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Synthesis of Tyrosine-Derived Tetrahydroisoquinolines by Lewis Acid Catalyzed Cyclization of *N*-(Phenylsulfonyl)alkyloxazolidinones

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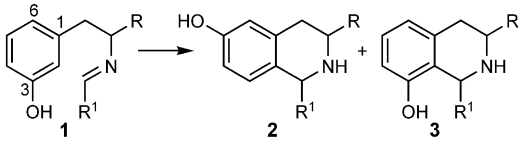
Dedicated to Professor Ekkehard Winterfeldt on the occasion of his 75th birthday

Keywords: Amino acids / Bromine / Protecting groups / Debromination / Oxazolidinones / Regioselectivity

N-Boc-protected tyrosine esters **5a**,**b** were converted into tetrahydroisoquinolines **13** and **14** in four steps by reduction and ring closure to oxazolidinones **9** and **10**, addition of benzenesulfinic acid and aldehydes to sulfones **11** and **12** and subsequent Lewis acid catalyzed cyclization. In the case of *m*-tyrosine derivative **5a**, selective protection with bromine prevented the formation of undesired regioisomers. Debromination of target compounds **13** was readily achieved under radical reduction conditions by using Bu_3SnH/AIBN. Tetrahydroisoquinolines **13** and **14** were isolated as single diastereomers whose *trans* configuration was confirmed by X-ray crystal structure analysis. Partial epimerization of *trans*-**13i** and *trans*-**21** to the corresponding *cis* diastereomers was achieved under basic conditions.

Introduction

Tetrahydroisoquinoline alkaloids have received much interest because of their tremendous structural diversity and broad spectrum of biological and pharmaceutical activities.[1] The most popular synthetic approaches towards tetrahydroisoquinolines are the Pictet–Spengler reaction,[2,3] the Bischler–Napieralski reaction,[4,5] and the Pomeranz–Fritsch reaction.[6–8] However, concerning *m*-tyrosine-derived precursors **1**, the above-mentioned cyclizations are hampered by the formation of regioisomers **2** and **3** (Scheme 1) or undesired byproducts such as oxazoles.[9]



Scheme 1. Possible regioisomers **2** and **3**.

A typical example for these regioisomers was reported by Myers in the total synthesis of (–)-quinocarcin.[10] To overcome the regioselectivity problem, Fukuyama introduced a bromine protecting group at C-6 of cyclization precursor **1**, and subjected these bromo-substituted *m*-tyrosines to Pictet–Spengler reactions.[11] Hashmi used substituted furylalanine derivatives in Au-catalyzed cycloisomerizations.[12] Upon searching for suitable methods we were attracted by the conversion of benzyl-substituted oxazolidinones with aldehydes and benzenesulfinic acid to the corresponding *N*-[1-(phenylsulfonyl)alkyl]oxazolidinones and their Lewis acid mediated ring closure to tricyclic tetrahydroisoquinoline derivatives published by Petrini.[13] This approach was used for the synthesis of azapodophyllotoxin[14] starting from DOPA.[13b] To the best of our knowledge, however, in no case was either *p*- or *m*-tyrosine considered as a starting material. Thus, we investigated the cyclization of tyrosine-derived *N*-[(phenylsulfonyl)alkyl]oxazolidinones as an extension of Petrini's methodology. The results are reported below.

Results and Discussion

The synthesis of cyclization precursors **9** and **10** commenced with the conversion of tyrosines **4a**,**b** to the corresponding Boc-protected amino acids[15] in 90 and 81% yield, respectively, following the method used by Jung[15a] (Scheme 2). The *N*-Boc derivatives were subsequently methylated with iodomethane in acetone in the presence of K_2CO_3 according to the protocol by Reddy[16a] to give compounds **5a**,**b**[16] in 97 and 76% yield, respectively.

Prior to reduction with $LiBH_4$ in Et_2O/MeOH to alcohol **7** (95%), *m*-tyrosine **5a** was brominated at the C-6 position with NBS in CH_2Cl_2 at room temperature to compound **6** (86%) (Scheme 2) to suppress cyclization to the undesired regioisomer. Tyrosine derivative **5b** was directly reduced to corresponding Boc-protected amino alcohol **8**[16a] in 80% yield.

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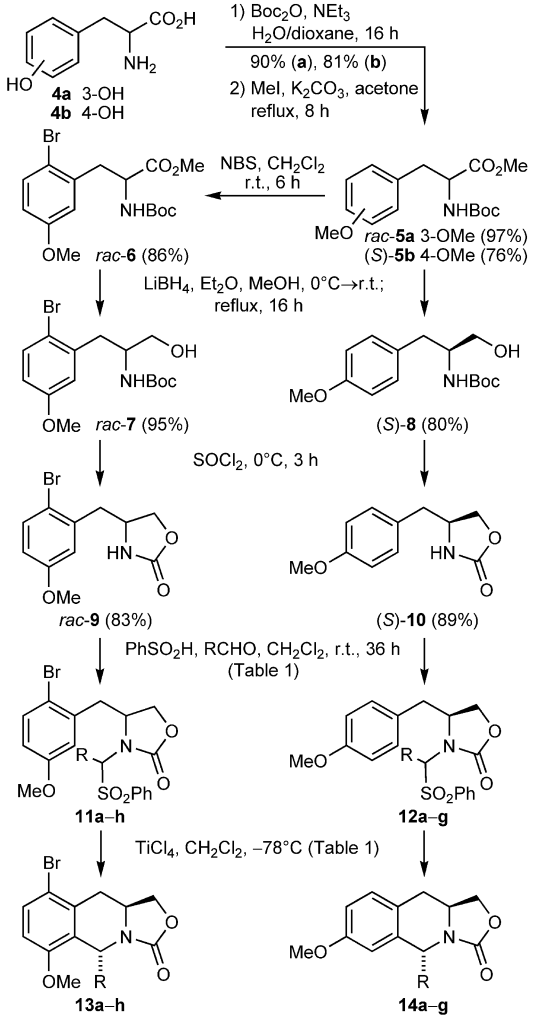


Scheme 2. Preparation of *m*- and *p*-tyrosine-derived oxazolidinones **9** and **10** and subsequent cyclization to corresponding tetrahydroisoquinolines **13** and **14**.

Treatment of amino alcohols **7** and **8** with thionyl chloride at 0 °C[13b] yielded oxazolidinones **9** and **10** in 83 and 89% yield, respectively. Crystallization of derivative **10** from Et_2O gave single crystals that were suitable for X-ray crystal structure analysis (Figure 1).[17]

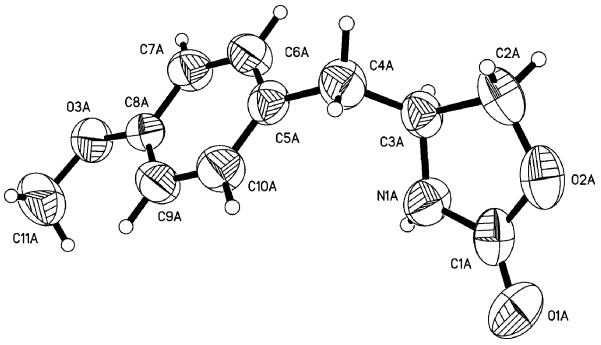


Figure 1. Molecular structure of 4-(4-methoxybenzyl)-1,3-oxazolidin-2-one (**10**) in the solid state (ORTEP presentation).

Following the protocol of Petrini,[13] compounds **9** and **10** were treated with benzenesulfinic acid and various aldehydes to give corresponding α-amidoalkylphenyl sulfones **11** and **12** as diastereomeric mixtures. The results are summarized in Table 1.

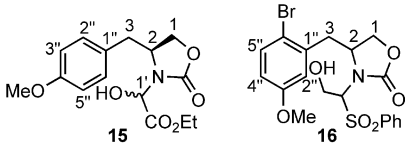
Whereas the addition reaction worked for aliphatic aldehydes and croton- and 2-benzyloxyacetaldehyde (Table 1, Entries 1–5, 9–13), benzaldehyde and glyoxal did not give sulfones **11f**,**g** and **12f**,**g** (Table 1, Entries 6, 7, 14, 15). In the reaction of tyrosine-based oxazolidinone **10** and glyoxal, hemiaminal **15** was isolated instead (Table 1). Under the conditions of the addition reaction, *m*-tyrosine-derived **9** afforded directly tricyclic tetrahydroisoquinoline **13f** in 4% yield. As derivative **11e** was difficult to isolate, the alter-

Table 1. Reaction of oxazolidinones **9** and **10** with aldehydes and $PhSO_2H$ to form *N*-[1-(phenylsulfonyl)alkyl]oxazolidinones **11** and **12** followed by cyclization to tetrahydroisoquinolines **13** and **14**[a].

Entry	Compound	RCHO	Oxazolidinones			Time	Isoquinolines	
		R =		Yield [%]	*dr*	[h]		Yield [%]
1	**9**	Pr	**11a**	78	51:49	0.75	**13a**	56
2	**9**	C_5H_{11}	**11b**	41	51:49	2.25	**13b**	80
3	**9**	*i*Pr	**11c**	37	58:42	2.5	**13c**	80
4	**9**	$CH{=}CHCH_3$	**11d**	52	67:33	1.0	**13d**	19
5	**9**	CH_2OBn	**11e**	38	55:45	6.5	**13e**	–[b]
6	**9**	Ph	**11f**	–	–	36	**13f**	4[c]
7	**9**	CO_2Et	**11g**	–	–	–	**13g**	–
8	**9**	CH_2OPMB	**11h**	40	56:44	1.0	**13h**	–[d]
9	**10**	Pr	**12a**	31	89:11	1.0	**14a**	68
10	**10**	C_5H_{11}	**12b**	11	57:43	2.0	**14b**	73
11	**10**	*i*Pr	**12c**	52	51:49	2.5	**14c**	28
12	**10**	$CH{=}CHCH_3$	**12d**	44	70:30	1.0	**14d**	–[e]
13	**10**	CH_2OBn	**12e**	22	68:32	0.75	**14e**	30
14	**10**	Ph	**12f**	–[f]	–	–	**14f**	–
15	**10**	CO_2Et	**12g**	–[g]	–	–	**14g**	–

[a] Reaction conditions according to Scheme 2. [b] Starting material **11e** was reisolated in 36% yield. [c] Under the reaction conditions starting material **9** was directly converted into **13f** (4%) and reisolated in 37%. [d] Oxazolidinone **16** was isolated in 50% (*dr* 52:48). [e] Starting material **12d** was reisolated in 68% yield. [f] Starting material **10** was reisolated in 37% yield. [g] Hemiaminal **15** was isolated in 51% yield (*dr* 71:29).

native paramethoxybenzyl (PMB) protecting group was used; addition product **11h** was obtained in 40% yield (Table 1, Entry 8).



N-[1-(Phenylsulfonyl)alkyl]oxazolidinones **11** and **12** were then cyclized in the presence of $TiCl_4$ in CH_2Cl_2 at –78 °C[13] to afford target compounds **13** and **14** (Scheme 2). As can be seen from Table 1, the ring closure of starting sulfones **11a**–**c** and **12a**–**c** proceeded uneventfully (Table 1, Entries 1–3, 9–11). Crotyl-substituted compound **12d**, however, did not react and was reisolated in 68% yield, whereas analogous *m*-tyrosine-based derivative **11d** gave the product in 19% yield (Table 1, Entries 4, 12). In contrast, from benzyloxymethyl-substituted oxazolidinones **11e** and **12e**, the reaction of tyrosine derivative **12e** afforded tricyclic compound **14e**, whereas **13e** was not formed (Table 1, Entries 5, 13). Under the cyclization conditions, the PMB protecting group in compound **11h** was removed and sulfone derivative **16** was isolated instead of desired tetrahydroisoquinoline **13h** (Table 1, Entry 8).

It should be noted that in all cases tetrahydroisoquinolines **13** and **14** were obtained as single diastereomers independent of the diastereomeric ratio of intermediate adducts **11** and **12**. The *trans* configuration was assigned according to NOE experiments for tyrosine-based tetrahydroisoquinoline **14e**. This assignment was further supported by X-ray crystal structure analysis of *m*-tyrosine derivative **13a** (Figure 2).[17]

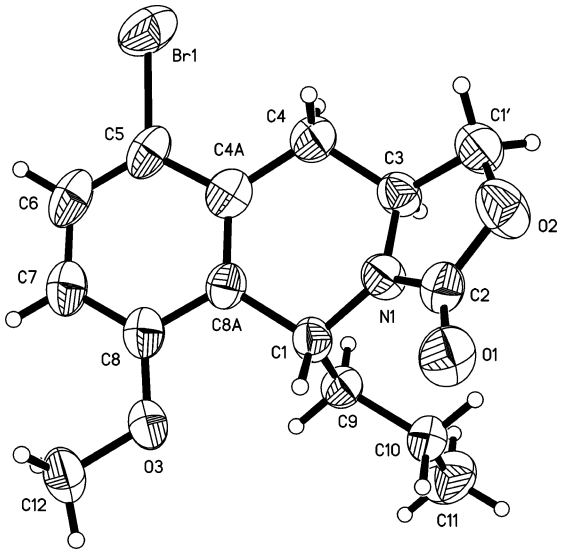
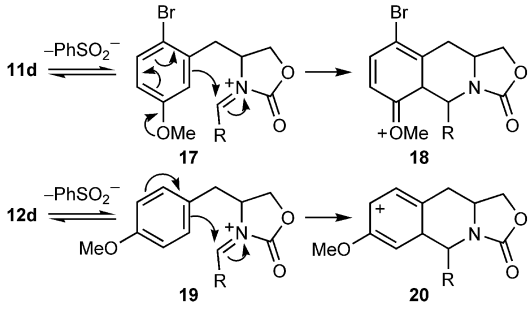


Figure 2. Molecular structure of 9-bromo-6-methoxy-5-propyl-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one (**13a**) in the solid state (ORTEP presentation).

The failure of initial adduct formation of benzaldehyde and glyoxal might be due to the oxazolidinone because Petrini reported the successful conversion of both aldehydes to the corresponding amido sulfones.[18] In our case, however, sulfinic acid partially reduced the aldehydes to the corresponding primary alcohols, RCH_2OH, which were found in all crude mixtures as byproducts.

The failure of ring closure in the case of crotyl-substituted oxazolidinone **12d** might be explained by the influence of the methoxy group. Although the charge delocalization through conjugation with R should be operative in both acyliminium ions **17** and **19**, presumably the +M effect of the methoxy substituent in *m*-tyrosine derivative **17** increases the nucleophilicity of the aromatic ring relative to tyrosine derivative **19** where such mesomeric activation is not possible (Scheme 3).



Scheme 3.

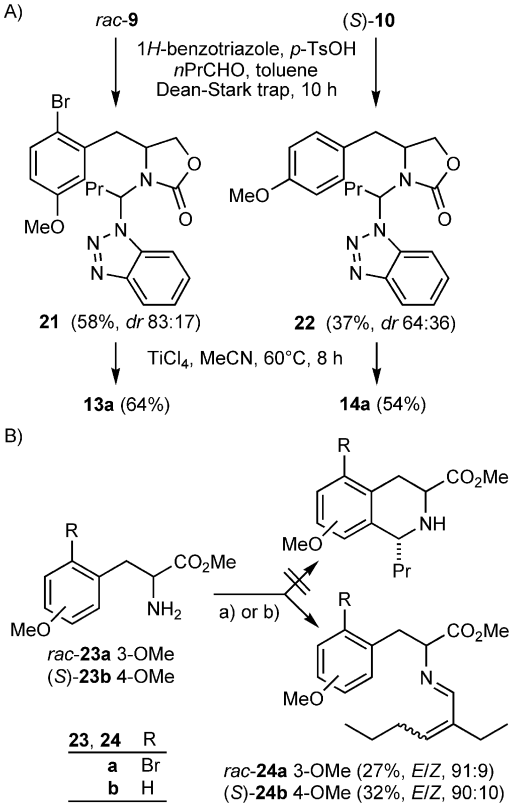
As shown in Scheme 4 for one example, alternative procedures were investigated for comparison. Following the benzotriazole method by Katritzky[14a] (A), tricyclic products **13a** and **14a** could be isolated in 64 and 54% yield, respectively.

