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A Straightforward Synthesis of L-Isoserinal

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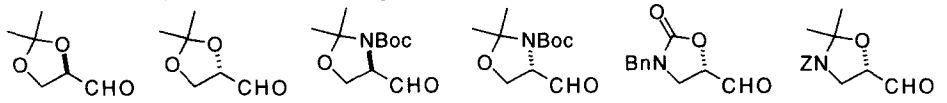
Abstract: A convenient preparation of L-isoserinal **3** in six steps and 32.8% overall yield employing D-glyceraldehyde acetonide **1** as starting material is described. The procedure is inexpensive, easily scaled up and proceeds without observable racemization. Copyright © 1996 Elsevier Science Ltd

Introduction

The synthesis of enantiomerically pure small molecules which could be used as synthetic building blocks constitutes an important issue in the context of the Organic Synthesis.[1] Among those molecules are polyfunctionalized aldehydes such as D- and L-glyceraldehyde **1** and D- and L-serinal **2**. Typically, several routes to both **1** and **2** have been described and the utility of these compounds in Organic Synthesis has been widely demonstrated.[2] The synthetic utility of compounds like **1** and **2** arises from the fact that they can be prepared from easily accessible starting materials. Both D- and L-glyceraldehyde are prepared from D-mannitol[3] and L-ascorbic acid,[4] respectively. Similarly, α-amino aldehydes **2** are prepared from the corresponding enantiomer of the natural α-amino acid, serine, in four steps.[5]

In this context, and as a part of a project directed to the synthesis of naturally occurring nitrogen-containing compounds,[6] we required the β-amino-α-alkoxy aldehyde **3**, namely isoserinal, N,O-protected in such a way that no acid-sensitive protecting groups were present in the molecule. This kind of protection has also been used successfully for preparing several serine-based chiral building blocks.[7] A similar synthetic approach used for preparing **2** is not very advisable for the synthesis of isoserinal derivatives since the precursor amino acid, isoserine, is not a natural product and it must be prepared in a stereoselective manner.[8]

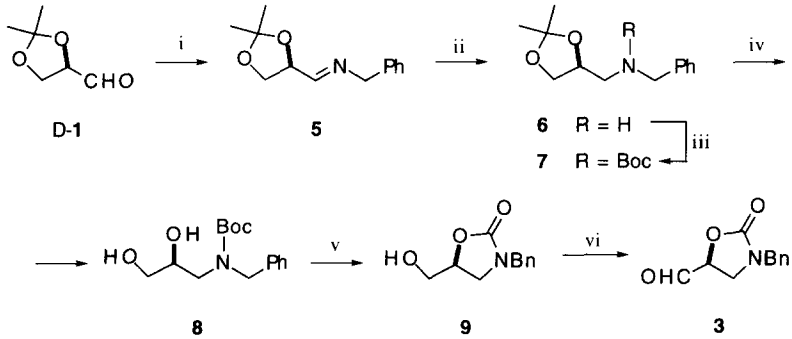


D-1 **L-1** **D-2** **L-2** **3** **4**

Until now only a diastereospecific route to the isoserinal derivative **4** is reported in the literature,[9] however that derivative is N,O-protected with acid-sensitive protecting groups. Also, it has been recently reported the preparation of several 5-substituted-2-oxazolidinones but in any case the aldehyde functionality was released.[10] Herein we describe in detail a new procedure which provides the new isoserinal derivative **3** in six steps and 32.8 % overall yield from readily available D-glyceraldehyde acetonide **1**. The same protocol should be amenable to the preparation of the antipode of **3** starting from L-glyceraldehyde.

Results and Discussion

D-Glyceraldehyde acetonide **1** was converted into the imine **5** by condensation of the former with benzylamine in diethyl ether as a solvent, and in the presence of magnesium sulfate as described.[11] The ^{1}H NMR spectrum of the crude product showed that imine **5** was obtained in near quantitative yield and pure enough for utilizing it without further purification (see experimental part). The reduction of **5** to the previously described secondary amine **6**[12] was achieved with sodium borohydride in methanol at 0 °C. Although the amine **6** can be purified, if required, by flash chromatography the crude material obtained after work-up can be used in the next step. This is particularly advisable in multigram-scale preparations (more than 2.0 g) since column chromatography of amine **6** requires excessive quantities of eluent due to its polarity. Protection of the amine **6** into the N-(tert-butoxycarbonyl) derivative **7** was initially carried out with Boc_2O in dioxane as a solvent but this was changed to Boc_2O in dichloromethane with catalytic 4-(dimethylamino)pyridine (DMAP) for speed and conversion reasons. Protection in dichloromethane was essentially completed in 24 h, whereas the use of dioxane as a solvent took several days and a lower chemical yield was observed. Compound **7** was consistently obtained from **6** in 80% yield, thus in about 72% overall yield from **1** after purification by column chromatography (Scheme 1).

