 346.1944.

Alcohol 4: LiAlH<sub>4</sub> (2.35 g, 60.2 mmol, 1.2 equiv.) was added at 0 °C to a solution of **3** (18.20 g, 50.1 mmol) in THF (400 mL), and the reaction mixture was stirred for 15 min at 0 °C. Water (2.4 mL) was then added dropwise at 0 °C, followed by 15% aqueous NaOH (2.4 mL) and water (7.2 mL). The cooling bath was removed and the reaction mixture was stirred for 45 min at room temp. The precipitate was filtered off and the solvents were removed in vacuo to afford the crude alcohol (18.25 g), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 2:1) to give pure 4 (12.52 g, 96%) as a colorless oil (two rotamers).  $[\alpha]_D^{25} = +31$  (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 4.01-3.59$  (m, 5 H), 2.74 (br., 0.5 H), 2.12 (br., 0.5 H), 1.92-1.36 (m, 19 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 152.5$ , 151.9, 93.8, 93.4, 80.4, 79.6, 67.1, 62.6, 62.4, 57.2, 30.1, 29.7, 29.5, 29.1, 28.5, 27.7, 26.9, 24.6, 23.3 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3444$ , 2979, 2936, 2871, 1694, 1478,

1455, 1392, 1257, 1174, 1086 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>13</sub>H<sub>25</sub>NNaO<sub>4</sub> 282.1681; found 282.1684.

Aldehvde 5: a solution of DMSO (8.20 mL, 114.6 mmol, 3.3 equiv.) in dichloromethane (30 mL) was added at -78 °C to a solution of oxalyl chloride (4.60 mL, 52.2 mmol, 1.5 equiv.) in dichloromethane (180 mL). The reaction mixture was stirred for 15 min at -78 °C, and a solution of 4 (9.05 g, 34.9 mmol) in dichloromethane (30 mL) was added. The reaction mixture was stirred for 45 min at -78 °C. Et<sub>3</sub>N (33.2 mL, 236.4 mmol, 6.8 equiv.) was then added at -78 °C, the cooling bath removed, and the reaction mixture was stirred for 1 h at room temp. The reaction was quenched by addition of water, and the aqueous phase was extracted with dichloromethane. The combined organic extracts were washed successively with 1 M HCl, water, aqueous NaHCO<sub>3</sub>, water, and brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and the solvent was removed in vacuo to give crude 5 (8.80 g, 98%). This aldehyde was used without any purification for the next step. An analytical sample (235 mg) was purified by flash chromatography on silica gel (heptanes/EtOAc, 4:1) to provide pure 5 (232 mg, 99%) as a colorless oil.  $[\alpha]_{D}^{25} = +26$  (*c* = 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta$  = 9.69 (s, 1 H), 3.96–3.77 (m, 2 H), 3.68 (m, 1 H), 2.52–2.24 (m, 2 H), 1.92–1.72 (m, 2 H), 1.52 (s, 3 H), 1.43 (m, 12 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CD<sub>3</sub>CN):  $\delta$  = 203.0, 174.7, 153.2, 152.8, 94.2, 80.5, 80.2, 67.6, 57.4, 40.8, 31.0, 29.4, 28.6, 28.0, 27.2, 26.8, 26.4, 24.8, 23.3 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 2979$ , 2937, 2876, 1725, 1694, 1390, 1367, 1257, 1173, 1084 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>13</sub>H<sub>23</sub>NNaO<sub>4</sub> 280.1525; found 280.1531.

Sulfone 7: Imidazole (10.9 g, 158 mmol, 2.5 equiv.) and tert-butyldiphenylsilyl chloride (17.5 mL, 66 mmol, 1.05 equiv.) were added to a solution of crude 13 (23.8 g) in DMF (80 mL). The reaction mixture was stirred for 2 h at room temp. and then quenched with a saturated aqueous NaHCO<sub>3</sub> solution. The mixture was stirred for 30 min and the aqueous phase was extracted with EtOAc. The extracts were washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub>, and filtered through Celite. The solvents were removed in vacuo and the residue was purified by flash chromatography on silica gel (heptanes/ EtOAc, 9:1 then 1:1) to give pure 7 (38.6 g, 87% from 73 mmol of 11) as a white solid.  $[\alpha]_{D}^{25} = -16$  (*c* = 1.0, CHCl<sub>3</sub>); m.p. 89–91 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.87 (m, 2 H), 7.61–7.49 (m, 7 H), 7.42–7.34 (m, 11 H), 5.04 (s, 2 H), 4.87 (d, J = 8.3 Hz, 1 H), 3.66-3.54 (m, 3 H), 3.20-2.99 (m, 2 H), 1.82-1.60 (m, 4 H), 1.03 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 156.1, 139.1, 136.5, 135.6, 134.9, 133.7, 133.0, 133.0, 130.0, 130.0, 129.3, 128.6, 128.2, 128.1, 127.9, 66.8, 65.5, 55.7, 51.7, 30.4, 26.9, 19.4, 19.3 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3440, 3020, 2932, 2860, 1717, 1507,$ 1306, 1219, 1208, 1148, 1113, 1086, 823 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>35</sub>H<sub>41</sub>NNaO<sub>5</sub>SSi 638.2372; found 638.2335.