In contrast, the direct Pictet–Spengler reaction (B) could not be applied to starting materials **23a**,**b**. Under the used conditions, condensation products **24a**,**b** were obtained instead of the desired bicycles. Derivatives **24** might be formed by an aldol-type condensation in analogy to a former publication by Ishii.[19] It should be noted that Tourwé and Hruby reported the failure of tetrahydroisoquinoline formation from tyrosine derivatives and formaldehyde by the Pictet–Spengler reaction.[20] It thus seems that the limitations of the Pictet–Spengler cyclization with regard to aliphatic aldehydes can be overcome by the Petrini and Katritzky methods.

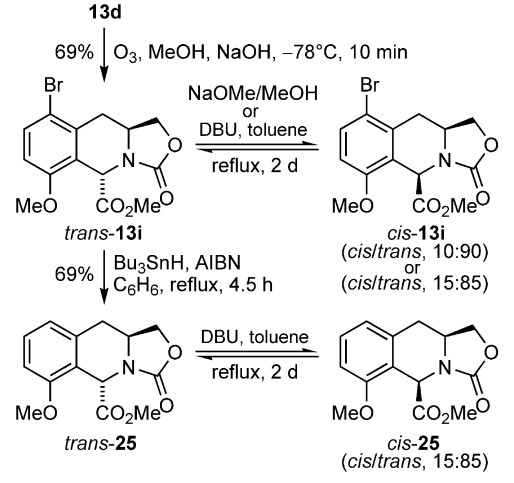
m-Tyrosine-derived tetrahydroisoquinolines **13a**,**b** were debrominated under radical reduction conditions by using Bu_3SnH in the presence of catalytic amounts of AIBN in refluxing benzene according to the method of Fukuyama[11,21] to afford the corresponding tricyclic products in 88 and 51% yield, respectively.

Next, the utilization of crotyl-substituted tetrahydroisoquinoline **13d** as a possible precursor to the AB system of the antitumor alkaloid quinocarcin[10,22,23] was investigated. Thus, derivative **13d** was ozonized in MeOH in the presence of NaOH at –78 °C to derivative **13i**, which was isolated in 69% yield (Scheme 5).

Its *trans* configuration was confirmed by X-ray crystal structure analysis (Figure 3).[17] It should be noted that corresponding ethyl ester **13g** could not be obtained by the



Scheme 4. Cyclization by (A) benzotriazole and (B) the Pictet–Spengler reaction. Reaction conditions: (a) 1. butyraldehyde (1.6 equiv.), molecular sieves 4 Å, CH_2Cl_2, r.t., 24 h; 2. TFA (3.2 equiv.), 0 °C, 16 h, 27% (**24a**), 32% (**24b**); (b) *p*-TsOH (0.1 equiv.), *n*PrCHO (1 equiv.), Dean–Stark trap, 16 h, 18% (**24a**), 14% (**24b**).



Scheme 5.

sulfinic acid route (Table 1). Radical-induced debromination of *trans*-**13i** gave derivative *trans*-**25** in 69% yield. Epimerization with NaOMe in MeOH heated at reflux led to complete decomposition of *trans*-**25**. In contrast, bromo derivative *trans*-**13i** epimerized partially under these conditions to yield a *trans*:*cis* mixture of **13i** in a 90:10 ratio. By using DBU in boiling toluene, however, both **13i** and **25** epimerized to *cis* configured analogues *cis*-**13i** and *cis*-**25** in a *trans*:*cis* ratio of 85:15. The isomers of **13i** could be separated by preparative HPLC [t_R(*cis*) = 6.59 min and t_R(*trans*) = 10.05 min] to afford *trans*- and *cis*-**13i** in 93 and 5% yield, respectively.

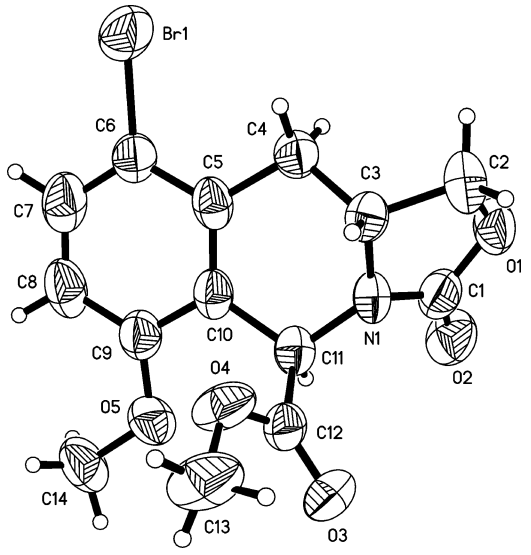


Figure 3. Molecular structure of methyl 9-bromo-6-methoxy-3-oxo-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinoline-5-carboxylate (**13i**) (ORTEP presentation).

Conclusions

It could be demonstrated that *N*-[1-(phenylsulfonyl)-alkyl]oxazolidinones **11** and **12** are valuable intermediates for the synthesis of tyrosine-derived tetrahydroisoquinolines **13** and **14**. Butyraldehyde was used to compare Petrini's method with Katritzky's benzotriazoles and the Pictet–Spengler cyclization. Whereas the latter completely failed, the methods by Petrini and Katritzky gave similar results. Thus, the used Petrini method complements the Pictet–Spengler reaction. In particular, *m*-tyrosine **4a** can be converted regioselectively via the *N*-[1-(phenylsulfonyl)alkyl]-oxazolidinones to the corresponding tetrahydroisoquinolines by employing bromine as a protecting group. This may open synthetic access to tetrahydroisoquinoline alkaloids.

Experimental Section

General: Melting points were determined with a Büchi SMP 20 and are uncorrected. NMR spectra were recorded with a Bruker Avance 300 or a Bruker Avance 500 (^{1}H: 300 or 500 MHz, ^{13}C: 75 or 125 MHz) with TMS as an internal standard. Signal assignments were made on the basis of DEPT experiments. IR spectra were recorded with a Bruker Vector 22 FTIR. Mass spectrometry was performed with a Finnigan MAT 95, Varian MAT 711, or Bruker Daltonics micrOTOF_Q. Chromatography was performed on silica gel 60 (230–400 mesh) (Macherey–Nagel). GC was performed with a Hewlett–Packard HP 6890, column HP 5TA (30 m × 0.32 mm), temperature program 16 °C min^{-1}, gradient from 80 to 300 °C. Commercial reagents were used without further purification. Bu-

tyraldehyde, isobutyraldehyde, crotonaldehyde, and hexanal, as well as all solvents, were distilled prior to use. Reactions were performed in oven-dried glassware under a N_2 atmosphere. The following compounds were prepared according to literature procedures: *N*-Boc protected tyrosines,[15a] **5a**,**b**,[16a] **8**,[16a] [(4-methoxybenzyl)oxy]-acetaldehyde,[24] and benzenesulfinic acid.[25]

Methyl 2-Bromo-*N*-(*tert*-butoxycarbonyl)-5-methoxyphenylalaninate (6): *N*-Bromosuccinimide (790 g, 4.44 mmol) was added portionwise to a solution of **5a** (1.25 g, 4.04 mmol) in absolute DMF (40 mL), and the reaction mixture was stirred at room temperature for 6 h. The solvent was removed, and the residue was chromatographed on SiO_2 (hexanes/EtOAc, 6:1) to give **6** as a colorless solid (1.36 g, 86%). M.p. 106–108 °C. R_f = 0.23 (hexanes/EtOAc, 6:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 [s, 9 H, C(CH_3)$_3$], 3.05 (dd, J = 8.3, 13.8 Hz, 1 H, 3-H$_A$), 3.27 (dd, J = 5.7, 13.8 Hz, 1 H, 3-H$_B$), 3.72 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 4.60–4.67 (m, 1 H, 2-H), 5.07 (d, J = 8.3 Hz, 1 H, NH), 6.68 (dd, J = 2.9, 8.7 Hz, 1 H, 4′-H), 6.75 (d, J = 2.9 Hz, 1 H, 2′-H), 7.42 (d, J = 8.7 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3 [C(CH$_3$)$_3$], 38.8 (C-3), 52.4 (OCH$_3$), 53.5 (C-2), 55.4 (OCH$_3$), 79.9 [C(CH$_3$)$_3$], 114.5 (C-2′, C-4′), 115.4 (C-6′), 116.7 (C-2′, C-4′), 133.4 (C-5′), 136.9 (C-1′), 155.0, 158.9 (C-3′, CO$_2$$t$Bu), 172.4 ($CO_2CH_3$) ppm. FTIR (ATR): $\tilde{\nu}$ = 1739 (s), 1689 (s), 1521 (s), 1480 (m), 1463 (m), 1440 (m), 1276 (br., m), 1240 (s), 1218 (s), 1157 (vs), 1041 (m), 1013 (m), 994 (m), 847 (m), 825 (m), 599 (br., m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 389 (7) [M]$^+$, 387 (7) [M]$^+$, 333 (13), 331 (13), 316 (10) [M – OC(CH$_3$)$_3$]$^+$, 314 (10) [M – OC(CH$_3$)$_3$]$^+$, 288 (2) [M – CO$_2$C(CH$_3$)$_3$]$^+$, 286 (2) [M – CO$_2$C(CH$_3$)$_3$]$^+$, 272 (35), 270 (29), 252 (43), 230 (11), 228 (11), 208 (22), 200 (10), 191 (30), 175 (2), 148 (9), 132 (3), 121 (6), 91 (3), 88 (20), 77 (2), 57 (100) [C(CH$_3$)$_3$]$^+$, 41 (7). $C_{16}H_{22}BrNO_5$ (388.25): calcd. C 49.50, H 5.71, N 3.61, Br 20.58; found C 49.71, H 5.79, N 3.61, Br 20.62.

***tert*-Butyl 1-(2-Bromo-5-methoxybenzyl)-2-hydroxyethylcarbamate (7):** To a solution of **6** (2.10 g, 5.41 mol) in absolute Et_2O (100 mL) in a Schlenk flask under inert gas at 0 °C was added lithiumborohydride (470 mg, 21.6 mmol) and absolute MeOH (10 mL), and the reaction mixture was stirred at 0 °C for a further 30 min. After warming to room temperature, the reaction mixture was heated at reflux for 16 h. Then a saturated solution of NH_4Cl (50 mL) was added, and the reaction mixture was stirred for 15 min. The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (3 × 100 mL), dried (Na_2SO_4), and concentrated. The residue was chromatographed on SiO_2 (hexanes/EtOAc, 2:1) to give **7** as a colorless solid (1.84 mg, 95%). M.p. 109–110 °C. R_f = 0.24 (hexanes/EtOAc, 2:1) ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, C(CH_3)$_3$], 2.17 (br. s, 1 H, OH), 2.74–2.96 (m, 1 H, 3-H$_A$), 2.99 (dd, J = 6.8, 13.7 Hz, 1 H, 3-H$_B$), 3.61 (dd, J = 4.6, 11.2 Hz, 1 H, 1-H$_A$), 3.70 (dd, J = 3.6, 11.2 Hz, 1 H, 1-H$_B$), 3.77 (s, 3 H, OCH_3), 3.87–3.94 (m, 1 H, 2-H), 4.91 (d, J = 7.8 Hz, 1 H, NH), 6.67 (dd, J = 3.0, 8.8 Hz, 1 H, 4′-H), 6.75 (br. s, 1 H, 2′-H), 7.42 (d, J = 8.8 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.3 [C(CH$_3$)$_3$], 37.5 (C-3), 53.1 (C-2), 55.5 (OCH$_3$), 64.5 (C-1), 79.7 [C(CH$_3$)$_3$], 114.1 (C-2′), 115.3 (C-6′), 116.7 (C-4′), 133.3 (C-5′), 138.6 (C-1′), 156.0, 159.0 (C-3′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1687 (vs), 1670 (m), 1573 (m), 1520 (s), 1475 (m), 1445 (m), 1418 (m), 1391 (m), 1366 (m), 1356 (m), 1318 (m), 1303 (m), 1280 (m), 1241 (s), 1166 (s), 1145 (m), 1091 (m), 1065 (m), 1015 (m), 1004 (s), 822 (m), 807 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 361, 359 (1) [M]$^+$, 330, 328 (1), 305, 303 (1), 274, 272 (4), 230, 228 (10), 224 (12), 203, 201 (7), 202, 200 (7) [M + H – HOCH$_2$CHNHC(O)OC(CH$_3$)$_3$]$^+$, 180 (6), 161 (2), 160 (26) [HOCH$_2$CHNHC(O)OC(CH$_3$)$_3$]$^+$, 121 (4), 104 (34), 60 (78), 57 (100) [C(CH$_3$)$_3$]$^+$, 42 (2), 41 (11), 28 (11). $C_{15}H_{22}BrNO_4$ (360.24): calcd. C 50.01, H 6.16, N 3.89; found C 50.09, H 6.23, N 3.86.

General Procedure for the Cyclization to Oxazolidinones 9 and 10: To an ice-cold solution of either **7** or **8** in absolute THF in a Schlenk flask under inert gas was added dropwise thionyl chloride (8 equiv.), and the reaction mixture was stirred at 0 °C for a further 3 h. After warming to room temperature, all volatile materials were removed and crude product **9** or **10** was chromatographed on SiO_2 (CH_2Cl_2/EtOAc, 3:1).

4-(2-Bromo-5-methoxybenzyl)-1,3-oxazolidin-2-one (9): From **7** (1.84 g, 5.12 mmol) in THF (100 mL) was obtained **9** as a colorless solid (1.21 g, 83%). M.p. 87–88 °C. R_f = 0.31 (CH_2Cl_2/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.94 (dd, J = 7.4, 13.5 Hz, 1 H, 3-H$_A$), 3.02 (dd, J = 5.6, 13.5 Hz, 1 H, 3-H$_B$), 3.79 (s, 3 H, OCH_3), 4.16–4.27 (m, 2 H, 1-H, 2-H), 4.43–4.52 (m, 1 H, 1-H), 5.73 (br. s, 1 H, NH), 6.71 (dd, J = 3.0, 8.7 Hz, 1 H, 4′-H), 6.77 (d, J = 3.0 Hz, 1 H, 2′-H), 7.45 (d, J = 8.7 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.6 (C-3), 52.0 (C-2), 55.5 (OCH$_3$), 69.5 (C-1), 114.4 (C-4′), 114.7 (C-6′), 117.2 (C-2′), 133.9 (C-5′), 136.4 (C-1′), 159.2, 159.3 (C-5′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1766 (vs), 1592 (m), 1579 (m), 1480 (m), 1470 (m), 1436 (m), 1404 (m), 1310 (m), 1239 (s), 1221 (s), 1177 (s), 1120 (m), 1114 (m), 1075 (m), 1007 (s), 948 (m), 937 (s), 889 (m), 822 (m), 812 (s), 762 (m), 705 (s), 657 (br., m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 287, 285 (22) [M]$^+$, 207 (12), 206 (100) [M – Br]$^+$, 202 (97) [H$_3$COC$_6$H$_4$BrCH$_2$ + H]$^+$, 200 (98) [MeOC$_6$H$_4$BrCH$_2$ + H]$^+$, 160, 158 (4), 171, 169 (3), 162 (13), 147 (1), 132 (1), 121 (29), 105 (3), 91 (9), 86 (86) [M – MeOC$_6$H$_4$BrCH$_2$]$^+$, 77 (9), 63 (3), 58 (5), 42 (20), 28 (2). $C_{11}H_{12}BrNO_3$ (286.12): calcd. C 46.18, H 4.23, N 4.90; found C 46.25, H 4.26, N 4.82.