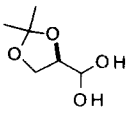


Reagents and conditions: i, $PhCH_2NH_2$, CH_2Cl_2, $MgSO_4$, r.t., 30 min. ii, $NaBH_4$, CH_3OH, 0 °C, 30 min. iii, Boc_2O, CH_2Cl_2, DMAP, r.t., 24 h. iv, TosOH, CH_3OH, reflux, 4 h. v, NaH, THF, 0 °C → r.t., 2h. vi, DMSO, $(COCl_2)$, Et_3N, -78 °C → 0 °C

Scheme 1

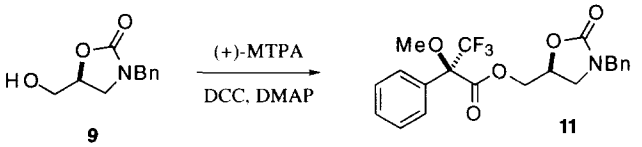
Quantitative deketalization of **7** using catalytic p-toluensulfonic acid in refluxing methanol afforded diol **8** which was sufficiently pure for use. It had been reported that cyclization of 1,2-dihydroxy carbamates into 2-oxazolidinones could be performed in the presence of a catalytic amount of imidazole in refluxing toluene.[13] However this procedure, in our hands, did give low yields when applied to compound **8**. We therefore investigated the cyclization under other conditions. Regioselective cyclization of diol **8** into oxazolidinone **9** was then achieved through sodium hydride deprotonation in dimethylformamide as a solvent. Nevertheless, we found that in multigram scale high levels of dimethylformamide entrained in product solid proved resistant to removal and was found to be detrimental in the subsequent oxidation step. In order to circumvent these problems other solvents were checked. Thus, smooth formation of **9** was accomplished by the use of sodium hydride in tetrahydrofuran at room temperature, thereby avoiding the use of dimethylformamide as solvent.

The final oxidation step was carried out under Swern conditions[14] (DMSO, $(COCl_2)$) and the aldehyde **3** was obtained in 60% yield. Notably, the use of different activating electrophiles,[15] such as DCC, acetic anhydride or phosphorous pentoxide, in DMSO caused lower yields and a more complex reaction mixture. Moreover, oxidation of primary alcohol **9** to provide aldehyde **3** failed when several metal-assisted oxidations, including chromium trioxide[16] and pyridinium chlorocromate[17] oxidations, were assayed. Examination of the crude product by ^{1}H NMR showed the product to exist predominantly as the hydrate **10** with some free aldehyde **3** noted (ca. 5-10%). The resonances corresponding to the free aldehyde **3** were observed by NMR when the spectra were recorded in DMSO-d_6 at 120 °C. The obtained aldehyde can be used without further purification showing a good reactivity in condensation and Wittig reactions as discussed below.



10

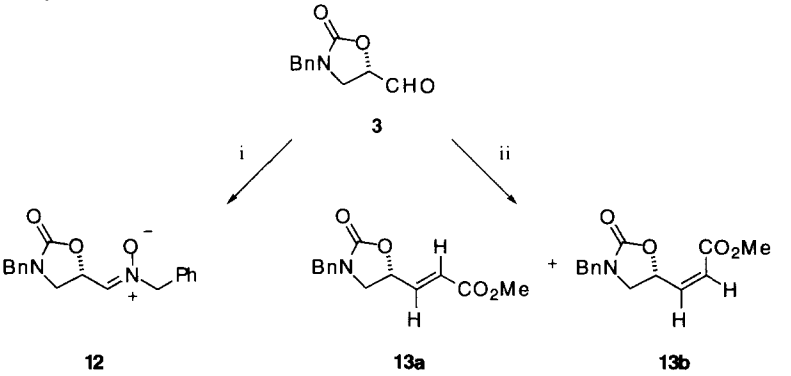
The enantiomeric purity of **3** was identical to that of the starting material **1** because the chemical reactions took place without affecting the asymmetric carbon atoms. In any case the stereochemical integrity of the process was determined by preparation of Mosher esters[14] of alcohol **9** prior to the oxidation step and from the same compound prepared by treating aldehyde **3** with sodium borohydride in methanol at 0 °C for 30 min (Scheme 2). Analysis of the 300 MHz ^{1}H and ^{19}F NMR spectra of these the esters showed the presence of only one diastereomer in each case at the limit of detection, indicating enantiomeric purity ≥ 95%.