**Diol 10:** LiBH<sub>4</sub> (247 mg, 10.8 mmol, 3 equiv.) and MeOH (0.44 mL, 10.8 mmol, 3 equiv.) were added successively, at 0 °C, to a solution of **9** (1.11 g, 3.59 mmol) in THF (20 mL). The reaction mixture was stirred for 4 h at 0 °C and was then quenched by addition of 1 M HCl. The reaction mixture was stirred for 20 min and then extracted with dichloromethane. The organic extracts were dried with Na<sub>2</sub>SO<sub>4</sub> and filtered through Celite. The solvents were removed in vacuo to afford the crude diol (768 mg), which was purified by flash chromatography on silica gel (dichloromethane/MeOH, 95:5) to yield pure **10** (718 mg, 79%) as a white solid.  $[a]_D^{25} = -16$  (c = 1.0, MeOH); m.p. 103–105 °C. <sup>1</sup>H NMR (300 MHz, MeOD):  $\delta = 7.39-7.23$  (m, 5 H), 5.07 (s, 2 H), 3.67–3.46 (m, 5 H), 1.73–1.28 (m, 4 H) ppm. <sup>13</sup>C NMR (75.5 MHz, MeOD):  $\delta = 158.7$ , 138.4, 129.4, 128.9, 128.7, 67.3, 65.4, 62.7, 54.2, 30.0, 28.6 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3436$ , 3024, 3009, 2947, 2881,

1708, 1511, 1226, 1069 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>13</sub>H<sub>19</sub>NNaO<sub>4</sub> 276.1212; found 276.1213.

Alcohol 11: pTsOH (13 mg, 0.07 mmol, 0.1 equiv.) and dimethoxypropane (0.85 mL, 6.72 mmol, 10 equiv.) were added, at room temp., to a solution of 10 (170 mg, 0.67 mmol) in dichloromethane (3 mL). The reaction mixture was stirred for 24 h at room temp. Et<sub>3</sub>N (10 µL) was then added and the solvents were evaporated in vacuo. Ethyl acetate and 1 M HCl were added to the residue, and the aqueous phase was extracted with EtOAc. The combined organic extracts were washed successively with 1 M HCl, water, saturated aqueous NaHCO<sub>3</sub>, water, and brine. The solvents were removed in vacuo to afford the crude alcohol (182 mg), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 1:1) to yield pure 11 (174 mg, 88%) as an oil.  $[\alpha]_D^{25} = +27$  (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.36 (m, 5 H), 5.14 (m, 2 H), 4.06-3.87 (m, 2 H), 3.78 (m, 1 H), 3.66 (m, 1 H), 3.56 (m, 1 H), 2.73 (0.5 H, br), 2.08 (0.5 H, br), 1.95-1.39 (m, 10 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 153.1, 152.3, 136.6, 136.3, 128.6, 128.1, 128.0, 128.0, 94.1, 93.7, 67.2, 66.6, 62.3, 57.8, 57.1, 30.0, 29.5, 29.2, 29.0, 27.6, 26.6, 24.6, 23.2 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} =$ 3456, 3026, 3013, 2941, 2881, 1694, 1412, 1352, 1255,  $1090 \text{ cm}^{-1}$ . HRMS (ESI)  $[M + Na]^+$ : m/z calcd. for C<sub>16</sub>H<sub>23</sub>NNaO<sub>4</sub> 316.1525; found 316.1522.

Sulfone 12: Triethylamine (11.4 mL, 81 mmol, 1.1 equiv.) was added to a solution of 11 (21.6 g, 74 mmol) in dichloromethane (400 mL) at -20 °C. Mesyl chloride (6.0 mL, 77 mmol, 1.04 equiv.) was then added dropwise over 10 min, and the reaction mixture was stirred at -20 °C for 30 min. The mixture was then washed with 1 M HCl, H<sub>2</sub>O, saturated aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, and brine, filtered through Celite, dried with Na<sub>2</sub>SO<sub>4</sub>, and the solvents evaporated in vacuo to give a colorless oil. The crude mesylate (27.4 g) was dissolved in THF (450 mL) and NaSPh (10.7 g, 77 mmol) was added carefully at 0 °C. The cooling bath was removed and the reaction mixture was stirred for 1 h. Magnesium monoperoxy phthalate (MMPP) (50.0 g, 81 mmol, 1.1 equiv.) and ethanol (135 mL) were then added at 0 °C. The bath was removed and the reaction mixture was stirred overnight. The solvents were removed in vacuo, the residue was diluted with EtOAc, and filtered. The solid was washed with EtOAc, and the filtrates were combined and washed with water. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried with Na2SO4 and filtered through Celite. The solvents were removed in vacuo to afford the crude sulfone (31.4 g). An analytical sample was purified by flash chromatography on silica (heptanes/EtOAc, 2:1) to give pure 12 as a colorless oil (two rotamers).  $[\alpha]_D^{25} = +20$  (c = 4.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.94 (m, 2 H), 7.72 (t, J = 7.2 Hz, 1 H), 7.62 (t, J = 7.7 Hz, 2 H), 7.39 (m, 5 H), 5.16 (s, 2 H), 4.05– 3.85 (m, 2 H), 3.76 (m, 1 H), 3.20 (m, 1 H), 3.05 (m, 1 H), 1.90-1.67 (m, 4 H), 1.67–1.45 (m, 6 H) ppm. <sup>13</sup>C NMR (75.5 MHz,  $CDCl_3$ ):  $\delta = 152.9, 152.1, 139.0, 136.4, 136.2, 133.8, 129.3, 128.6,$ 128.2, 128.0, 94.2, 93.7, 67.1, 67.0, 66.7, 57.3, 56.4, 55.8, 32.2, 31.4, 27.5, 26.6, 24.5, 23.0, 19.4, 19.3 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3028, 3011$ , 2941, 2881, 1697, 1448, 1410, 1352, 1148, 1087, 837 cm<sup>-1</sup>. HRMS (ESI)  $[M + Na]^+$ : m/z calcd. for C<sub>22</sub>H<sub>27</sub>NNaO<sub>5</sub>S 440.1508; found 440.1479.