(4*S*)-4-(4-Methoxybenzyl)-1,3-oxazolidin-2-one (10): From **8** (959 mg, 3.41 mmol) in THF (60 mL) was obtained **10** as colorless crystals (632 mg, 89%). M.p. 75 °C. R_f = 0.20 (CH_2Cl_2/EtOAc, 3:1). $[\alpha]_D^{22}$ = –55.9 (c = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.80 (dd, J = 6.6, 13.8 Hz, 1 H, 3-H$_A$), 2.83 (dd, J = 7.2, 13.8 Hz, 1 H, 3-H$_B$), 3.79 (s, 3 H, OCH_3), 4.02–4.07 (m, 1 H, 2-H), 4.13 (dd, J = 5.5, 8.7 Hz, 1 H, 1-H$_A$), 4.43 (dd, J = 8.0, 8.7 Hz, 1 H, 1-H$_B$), 5.72 (br. s, 1 H, NH), 6.85–6.88 (m, 2 H, 3′-H, 5′-H), 7.09–7.10 (m, 2 H, 2′-H, 6′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.5 (C-3), 53.9 (C-2), 55.3 (OCH$_3$), 69.6 (C-1), 114.4 (C-3′, C-5′), 127.9 (C-1′), 130.0 (C-2′,C-6′), 158.8, 159.4 (C-4′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1740 (vs), 1512 (s), 1243 (s), 1178 (m), 1026 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 208 (1) [M + H]$^+$, 207 (10) [M]$^+$, 123 (2), 122 (26), 121 (100) [CH$_2$C$_6$H$_5$OMe]$^+$, 107 (2), 91 (3), 78 (4), 65 (3), 51 (1), 42 (4), 32 (3), 28 (30), 18 (24). $C_{11}H_{13}NO_3$ (207.23): calcd. C 63.76, H 6.32, N 6.76; found C 63.73, H 6.34, N 6.66.

General Procedure for the Preparation of Sulfones 11 and 12: To a solution of either **9** or **10** (100–150 mg, 1 equiv.) in CH_2Cl_2 (5–7 mL) in a Schlenk flask under inert gas were successively added benzenesulfinic acid (2 equiv.), the respective aldehyde (1.5 equiv.), and $MgSO_4$ (100–150 mg), and the reaction mixture was stirred for 36 h at room temperature. Then, the mixture was filtered through a sintered-glass frit (bottom layer: 1 cm sand, top layer: 1 cm Florisil) with CH_2Cl_2. The filtrate was concentrated and crude sulfone **10** or **11** was chromatographed on SiO_2.

4-(2-Bromo-5-methoxybenzyl)-3-[1-(phenylsulfonyl)butyl]-1,3-oxazolidin-2-one (11a): Yield: 132 mg (78%), colorless foam. R_f = 0.13 (hexanes/EtOAc, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94–1.04 (m, 3 H, 4′′-H), 1.30–1.57 (m, 2 H, 3′′-H), 2.06–2.18 (m, 0.5 H, 2′′-H), 2.22–2.35 (m, 1 H, 2′′-H), 2.39–2.52 (m, 0.5 H, 2′′-H), 2.81 (dd, J = 11.2, 13.1 Hz, 0.5 H, 3-H$_A$), 2.85 (dd, J = 11.2, 13.4 Hz,

0.5 H, 3-H_A), 3.31 (dd, J = 3.6, 13.1 Hz, 0.5 H, 3-H_B), 3.70 (br. d, J = 13.4 Hz, 0.5 H, 3-H_B), 3.80 (2 s, 3 H, OCH_3), 3.90–3.95 (m, 0.5 H, 1-H), 4.08–4.18 (m, 1.5 H, 1-H), 4.24–4.33 (m, 0.5 H, 2-H), 4.64–4.76 (m, 0.5 H, 2-H), 4.93 (br. d, J = 9.2 Hz, 0.5 H, 1′′-H), 5.15 (t, J = 7.4 Hz, 0.5 H, 1′′-H), 6.73 (ddd, J = 1.8, 2.9, 8.7 Hz, 1 H, 4′-H), 6.78 (dd, J = 2.4, 2.9 Hz, 1 H, 2′-H), 7.47 (dd, J = 3.8, 8.7 Hz, 1 H, 5′-H), 7.55–7.63 (m, 2 H, m-C_6H_5), 7.66–7.73 (m, 1 H, p-C_6H_5), 7.92–7.96 (m, 1 H, o-C_6H_5), 7.99–8.03 (m, 1 H, o-C_6H_5) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.45, 13.50 (C-4′′), 19.3, 19.7 (C-3′′), 26.8, 27.4 (C-2′′), 40.0, 40.3 (C-3), 53.4 (C-2), 55.6 (OCH$_3$), 66.9, 67.0 (C-1), 74.6, 75.7 (C-1′′), 114.5, 114.6 (C-4′), 114.8, 115.1 (C-6′), 117.7, 117.8 (C-2′), 128.7 (o-C_6H_5), 129.28, 129.32, 129.5 (o-, m-C_6H_5), 134.0 (C-5′), 134.3, 134.5 (p-C_6H_5), 135.8, 135.9, 136.9, 137.4 (C-1′, C-6′, i-C_6H_5), 157.1, 159.2 (C=O, C-3′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1753 (vs), 1473 (m), 1446 (m), 1403 (m), 1305 (m), 1240 (m), 1199 (m), 1163 (m), 1143 (s), 1079 (m), 1044 (m), 1012 (m), 722 (m), 687 (m), 600 (m), 577 (m), 555 (m), 540 (m), 522 (m) cm^{-1}. MS (FAB, 3-nitrobenzyl alcohol + NaI): m/z (%) = 506 (48) [M + Na]$^+$, 504 (46) [M + Na]$^+$, 479 (2), 477 (2), 413 (2), 364 (27) [M + Na – PhSO$_2$H]$^+$, 362 (27) [M + Na – PhSO$_2$H]$^+$, 342 (22) [M – SO$_2$Ph]$^+$, 340 (23) [M – SO$_2$Ph]$^+$, 329 (15), 327 (13), 284 (3), 218 (1), 199 (16) [$H_3COC_6H_3BrCH_2$]$^+$, 176 (100) [3-$NO_2C_6H_5$ + Na]$^+$, 172 (21), 136 (9), 95 (7), 92 (11), 69 (11), 55 (15). HRMS (FAB): calcd. for $C_{21}H_{24}BrNNaO_5S^+$ [M + Na]$^+$ 504.0451; found 504.0452.

4-(2-Bromo-5-methoxybenzyl)-3-[1-(phenylsulfonyl)hexyl]-1,3-oxazolidin-2-one (11b): Yield: 74 mg (41%), colorless foam. R_f = 0.25 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82–0.96 (m, 3 H, 6′′-H), 1.21–1.61 (m, 6 H, 3′′-H, 4′′-H, 5′′-H), 2.09–2.23 (m, 0.56 H, 2′′-H), 2.24–2.35 (m, 1.01 H, 2′′-H), 2.35–2.52 (m, 0.53 H, 2′′-H), 2.81 (dd, J = 7.8, 13.1 Hz, 0.5 H, 3-H), 2.85 (dd, J = 7.6, 13.1 Hz, 0.5 H, 3-H), 3.31 (dd, J = 3.5, 13.1 Hz, 0.52 H, 3-H), 3.70–3.76 (m, 0.53 H, 3-H), 3.80 (2 s, 1.5 H, OCH_3), 3.88–3.98 (m, 0.56 H, 1-H), 4.05–4.23 (m, 1.69 H, 1-H), 4.22–4.35 (m, 0.56 H, 2-H), 4.63–4.77 (m, 0.52 H, 2-H), 4.92 (br. d, J = 9.8 Hz, 0.49 H, 1′′-H), 5.09–5.19 (m, 0.48 H, 1′′-H), 6.73 (dd, J = 2.9, 8.8 Hz, 1 H, 4′-H), 6.78 (dd, J = 1.8, 2.9 Hz, 1 H, 2′-H), 7.45 (dd, J = 4.2, 8.8 Hz, 1 H, 5′-H), 7.55–7.63 (m, 2 H, m-$SO_2C_6H_5$), 7.66–7.73 (m, 1 H, p-$SO_2C_6H_5$), 7.92–7.95 (m, 1 H, o-$SO_2C_6H_5$), 7.99–8.01 (m, 1 H, o-$SO_2C_6H_5$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.89, 13.90 (C-6′′), 22.3 (C-4′′, C-5′′), 24.8, 25.4 (C-2′′), 25.6, 26.6 (C-3′′), 31.09, 31.13 (C-4′′, C-5′′), 40.0, 40.3 (C-3), 53.13, 53.20 (C-2), 55.9 (OCH$_3$), 66.8, 67.0 (C-1), 74.9, 75.9 (C-1′′), 114.49, 114.54 (C-4′), 114.8, 115.1 (C-6′), 117.7, 117.8 (C-2′), 128.7, 129.27 (o-$SO_2C_6H_5$), 129.31, 129.4 (m-$SO_2C_6H_5$), 134.0 (C-5′), 134.3, 134.5 (p-$SO_2C_6H_5$), 135.8, 135.9, 136.9, 137.4 (C-1′, i-$SO_2C_6H_5$), 158.1, 159.2 (C-3′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1755 (vs), 1471 (m), 1446 (m), 1403 (m), 1304 (m), 1241 (m), 1217 (m), 1144 (s), 1081 (m), 1044 (m), 1013 (m), 724 (m), 688 (m), 620 (m), 601 (m), 579 (m) cm^{-1}. MS (FAB, 3-nitrobenzyl alcohol + NaI): m/z (%) = 684 (5), 682 (5), 649 (3), 545 (2), 534 (100) [M + Na]$^+$, 532 (94) [M + Na]$^+$, 499 (9), 476 (9), 474 (8), 413 (2), 392 (82) [M + Na – PhSO$_2$H]$^+$, 390 (81) [M + Na – PhSO$_2$H]$^+$, 370 (32) [M – PhSO$_2$]$^+$, 368 (37) [M – PhSO$_2$]$^+$, 349 (7), 323 (19), 259 (1), 214 (5), 205 (10), 187 (27), 176 (12), 133 (10), 119 (14), 109 (11), 105 (14). HRMS (FAB): calcd. for $C_{23}H_{28}BrNNaO_5S^+$ [M + Na]$^+$ 532.0764; found 532.0768.

4-(2-Bromo-5-methoxybenzyl)-3-[2-methyl-1-(phenylsulfonyl)-propyl]-1,3-oxazolidin-2-one (11c): Yield: 62 mg (37%), colorless foam. R_f = 0.24 and 0.27 (hexanes/EtOAc, 3:1). Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.19 [br. d, J = 6.5 Hz, 3 H, CH(CH_3)$_2$], 1.27 [d, J = 6.5 Hz, 3 H, CH(CH_3)$_2$], 2.73–2.84 [m, 1 H, CH(CH$_3$)$_2$], 2.89 (br. t, J = 13.0 Hz, 1 H, 3-H_A), 3.39 (dd, J = 3.7, 13.0 Hz, 1 H, 3-H_B), 3.64–3.72 (m, 1 H, 1-H_A), 3.80 (s, 3 H, OCH_3), 4.06 (dd, J = 3.4, 8.8 Hz, 1 H, 1-H_B), 4.59 (br. s, 1 H, 2-H), 5.04 (br. d, J = 10.8 Hz, 1 H, CHSO$_2$C$_6$H$_5$), 6.72 (dd, J = 3.0, 8.8 Hz, 1 H, 4′-H), 6.78 (d, J = 3.0 Hz, 1 H, 2′-H), 7.60 (d, J = 8.8 Hz, 1 H, 5′-H), 7.55–7.58 (m, 2 H, m-$SO_2C_6H_5$), 7.64–7.67 (m, 1 H, p-$SO_2C_6H_5$), 7.94 (br. d, J = 7.3 Hz, 2 H, o-$SO_2C_6H_5$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.4 [CH(CH_3)$_2$], 21.4 [CH(CH_3)$_2$], 28.5 (C-3), 53.8 (C-2), 55.6 (OCH$_3$), 67.1 (C-1), 81.2 (CHSO$_2$C$_6$H$_5$), 114.6 (C-4′), 115.0 (C-6′), 117.5 (C-2′), 127.9 (o-$SO_2C_6H_5$), 129.3 (m-$SO_2C_6H_5$), 134.0 (C-5′), 134.1 (p-$SO_2C_6H_5$), 135.2, 135.9 (C-1′, i-$SO_2C_6H_5$), 159.2 (C=O, C-3′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1751 (vs), 1474 (m), 1407 (m), 1302 (m), 1241 (m), 1142 (m), 1075 (m), 599 (m), 585 (m), 561 (m) cm^{-1}. MS (FAB, 3-nitrobenzyl alcohol + NaI): m/z (%) = 538 (1), 506 (100) [M + Na]$^+$, 504 (96) [M + Na]$^+$, 479 (5), 418 (1), 395 (1), 364 (79) [M + Na – PhSO$_2$H]$^+$, 362 (80) [M + Na – PhSO$_2$H]$^+$, 342 (52) [M – PhSO$_2$]$^+$, 340 (52) [M – PhSO$_2$]$^+$, 329 (13), 296 (2), 284 (5), 245 (2), 218 (4), 201 (5), 187 (18), 154 (11), 107 (6), 79 (4), 55 (4), 28 (2). HRMS (FAB): calcd. for $C_{21}H_{24}BrNNaO_5S^+$ [M + Na]$^+$ 504.0451; found 504.0438.

4-(2-Bromo-5-methoxybenzyl)-3-[(2*E*)-1-(phenylsulfonyl)but-2-enyl]-1,3-oxazolidin-2-one (11d): Yield: 88 mg (52%), colorless foam. R_f = 0.13 (hexanes/EtOAc, 5:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, J = 6.9 Hz, 1.98 H, 4′′-H), 1.51 (d, J = 6.9 Hz, 1.02 H, 4′′-H), 2.61 (dd, J = 9.6, 13.7 Hz, 0.33 H, 3-H), 2.67 (dd, J = 9.6, 13.7 Hz, 0.67 H, 3-H), 3.38–3.46 (m, 1 H, 3-H), 3.68–3.77 (m, 1 H, 3′′-H), 3.79, 3.80 (2 s, 3 H, OCH_3), 4.11–4.27 (m, 2 H, 1-H), 4.26–4.46 (m, 1 H, 2-H), 5.23 (dd, J = 8.3, 14.6 Hz, 0.66 H, 2′′-H), 5.24 (dd, J = 8.7, 14.6 Hz, 0.34 H, 2′′-H), 6.57 (d, J = 14.6 Hz, 0.33 H, 1′′-H), 6.60 (d, J = 14.6 Hz, 0.67 H, 1′′-H), 6.70–6.76 (m, 2 H, 3′-H, 4′-H), 7.43–7.49 (m, 1 H, 5′-H), 7.51–7.55 (m, 2 H, m-$SO_2C_6H_5$), 7.56–7.69 (m, 1 H, p-$SO_2C_6H_5$), 7.85–7.91 (m, 2 H, o-$SO_2C_6H_5$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 14.2 (C-4′′), 36.3, 36.8 (C-3), 53.1, 53.2 (C-2), 55.59, 55.63 (OCH$_3$), 62.2, 62.5 (C-3′′), 65.9, 66.2 (C-1), 103.5, 104.1 (C-2′′), 114.66, 114.73 (C-3′, C-4′), 114.8 (C-6′), 117.8, 118.0 (C-3′, C-4′), 128.2, 128.4 (C-1′′), 129.0, 129.05, 129.11, 129.2 (o-, m-$SO_2C_6H_5$), 133.9, 134.0 (C-5′, p-$SO_2C_6H_5$), 135.4, 135.6, 136.9, 137.2 (C-1′, i-$SO_2C_6H_5$), 154.7, 159.2 (C=O, C-3′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1753 (vs), 1663 (m), 1475 (m), 1446 (m), 1408 (s), 1291 (m), 1224 (m), 1135 (s), 1082 (s), 1012 (m), 951 (m), 757 (m), 728 (s), 690 (s), 666 (m), 599 (m), 586 (m), 570 (m), 547 (m) cm^{-1}. MS (ESI): m/z (%) = 983 (6) [2 M + Na]$^+$, 520 (21) [M + K]$^+$, 518 (18) [M + K]$^+$, 504 (100) [M + Na]$^+$, 502 (95) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{21}H_{22}BrNNaO_5S^+$ [M + Na]$^+$ 502.0300; found 502.0303.