9 **11**

Scheme 2

The β-amino aldehyde **3** has proven to be a useful intermediate in Organic Synthesis (Scheme 3). The reaction of **3** with benzylhydroxylamine[18] following our previously described conditions[19] afforded nitrone **12** in 68 % yield after column chromatography. The Wittig reaction of **3** with (methoxycarbonylmethylene)-triphenylphosphorane in chloroform afforded a 70 % yield of the α,β-unsaturated ester **13** as a 60:40 mixture of E/Z isomers according to ^{1}H NMR.



12 **13a** **13b**

Reagents and conditions: i, $PhCH_2NHOH$, CH_2Cl_2, $MgSO_4$, r.t., 4 h. ii, $Ph_3P{=}CO_2Me$, $CHCl_3$, r.t., 48 h.

Scheme 3

In conclusion we have achieved a simple and convenient synthesis on a multigram scale of L-isoserinal in enantiomerically pure form. We expect the L-isoserinal derivative **3** to find several synthetic applications of broad utility as new C_3 chiral building block in Organic Synthesis.

Experimental

General Methods. All moisture-sensitive reactions were performed under an argon atmosphere using oven-dried glassware. Solvents were dried over standard drying agents[20] and freshly distilled prior to use. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz Varian Unity spectrometer at room temperature, unless otherwise specified. Chemical shifts are given in parts per million downfield from tetramethylsilane. Optical rotations were measured using a Perkin Elmer 214 polarimeter. Elemental analyses were performed on a 1106 Microanalyzer (Carlo Erba). All reactions were monitored by TLC on silica gel plates (Merck Kiesel gel 60 F254) and visualized by spraying with either 1M aqueous KMnO4 or a solution of 2,4-dinitrophenylhydrazine in methanolic sulfuric acid and heated. Flash column chromatography[21] was performed on silica gel 60 F254.

N-(2,3-O-isopropylidene-D-glycerylidene)benzylamine (5). To a well-stirred solution of D-glyceraldehyde[3] (13 g, 0.1 mol) in diethyl ether (300 mL), anhydrous magnesium sulfate (18 g, 0.15 mol) was added and the resulting suspension was treated with freshly distilled benzylamine (10.7 g, 0.1 mol). The resulting reaction mixture was vigorously stirred for 1 h at which time the salts was filtered off and the resulting solution was washed with brine (3 x 150 mL). The organic layer was dried (Na_2SO_4) and evaporated to yield 21.5 g (99%) of the crude imine **5** as an oil. This material was sufficiently pure for use as judge by NMR spectroscopy. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.36 (s, 3H), 1.43 (s, 3H), 3.94 (dd, 1H, J = 8.6, 6.2 Hz), 4.20 (dd, 1H, J = 8.6, 6.9 Hz), 4.59 (s, 2H), 4.62 (ddd, 1H, J = 6.9, 6.2, 5.1 Hz), 7.23-7.38 (m, 5H), 7.74 (dt, 1H, J = 5.1, 1.5 Hz).

N-Benzyl-N-[O-2,3-isopropylidene-2(S),3-dihydroxypropyl]amine (6). A solution of imine **5** (20 g, 0.092 mol) in methanol (300 mL) was cooled (0 °C) and $NaBH_4$ (7.23 g, 0.184 mol) was added portionwise. After 30 min at 0 °C the solution was diluted with acetone (10 mL) and concentrated to nearly dryness. The residue was partitioned between brine (200 mL) and dichloromethane (200 mL). The aqueous layer was extracted twice (100 mL) with dichloromethane. The organic extracts were joined, dried (Na_2SO_4) and concentrated to yield the crude secondary amine **6** (18.33 g, 91%) which was used in the next step without further purification. An analytical sample can be obtained by flash chromatography using ethyl acetate as an eluent (R_f = 0.43). Oil; $[\alpha]^{20}_D$ = + 5.8° (c 1.04, $CHCl_3$) [Lit.[12a] $[\alpha]^{20}_D$ = + 5.5° (c 0.054, $CHCl_3$)]; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.34 (s, 3H), 1.40 (s, 3H), 1.60 (bs, 1H), 2.72 (d, 2H, J = 5.4 Hz), 3.66 (dd, 1H, J = 8.1, 6.6 Hz), 3.80 (s, 2H), 4.00 (dd, 1H, J = 8.1, 6.4 Hz), 4.23 (p, 1H, J = 6.2 Hz), 7.19-7.28 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 25.22, 26.68, 51.50, 53.73, 67.30, 75.22, 108.85, 126.71, 127.84, 128.14, 140.02.