Hydroxy Sulfone 13:  $CeCl_3$ ·7  $H_2O$  (34.0 g, 90 mmol, 1.2 equiv.) and oxalic acid (346 mg, 3.8 mmol, 0.05 equiv.) were added, at room temp., to a solution of crude 12 (31.4 g) in acetonitrile (350 mL), and the reaction mixture was stirred overnight. The mixture was neutralized with solid NaHCO<sub>3</sub>, and concentrated in vacuo. The residue was dissolved in EtOAc, filtered through Celite, dried with Na<sub>2</sub>SO<sub>4</sub>, and the solvent was removed in vacuo to give a pale-

yellow oil (24.1 g). An analytical sample was purified by flash chromatography on silica gel (heptanes/EtOAc, 2:3) to give pure **13** as a colorless oil.  $[\alpha]_{25}^{25} = -21$  (c = 5.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.74$  (d, J = 7.5 Hz, 2 H), 7.48 (t, J = 7.3 Hz, 1 H), 7.38 (t, J = 7.5 Hz, 2 H), 7.17 (m, 5 H), 5.48 (d, J = 8.5 Hz, 1 H), 4.90 (s, 2 H), 3.55–3.25 (m, 3 H), 2.96 (m, 2 H), 1.75–1.30 (m, 4 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 156.5$ , 138.6, 136.3, 133.6, 129.2, 128.4, 127.9, 127.8, 66.5, 64.2, 55.4, 52.1, 29.6, 19.1 ppm. IR (CHCl<sub>3</sub>):  $\tilde{\nu} = 3435$ , 3024, 2955, 1712, 1508, 1306, 1228, 1148, 1087 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m/z* calcd. for C<sub>19</sub>H<sub>23</sub>NNaO<sub>5</sub>S 400.1195; found 400.1205.

**Mosher's Ester 14:** The general procedure F was applied.  $[\alpha]_{D5}^{25} = +53 \ (c = 1.0, \text{ CHCl}_3)$ . <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta = 7.54$ -7.42 (m, 5 H), 4.33 (m, 2 H), 3.92–3.71 (m, 2 H), 3.64 (m, 1 H), 3.52 (m, 3 H), 1.74–1.52 (m, 4 H), 1.50–1.36 (15H). IR (neat):  $\tilde{v} = 2974$ , 1749, 1696, 1390, 1260, 1170, 1085 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>23</sub>H<sub>32</sub>F<sub>3</sub>NNaO<sub>6</sub> 498.2079; found 498.2061.

**Mosher's Ester 15:** The general procedure F was applied.  $[\alpha]_{D}^{25} = -10 \ (c = 0.8, \text{CHCl}_3)$ . <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta = 7.54-7.42 \ (m, 5 \text{ H}), 4.33 \ (m, 2 \text{ H}), 3.91-3.70 \ (m, 2 \text{ H}), 3.64 \ (m, 1 \text{ H}), 3.52 \ (m, 3 \text{ H}), 1.73-1.50 \ (m, 4 \text{ H}), 1.49-1.35 \ (15\text{H}).$  IR (film):  $\tilde{v} = 2978, 1748, 1694, 1390, 1259, 1170, 1086 \ \text{cm}^{-1}$ . HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>23</sub>H<sub>32</sub>F<sub>3</sub>NNaO<sub>6</sub> 498.2079; found 498.2077.

**Mosher's Ester 16:** The general procedure F was applied.  $[\alpha]_{25}^{25} = +45 \ (c = 0.3, \text{CHCl}_3)$ . <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta = 7.54$ -7.41 (m, 5 H), 7.35 (m, 5 H), 5.16–4.98 (m, 2 H), 4.29 (m, 2 H), 3.90 (m, 2 H), 3.68 (m, 1 H), 3.49 (br. s, 3 H), 1.73–1.54 (m, 4 H), 1.50 (br. s, 3 H), 1.42 (br. s, 3 H). IR (neat):  $\tilde{v} = 3025$ , 2982, 1751, 1700, 1696, 1410, 1351, 1260, 1170, 1089 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>26</sub>H<sub>30</sub>F<sub>3</sub>NNaO<sub>6</sub> 532.1923; found 532.1929.