3-[2-(Benzyloxy)-1-(phenylsulfonyl)ethyl]-4-(2-bromo-5-methoxybenzyl)-1,3-oxazolidin-2-one (11e): Yield: 75 mg (38%), colorless foam. R_f = 0.10 (hexanes/EtOAc, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.79 (dd, J = 10.7, 13.7 Hz, 0.5 H, 3-H_A), 2.87 (dd, J = 10.7, 13.7 Hz, 0.5 H, 3-H_A), 3.29 (dd, J = 3.7, 13.7 Hz, 0.5 H, 3-H_B), 3.62 (dd, J = 3.7, 13.7 Hz, 0.5 H, 3-H_B), 3.73, 3.74 (2 s, 3 H, OCH_3), 3.77–3.88 (m, 2 H, CHCH$_2$OCH_2C$_6$H$_5$), 4.06–4.39 (m, 3 H, 2-H, 1-H, CHCH_2OCH$_2$C$_6$H$_5$), 4.50–4.61 (m, 2 H, 1-H, CHCH_2OCH$_2$C$_6$H$_5$), 5.14–5.18 (m, 0.5 H, CHCH$_2$OCH$_2$C$_6$H$_5$), 5.38–5.43 (m, 0.5 H, CHCH$_2$OCH$_2$C$_6$H$_5$), 6.70 (ddd, J = 1.0, 3.0, 8.8 Hz, 1 H, 4′-H), 6.75 (dd, J = 1.0, 3.0 Hz, 1 H, 2-H), 7.18–7.36 (m, 5 H, o-, m-, p-CH$_2$C$_6$H$_5$), 7.44 (dd, J = 1.6, 8.8 Hz, 1 H, 5′-H), 7.52–7.60 (m, 2 H, m-$SO_2C_6H_5$), 7.65–7.72 (m, 1 H, p-$SO_2C_6H_5$), 7.89–7.98 (m, 2 H, o-$SO_2C_6H_5$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.3, 39.6 (C-3), 48.3 (C-2), 50.0 (CHCH$_2$OCH$_2$C$_6$H$_5$), 55.49, 55.50 (OCH$_3$), 68.9 (C-1), 70.2 (CHCH$_2$OCH$_2$C$_6$H$_5$), 72.6 (CHCH$_2$OCH$_2$C$_6$H$_5$), 110.0 (C-2′), 116.0 (C-6′), 117.5, 117.7 (C-4′), 127.6, 127.8, 127.9, 128.0, 128.1

(*o*-, *m*-, *p*-$CH_2C_6H_5$), 128.5, 129.1 (*o*-$SO_2C_6H_5$), 129.3, 129.4 (*m*-$SO_2C_6H_5$), 131.8 (C-5′), 134.4 (*p*-$SO_2C_6H_5$), 155.1, 156.3, 156.7, 159.1 (C-3′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1746 (vs), 1460 (m), 1438 (m), 1409 (m), 1289 (m), 1241 (m), 1216 (m), 1145 (m), 1079 (s), 1011 (m), 984 (m), 806 (m), 737 (s), 697 (s), 688 (s), 600 (m), 581 (s), 553 (m), 523 (m) cm^{-1}. MS (ESI): *m*/*z* (%) = 600 (6) $[M + K]^+$, 598 (6) $[M + K]^+$, 584 (86) $[M + Na]^+$, 582 (100) $[M + Na]^+$, 560 (4), 558 (4), 487 (2), 473 (3), 458 (4), 456 (4), 442 (89) $[M + H + Na - SO_2Ph]^+$, 440 (87) $[M + H + Na - SO_2Ph]^+$, 420 (2), 418 (2), 387 (3), 362 (7). HRMS (ESI): calcd. for $C_{26}H_{26}BrNNaO_6S^+$ $[M + Na]^+$ 582.0556; found 582.0549.

4-(2-Bromo-5-methoxybenzyl)-3-[2-[(4-methoxybenzyl)oxy]-1-(phenylsulfonyl)ethyl]-1,3-oxazolidin-2-one (11h): Yield: 79 mg (40%), colorless solid. M.p. 37–40 °C. R_f = 0.33 (hexanes/EtOAc, 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.77 (dd, *J* = 10.6, 13.6 Hz, 1 H, 3-H), 2.86 (dd, *J* = 10.9, 13.6 Hz, 1 H, 3-H), 3.24 (dd, *J* = 3.8, 13.6 Hz, 0.55 H, 3-H), 3.61 (dd, *J* = 3.6, 13.6 Hz, 0.48 H, 3-H), 3.74, 3.77, 3.78, 3.79 (4 s, 6 H, OCH_3), 4.08 (q, *J* = 8.1 Hz, 0.67 H, 1-H), 4.11–4.17 (m, 1.9 H, 1-H, $CHCH_2OCH_2C_6H_5OCH_3$), 4.19 (dd, *J* = 5.3, 11.2 Hz, 0.62 H, $CHCH_2OCH_2C_6H_5OCH_3$), 4.24–4.35 (m, 1.5 H, 2-H, $CHCH_2OBn$), 4.41 (d, *J* = 11.4 Hz, 0.46 H, $OCH_2C_6H_5OCH_3$), 4.46 (d, *J* = 11.4 Hz, 0.47 H, $OCH_2C_6H_5OCH_3$), 4.47 (d, *J* = 11.4 Hz, 0.54 H, $OCH_2C_6H_5OCH_3$), 4.53 (d, *J* = 11.4 Hz, 0.57 H, $OCH_2C_6H_5OCH_3$), 4.60–4.65 (m, 0.58 H, 2-H), 5.15 (dd, *J* = 5.1, 8.7 Hz, 0.47 H, $CHCH_2OCH_2C_6H_5OCH_3$), 5.38 (dd, *J* = 5.5, 7.5 Hz, 0.53 H, $CHCH_2OCH_2C_6H_5OCH_3$), 6.70 (dd, *J* = 1.2, 3.1 Hz, 1 H, 4′-H), 6.71 (dd, *J* = 1.2, 3.1 Hz, 0.5 H, 4′-H), 6.74 (dd, *J* = 3.0, 4.5 Hz, 1 H, 2′-H), 6.81–6.85 (m, 2 H, *o*-$C_6H_5OCH_3$), 7.14–7.20 (m, 2 H, *m*-$C_6H_5OCH_3$), 7.44 (dd, *J* = 2.5, 8.8 Hz, 1 H, 5′-H), 7.52–7.60 (m, 2 H, *m*-$SO_2C_6H_5$), 7.65–7.72 (m, 1 H, *p*-$SO_2C_6H_5$), 7.89–7.91 (m, 1 H, *o*-$SO_2C_6H_5$), 7.96–7.98 (m, 1 H, *o*-$SO_2C_6H_5$) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 39.5, 40.3 (C-3), 53.5 (C-2), 55.26, 55.28, 55.50, 55.54 (OCH_3), 62.9, 63.7 ($CHCH_2OCH_2C_6H_5OCH_3$), 67.16, 67.22 (C-1), 73.0, 73.1 ($OCH_2C_6H_5$), 73.6, 74.6 ($CHCH_2OCH_2C_6H_5OCH_3$), 113.9, 114.0 (*o*-$C_6H_5OCH_3$), 114.4, 114.6 (C-4′), 114.8, 115.1 (C-6′), 117.5, 117.7 (C-2′), 128.3, 128.5 (C-1′, *i*-$SO_2C_6H_5$, *p*-$C_6H_5OCH_3$), 128.7, 129.1 (*o*-$SO_2C_6H_5$), 129.3, 129.4 (*m*-$SO_2C_6H_5$), 129.6, 129.8 (*m*-$C_6H_5OCH_3$), 134.4, 134.5 (*p*-$SO_2C_6H_5$), 135.9, 136.0 (C-1′, *i*-$SO_2C_6H_5$, *p*-$C_6H_5OCH_3$), 137.6, 137.8 (C-1′, *i*-$SO_2C_6H_5$, *p*-$C_6H_5OCH_3$), 159.12, 159.16, 159.55, 159.57, 157.5, 157.9 (C-3′, *i*-$C_6H_5OCH_3$, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1754 (vs), 1513 (m), 1473 (m), 1446 (m), 1405 (m), 1304 (m), 1242 (s), 1210 (m), 1174 (m), 1144 (s), 1080 (m), 1062 (m), 1031 (m), 1012 (m), 815 (m), 756 (m), 724 (m), 687 (m), 584 (s), 552 (m), 522 (m) cm^{-1}. MS (FAB, 3-nitrobenzyl alcohol + NaI): *m*/*z* (%) = 764 (2), 686 (1), 614 (96) $[M + Na]^+$, 612 (89) $[M + Na]^+$, 472 (11) $[M + H + Na - SO_2Ph]^+$, 470 (11) $[M + H + Na - SO_2Ph]^+$, 352 (4), 329 (48), 307 (4), 245 (2), 187 (3), 177 (5), 154 (38), 121 (100) $[CH_2C_6H_5OCH_3]^+$, 83 (11), 81 (9), 69 (16), 57 (16), 43 (7). HRMS (FAB): calcd. for $C_{27}H_{28}BrNNaO_7S^+$ $[M + Na]^+$ 612.0662; found 612.0661.

(4*S*)-4-(4-Methoxybenzyl)-3-[1-(phenylsulfonyl)butyl]-1,3-oxazolidin-2-one (12a): With butyraldehyde. Yield: 90 mg (31%), colorless solid. M.p. 94–96 °C. R_f = 0.27 and 0.22 (hexanes/EtOAc, 3:1). $[\alpha]_D^{22}$ = +97.35 (*c* = 1.0, CH_2Cl_2). Major diastereomer: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.4 Hz, 2 H, 4′′-H), 1.43–1.66 (m, 2 H, 3′′-H), 2.08–2.30 (m, 1 H, 2′′-H), 2.60 (dd, *J* = 11.3, 13.1 Hz, 1 H, 3-H_A), 3.30 (dd, *J* = 3.6, 13.1 Hz, 1 H, 3-H_B), 3.81 (s, 3 H, OCH_3), 3.88 (dd, *J* = 8.0, 8.8 Hz, 1 H, 1-H_A), 3.99 (dd, *J* = 4.3, 8.8 Hz, 1 H, 1-H_B), 4.50–4.59 (m, 1 H, 2-H), 5.19 (dd, *J* = 4.3, 10.9 Hz, 1 H, 1′′-H), 6.85–6.91 (m, 2 H, 3′-H, 5′-H), 7.11–7.16 (m, 2 H, 2′-H, 6′-H), 7.56–7.61 (m, 2 H, *m*-C_6H_5), 7.67–7.72 (m, 1 H, *p*-C_6H_5), 7.92–7.95 (m, 2 H, *o*-C_6H_5) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4 (C-4′′), 19.1 (C-3′′), 27.7 (C-2′′), 38.9 (C-3), 55.3 (OCH_3), 67.6 (C-1), 74.4 (C-1′′), 114.5 (C-3′, C-5′), 127.2 (C-1′), 128.6 (*o*-C_6H_5), 129.5 (*m*-C_6H_5), 130.2 (C-2′, C-6′), 134.6 (*p*-C_6H_5), 136.9 (*i*-C_6H_5), 158.2, 158.9 (C=O, C-5′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1749 (vs), 1512 (s), 1446 (m), 1403 (m), 1304 (m), 1289 (m), 1246 (s), 1195 (m), 1178 (m), 1143 (s), 1079 (m), 1029 (m), 999 (m), 758 (m), 722 (m), 714 (m), 687 (m), 614 (m), 576 (s), 549 (m), 535 (m), 524 (m) cm^{-1}. MS (CI, 70 eV): *m*/*z* (%) = 523 (9) [2 (M – $C_6H_5SO_2$) – H]$^+$, 474 (1), 469 (13), 458 (3), 415 (6), 375 (4), 350 (4), 332 (13), 258 (2), 278 (7), 267 (25), 262 (80) $[M - C_6H_5SO_2]^+$, 251 (15), 218 (7), 208 (46), 178 (3), 159 (6), 147 (11), 143 (71), 125 (100), 121 (33) $[CH_2C_6H_5OCH_3]^+$, 94 (7), 78 (21), 55 (16). $C_{21}H_{25}NO_5S$ (403.49): calcd. C 62.51, H 6.25, N 3.47; found C 62.31, H 6.23, N 3.37.

(4*S*)-4-(4-Methoxybenzyl)-3-[1-(phenylsulfonyl)hexyl]-1,3-oxazolidin-2-one (12b): With hexanal. Yield: 147 mg (11%). Colorless foam. R_f = 0.13 and 0.17 (hexanes/EtOAc, 7:2). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.85–0.88 (m, 3 H, 6′′-H), 1.26–1.61 (m, 6 H, 3′′-H, 4′′-H, 5′′-H), 2.09–2.23 (m, 1 H, 2′′-H_A), 2.23–2.30 (m, 1 H, 2′′-H_B), 2.59 (dd, *J* = 11.4, 13.1 Hz, 0.56 H, 3-H), 2.68 (dd, *J* = 10.3, 13.5 Hz, 0.42 H, 3-H), 3.30 (dd, *J* = 3.7, 13.1 Hz, 0.55 H, 3-H), 3.46–3.55 (m, 0.45 H, 3-H), 3.80 (2 s, 3 H, OCH_3), 3.88 (dd, *J* = 8.1, 8.8 Hz, 0.56 H, 1-H), 3.99 (dd, *J* = 4.4, 8.8 Hz, 0.56 H, 1-H), 4.06–4.16 (m, 1.32 H, 1-H, 2-H), 4.52–4.56 (m, 0.53 H, 2-H), 4.84 (br. d, *J* = 6.6 Hz, 0.38 H, 1′′-H), 5.17 (br. d, *J* = 9.1 Hz, 0.51 H, 1′′-H), 6.86–6.88 (m, 1 H, 3′-H, 5′-H), 6.88–6.90 (m, 1 H, 3′-H, 5′-H), 7.12–7.15 (m, 1 H, 2′-H, 6′-H), 7.14 (m, 1 H, 2′-H, 6′-H), 7.57–7.61 (m, 2 H, *m*-$SO_2C_6H_5$), 7.70–7.71 (m, 1 H, *p*-$SO_2C_6H_5$), 7.93 (d, *J* = 7.3 Hz, 1 H, *o*-$SO_2C_6H_5$), 7.97 (d, *J* = 7.3 Hz, 1 H, *o*-$SO_2C_6H_5$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.88, 13.90 (C-6′′), 22.27, 22.30, 24.8, 25.4, 25.7, 25.9, 31.05, 31.10 (C-2′′, C-3′′, C-4′′, C-5′′), 38.9, 39.0 (C-3), 55.29, 55.31 (C-2, OCH_3), 55.9 (C-2), 67.57, 67.60 (C-1), 74.6, 75.9 (C-1′′), 114.5 (C-3′, C-5′), 127.2 (C-1′), 128.6, 129.27 (*o*-$SO_2C_6H_5$), 129.30, 129.5 (*m*-$SO_2C_6H_5$), 130.1, 130.2 (C-2′, C-6′), 134.3, 134.6 (*p*-$SO_2C_6H_5$), 136.9, 137.1 (*i*-$SO_2C_6H_5$), 158.2, 158.8, 158.9 (C-4′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1752 (vs), 1512 (m), 1404 (m), 1303 (m), 1247 (s), 1178 (m), 1144 (s), 1080 (m), 1030 (m), 751 (m), 722 (m), 715 (m), 688 (m), 578 (s), 550 (m) cm^{-1}. MS (FAB, 3-nitrobenzyl alcohol + NaI): *m*/*z* (%) = 885 (2) [2 M + Na]$^+$, 604 (7), 454 (100) $[M + Na]^+$, 413 (2), 328 (2), 312 (1) $[M + Na - PhSO_2H]^+$, 290 (56) $[M - PhSO_2]^+$, 197 (2), 187 (13), 165 (5), 121 (14) $[H_3COC_6H_5CH_2]^+$, 55 (19). HRMS (FAB): calcd. for $C_{23}H_{29}NNaO_5S$ $[M + Na]^+$ 454.1659; found 454.1670.