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.72; H, 8.29; N, 6.40.

N-Benzyl-N-(tert-butoxycarbonyl)-N-[O-2,3-isopropylidene-2(S),3-dihydroxypropyl]amine (7). The crude secondary amine **6** (18 g, 0.082 mol) was dissolved in dichloromethane (250 mL), and DMAP (0.1 g, 0.82 mmol) and ditert-butyldicarbonate (26.81 g, 0.123 mol) were added. The mixture was stirred at room temperature for 24 h, cooled in ice and treated with cold (0 °C) 1M $KHSO_4$ for 15 min. The organic layer was separated, washed with brine (2 x 100 mL), dried (Na_2SO_4) and concentrated under reduced pressure.

Purification by flash chromatography (silica gel, 80:20 hexane-diethyl ether) of the residue afforded 21.1 g (80%) of pure **7** as an oil. R_f = 0.22 (80:20 hexane-diethyl ether); $[\alpha]^{20}_D$ = -19.8° (c 1.88, $CHCl_3$); ^1H NMR ($CDCl_3$, 55 °C, 300 MHz) δ 1.31 (s, 3H), 1.38 (s, 3H), 1.45 (s, 9H), 3.20 (dd, 1H, J = 14.5, 6.1 Hz), 3.45 (bd, 1H, J = 14.5 Hz), 3.60 (dd, 1H, J = 8.3, 6.8 Hz), 3.90 (dd, 1H, J =8.3, 6.2 Hz), 4.24 (p, 1H, J = 5.9 Hz), 4.45 (d, 1H, J = 15.6 Hz), 4.62 (d, 1H, J = 15.6 Hz), 7.29-7.58 (m, 5H); ^{13}C NMR ($CDCl_3$, 55 °C, 75.5 MHz) δ 25.55, 26.83, 28.42, 49.05, 49.60, 67.51, 75.46, 80.08, 109.20, 127.14, 127.56, 128.46, 138.54, 155.89.

Anal. Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.47; N, 4.36. Found: C, 67.01; H, 8.67; N, 4.57.

N-Benzyl-N-(tert-butoxycarbonyl)-N-[2(S),3-dihydroxypropyl]amine (8). A solution of **7** (21 g, 0.065 mol) and p-TosOH•H_2O (3.0 g, 0.016 mol) in methanol (400 mL) was heated at reflux for 4 h, then cooled to room temperature and treated with solid $NaHCO_3$ (3.75 g, 0.045 mol). After stirring for 15 min the mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was partitioned between ethyl acetate (300 mL) and brine (300 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated to give essentially pure **8** (18.27 g, 100%) as a sticky oil. This crude material was used in the next step without further purification. R_f = 0.25 (diethyl ether); ^1H NMR ($CDCl_3$+D_2O, 300 MHz) δ 1.45 (s, 9H), 3.30 (dd, 1H, J = 14.7, 6.1 Hz); 3.35 (dd, 1H, J = 14.7, 5.3 Hz); 3.47 (dd, 1H, J = 11.6, 4.8 Hz); 3.54 (dd, 1H, J = 11.6, 4.0 Hz); 3.72 (dddd, J = 6.1, 5.3, 4.8, 4.0 Hz), 4.46 (s, 2H), 7.19-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$+D_2O, 75.5 MHz) δ 28.06, 49.37, 52.17, 63.66, 70.76, 80.67, 127.14, 127.46, 128.33, 133.16, 137.79.