**Mosher's Ester 17:** The general procedure F was applied.  $[\alpha]_D^{-5} = -8 \ (c = 0.3, \text{ CHCl}_3)$ . <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta = 7.45 \ (m, 5 \text{ H})$ , 7.35 (m, 5 H), 5.14–4.96 (m, 2 H), 4.29 (m, 2 H), 3.87 (m, 2 H), 3.68 (m, 1 H), 3.50 (br. s, 3 H), 1.75–1.56 (m, 4 H), 1.50 (br. s, 3 H), 1.42 (br. s, 3 H). IR (neat):  $\tilde{v} = 3030, 2962, 1744, 1700, 1696, 1410, 1351, 1261, 1170, 1091 \text{ cm}^{-1}$ . HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>26</sub>H<sub>30</sub>F<sub>3</sub>NNaO<sub>6</sub> 532.1923; found 532.1904.

β-Hydroxy Sulfone 18: a 1.6 M solution of nBuLi in hexanes (20 mL, 32.0 mmol, 2.2 equiv.) was added dropwise, at -78 °C, to a solution of 7 (8.84 g, 14.4 mmol) in THF (140 mL). After stirring for 20 min, a solution of 5 (4.15 g, 16.2 mmol, 1.1 equiv.) in THF (10 mL) was added dropwise. The reaction mixture was stirred for 1.5 h at -78 °C, the bath was then removed, and the mixture was stirred for an additional 30 min. The reaction was then quenched with a saturated solution of NH<sub>4</sub>Cl and stirred for 10 min. The aqueous phase was extracted with EtOAc and the extracts were washed with water and brine. The organic phase was dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and concentrated in vacuo to afford a crude mixture (13.10 g), which was then purified by flash chromatography on silica gel (dichloromethane/EtOAc, 29:1 then 9:1) to give 1.06 g (12%) of recovered starting sulfone 7, and pure 18 (10.70 g, 85%) as a white foam (mixture of diastereomers and rotamers). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta$  = 7.89 (m, 2 H), 7.74– 7.51 (m, 7 H), 7.51-7.25 (m, 11 H), 5.55 (m, 1 H), 5.07 (m, 2 H), 4.26-3.04 (m, 9 H), 2.00-1.36 (m, 23 H), 1.03 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CD<sub>3</sub>CN):  $\delta$  = 157.2, 157.1, 152.9, 152.8, 152.7, 140.7, 139.5, 138.3, 136.4, 134.6, 134.2, 130.8, 130.2, 129.6, 129.4, 129.3, 128.8, 128.6, 94.0, 80.4, 79.8, 70.4, 69.8, 69.3, 67.6, 66.8, 58.1, 57.8, 53.9, 53.7, 32.6, 31.7, 31.1, 30.9, 30.3, 30.2, 28.7, 28.0, 27.8, 27.3, 24.9, 23.5, 22.3, 20.7, 19.8 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3437$ , 3019, 2933, 2860, 1709, 1689, 1511, 1394, 1367, 1212, 1145, 1111,

823 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>48</sub>H<sub>64</sub>N<sub>2</sub>NaO<sub>9</sub>SSi 895.4000; found 895.3974.

Carboxylic Acid 19: According to the general procedure A, oxazolidine 18 (2.05 g, 2.3 mmol) afforded the crude carboxylic acid (1.95 g), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 3:1 then 1:1) to yield pure 19 (1.51 g, 76%, mixture of diastereomers and rotamers) as a white foam. <sup>1</sup>H NMR  $(300 \text{ MHz}, \text{CDCl}_3)$ :  $\delta = 8.95$  (br. s, 1 H), 7.78 (m, 2 H), 7.63 (m, 5 H), 7.52 (m, 2 H), 7.45–7.30 (m, 11 H), 6.3 (m, 1 H), 5.45 (m, 1 H), 5.18-5.03 (m, 2 H), 4.39-4.14 (m, 2 H), 3.60 (m, 3 H), 3.06 (m, 1 H), 2.77 (m, 1 H), 2.32–1.78 (m, 4 H), 1.74–1.34 (m, 11 H), 1.06 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.3, 175.4, 175.3, 156.3, 155.8, 136.3, 136.2, 135.5, 134.3, 132.9, 129.9, 129.3, 129.1, 128.5, 128.2, 128.1, 127.8, 81.7, 80.1, 74.5, 74.1, 66.9, 65.2, 65.1, 52.5, 51.9, 51.8, 41.2, 40.8, 28.5, 28.3, 26.8, 26.1, 25.8, 23.8, 23.4, 19.2 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3436$ , 3015, 2933, 2860, 1714, 1505, 1310, 1154, 1113, 823 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>45</sub>H<sub>56</sub>N<sub>2</sub>NaO<sub>10</sub>SSi 867.3323; found 867.3364.