(4*S*)-4-(4-Methoxybenzyl)-3-[2-methyl-1-(phenylsulfonyl)propyl]-1,3-oxazolidin-2-one (12c): With isobutyraldehyde. Yield: 102 mg (52%). Colorless foam. R_f = 0.22 (hexanes/EtOAc, 7:2). Major diastereomer: ^1H NMR (300 MHz, $CDCl_3$): δ = 1.18 [d, *J* = 6.5 Hz, 3 H, $CH(CH_3)_2$], 1.28 [d, *J* = 6.5 Hz, 3 H, $CH(CH_3)_2$], 2.63 (dd, *J* = 11.7, 13.0 Hz, 1 H, 3-H_A), 2.66–2.76 [m, 1 H, $CH(CH_3)_2$], 3.36 (dd, *J* = 3.3, 13.0 Hz, 1 H, 3-H_B), 3.53–3.75 (m, 1 H, 1-H_A), 3.80 (s, 3 H, OCH_3), 3.94 (dd, *J* = 4.4, 8.8 Hz, 1 H, 1-H_B), 4.33–4.49 (m, 1 H, 2-H), 5.05 (br. d, *J* = 10.4 Hz, 1 H, $CHSO_2C_6H_5$), 6.85–6.90 (m, 2 H, 3′-H, 5′-H), 7.10–7.15 (m, 2 H, 2′-H, 6′-H), 7.53–7.59 (m, 2 H, *m*-$SO_2C_6H_5$), 7.63–7.69 (m, 1 H, *p*-$SO_2C_6H_5$), 7.94 (d, *J* = 7.3 Hz, 2 H, *o*-$SO_2C_6H_5$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.4, 21.2 [$CH(CH_3)_2$], 28.6 [$CH(CH_3)_2$], 39.0 (C-3), 55.3 (OCH_3), 55.7 (C-2), 67.6 (C-1), 80.7 ($CHSO_2C_6H_5$), 114.5 (C-3′, C-5′), 127.2 (C-1′), 127.8 (*o*-$SO_2C_6H_5$), 129.3 (*m*-$SO_2C_6H_5$), 130.2 (C-2′, C-6′), 134.2 (*p*-$SO_2C_6H_5$), 139.2 (*i*-$SO_2C_6H_5$), 158.9 (C=O, C-4′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1748 (vs), 1512 (s), 1446 (m), 1301 (m), 1247 (s), 1178 (m), 1141 (s), 1073 (m), 1029 (m), 759 (m), 729 (m), 712 (m), 689 (m), 608 (m), 578 (s), 546 (m), 523 (m) cm^{-1}. MS

(FAB, 3-nitrobenzyl alcohol + NaI): *m/z* (%) = 487 (2), 449 (1), 434 (2), 426 (100) $[M + Na]^+$, 402 (1), 363 (4), 337 (1), 300 (1), 285 (14), 284 (81) $[M + Na – PhSO_2H]^+$, 262 (82) $[M – PhSO_2]^+$, 230 (1), 189 (1), 187 (18), 165 (1), 147 (7), 133 (7), 121 (18) $[H_3COC_6H_5CH_2]^+$, 92 (10), 72 (9), 63 (18), 51 (1), 27 (1). HRMS (FAB): calcd. for $C_{21}H_{25}NNaO_5S$ $[M + Na]^+$ 426.1346; found 426.1340.

(4*S*)-4-(4-Methoxybenzyl)-3-[(2*E*)-1-(phenylsulfonyl)but-2-enyl]-1,3-oxazolidin-2-one (12d): With crotonaldehyde. Yield: 86 mg (44%). Colorless foam. R_f = 0.12 (hexanes/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48 (d, J = 7.0 Hz, 2.1 H, 4′′-H), 1.52 (d, J = 7.0 Hz, 0.9 H, 4′′-H), 2.70–2.80 (m, 1 H, 3-H_A), 3.00 (dd, J = 3.1, 14.1 Hz, 0.3 H, 3-H_B), 3.05 (dd, J = 3.1, 14.1 Hz, 0.7 H, 3-H_B), 3.77–3.81 (m, 1 H, 3′′-H), 3.80 (s, 3 H, OCH_3), 4.17–4.27 (m, 3 H, 1-H, 2-H), 5.00 (dd, J = 9.0, 14.7 Hz, 0.2 H, 1′′-H), 5.05 (dd, J = 8.0, 14.7 Hz, 0.8 H, 1′′-H), 6.58 (dd, J = 0.8, 14.7 Hz, 0.3 H, 2′′-H), 6.60 (dd, J = 0.8, 14.7 Hz, 0.7 H, 2′′-H), 6.85 (d, J = 8.7 Hz, 0.3 H, 3′-H, 5′-H), 6.84–6.88 (m, 2 H, 3′-H, 5′-H), 6.98–7.01 (m, 0.6 H, 2′-H, 6′-H), 7.03–7.06 (m, 1.4 H, 2′-H, 6′-H), 7.52–7.56 (m, 2 H, *m*-$SO_2C_6H_5$), 7.63–7.69 (m, 1 H, *p*-$SO_2C_6H_5$), 7.86–7.89 (m, 2 H, *o*-$SO_2C_6H_5$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.9, 14.3 (C-4′′), 34.9, 35.3 (C-3), 54.6, 54.9 (C-2), 55.3 (OCH_3), 62.1, 62.5 (C-3′′), 66.4, 66.7 (C-1), 102.7, 103.5 (C-1′′), 114.4, 114.5 (C-2′, C-6′), 126.3, 126.5 (C-1′), 128.5, 128.6 (C-2′′), 128.9, 129.1, 129.2 (*o*-, *m*-$SO_2C_6H_5$), 130.37, 130.42 (C-3′, C-5′), 133.89, 133.91 (*p*-$SO_2C_6H_5$), 136.9, 137.2 (*i*-$SO_2C_6H_5$), 154.8, 159.0 (C-4′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1750 (vs), 1661 (m), 1512 (m), 1410 (s), 1301 (m), 1247 (s), 1179 (m), 1138 (s), 1115 (m), 1083 (m), 1068 (m), 1026 (m), 1000 (m), 952 (m), 818 (m), 754 (m), 728 (s), 690 (m), 666 (m), 587 (m), 547 (m) cm^{-1}. MS (ESI): *m/z* (%) = 825 (4) $[2 M + Na]^+$, 440 (27) $[M + K]^+$, 425 (27) $[M + Na + H]^+$, 424 (100) $[M + Na]^+$. HRMS (ESI): calcd. for $C_{21}H_{23}NNaO_5S^+$ $[M + Na]^+$ 424.1189; found 424.1188.

(4*S*)-3-[2-(Benzyloxy)-1-(phenylsulfonyl)ethyl]-4-(4-methoxybenzyl)-1,3-oxazolidin-2-one (12e): With benzyloxyacetaldehyde. Yield: 78 mg (22%). Colorless foam. R_f = 0.17 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.58 (dd, J = 10.5, 13.5 Hz, 0.7 H, 3-H), 2.69 (dd, J = 10.5, 14.0 Hz, 0.3 H, 3-H), 3.15 (dd, J = 3.8, 13.5 Hz, 0.7 H, 3-H), 3.41 (dd, J = 3.8, 14.0 Hz, 0.3 H, 3-H), 3.78 (s, 3 H, OCH_3), 4.02–4.27 (m, 4.5 H, 2-H, 2′′-H, O$CH_2C_6H_5$), 4.40–4.62 (m, 2.9 H, 1-H, 2-H), 5.14 (dd, J = 5.1, 8.9 Hz, 0.3 H, 1′′-H), 5.38 (dd, J = 5.4, 6.7 Hz, 0.6 H, 1′′-H), 6.78–6.83 (m, 2 H, 3′-H, 5′-H), 6.92–6.97 (m, 0.6 H, 2′-H, 6′-H), 7.00–7.05 (m, 1.4 H, 2′-H, 6′-H), 7.24–7.38 (m, 5 H, *o*-, *m*-, *p*-$OCH_2C_6H_5$), 7.52–7.60 (m, 2 H, *m*-$C_6H_5SO_2$), 7.64–7.72 (m, 2 H, *p*-$C_6H_5SO_2$), 7.88–7.98 (m, 2 H, *o*-$C_6H_5SO_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.6, 39.1 (C-3), 55.3 (OCH_3), 55.4, 55.8 (C-2), 63.1, 64.8 (C-2′′), 67.7, 67.9 (O$CH_2C_6H_5$), 73.4, 73.6 (C-1′′), 74.6 (C-1′′), 114.28, 114.34 (C-3′, C-5′), 127.2, 127.3 (C-1′), 128.1, 128.2 (*o*-, *m*-, *p*-$OCH_2C_6H_5$), 128.3 (*o*-$OCH_2C_6H_5$), 128.5, 128.65, 128.68, 129.1 (*o*-$C_6H_5SO_2$), 129.3, 129.4 (*m*-$C_6H_5SO_2$), 130.0, 130.3 (C-2′, C-6′), 134.4, 134.5 (*p*-$C_6H_5SO_2$), 136.5, 136.7, 137.6, 137.7 (*i*-$OCH_2C_6H_5$, *i*-$C_6H_5SO_2$), 157.6, 158.0, 158.7, 158.8 (C-4′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1752 (vs), 1512 (s), 1405 (m), 1304 (m), 1247 (s), 1214 (m), 1178 (m), 1144 (s), 1114 (m), 1079 (m), 1029 (m), 736 (m), 698 (m), 687 (s) 578 (s) cm^{-1}. MS (CI, 70 eV): *m/z* (%) = 697 (1) $[2 (M – C_6H_5SO_2) + C_2H_5]^+$, 679 (10) $[2 (M – C_6H_5SO_2) + H]^+$, 589 (6), 550 (1), 499 (5), 460 (6), 430 (10), 390 (1), 368 (4), 340 (100) $[M – C_6H_5SO_2]^+$, 322 (3), 262 (3), 250 (48), 218 (31), 176 (5), 147 (17), 121 (65) $[H_3COC_6H_5CH_2]^+$, 91 (33) $[C_7H_7]^+$, 77 (5), 65 (3). $C_{26}H_{27}NO_6S$ (481.56): calcd. C 64.85, H 5.65, N 2.91; found C 64.94, H 5.70, N 2.79.

Ethyl Hydroxy[4-(4-methoxybenzyl)-2-oxo-1,3-oxazolidin-3-yl]acetate (15): Yield: 77 mg (51%). Colorless oil. R_f = 0.15 (hexanes/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35, 1.36 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 2.63 (dd, J = 9.5, 13.8 Hz, 0.29 H, 3-H_A), 2.79 (dd, J = 8.7, 13.8 Hz, 0.75 H, 3-H_A), 3.06 (dd, J = 4.2, 13.9 Hz, 0.27 H, 3-H_B), 3.17 (dd, J = 4.7, 13.9 Hz, 0.75 H, 3-H_B), 3.80 (s, 3 H, OCH_3), 4.05 (dd, J = 6.1, 8.2 Hz, 1 H, 1-H_A), 4.10–4.18 (m, 1 H, 2-H), 4.21 (dd, J = 8.2, 16.4 Hz, 1 H, 1-H_B), 4.37 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.31 (s, 0.7 H, 1′′-H), 5.41 (s, 0.23 H, 1′′-H), 6.83–6.88 (m, 2 H, 3′-H, 5′-H), 7.07–7.14 (m, 2 H, 2′-H, 6′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.07, 14.13 (CH_2CH_3), 38.1, 38.8 (C-3), 55.2, 55.8 (C-2), 55.3 (OCH_3), 63.16, 63.27 (CH_2CH_3), 67.60, 67.63 (C-1), 74.8, 74.9 (C-1′′), 114.38, 114.39 (C-3′, C-5′), 126.95, 127.05 (C-1′), 130.08, 130.16 (C-2′, C-6′), 157.4, 157.6 (COH), 158.8 (C-4′), 169.1, 170.3 (COO) ppm. FTIR (ATR): $\tilde{\nu}$ = 1734 (vs), 1512 (s), 1418 (br., m), 1299 (m), 1243 (br., s), 1178 (s), 1113 (m), 1067 (br., m), 1023 (br., s) cm^{-1}. MS (FAB, 3-nitrobenzyl alcohol): *m/z* (%) = 332 (6) $[M + Na]^+$, 310 (12) $[M + H]^+$, 309 (14) $[M]^+$, 292 (40) $[M + OH]^+$, 259 (4), 236 (9), 218 (100) $[M – H – CO_2-C_2H_5]^+$, 208 (5), 188 (5), 174 (7), 151 (6), 147 (14), 121 (21) $[CH_2C_6H_5OCH_3]^+$, 107 (7), 91 (9), 83 (8), 69 (10), 57 (12), 43 (13). HRMS (FAB): calcd. for $C_{15}H_{19}NO_6$ $[M]^+$ 309.1212; found 309.1220.

4-(2-Bromo-5-methoxybenzyl)-3-[2-hydroxy-1-(phenylsulfonyl)ethyl]-1,3-oxazolidin-2-one (16): Yield: 19 mg (50%). Colorless crystalline solid. M.p. 124–125 °C. R_f = 0.12 and 0.17 (hexanes/EtOAc, 2:1). Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.74 (t, J = 6.7 Hz, 1 H, OH), 2.92 (dd, J = 10.8, 13.4 Hz, 1 H, 3-H_A), 3.41 (dd, J = 3.7, 13.4 Hz, 1 H, 3-H_B), 3.79 (s, 3 H, OCH_3), 4.10 (dd, J = 7.7, 8.8 Hz, 1 H, 1-H_A), 4.22 (dd, J = 2.7, 8.8 Hz, 1 H, 1-H_B), 4.44 (dd, J = 5.6, 6.7 Hz, 1 H, CH_2OH), 4.64–4.72 (m, 1 H, 2-H), 5.25 (t, J = 5.6 Hz, 1 H, CHCH$_2$OH), 6.72 (dd, J = 3.0, 8.8 Hz, 1 H, 4′-H), 6.83 (d, J = 3.0 Hz, 1 H, 2′-H), 7.47 (d, J = 8.8 Hz, 1 H, 5′-H), 7.57–7.69 (m, 2 H, *m*-$SO_2C_6H_5$), 7.71–7.74 (m, 1 H, *p*-$SO_2C_6H_5$), 7.93–7.99 (m, 2 H, *o*-$SO_2C_6H_5$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.6 (C-3), 54.4 (C-2), 55.6 (OCH_3), 58.7 (CH_2OH), 67.5 (C-1), 75.1 (CHCH$_2$OH), 114.6 (C-4′), 115.2 (C-6′), 117.5 (C-2′), 128.6 (*o*-$SO_2C_6H_5$), 129.6 (*m*-$SO_2C_6H_5$), 133.9 (C-5′), 134.8 (*p*-$SO_2C_6H_5$), 136.1, 137.4 (C-1′, *i*-$SO_2C_6H_5$), 158.2, 159.2 (C-3′, C=O) ppm. FTIR (ATR): $\tilde{\nu}$ = 1717 (vs), 1470 (m), 1415 (m), 1322 (m), 1308 (m), 1281 (m), 1252 (m), 1233 (m), 1218 (m), 1197 (m), 1183 (m), 1162 (m), 1145 (m), 1133 (m), 1116 (m), 1085 (m), 1069 (m), 1055 (m), 1000 (m), 806 (m), 774 (m), 766 (m), 727 (m), 686 (m), 609 (m), 598 (m), 576 (m) cm^{-1}. MS (ESI): *m/z* (%) = 963 (9) $[2 M + Na]^+$, 510 (15) $[M + K]^+$, 508 (13) $[M + K]^+$, 494 (100) $[M + Na]^+$, 492 (93) $[M + Na]^+$, 352 (42), 350 (45). HRMS (ESI): calcd. for $C_{19}H_{20}BrNNaO_6S^+$ $[M + Na]^+$ 492.0087; found 492.0088.

General Procedure for the Preparation of Tetrahydroisoquinolines 13 and 14: To a solution of either **11** or **12** (1 equiv.) in CH_2Cl_2 (3–5 mL) in a Schlenk flask under inert gas at –78 °C was added $TiCl_4$ (ca. 3.5 equiv.) by syringe, and the reaction mixture was stirred for the given time (Table 1). After the addition of brine (10 mL), the reaction mixture was warmed to room temperature. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried (Na_2SO_4) and concentrated. Crude product **13** or **14** was chromatographed on SiO_2 with hexanes/EtOAc.