3-Benzyl-5-(hydroxymethyl)oxazolidin-2-one (9). To a cooled solution (0 °C) of **8** (18.0 g, 0.064 mol) in anhydrous THF (600 mL), sodium hydride (0.064 mol) as a 60% dispersion in mineral oil (2.56 g) was added. The suspension was stirred at room temperature for 2 h, then diluted with methanol (5 mL) and concentrated under reduced pressure. Flash chromatography of the residue (silica gel, 10:1 diethyl ether-methanol) afforded pure **9** (10.1 g, 76%) as a white solid; mp 82 °C; R_f = 0.10 (diethyl ether); $[\alpha]^{20}_D$ = + 38.8° (c 1.19, $CHCl_3$); ^1H NMR ($CDCl_3$+D_2O, 300 MHz) δ 3.30 (dd, 1H, J = 8.6, 6.7 Hz), 3.40 (t, 1H, J =8.8 Hz), 3.58 (dd, 1H, J = 12.6, 4.4 Hz), 3.79 (dd, 1H, J =12.6, 3.4 Hz), 4.31 (d, 1H, J = 15.7 Hz), 4.44 (d, 1H, J = 15.7 Hz), 4.53 (dddd, 1H, J = 9.0, 6.7, 4.4, 3.4 Hz), 7.26-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$+D_2O, 75.5 MHz) δ 45.01, 48.00, 62.66, 73.49, 127.79, 127.80, 128.61, 135.36, 158.01.

Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.61; H, 6.46; N, 6.90.

3-Benzyl-5-formyloxazolidin-2-one (L-isoserinal) (3). To a cold solution (-70 °C) of oxalyl chloride (6.9 mL, 0.081 mol) in dry dichloromethane (150 mL) was added dropwise dry DMSO (10.9 mL, 0.166 mol). The mixture was stirred for 10 min at which time a solution of **9** (10 g, 0.048 mol) in dichloromethane (50 mL) was added dropwise within 10 min and stirring was continued for 20 min. Triethylamine (20 mL, 0.144 mol) was added and the mixture was stirred for 5 min, and then allowed to warm to 0 °C. The mixture was filtered with suction through a bed of Celite, and concentrated to a small volume with a bath temperature below 30 °C. The residue was partitioned between ethyl acetate (150 mL) and brine (100 mL). The organic layer was separated, washed twice with brine (100 mL), dried (Na_2SO_4) and concentrated under reduced pressure with a bath temperature below 30 °C to afford crude L-isoserinal **3** (5.9 g, 60%) as a colourless oil. Purification of the aldehyde by flash chromatography led to considerable loss of material and extensive decomposition. The crude aldehyde was suitable for use without further purification as judged by ^1H NMR and it is advisable to be used immediately in next reactions. Optical measurements of this material were not very useful since they were in general quite variable: $[\alpha]^{20}_D$ = + 22.1° to + 30.5° (c 1.80, $CHCl_3$); ^1H NMR (DMSO-d_6, 120 °C, 300 MHz) δ

3.52 (dd, 1H, J = 9.2, 5.4 Hz), 3.68 (t, 1H, J = 9.3 Hz), 4.37 (s, 2H), 5.01 (dd, 1H, J = 9.4, 5.4 Hz), 7.25-7.36 (m, 5H), 9.65 (s, 1H).

Determination of the Enantiomeric Purity of L-isoserinal (3). Preparation of Mosher ester (11). To a solution of the alcohol **9** (50 mg, 0.24 mmol), prepared from **8** as described above, 1,3-dicyclohexylcarbodiimide (57.6 mg, 0.27 mmol), and 4-(dimethylamino)pyridine (8 mg, 0.064 mmol) in dichloromethane (15 mL) was added 2.72 mL of 0.09 M (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) in dichloromethane. This solution was stirred at room temperature and after 16 h, TLC (40:60 hexane-diethyl ether) showed the complete conversion into the Mosher ester (R_f = 0.12) at the expense of starting material (R_f = 0.02). The reaction mixture was filtered through cotton and concentrated under reduced pressure to dryness. Both ^1H and ^{19}F NMR of the crude residue (110 mg) showed that only one diastereomer was present. The crude Mosher ester **11** was purified by flash chromatography (silica gel, 40:60 hexane-diethyl ether) to give 85 mg (84%) of pure **11** as a colourless oil; $[\alpha]^{20}_D$ = +53.6° (c 1.46, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.10 (dd, 1H, J = 8.9, 6.4 Hz), 3.42 (t, 1H, J = 9.0 Hz), 3.50 (s, 3H), 4.12 (d, 1H, J = 14.9 Hz), 4.27 (dd, 1H, J = 12.1, 4.3 Hz), 4.45 (d, 1H, J = 14.9 Hz), 4.57 (dd, 1H, J =12.1, 3.5 Hz), 4.72 (dddd, 1H, J = 9.0, 6.4, 4.3, 3.5 Hz), 7.10-7.20 (m, 2H), 7.25-7.32 (m, 3H), 7.34-7.44 (m, 3H), 7.45-7.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 45.32, 48.19, 55.53, 65.37, 69.70, 84.74 (q, J = 27.5 Hz), 123.10 (q, J = 286.7 Hz), 127.26, 128.071 (2C), 128.63, 128.87, 129.86, 131.63, 135.14, 156.97, 166.29. ^{19}F NMR ($CDCl_3$, 300 MHz) δ -72.15.