**Piperidine 20:** According to the general procedure B, carboxylic acid **19** (315 mg, 0.37 mmol) afforded the crude piperidine **20** (176 mg, 84%) as a clear oil, which was used as-is for the next step. <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD):  $\delta$  = 7.65 (m, 4 H), 7.48–7.30 (m, 6 H), 3.95 (m, 1 H), 3.70 (m, 2 H), 3.07 (m, 1 H), 2.90 (m, 1 H), 2.05–1.44 (m, 10 H), 1.41 (s, 9 H), 1.05 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CD<sub>3</sub>OD):  $\delta$  = 178.7, 157.5, 136.7, 134.1, 131.2, 129.0, 80.1, 66.7, 59.7, 58.4, 56.6, 31.8, 30.8, 30.4, 28.9, 27.7, 27.5, 23.9, 20.1 ppm. HRMS (ESI) [M + H]<sup>+</sup>: *m*/*z* calcd. for C<sub>31</sub>H<sub>47</sub>N<sub>2</sub>O<sub>5</sub>Si 555.3254; found 555.3262; [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>31</sub>H<sub>46</sub>N<sub>2</sub>NaO<sub>5</sub>Si 577.3074; found 555.3079.

**Lactam 21:** According to the general procedure C, amino acid **20** (128 mg, 0.23 mmol) afforded the crude lactam (126 mg), which was purified by flash chromatography on silica gel (heptanes/ EtOAc, 5:1) to give pure **21** (95 mg, 77%) as a colorless oil. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -20 (c = 1.3, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.71– 7.62 (m, 4 H), 7.46–7.33 (m, 6 H), 5.59 (m, 1 H), 4.04 (m, 1 H), 3.96–3.77 (m, 3 H), 3.38 (m, 1 H), 2.35 (m, 1 H), 2.09–1.44 (m, 10 H), 1.44 (s, 9 H), 1.07 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 170.5, 155.9, 135.7, 133.8, 133.7, 129.7, 127.7, 79.4, 65.4, 57.8, 54.7, 51.3, 30.4, 28.4, 27.7, 27.0, 25.2, 23.9, 20.2, 19.3 ppm. IR (CHCl<sub>3</sub>):  $\tilde{\nu}$  = 3407, 3073, 3011, 2951, 2860, 1705, 1651, 1465, 1428, 1167, 1112, 824 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>31</sub>H<sub>44</sub>N<sub>2</sub>NaO<sub>4</sub>Si 559.2968; found 559.2964.

Alcohol 22: According to the general procedure D, compound 21 (148 mg, 0.28 mmol) afforded the crude alcohol (157 mg), which was purified by flash chromatography on silica gel (heptanes/ EtOAc, 4:1 to pure EtOAc) to give 22 (81 mg, 99%) as a white foam. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -26 (c = 1.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 5.50 (m, 1 H), 4.58 (m, 1 H), 4.04 (m, 1 H), 3.86 (m, 1 H), 3.73 (m, 1 H), 3.42 (m, 1 H), 3.24 (m, 1 H), 2.33 (m, 1 H), 2.20–1.85 (m, 2 H), 1.83–1.52 (m, 7 H), 1.42 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 169.8, 156.0, 79.7, 64.7, 64.1, 59.5, 52.6, 32.2, 28.5, 27.3, 26.5, 25.0, 23.7 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v}$  = 3413, 3007, 2950, 1707, 1630, 1468, 1333, 1262, 1165, 1010, 821 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>15</sub>H<sub>26</sub>N<sub>2</sub>NaO<sub>4</sub> 321.1790; found 321.1782.

Methyl Ester 23: An aqueous solution of 5% NaHCO<sub>3</sub> (0.21 mL), KBr (6 mg, 0.05 mmol, 0.1 equiv.), and TEMPO (81 mg, 0.51 mmol, 1.1 equiv.) was added, at 0 °C, to a solution of 22 (137 mg, 0.46 mmol) in acetone (4 mL). A solution of 5% NaOCl (0.14 mL) was then added dropwise and the reaction mixture was stirred for 1 h at 0 °C. A solution of 5% NaOCl (0.07 mL) was again added and the stirring was continued for an additional hour.

The reaction mixture was acidified to pH 6 with a solution of 10%KHSO<sub>4</sub>. The solvents were removed in vacuo, and the residue was directly purified by flash chromatography on silica gel (heptanes/ EtOAc, 1:4 then dichloromethane/MeOH, 9:1). The carboxylic acid obtained (130 mg) was dissolved in toluene/methanol (5 mL, 4:1) and TMSCHN<sub>2</sub> (0.22 mL, 0.44 mmol) was added dropwise. The reaction mixture was stirred for 5 min and was then quenched with acetic acid. The solvents were removed in vacuo and the residue was purified by flash chromatography on silica gel (heptanes/ EtOAc, 3:1) to afford 23 (126 mg, 84%) as a colorless oil.  $\left[\alpha\right]_{D}^{25}$  =  $-10 (c = 1.1, CHCl_3)$ . <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 5.52$  (br. s, 1 H), 4.18–4.07 (m, 2 H), 3.72 (s, 3 H), 3.51 (m, 1 H), 2.40 (m, 1 H), 2.15–1.48 (m, 9 H), 1.42 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz,  $CDCl_3$ ):  $\delta = 171.6, 170.7, 155.8, 79.5, 56.6, 54.7, 52.3, 51.2, 30.0,$ 28.4, 27.2, 25.4, 25.0, 20.3 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v}$  = 3417, 3022, 2990, 2952, 1736, 1707, 1654, 1498, 1208, 1166 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>16</sub>H<sub>26</sub>N<sub>2</sub>O<sub>5</sub>Na 349.1739; found 349.1776.