9-Bromo-6-methoxy-5-propyl-1,5,10,10a-tetrahydro[1,3]oxazolo-[3,4-*b*]isoquinolin-3-one (13a): Yield: 22 mg (56%). Colorless crystalline solid. M.p. 137 °C. R_f = 0.33 (hexanes/EtOAc, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, J = 7.2 Hz, 3 H,

$CH_2CH_2CH_3$), 1.28–1.59 (m, 3 H, $CH_2CH_2CH_3$), 1.92–1.93 (m, 1 H, $CH_2CH_2CH_3$), 2.64 (dd, J = 10.4, 17.0 Hz, 1 H, 10-H_A), 3.12 (dd, J = 5.5, 17.0 Hz, 1 H, 10-H_B), 3.83 (s, 3 H, OCH_3), 4.07–4.16 (m, 1 H, 10a-H), 4.19 (dd, J = 3.3, 8.6 Hz, 1 H, 1-H), 4.55 (dd, J = 7.8, 8.6 Hz, 1 H, 1-H), 5.03 (dd, J = 2.5, 10.1 Hz, 1 H, 5-H), 6.68 (d, J = 8.8 Hz, 1 H, 7-H), 7.42 (d, J = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 ($CH_2CH_2CH_3$), 19.7 ($CH_2CH_2CH_3$), 34.2 (C-10), 36.0 ($CH_2CH_2CH_3$), 47.0 (C-10a), 48.8 (C-5), 55.6 (OCH_3), 68.7 (C-1), 110.1 (C-7), 115.8 (C-9), 128.5 (C-9a, C-5a), 131.2 (C-8), 131.6 (C-9a, C-5a), 155.0, 156.8 (C-6, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1739 (vs), 1460 (m), 1425 (m), 1289 (m), 1273 (m), 1255 (s), 1230 (m), 1079 (s), 1044 (m), 1014 (m), 993 (m), 966 (m), 820 (m), 756 (m), 619 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 341 (4) $[M]^+$, 339 (4) $[M]^+$, 298 (99) $[M - (CH_2)_2CH_3]^+$, 296 (100) $[M - (CH_2)_2CH_3]^+$, 281 (1), 254 (2), 252 (2), 239 (7), 237 (7), 225 (9), 217 (6), 196 (2), 173 (24), 158 (6), 146 (10), 130 (10), 103 (5), 77 (3), 63 (1), 36 (2). $C_{15}H_{18}BrNO_3$ (340.21): calcd. C 52.96, H 5.33, N 4.12; found C 52.89, H 5.31, N 4.11.

9-Bromo-6-methoxy-5-pentyl-1,5,10,10a-tetrahydro[1,3]oxazolo-[3,4-*b*]isoquinolin-3-one (13b): Yield: 29 mg (80%). Colorless crystalline solid. M.p. 86–87 °C. R_f = 0.23 (hexanes/EtOAc, 6:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.0 Hz, 3 H, 5′-H), 1.22–1.55 (m, 7 H, 1′-H, 2′-H, 3′-H, 4′-H), 1.83–1.96 (m, 1 H, 1′-H), 2.64 (dd, J = 10.4, 17.0 Hz, 1 H, 10-H_A), 3.11 (dd, J = 5.6, 17.0 Hz, 1 H, 10-H_B), 3.82 (s, 3 H, OCH_3), 4.06–4.16 (m, 1 H, 10a-H), 4.19 (dd, J = 3.2, 8.6 Hz, 1 H, 1-H), 4.58 (dd, J = 7.8, 8.6 Hz, 1 H, 1-H), 4.99–5.02 (m, 1 H, 5-H), 6.66 (d, J = 8.8 Hz, 1 H, 7-H), 7.42 (d, J = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (C-5′), 22.5, 26.1, 31.2 (C-2′, C-3′, C-4′), 33.7 (C-1′), 34.2 (C-10), 47.0 (C-10a), 49.1 (C-5), 55.6 (OCH_3), 68.7 (C-1), 110.1 (C-7), 115.8 (C-9), 128.6 (C-9a, C-5a), 131.2 (C-8), 131.6 (C-9a, C-5a), 155.0, 156.8 (C-6, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 2958 (m), 2920 (m), 1735 (vs), 1700 (m), 1291 (m), 1267 (m), 1246 (m), 1230 (m), 1200 (m), 1169 (m), 1134 (m), 1111 (m), 1082 (s), 1070 (s), 1052 (m), 1002 (m), 976 (m), 965 (m), 877 (m), 810 (m), 762 (m), 621 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 369 (3) $[M]^+$, 367 (3) $[M]^+$, 299 (1), 298 (99) $[M - C_5H_{11}]^+$, 296 (100) $[M - C_5H_{11}]^+$, 254 (1), 252 (1), 239 (3), 237 (3), 225 (5), 217 (2), 173 (12), 146 (4), 115 (2). $C_{17}H_{22}BrNO_3$ (368.27): calcd. C 55.44, H 6.02, N 3.80; found C 55.23, H 5.93, N 3.65.

9-Bromo-5-isopropyl-6-methoxy-1,5,10,10a-tetrahydro[1,3]oxazolo-[3,4-*b*]isoquinolin-3-one (13c): Yield: 18 mg (80%). Colorless crystalline solid. M.p. 161 °C. R_f = 0.39 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 [d, J = 7.1 Hz, 3 H, $CH(CH_3)_2$], 1.06 [d, J = 6.8 Hz, 3 H, $CH(CH_3)_2$], 2.36 [sept.d, J_d = 5.2, $J_{sept.}$ = 6.9 Hz, 1 H, $CH(CH_3)_2$], 2.64 (dd, J = 9.6, 17.1 Hz, 1 H, 10-H_A), 3.15 (dd, J = 6.2, 17.1 Hz, 1 H, 10-H_B), 3.81 (s, 3 H, OCH_3), 4.12 (dd, J = 3.6, 8.6 Hz, 1 H, 1-H), 4.24–4.33 (m, 1 H, 10a-H), 4.59 (dd, J = 7.9, 8.6 Hz, 1 H, 1-H), 4.98 (d, J = 5.2 Hz, 1 H, 5-H), 6.67 (d, J = 8.8 Hz, 1 H, 7-H), 7.44 (d, J = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.1, 19.9 [$CH(CH_3)_2$], 32.0 [$CH(CH_3)_2$], 33.8 (C-10), 49.1 (C-10a), 53.8 (C-5), 55.5 (OCH_3), 68.8 (C-1), 110.1 (C-7), 115.8 (C-9), 127.3 (C-5a), 131.3 (C-8), 132.3 (C-9a), 155.4, 157.7 (C-3, C-6) ppm. FTIR (ATR): $\tilde{\nu}$ = 1734 (vs), 1458 (m), 1434 (m), 1421 (m), 1412 (m), 1384 (m), 1290 (m), 1252 (m), 1224 (m), 1069 (s), 1009 (m), 980 (m), 880 (m), 802 (m), 756 (m), 703 (m), 629 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 341 (22) $[M]^+$, 339 (21) $[M]^+$, 298 (99) $[M - CH(CH_3)_2]^+$, 296 (100) $[M - CH(CH_3)_2]^+$, 254 (2), 239 (5), 237 (5), 224 (7), 173 (19), 158 (3), 146 (7), 130 (5), 103 (2), 77 (1), 41 (1), 28 (3). $C_{15}H_{18}BrNO_3$ (340.21): calcd. C 52.96, H 5.33, N 4.12; found C 53.00, H 5.40, N 4.02.

9-Bromo-6-methoxy-5-[(1*E*)-prop-1-enyl]-1,5,10,10a-tetrahydro[1,3]-oxazolo[3,4-*b*]isoquinolin-3-one (13d): Yield: 5 mg (19%). Colorless crystalline solid. M.p. 132–133 °C (Et_2O). R_f = 0.20 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.66 (s, 1.5 H, 3′-H), 1.68 (t, J = 1.5 Hz, 1.5 H, 3′-H), 2.64 (dd, J = 10.2, 16.9 Hz, 1 H, 10-H_A), 3.14 (dd, J = 5.2, 16.9 Hz, 1 H, 10-H_B), 3.81 (s, 3 H, OCH_3), 4.05–4.18 (m, 2 H, 10a-H, 1-H), 4.61 (dd, J = 7.6, 8.3 Hz, 1 H, 1-H), 5.34–5.46 (m, 1 H, 2′-H), 5.55–5.64 (m, 2 H, 5-H, 1′-H), 6.68 (d, J = 8.8 Hz, 1 H, 7-H), 7.46 (d, J = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.6 (C-3′), 34.5 (C-10), 47.3 (C-10a), 49.5 (C-5), 55.7 (OCH_3), 69.0 (C-1), 110.2 (C-7), 115.8 (C-9), 126.1 (C-5a), 127.3 (C-2′), 127.8 (C-1′), 131.6 (C-8), 132.2 (C-9a), 155.4, 156.4 (C-6, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1742 (vs), 1459 (m), 1436 (m), 1412 (m), 1288 (m), 1258 (m), 1218 (m), 1081 (m), 1023 (m), 966 (m), 803 (m), 744 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 339 (47) $[M]^+$, 337 (46) $[M]^+$, 324 (7), 322 (6), 308 (30), 306 (30), 298 (45) $[M - CH{=}CHCH_3]^+$, 296 (100) $[M - CH{=}CHCH_3]^+$, 294 (51), 264 (8), 239 (10), 237 (11), 225 (13), 207 (7), 183 (5), 173 (35), 158 (27), 146 (14), 130 (15), 128 (10), 89 (4), 77 (7), 73 (2), 39 (3). HRMS (ESI): calcd. for $C_{15}H_{16}BrNNaO_3^+$ $[M + Na]^+$ 360.0206; found 360.0189.

9-Bromo-6-methoxy-5-phenyl-1,5,10,10a-tetrahydro[1,3]oxazolo-[3,4-*b*]isoquinolin-3-one (13f): Yield: 5 mg (4%). Colorless solid. M.p. 200–201 °C. R_f = 0.23 (hexanes/EtOAc, 5:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.73 (dd, J = 10.6, 17.0 Hz, 1 H, 10-H_A), 3.23 (dd, J = 5.3, 17.0 Hz, 1 H, 10-H_B), 3.60 (s, 3 H, OCH_3), 3.91–3.96 (m, 1 H, 10a-H), 4.14 (dd, J = 4.8, 8.7 Hz, 1 H, 1-H), 4.47 (dd, J = 8.0, 8.7 Hz, 1 H, 1-H), 6.21 (s, 1 H, 5-H), 6.68 (d, J = 8.8 Hz, 1 H, 7-H), 7.15–7.17 (m, 2 H, 3′-H), 7.25–7.30 (m, 3 H, 2′-H, 4′-H), 7.54 (d, J = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 34.7 (C-10), 46.9 (C-10a), 52.0 (C-5), 55.7 (OCH_3), 68.9 (C-1), 110.4 (C-7), 115.8 (C-9), 125.4 (C-9a), 127.6 (C-3′), 127.7 (C-4′), 128.4 (C-2′), 132.1 (C-8), 133.0 (C-1′, C-5a), 140.6 (C-1′, C-5a), 155.6, 156.1 (C-6, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1733 (vs), 1455 (m), 1411 (m), 1386 (m), 1287 (s), 1259 (s), 1223 (m), 1083 (m), 1068 (s), 1014 (m), 983 (m), 809 (m), 754 (m), 602 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 376 (18) $[M + H]^+$, 375 (100) $[M]^+$, 374 (18) $[M + H]^+$, 373 (100) $[M]^+$, 358 (1), 330 (4), 328 (4), 314 (9), 298 (75) $[M - C_6H_5]^+$, 296 (76) $[M - C_6H_5]^+$, 252 (2), 239 (5), 237 (5), 226 (37), 224 (37), 209 (13), 194 (7), 178 (9), 173 (19), 146 (10), 130 (6), 104 (6), 77 (5), 51 (2), 39 (1). HRMS (ESI): calcd. for $C_{18}H_{16}BrNNaO_3^+$ $[M + Na]^+$ 396.0206; found 396.0205.

Methyl 9-Bromo-6-methoxy-3-oxo-1,5,10,10a-tetrahydro[1,3]-oxazolo[3,4-*b*]isoquinoline-5-carboxylate (13i): To a solution of **13d** (42 mg, 0.124 mmol) in CH_2Cl_2 (5 mL) at –78 °C was added a solution of NaOH (2.5 M in MeOH, 248 μL, 24.8 mg, 620 μmol NaOH). Then, O_3 was passed through the mixture for 10 min followed by oxygen for 5 min. Et_2O and H_2O (4 mL each) were added, and the reaction mixture was warmed to room temperature. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give **13i** as a colorless solid. Yield: 34 mg (69%). M.p. 157–158 °C (Et_2O). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.64 (dd, J = 10.7, 16.6 Hz, 1 H, 10-H_A), 3.19 (dd, J = 4.7, 16.6 Hz, 1 H, 10-H_B), 3.78 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, OCH_3), 4.17–4.21 (m, 1 H, 10a-H), 4.23 (dd, J = 3.7, 8.6 Hz, 1 H, 1-H), 4.60 (dd, J = 7.6, 8.6 Hz, 1 H, 1-H), 5.60 (s, 1 H, 5-H), 6.70 (d, J = 8.8 Hz, 1 H, 7-H), 7.52 (d, J = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.5 (C-10), 48.6 (C-10a), 52.2 (C-5), 52.8 (CO_2CH_3), 55.9 (OCH_3), 68.5 (C-1), 110.1 (C-7), 115.9 (C-9), 121.6 (C-5a), 132.6 (C-8), 133.0 (C-9a), 155.7, 156.3 (C-3, C-6), 170.2 (CO_2CH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1750 (vs), 1731 (vs), 1578 (m), 1464 (m), 1436 (m), 1416 (m), 1287 (s), 1245 (s), 1217 (m),

1201 (m), 1191 (m), 1080 (s), 1001 (m), 968 (m), 811 (m), 763 (m), 753 (m), 615 (m) cm^{-1}. MS (ESI): *m/z* (%) = 735 (7) [2 M + Na]$^+$, 396 (5), 394 (5), 380 (92) [M + Na]$^+$, 378 (100) [M + Na]$^+$, 272 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{14}H_{14}BrNNaO_5^+$ [M + Na]$^+$ 377.9948; found 377.9950.

7-Methoxy-5-propyl-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one (14a): Yield: 19 mg (68%). Colorless oil. R_f = 0.32 (hexanes/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 [t, *J* = 7.3 Hz, 3 H, $(CH_2)_2CH_3$], 1.40–1.58 (m, 2 H, $CH_2CH_2CH_3$), 1.67–1.79 (m, 1 H, $CH_2CH_2CH_3$), 1.82–1.93 (m, 1 H, $CH_2CH_2CH_3$), 2.82–2.85 (m, 2 H, 10-H), 3.80 (s, 3 H, OCH_3), 3.99–4.08 (m, 1 H, 10a-H), 4.14 (dd, *J* = 3.1, 8.6 Hz, 1 H, 1-H), 4.53 (dd, *J* = 7.8, 8.6 Hz, 1 H, 1-H), 4.87 (dd, *J* = 3.8, 9.7 Hz, 1 H, 5-H), 6.70 (d, *J* = 2.6 Hz, 1 H, 6-H), 6.76 (dd, *J* = 2.6, 8.4 Hz, 1 H, 8-H), 7.02 (d, *J* = 8.4 Hz, 1 H, 9-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 [$(CH_2)_2CH_3$], 19.4 ($CH_2CH_2CH_3$), 33.2 (C-10), 39.4 ($CH_2CH_2CH_3$), 48.6 (C-10a), 52.7 (C-5), 55.4 (OCH_3), 68.3 (C-1), 111.9 (C-6), 113.1 (C-8), 123.4 (C-9a), 130.2 (C-9), 137.5 (C-5a), 157.2, 158.4 (C-3, C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 1738 (vs), 1502 (m), 1415 (m), 1271 (m), 1226 (m), 1203 (m), 1177 (m), 1068 (m), 1034 (m), 1003 (m), 991 (m), 961 (m), 887 (m), 763 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 261 (13) [M]$^+$, 219 (13), 218 (100) [M – C_3H_7]$^+$, 174 (14), 159 (5), 147 (16), 131 (9), 115 (3), 91 (3), 77 (2), 65 (1), 51 (1), 27 (1). $C_{15}H_{19}NO_3$ (261.32): calcd. C 68.94, H 7.33, N 5.36; found C 69.06, H 7.43, N 5.09.