Anal. Calcd for $C_{21}H_{20}NO_5F_3$: C, 59.57; H, 4.76; N, 3.31. Found: C, 59.59; H, 4.90; N, 3.18.

Identical results were obtained when the Mosher ester **11** was prepared from a sample of **9** obtained by the reduction of freshly prepared crude aldehyde **3** with $NaBH_4$ in methanol (0 °C, 30 min).

(Z)-N-](3-Benzyl-2-oxazolidinone-5-yl)methylidene]benzylamine N-oxide (12). To a well-stirred solution of the crude aldehyde **3** (1.0 g, 4.88 mmol) in dichloromethane (40 mL), N-benzylhydroxylamine[18] (0.6 g, 4.88 mmol) and anhydrous magnesium sulfate (0.6 g, 5 mmol) were added in one portion and the stirring was maintained at room temperature for 4 h. The mixture was filtered and the filtrate evaporated to yield the crude product. Purification by flash chromatography (silica gel, 30:70 hexane-ethyl acetate) afforded pure **12** (1.03 g, 68%) as a white solid; mp 148 °C; R_f = 0.20 (30:70 hexane-ethyl acetate); $[\alpha]^{20}_D$ = -105.7° (c 0.37, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.25 (dd, 1H, J = 9.3, 6.6 Hz), 3.81 (t, 1H, J = 9.3 Hz), 4.32 (d, 1H, J = 14.9 Hz), 4.40 (d, 1H, J = 14.9 Hz), 4.84 (ABq, 2H, J = 14.6 Hz, Δδ = 0.01), 5.35-5.43 (m, 1H), 6.90 (d, 1H, J = 4.4 Hz), 7.20-7.43 (m, 10H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 47.81, 48.33, 69.03, 69.13, 128.11, 128.25, 128.85, 129.19, 129.53 (2C), 131.46, 135.15, 136.38.

Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.98; H, 5.76; N, 9.12.

Methyl 3-(3-benzyl-2-oxazolidinone-5-yl)propenoate (13). To a well-stirred solution of methyl (triphenylphosphoranylidene)acetate (1.67 g, 5 mmol) in chloroform (25 mL) a solution of aldehyde **3** (1.0 g, 4.88 mmol) in the same solvent (25 mL) was added. The reaction mixture was stirred at room temperature for 48 h. Filtration through celite, evaporation of the solvent under reduced pressure and flash chromatography (silica gel, 60:40 hexane-diethyl ether) of the residue gave first **13b** (Z-isomer) (0.36 g, 28%) as an oil; R_f = 0.28 (Hexane-diethyl ether, 60:40); $[\alpha]^{20}_D$ = -135.5° (c 1.21, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.06 (dd, 1H, J = 9.1, 6.9 Hz), 3.67 (s, 3H), 3.87 (t, 1H, J = 9.2 Hz), 4.40 (ABq, 2H, J = 14.9 Hz, Δδ = 0.04), 5.82 (dddd, 1H, J = 9.1, 6.9, 6.4, 1.9 Hz), 5.88 (dd, 1H, J = 11.5, 1.9 Hz), 6.44 (dd, 1H, J =11.5, 6.4 Hz), 7.20-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 48.31, 49.99, 51.75, 70.94, 121.13, 127.99, 128.11, 128.82, 135.43, 147.97.

Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.42; H, 5.98; N, 5.40.

Eluted second was **13a** (E-isomer) (0.54 g, 42%) as an oil; R_f = 0.16 (Hexane-diethyl ether, 60:40); $[\alpha]^{20}_D$ = + 34.6° (c 0.76, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.14 (dd, 1H, J = 8.8, 6.8 Hz), 3.59 (t, 1H, J = 8.9 Hz), 3.73 (s, 3H), 4.36 (d, 1H, J = 14.8 Hz), 4.45 (d, 1H, J = 14.8 Hz), 5.05 (dddd, 1H, J = 9.0, 6.8, 5.0, 1.8 Hz), 6.14 (dd, 1H, J = 15.6, 1.8 Hz), 6.81 (dd, 1H, J =15.6, 5.0 Hz), 7.20-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 48.35, 48.62, 51.95, 71.24, 122.82, 128.11 (2C), 128.92, 135.18, 142.35, 157.18, 169.89.

Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.40; H, 5.63; N, 5.69.

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