β-Keto Sulfone 24: IBX (3.8 g, 13.8 mmol, 3 equiv.) was added to a solution of 18 (4.0 g, 4.6 mmol) in DMSO (50 mL) and the reaction mixture was stirred for 4 h at room temperature. After cooling to 0 °C, the reaction was quenched with water. Diethyl ether was added, and the white solid was washed with diethyl ether and removed by filtration. The two layers were separated, and the aqueous phase was extracted with diethyl ether. The organic extracts were washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and concentrated in vacuo to give crude 24 (4.0 g), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 3:1) to afford pure 24 as a white foam (3.8 g, 95%, mixture of diastereomers and rotamers). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.80$ – 7.46 (m, 9 H), 7.46–7.28 (m, 11 H), 5.13–4.80 (m, 3 H), 4.25 (m, 1 H), 3.99–3.77 (m, 2 H), 3.76–3.44 (m, 4 H), 3.02–2.45 (m, 2 H), 2.11-1.36 (m, 21 H), 1.02 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz,  $CDCl_3$ ):  $\delta = 201.6, 201.3, 156.1, 152.7, 152.4, 151.9, 136.7, 136.4,$ 135.6, 134.4, 133.0, 130.0, 129.4, 129.2, 128.7, 128.2, 127.9, 93.9, 93.6, 80.3, 79.9, 74.8, 74.5, 74.3, 67.3, 67.0, 66.8, 65.7, 65.3, 65.1, 56.8, 56.5, 56.2, 52.4, 51.8, 42.0, 41.8, 41.6, 28.9, 28.5, 28.0, 27.7, 27.3, 27.0, 24.5, 24.0, 23.5, 23.3, 19.4 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v}$  = 3687, 3030, 3015, 2934, 1717, 1684, 1507, 1394, 1226, 1106, 931, 821 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C48H62N2NaO9SSi 893.3843; found 893.3839.

Oxazolidine 25: K<sub>2</sub>CO<sub>3</sub> (0.83 g, 6.0 mmol, 2 equiv.) and MeI (0.57 mL, 9.0 mmol, 3 equiv.) were added, at room temperature, to a solution of 24 (2.60 g, 3.0 mmol) in DMF (10 mL). After stirring for 4 h, MeI (0.29 mL, 4.5 mmol, 1.5 equiv.) was added and the mixture was stirred for an additional 4 h. The reaction was then quenched with water, neutralized with 1 M HCl, and extracted with diethyl ether. The organic phase was washed with H<sub>2</sub>O, a 10% solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, and brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered through Celite, and concentrated in vacuo to give crude 25 (2.57 g), which was purified by flash chromatography on silica gel (heptanes/ EtOAc, 3:1) to afford pure 25 (2.55 g, 97%, mixture of diastereomers and rotamers) as a white foam. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.77-7.57$  (m, 7 H), 7.55-7.28 (m, 13 H), 5.24-4.94 (m, 3 H), 4.05-3.82 (m, 2 H), 3.80-3.50 (m, 4 H), 3.14-2.70 (m, 2 H), 2.49–1.69 (m, 6 H), 1.68–1.41 (m, 18 H), 1.04 (s, 9 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 204.1, 203.8, 203.7, 156.1, 156.0, 152.5, 152.4, 151.8, 136.6, 135.5, 135.0, 134.8, 134.2, 132.9, 130.2, 130.0, 128.9, 128.5, 128.1, 127.8, 93.8, 93.4, 80.1, 80.0, 79.7, 76.3, 76.1, 67.3, 67.0, 66.6, 65.5, 65.3, 56.8, 56.5, 56.3, 53.5, 52.7, 37.6, 37.1, 36.9, 29.6, 29.5, 29.3, 28.4, 28.0, 27.8, 27.7, 26.9, 26.4, 26.2, 24.4, 23.1, 22.7, 19.2, 16.3, 16.0, 15.8 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} =$ 3440, 3071, 3019, 3014, 2971, 1713, 1689, 1505, 1393, 1378, 1146,

1106,  $822 \text{ cm}^{-1}$ . HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for  $C_{49}H_{64}N_2NaO_9SSi$  907.4000; found 907.3960.