7-Methoxy-5-pentyl-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one (14b): Yield: 59 mg (73%). Colorless oil. R_f = 0.25 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.0 Hz, 3 H, 5′-H), 1.26–1.52 (m, 6 H, 2′-H, 3′-H, 4′-H), 1.66–1.79 (m, 1 H, 1′-H), 1.84–1.96 (m, 1 H, 1′-H), 2.82–2.85 (m, 2 H, 10-H), 3.79 (s, 3 H, OCH_3), 3.98–4.07 (m, 1 H, 10a-H), 4.14 (dd, *J* = 3.0, 8.6 Hz, 1 H, 1-H), 4.54 (dd, *J* = 7.8, 8.6 Hz, 1 H, 1-H), 4.86 (dd, *J* = 3.7, 9.6 Hz, 1 H, 5-H), 6.70 (d, *J* = 2.6 Hz, 1 H, 6-H), 6.76 (dd, *J* = 2.6, 8.4 Hz, 1 H, 8-H), 7.01 (d, *J* = 8.4 Hz, 1 H, 9-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-5′), 22.6, 25.7, 31.6 (C-2′, C-3′, C-4′), 33.2 (C-10), 37.2 (C-1′), 48.7 (C-10a), 53.0 (C-5), 55.4 (OCH_3), 68.3 (C-1), 111.9 (C-6), 113.0 (C-8), 123.7 (C-9a), 130.2 (C-9), 137.5 (C-5a), 157.2, 158.4 (C-7, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1740 (vs), 1502 (m), 1414 (m), 1269 (m), 1244 (m), 1222 (s), 1176 (m), 1098 (m), 1067 (m), 1037 (m), 1007 (m), 970 (m), 760 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 289 (7) [M]$^+$, 219 (13), 218 (100) [M – C_5H_{11}]$^+$, 174 (9), 159 (2), 147 (6), 131 (3), 115 (1), 91 (1), 28 (1). HRMS (ESI): calcd. for $C_{17}H_{23}NNaO_3^+$ [M + Na]$^+$ 312.1570; found 312.1568.

5-Isopropyl-7-methoxy-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one (14c): Yield: 9 mg (28%). Colorless oil. R_f = 0.11 (hexanes/EtOAc, 6:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 [d, *J* = 6.9 Hz, 3 H, $CH(CH_3)_2$], 1.16 [d, *J* = 6.8 Hz, 3 H, $CH(CH_3)_2$], 2.36 [sept.d, J_d = 4.0, $J_{sept.}$ = 6.8 Hz, 1 H, $CH(CH_3)_2$], 2.79–2.82 (m, 2 H, 10-H), 3.80 (s, 3 H, OCH_3), 4.01–4.09 (m, 1 H, 10a-H), 4.12 (dd, *J* = 2.4, 8.6 Hz, 1 H, 1-H), 4.54 (dd, *J* = 7.6, 8.6 Hz, 1 H, 1-H), 4.79 (d, *J* = 4.0 Hz, 1 H, 5-H), 6.75–6.89 (m, 2 H, 6-H, 8-H), 7.01–7.04 (m, 1 H, 9-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.6, 20.3 [$CH(CH_3)_2$], 32.9 (C-10), 35.0 [$CH(CH_3)_2$], 51.0 (C-10a), 55.3 (OCH_3), 58.0 (C-5), 67.9 (C-1), 111.9, 113.0 (C-6, C-8), 124.3 (C-9a), 130.2 (C-9), 136.4 (C-5a), 158.3, 158.4 (C-7, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1729 (vs), 1501 (m), 1407 (m), 1276 (m), 1258 (m), 1245 (m), 1222 (m), 1176 (m), 1154 (m), 1065 (m), 1037 (m), 1008 (m), 763 (m), 594 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 262 (1) [M + H]$^+$, 261 [M]$^+$, 219 (12), 218 (100) [M – $CH(CH_3)_2$]$^+$, 174 (12), 159 (3), 147 (10), 145 (7), 131 (5), 115 (1), 91 (1), 77 (1), 28 (2). HRMS (ESI): calcd. for $C_{15}H_{19}NNaO_3^+$ [M + Na]$^+$ 284.1257; found 284.1263.

5-(Benzyloxy)methyl-7-methoxy-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one (14e): Yield: 9 mg (30%). Colorless oil. R_f = 0.21 (hexanes/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.79 (dd, *J* = 11.0, 15.3 Hz, 1 H, 10-H_A), 2.87 (dd, *J* = 4.7, 15.3 Hz, 1 H, 10-H_B), 3.75 (s, 3 H, OCH_3), 3.80 (dd, *J* = 5.3, 10.2 Hz, 1 H, $CHCH_2OCH_2Ph$), 3.89 (dd, *J* = 3.7, 10.2 Hz, 1 H, $CHCH_2OCH_2Ph$), 4.11 (dd, *J* = 4.1, 8.6 Hz, 1 H, 1-H), 4.16–4.22 (m, 1 H, 10a-H), 4.43 (d, *J* = 12.2 Hz, 1 H, OCH_2Ph), 4.53 (dd, *J* = 7.9, 8.6 Hz, 1 H, 1-H), 4.61 (d, *J* = 12.2 Hz, 1 H, OCH_2Ph), 5.03 (t, *J* = 4.4 Hz, 1 H, 5-H), 6.71 (d, *J* = 2.6 Hz, 1 H, 6-H), 6.79 (dd, *J* = 2.6, 8.4 Hz, 1 H, 8-H), 7.05 (d, *J* = 8.4 Hz, 1 H, 9-H), 7.19–7.21 (m, 1 H, *p*-$PhCH_2O$), 7.25–7.35 (m, 4 H, *o*-, *m*-$PhCH_2O$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.4 (C-10), 49.7 (C-10a), 52.5 (C-5), 55.3 (OCH_3), 68.5 (C-1), 72.98 (CH_2OCH_2Ph), 73.04 ($PhCH_2O$), 111.6 (C-6), 113.6 (C-8), 124.5 (C-9a, C-5a, *i*-$PhCH_2O$), 127.67 (*o*-, *m*-$PhCH_2O$), 127.71 (*p*-$PhCH_2O$), 128.4 (*o*-, *m*-$PhCH_2O$), 130.3 (C-9), 133.7, 137.9 (C-9a, C-5a, *i*-$PhCH_2O$), 157.0, 158.4 (C-3, C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 1741 (s), 1424 (m), 1222 (m), 1103 (m), 1068 (m), 1027 (m), 742 (m), 697 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 339 (11) [M]$^+$, 233 (1), 219 (11), 218 (100) [M – $CH(CH_3)_2$]$^+$, 207 (2), 174 (8), 159 (2), 147 (7), 131 (5), 130 (2), 91 (7), 32 (1), 28 (7). HRMS (ESI): calcd. for $C_{20}H_{21}NNaO_4^+$ [M + Na]$^+$ 362.1363; found 362.1359.

General Procedure for the Debromination of 13: To a solution of **13** (1 equiv.) in benzene was added Bu_3SnH (ca. 1.1 equiv.) and AIBN (ca. 0.1 equiv.), and the reaction mixture was heated at reflux for 3.5–4.5 h. After cooling to room temperature, H_2O (10 mL) was added. The layers were separated, and the organic layer was washed with brine (3 × 10 mL) and dried (Na_2SO_4). The solvent was removed, and the residue was chromatographed on SiO_2 with hexanes/EtOAc.

6-Methoxy-5-propyl-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one: From **13a** (7.40 mg, 21.7 μmol) in benzene (1 mL). Yield: 5 mg (88%). Colorless solid. M.p. 93–95 °C. R_f = 0.18 (hexanes/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.2 Hz, 3 H, 3′-H), 1.44–1.55 (m, 3 H, 1′-H_A, 2′-H), 1.91–1.99 (m, 1 H, 1′-H_B), 2.87 (dd, *J* = 10.3, 16.1 Hz, 1 H, 10-H_A), 2.94 (dd, *J* = 5.3, 16.1 Hz, 1 H, 10-H_B), 3.83 (s, 3 H, OCH_3), 4.10–4.15 (m, 2 H, 10a-H, 1-H), 4.52–4.56 (m, 1 H, 1-H), 5.03–5.05 (m, 1 H, 5-H), 6.70 (d, *J* = 7.7 Hz, 1 H, 9-H), 6.73 (d, *J* = 8.2 Hz, 1 H, 7-H), 7.15 (dd, *J* = 7.7, 8.2 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.7 (C-3′), 19.8 (C-2′), 33.3 (C-10), 36.3 (C-1′), 47.2 (C-10a), 49.1 (C-5), 55.3 (OCH_3), 68.5 (C-1), 108.5 (C-7), 121.3 (C-9), 126.0 (C-5a), 127.5 (C-8), 132.3 (C-9a), 155.9, 157.0 (C-6, C-3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1726 (vs), 1471 (m), 1459 (m), 1441 (m), 1430 (m), 1420 (m), 1269 (m), 1253 (m), 1237 (s), 1098 (m), 1086 (m), 1065 (m), 1005 (m), 968 (m), 780 (m), 759 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 261 (2) [M]$^+$, 219 (13), 218 (100) [M – C_3H_7]$^+$, 203 (1), 174 (3), 160 (1), 159 (7), 147 (7), 131 (3), 115 (2), 103 (1), 91 (1), 77 (1). HRMS (ESI): calcd. for $C_{15}H_{19}NNaO_3^+$ [M + Na]$^+$ 284.1257; found 284.1251.

6-Methoxy-5-pentyl-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one: From **13b** (21 mg, 57.0 μmol) in benzene (6 mL). Yield: 9 mg (51%). Colorless solid. M.p. 82–84 °C. R_f = 0.18 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.95 (m, 3 H, 5′-H), 1.19–1.56 (m, 6 H, 2′-H, 3′-H, 4′-H), 1.61–1.75 (m, 1 H, 1′-H), 1.92–2.05 (m, 1 H, 1′-H), 2.82–2.98 (m, 2 H, 10-H), 3.83 (s, 3 H, OCH_3), 4.07–4.16 (m, 2 H, 3-H, 1-H), 4.51–4.57 (m, 1 H, 1-H), 5.00–5.03 (m, 1 H, 5-H), 6.70 (d, *J* = 7.7 Hz, 1 H, 9-H), 6.73 (d, *J* = 8.1 Hz, 1 H, 7-H), 7.15 (dd, *J* = 7.7, 8.1 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1 (C-5′), 22.5, 26.2, 31.4 (C-2′, C-3′, C-4′), 33.3 (C-10), 34.0 (C-1′), 47.2 (C-10a), 49.4 (C-5), 55.3

(OCH_3), 68.5 (C-1), 108.5 (C-7), 121.3 (C-9), 126.0 (C-5a), 127.5 (C-8), 132.3 (C-9a), 155.9, 157.0 (C-3, C-6) ppm. FTIR (ATR): $\tilde{\nu}$ = 1734 (vs), 1469 (m), 1434 (m), 1422 (m), 1261 (m), 1238 (m), 1074 (m), 1010 (m), 778 (m), 753 (m), 731 (m), 708 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 289 (12) $[M]^+$, 219 (14), 218 (100) $[M - C_5H_{11}]^+$, 203 (1), 174 (4), 159 (7), 147 (13), 131 (3), 115 (2), 91 (1). HRMS (ESI): calcd. for $C_{17}H_{23}NNaO_3^+$ $[M + Na]^+$ 312.1576; found 312.1574.

3-[1-(1*H*-1,2,3-Benzotriazol-1-yl)butyl]-4-(2-bromo-5-methoxybenzyl)-1,3-oxazolidin-2-one (21): Butyraldehyde (15.4 μL, 12.6 mg, 175 μmol) was added to a suspension of *rac*-**9** (50.0 mg, 175 μmol), 1*H*-benzotriazole (20.8 mg, 175 μmol) and *p*-toluenesulfonic acid (3.33 mg, 17.5 μmol) in absolute toluene (10 mL), and the reaction mixture was heated at reflux with a Dean–Stark trap for 10 h. After dilution with toluene (20 mL), the reaction mixture was washed with a NaOH solution (2 N; 2×40 mL) and a saturated NH_4Cl solution (2×40 mL), dried (Na_2SO_4), and concentrated. The residue (79 mg) was chromatographed on SiO_2 (hexanes/EtOAc, 4.5:1) to give a diastereomeric mixture of **21** (*dr* 83:17 by ^1H NMR spectroscopy). Yield: 47 mg (58%). Colorless foam. R_f = 0.18 (hexanes/EtOAc, 4.5:1). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.4 Hz, 0.5 H, $CHCH_2CH_2CH_3$), 1.09 (t, *J* = 7.4 Hz, 2.5 H, $CHCH_2CH_2CH_3$), 1.51 (sext, *J* = 7.4 Hz, 2 H, $CHCH_2CH_2CH_3$), 1.99 (dd, *J* = 10.9, 13.3 Hz, 2.5 H, 3-H_A), 2.32 (dd, *J* = 10.5, 13.5 Hz, 0.5 H, 3-H_A), 2.79–2.87 (m, 1 H, $CHCH_2CH_2CH_3$), 2.90–2.99 (m, 1 H, $CHCH_2CH_2CH_3$), 3.08 (dd, *J* = 4.0, 13.4 Hz, 1 H, 3-H_B), 3.69 (s, 2.5 H, OCH_3), 3.73 (s, 0.5 H, OCH_3), 4.03–4.14 (m, 2 H, 1-H), 4.37–4.43 (m, 0.5 H, 2-H), 4.43–4.49 (m, 2.5 H, 2-H), 6.48 (d, *J* = 3.0 Hz, 0.83 H, 2′-H), 6.56 (d, *J* = 3.0 Hz, 0.17 H, 2′-H), 6.61–6.74 (m, 2 H, $CHCH_2CH_2CH_3$, 4′-H), 7.38–7.44 (m, 2 H, 5′-H, 3′′-H, 4′′-H), 7.52–7.57 (m, 2 H, 3′′-H, 4′′-H), 8.02 (d, *J* = 8.4 Hz, 1 H, 2′′-H, 5′′-H), 8.07 (d, *J* = 8.4 Hz, 1 H, 2′′-H, 5′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.4, 13.5 ($CHCH_2CH_2CH_3$), 19.1, 19.3 ($CHCH_2CH_2CH_3$), 32.1, 32.7 ($CHCH_2CH_2CH_3$), 38.9, 40.0 (C-3), 52.1, 52.5 (C-2), 55.4, 55.5 (OCH_3), 66.5, 66.6 ($CHCH_2CH_2CH_3$), 66.7, 66.9 (C-1), 110.2, 110.9 (C-2′′, C-5′′), 114.4, 114.6 (C-4′), 114.75, 114.84 (C-6′), 117.0, 117.4 (C-2′), 119.8, 119.9 (C-2′′, C-5′′), 124.6, 124.7 (C-3′′, C-4′′), 128.1, 128.3 (C-3′′, C-4′′), 132.9 (C-1′′, C-6′′), 133.9 (C-5′), 135.7 (C-1′), 145.9, 146.1 (C-1′′, C-6′′), 157.8, 158.5, 158.98, 159.04 (C=O, C-3′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1747 (s), 1473 (m), 1453 (m), 1411 (m), 1239 (m), 1157 (m), 1078 (m), 1046 (m), 1012 (m), 747 (s) cm^{-1}. MS (ESI): *m*/*z* (%) = 483 (75) $[M + Na]^+$, 481 (83) $[M + Na]^+$, 364 (92) [M – benzotriazolyl + H + $Na]^+$, 362 (92) [M – benzotriazole + H + $Na]^+$, 342 (27) $[M + H]^+$, 340 (30) $[M + H]^+$, 149 (4), 132 (7), 104 (2). HRMS (ESI): calcd. for $C_{21}H_{23}BrN_4NaO_3^+$ $[M + Na]^+$ 481.0846; found 481.0853.

3-[1-(1*H*-1,2,3-Benzotriazol-1-yl)butyl]-4-(4-methoxybenzyl)-1,3-oxazolidin-2-one (22): As described above from (*S*)-**10** (50.0 mg, 241 μmol), 1*H*-benzotriazole (28.7 mg, 241 μmol), and *p*-TsOH (4.58 mg, 24.1 μmol) in absolute toluene (10 mL) and butyraldehyde (21.3 μL, 17.4 mg, 241 μmol) to give a diastereomeric mixture of **22** (*dr* = 64:36). Yield: 34 mg (37%). Colorless foam. R_f = 0.16 (hexanes/EtOAc, 4.5:1). $[\alpha]_D^{22}$ = –112.9 (*c* = 0.036, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.4 Hz, 1.7 H, $CHCH_2CH_2CH_3$), 1.09 (t, *J* = 7.4 Hz, 1.3 H, $CHCH_2CH_2CH_3$), 1.42–1.54 (m, 2 H, $CHCH_2CH_2CH_3$), 1.89 (dd, *J* = 10.5, 13.5 Hz, 0.64 H, 3-H_A), 2.56–2.63 (m, 0.36 H, $CHCH_2CH_2CH_3$), 2.66–2.76 (m, 1.64 H, $CHCH_2CH_2CH_3$, 3-H_A, 3-H_B), 2.85–2.96 (m, 1 H, $CHCH_2CH_2CH_3$), 3.68 (dd, *J* = 3.9, 13.1 Hz, 0.36 H, 3-H_B), 3.75 (s, 1.7 H, OCH_3), 3.77 (s, 1.3 H, OCH_3), 3.93–4.00 (m, 1 H, 1-H_A), 4.08–4.13 (m, 1 H, 1-H_B), 4.14–4.19 (m, 1 H, 2-H), 6.61 (d, *J* = 7.6 Hz, 0.64 H, $CHCH_2CH_2CH_3$), 6.77 (d, *J* = 8.7 Hz, 1.28 H, 3′-H), 6.81 (d, *J* = 8.7 Hz, 0.72 H, 3′-H), 6.90 (d, *J* = 8.7 Hz, 1.28 H, 2′-H), 7.04 (d, *J* = 8.7 Hz, 0.72 H, 2′-H), 7.39–7.44 (m, 1 H, 3′′-H, 4′′-H), 7.52–7.57 (m, 1 H, 3′′-H, 4′′-H), 7.76 (d, *J* = 8.4 Hz, 0.72 H, 2′′-H, 5′′-H), 8.01 (d, *J* = 8.4 Hz, 1.28 H, 2′′-H, 5′′-H), 8.07 (d, *J* = 8.4 Hz, 1.28 H, 2′′-H, 5′′-H), 8.11 (d, *J* = 8.4 Hz, 0.72 H, 2′′-H, 5′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.4, 13.5 ($CHCH_2CH_2CH_3$), 19.1, 19.3 ($CHCH_2CH_2CH_3$), 32.0, 35.0 ($CHCH_2CH_2CH_3$), 37.7, 39.4 (C-3), 54.2 (C-2), 55.2 (OCH_3), 66.5, 67.3 ($CHCH_2CH_2CH_3$), 67.4, 67.5 (C-1), 110.2, 110.9 (C-2′′, C-5′′), 114.27, 114.35 (C-3′), 119.8, 119.9 (C-2′′, C-5′′), 124.6, 124.8 (C-3′′, C-4′′), 127.0, 127.1 (C-1′), 128.2, 128.4 (C-3′′, C-4′′), 130.9 (C-2′), 132.86, 132.91 (C-1′′, C-6′′), 145.8, 146.1 (C-1′′, C-6′′), 157.8, 158.6, 158.7, 158.8 (C=O, C-4′) ppm. FTIR (ATR): $\tilde{\nu}$ = 1745 (s), 1512 (m), 1410 (m), 1245 (s), 1178 (m), 1155 (m), 1076 (m), 1030 (m), 1002 (m), 780 (m), 769 (m), 747 (s) cm^{-1}. MS (ESI): *m*/*z* (%) = 403 (100) $[M + Na]^+$, 338 (19) $[M + H - CH_2CH_2CH_3]^+$, 284 (19) [M – H – benzotriazolyl]$^+$. HRMS (ESI): calcd. for $C_{21}H_{24}N_4NaO_3^+$ $[M + Na]^+$ 403.1741; found 403.1722.

General Procedure for the Preparation of Compounds 13a,14a by Benzotriazole: To a solution of **23** or **24** (1 equiv.) in absolute acetonitrile (5 mL) was added $TiCl_4$ (1.5 equiv.) by syringe, and the reaction mixture was heated at 60 °C for 8 h. After the addition of H_2O (10 mL), the reaction mixture was extracted with Et_2O (2×30 mL). The combined extracts were washed with a NaOH solution (2 N; 2×20 mL) and a saturated NH_4Cl solution (2×30 mL), dried (Na_2SO_4), and concentrated. The residue was chromatographed on SiO_2 (hexanes/EtOAc, 3:1) to give product **13a** [64%, R_f = 0.26 (hexanes/EtOAc, 3:1)] as colorless crystals or **14a** [54%, R_f = 0.13 (hexanes/EtOAc, 3:1)] as a colorless oil.

Cyclization of Derivatives 23a,b by the Pictet–Spengler Reaction

Method A: To a solution of **23a** (72 mg, 250 μmol) or **23b** (76 mg, 363 μmol) in absolute CH_2Cl_2 (5 mL) were added molecular sieves 4 Å (100 mg) and butyraldehyde (35.3 μL, 28.8 mg, 400 μmol for **23a**, 51.3 μL, 41.9 mg, 581 μmol for **23b**), and the reaction mixture was stirred at room temperature for 24 h. Then, the reaction mixture was cooled to 0 °C and trifluoroacetic acid (59.4 μL, 91.2 mg, 800 μmol for **23a**, 86.0 μL, 132 mg, 1.16 mmol for **23b**) was added dropwise by syringe, and the mixture was stirred at 0 °C for a further 16 h. After filtration, the filtrate was concentrated and the residue chromatographed on basic Al_2O_3 (hexanes/EtOAc, 20:1) to give **24a** or **24b** (*E*/*Z*, 90:10 by ^1H NMR spectroscopy).

Methyl 2-Bromo-*N*-[2-ethylhex-2-enylidene]-5-methoxyphenylalaninate (24a): Yield: 27 mg (27%). Light yellow oil. R_f = 0.29 (hexanes/EtOAc, 4.5:1). Major diastereomer: ^1H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.4 Hz, 3 H, 4′′′-H), 0.97 (t, *J* = 7.5 Hz, 3 H, 4′′-H), 1.42 (sext, *J* = 7.4 Hz, 2 H, 3′′′-H), 2.17 (ddd, *J* = 1.7, 7.4, 14.8 Hz, 2 H, 2′′′-H), 2.29–2.42 (m, 2 H, 3′′-H), 3.09 (dd, *J* = 9.0, 13.5 Hz, 1 H, 3-H_A), 3.49 (dd, *J* = 5.2, 13.5 Hz, 1 H, 3-H_B), 3.71, 3.74 (2 s, 3 H, OCH_3), 4.15 (dd, *J* = 5.2, 9.0 Hz, 1 H, 2-H), 5.69 (t, *J* = 7.4 Hz, 3 H, 1′′′-H), 6.63 (dd, *J* = 3.1, 8.8 Hz, 1 H, 4′-H), 6.71 (d, *J* = 3.1 Hz, 1 H, 3′-H), 7.39 (d, *J* = 8.8 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.6 (C-4′′), 13.9 (C-4′′′), 19.0 (C-3′′), 22.3 (C-3′′′), 30.3 (C-2′′′), 40.0 (C-3), 52.2, 55.4 (2 x OCH_3), 72.1 (C-2), 114.6 (C-4′), 115.1 (C-6′), 117.2 (C-2′), 133.2 (C-5′), 137.9 (C-1′), 141.7 (C-2′′), 143.6 (C-1′′′), 158.5 (C-3′), 167.8 (C-1′′), 172.3 (CO_2CH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 2958 (m), 1738 (m), 1613 (m), 1512 (s), 1245 (s), 1201 (m), 1175 (m), 1162 (m), 1034 (m), 823 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 397 (7) $[M]^+$, 395 (7) $[M]^+$, 368 (2), 366 (2), 338 (5) [M – $CO_2Me]^+$, 336 (5) [M – $CO_2Me]^+$, 316 (100) [M – Br]$^+$, 300 (7), 284 (14), 260 (12), 244 (3), 228 (5), 218 (9), 196 (25) [M – $CH_2C_6H_4(OMe)Br]^+$, 186 (9), 158 (7), 136 (9), 109 (3), 91 (1), 69 (3). $C_{19}H_{26}BrNO_3$ (396.32):

calcd. C 57.58, H 6.61, N 3.53; found C 57.83, H 6.71, N 3.37. HRMS (ESI): calcd. for $C_{19}H_{26}BrNNaO_3^+$ [M + Na]$^+$ 418.0988; found 418.0969.

Methyl *N*-(2-Ethylhex-2-enylidene)-*O*-methyl-L-tyrosinate (24b): Yield: 37 mg (32%). Light yellow oil. R_f = 0.27 (hexanes/EtOAc, 4.5:1). Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.4 Hz, 3 H, 4′′′-H), 0.98 (t, J = 7.5 Hz, 3 H, 4′′-H), 1.36–1.48 (m, 2 H, 3′′′-H), 2.14–2.21 (m, 2 H, 2′′′-H), 2.28–2.47 (m, 2 H, 3′′-H), 3.00 (dd, J = 8.9, 13.6 Hz, 1 H, 3-H_A), 3.24 (dd, J = 5.2, 13.6 Hz, 1 H, 3-H_B), 3.71, 3.77 (2 s, 3 H, OCH_3), 3.94 (dd, J = 5.2, 8.9 Hz, 1 H, 2-H), 5.67 (t, J = 7.4 Hz, 3 H, 1′′′-H), 6.78 (d, J = 8.8 Hz, 2 H, 3′-H, 5′-H), 7.06 (d, J = 8.8 Hz, 2 H, 2′-H, 6′-H), 7.37 (s, 1 H, 1′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.7 (C-4′′), 13.9 (C-4′′′), 19.0 (C-3′′), 22.4 (C-3′′′), 30.2 (C-2′′′), 39.0 (C-3), 52.1, 55.2 (2 x OCH_3), 75.2 (C-2), 113.6 (C-3′, C-5′), 129.8 (C-1′), 130.7 (C-2′, C-6′), 141.7 (C-2′′), 143.3 (C-1′′′), 158.2 (C-4′), 167.3 (C-1′′), 172.7 (CO_2CH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 2958 (m), 1738 (m), 1612 (m), 1512 (s), 1245 (s), 1201 (m), 1168 (m), 1110 (m), 1034 (m), 823 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 317 (69) [M]$^+$, 302 (1), 288 (4), 274 (4), 258 (14) [M – CO_2Me]$^+$, 242 (1), 214 (3), 196 (100) [M – $CH_2C_6H_4$OMe]$^+$, 186 (1), 165 (2), 164 (20), 151 (3), 136 (28), 121 (85) [$CH_2C_6H_4$OMe]$^+$, 108 (6), 91 (3), 77 (3), 55 (2), 41 (2). $C_{19}H_{27}NO_3$ (317.42): calcd. C 71.89, H 8.57, N 4.41; found C 71.79, H 8.76, N 4.32. HRMS (ESI): calcd. for $C_{19}H_{27}NNaO_3^+$ [M + Na]$^+$ 340.1883; found 340.1872.

Method B: To a solution of **23a** or **23b** (1 equiv.) in absolute toluene (10 mL) was added *p*-TsOH (0.1 equiv.) and butyraldehyde (1 equiv.), and the reaction mixture was heated at reflux with a Dean–Stark trap for 16 h. After dilution with toluene (10 mL), the reaction mixture was poured into a saturated $NaHCO_3$ solution (25 mL). The layers were separated, and the organic layer was washed with a NaOH solution (0.5 N; 2 × 25 mL) and a saturated $NaHCO_3$ solution (2 × 20 mL), dried (Na_2SO_4), and concentrated. The residue was chromatographed on basic Al_2O_3 (hexanes/EtOAc, 20:1) to give **24a** [18%, R_f = 0.19 (hexanes/EtOAc, 20:1)] or **24b** [14%, R_f = 0.15 (hexanes/EtOAc, 20:1)] as colorless oils.

Methyl 6-Methoxy-3-oxo-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]-isoquinoline-5-carboxylate (25): From **13i** (15 mg, 41.1 μmol) in benzene (4 mL). Yield: 8 mg (69%). Colorless solid. M.p. 111–112 °C. R_f = 0.07 (hexanes/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.87 (dd, J = 10.6, 15.8 Hz, 1 H, 10-H_A), 2.96 (dd, J = 4.8, 15.8 Hz, 1 H, 10-H_B), 3.78 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, OCH_3), 4.16 (dd, J = 3.6, 8.5 Hz, 1 H, 1-H), 4.19–4.28 (m, 1 H, 10a-H), 4.57 (dd, J = 7.6, 8.5 Hz, 1 H, 1-H), 5.59 (s, 1 H, 5-H), 6.77 (d, J = 7.8 Hz, 1 H, 7-H), 6.78 (d, J = 8.2 Hz, 1 H, 9-H), 7.25 (dd, J = 7.8, 8.2 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.9 (C-10), 48.8 (C-10a), 52.4 (C-5), 52.6 (CO_2CH_3), 55.6 (OCH_3), 68.4 (C-1), 108.6 (C-7), 119.1 (C-5a), 121.6 (C-9), 129.0 (C-8), 133.5 (C-9a), 156.47, 156.53 (C-3, C-6), 170.8 (CO_2CH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1739 (vs), 1585 (m), 1472 (m), 1443 (m), 1412 (m), 1381 (m), 1337 (m), 1263 (m), 1238 (m), 1194 (m), 1167 (s), 1076 (m), 1007 (m), 987 (m), 959 (m), 781 (m), 768 (m), 741 (m), 727 (m), 707 (m), 665 (m), 620 (m) cm^{-1}. MS (ESI): *m*/*z* (%) = 577 (2) [2 M + Na]$^+$, 365 (28), 316 (6), 300 (100) [M + Na]$^+$, 278 (2), 244 (1), 218 (1) [M – CO_2CH_3]$^+$. HRMS (ESI): calcd. for $C_{14}H_{15}NNaO_5^+$ [M + Na]$^+$ 300.0842; found 300.0839.

Methyl 9-Bromo-6-methoxy-3-oxo-1,5,10,10a-tetrahydro[1,3]-oxazolo[3,4-*b*]isoquinoline-5-carboxylate (*cis*-13i)

Method A: To a solution of *trans*-**13i** (5.00 mg, 14.0 μmol) in absolute MeOH (2 mL) was added 3% NaOMe/MeOH (2.63 μL, 75.6 μg, 1.40 μmol), and the reaction mixture was stirred at room temperature for 2 d. Additional 3% NaOMe/MeOH (23.7 μL, 680 μg, 12.6 μmol) was added, and the reaction mixture was heated at reflux for 2 d (*trans*:*cis*, 90:10 by GC). HCl-saturated MeOH (2 mL) was added, and the reaction mixture was concentrated. The residue was taken up in $CHCl_3$ (10 mL), washed with a saturated $NaHCO_3$ solution (3 × 10 mL) and brine (2 × 20 mL), dried (Na_2SO_4), and concentrated. The residue was chromatographed on SiO_2 (hexanes/EtOAc, 2:1) to give a mixture of *cis*/*trans*-**13i** as a colorless solid (4 mg, *trans*/*cis*, 90:10). The isomers were separated by preparative HPLC on a column Kromasil (250 × 20 mm, 100 Sil 5 μm) (MZ-Analysentechnik) with 2-PrOH in hexane (gradient from 0–10%, flow 7 mL min^{-1}).

Method B: To a solution of *trans*-**13i** (5.00 mg, 14.7 μmol) in toluene (3 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (2.23 μL, 2.27 mg, 14.7 μmol) by syringe, and the reaction mixture was heated at reflux for 24 h. After the addition of more DBU (20.1 μL, 132 μmol), the reaction mixture was heated at reflux for 24 h (7% conversion to *cis*-**13i**), which resulted in a mixture of *cis*/*trans*-**13i** in a *trans*/*cis* ratio of 85:15 (by GC).

Methyl 6-Methoxy-3-oxo-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]-isoquinoline-5-carboxylate (*cis*-25): As described above under method b to give a mixture of *cis*/*trans*-**25** in a *trans*/*cis* ratio of 85:15 (by GC).

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