Carboxylic Acid 26: According to the general procedure A, oxazolidine 25 (2.53 g, 2.9 mmol) afforded the crude carboxylic acid (2.48 g), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 2:1 then 1:2) with 30 to 70% EtOAc in heptanes to afford pure 26 (1.78 g, 72%, a mixture of diastereomers and rotamers) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.71$ – 7.55 (m, 7 H), 7.53–7.29 (m, 13 H), 5.46–4.91 (m, 4 H), 4.32 (m, 1 H), 3.59 (m, 3 H), 3.08–2.83 (m, 2 H), 2.28–2.01 (m, 2 H), 1.94– 1.48 (m, 4 H), 1.43 (s, 9 H), 1.03 (s, 9 H), 0.88 (m, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 204.3, 204.0, 175.6, 175.3, 175.0, 156.6, 156.5, 155.8, 136.5, 136.3, 136.0, 135.7, 134.9, 134.4, 133.1, 133.0, 130.3, 130.0, 130.0, 129.0, 128.7, 128.3, 128.2, 128.0, 80.3, 76.4, 76.2, 67.2, 67.1, 65.4, 64.5, 53.6, 53.0, 52.7, 52.5, 36.5, 29.8, 29.5, 29.2, 28.4, 27.0, 26.3, 26.1, 22.8, 19.4, 16.1 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3435, 3012, 2929, 2858, 1711, 1505, 1306, 1216, 1146 \text{ cm}^{-1}$ . HRMS (ESI)  $[M + Na]^+$ : m/z calcd. for  $C_{46}H_{58}N_2NaO_{10}SSi$ 881.3479; found 881.3464.

**Piperidine 27:** According to the general procedure B, carboxylic acid **26** (1.68 g, 2.0 mmol) afforded the crude piperidine (914 mg, 82%) as a clear oil, which was used as-is for the next step. <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD):  $\delta$  = 7.75–7.55 (m, 4 H), 7.50–7.30 (m, 6 H), 4.04–3.46 (m, 4 H), 3.18 (m, 2 H), 2.21–1.51 (m, 9 H), 1.44 (s, 9 H), 1.11–0.88 (m, 12 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CD<sub>3</sub>OD):  $\delta$  = 178.1, 157.6, 157.2, 136.7, 136.0, 134.0, 133.8, 131.3, 131.2, 129.0, 128.6, 80.1, 71.0, 70.9, 66.2, 65.9, 63.5, 60.4, 59.6, 56.2, 56.1, 35.8, 33.1, 30.8, 30.6, 29.7, 29.3, 29.1, 28.8, 27.9, 27.6, 27.4, 22.3, 20.1, 18.6, 11.1 ppm. ESI [M + Na]<sup>+</sup>: *m/z* = 591; [M + H]<sup>+</sup>: *m/z* = 569.

**Lactams 28a and 28b:** According to the general procedure C, amino acid **27** (730 mg, 1.3 mmol) afforded a crude mixture of two diastereomers (631 mg), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 9:1) to give pure **28a** (465 mg, 66%, TLC  $R_{\rm f} = 0.50$  in EtOAc/heptanes 1:2) as a colorless oil and **28b** (87 mg, 12%, TLC  $R_{\rm f} = 0.55$  in EtOAc/heptanes 1:2) also as a colorless oil.

**28a:**  $[\alpha]_D^{25} = -10$  (c = 4.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.72-7.62$  (m, 4 H), 7.44–7.31 (m, 6 H), 5.61 (br. s, 1 H), 4.16 (m, 1 H), 4.00 (m, 1 H), 3.90 (dd, 1 H, J = 3.8 Hz, 9.4 Hz), 3.71 (t, J = 9.2 Hz, 1 H), 3.58 (m, 1 H), 2.33 (m, 1 H), 2.04 (m, 1 H), 1.96 (m, 1 H), 1.85 (m, 1 H), 1.73 (m, 1 H), 1.58–1.40 (m, 13 H), 1.08 (s, 9 H), 0.90 (d, J = 7.0 Hz, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 172.1$ , 155.6, 135.6, 133.6, 133.5, 129.7, 127.7, 79.3, 62.4, 56.1, 55.5, 50.8, 32.9, 28.4, 26.9, 26.3, 26.0, 23.1, 22.8, 19.3, 16.4 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3415$ , 3073, 3009, 2962, 2933, 2860, 1705, 1651, 1493, 1209, 1112, 823 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>32</sub>H<sub>46</sub>N<sub>2</sub>NaO<sub>4</sub>Si 573.3125; found 573.3118.

**28b:**  $[\alpha]_D^{25} = -23$  (c = 1.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD):  $\delta = 7.69-7.60$  (m, 4 H), 7.48–7.34 (m, 6 H), 4.03 (m, 1 H), 3.92 (m, 2 H), 3.73 (m, 1 H), 3.05 (m, 1 H), 2.05–1.52 (m, 9 H), 1.43 (s, 9 H), 1.05 (s, 9 H), 0.87 (d, J = 6.4 Hz, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CD<sub>3</sub>OD):  $\delta = 172.3$ , 158.0, 136.8, 134.8, 134.7, 130.9, 128.9, 80.4, 66.4, 63.1, 60.1, 52.1, 35.5, 31.4, 28.8, 27.5, 26.0, 25.4, 20.1, 18.9 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3414$ , 3073, 3015, 2932, 2859, 17005, 1651, 1494, 1463, 1166, 1112, 823 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: m/z calcd. for C<sub>32</sub>H<sub>46</sub>N<sub>2</sub>NaO<sub>4</sub>Si 573.3125; found 573.3139.

Alcohol 29a: According to the general procedure D, lactam 28a (197 mg, 0.36 mmol) afforded the crude alcohol (221 mg), which was purified by flash chromatography on silica gel (heptanes/ EtOAc, 3:1 then pure EtOAc) to give 29a (106 mg, 95%) as a clear oil.  $[\alpha]_{25}^{25} = -22$  (c = 1.9, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 5.52$  (m, 1 H), 4.53 (m, 1 H), 4.02 (m, 1 H), 3.82 (m, 1 H), 3.65

(m, 1 H), 3.52 (m, 1 H), 3.22 (m, 1 H), 2.25 (m, 1 H), 2.04 (m, 1 H), 1.85 (m, 2 H), 1.73–1.44 (m, 5 H), 1.38 (s, 9 H), 0.92 (d, J = 7.0 Hz, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 170.7$ , 155.8, 79.5, 64.4, 63.8, 60.1, 52.1, 34.8, 31.3, 28.3, 25.9, 24.8, 23.0, 15.0 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3414$ , 3007, 2937, 2878, 1708, 1630, 1492, 1468, 1336, 1165 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m/z* calcd. for C<sub>16</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>4</sub> 335.1947; found 335.1950.

Alcohol 29b: According to the general procedure D, lactam 28b (59 mg, 0.13 mmol) afforded the crude alcohol (65 mg), which was purified by flash chromatography on silica gel (heptanes/EtOAc, 3:1 then pure EtOAc) to give 29b (32 mg, 96%) as a clear oil.  $[\alpha]_{25}^{25} = -50$  (c = 0.6, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 5.45$  (br. s, 1 H), 4.56 (dd, J = 3.8, 9.6 Hz, 1 H), 4.05 (dt, J = 11.7, 5.8 Hz, 1 H), 3.86 (m, 1 H), 3.72 (m, 1 H), 3.24 (m, 1 H), 3.00 (dt, J = 10.4, 4.1 Hz, 1 H), 2.31 (m, 1 H), 2.05–1.58 (m, 7 H), 1.42 (s, 9 H), 1.35–1.22 (m, 1 H), 0.88 (d, J = 6.4 Hz, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 170.2$ , 156.1, 79.7, 65.6, 64.7, 64.2, 52.6, 35.2, 33.4, 28.5, 26.9, 24.6, 23.5, 18.5 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3417$ , 3020, 3008, 2981, 2934, 1708, 1631, 1468, 1219, 1166 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>16</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>4</sub> 335.1947; found 335.1944.

**Methyl Ester 30a:** According to the general procedure E, alcohol **29a** (75 mg, 0.24 mmol) afforded the crude methyl ester, which was purified by flash chromatography on silica gel (heptanes/EtOAc, 4:1) to give **30a** (56 mg, 69%) as a colorless oil.  $[\alpha]_D^{25} = +16$  (c = 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 5.53$  (m, 1 H), 4.50 (m, 1 H), 4.30 (m, 1 H), 3.81–3.64 (m, 4 H), 2.37 (m, 1 H), 2.12–1.71 (m, 6 H), 1.66–1.40 (m, 11 H), 1.00 (d, J = 7.0 Hz, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 173.4$ , 172.7, 155.7, 79.6, 55.4, 54.8, 52.3, 50.5, 32.8, 28.5, 25.9, 25.4, 25.2, 22.0, 16.6 ppm. IR (CHCl<sub>3</sub>):  $\tilde{\nu} = 3423$ , 3024, 3015, 2954, 1741, 1706, 1658, 1498, 1220, 1167 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>17</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>5</sub> 363.1896; found 363.1898.

**Methyl Ester 30b:** According to the general procedure E, alcohol **29b** (28 mg, 0.09 mmol) afforded the crude methyl ester, which was purified by flash chromatography on silica gel (heptanes/EtOAc, 4:1) to afford **30b** (21 mg, 69%) as a colorless oil.  $[\alpha]_D^{25} = -22$  (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 5.52$  (m, 1 H), 4.10 (m, 2 H), 3.72 (s, 3 H), 3.07 (m, 1 H), 2.39 (m, 1 H), 2.18–1.52 (m, 8 H), 1.42 (s, 9 H), 0.92 (d, J = 6.4 Hz, 3 H) ppm. <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta = 171.8$ , 171.1, 155.9, 79.7, 61.2, 56.4, 52.4, 51.2, 34.5, 30.2, 28.5, 25.2, 25.2, 24.6, 18.6 ppm. IR (CHCl<sub>3</sub>):  $\tilde{v} = 3422$ , 3019, 2963, 2935, 1740, 1707, 1655, 1497, 1368, 1226, 1166 cm<sup>-1</sup>. HRMS (ESI) [M + Na]<sup>+</sup>: *m*/*z* calcd. for C<sub>17</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>5</sub> 363.1896; found 363.1879.

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