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Silver(I)-promoted asymmetric halomethoxylation of chiral α,β-unsaturated carboxylic acid derivatives: enantioselective synthesis of N-protected *syn*-β-methoxy-α-amino acids

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Abstract—Asymmetric halomethoxylation of chiral α,β-unsaturated carboxylic acid derivatives was performed with halogens (Br_2/I_2) promoted by silver(I) salts with high regio- and *anti*-selectivity and moderate to good diastereoselectivity. Reagent controlled diastereoselectivity was observed for *N*-cinnamoyl-2-oxazolidinone substrates especially for cinnamoyl and electron-deficient cinnamoyl substrates, when Ag_2O was used as a promoter instead of $AgNO_3$. Enoyl substrates containing Oppolzer's sultam chiral auxiliary are independent of the counter ion of the Ag(I) salt. This method was applied to a short synthesis of both enantiomers of N-protected *syn*-β-methoxyphenylalanine, and N- and O-protected *syn*-β-methoxytyrosine, unusual amino acid components of biologically active cyclic peptide and depsipeptide antibiotics.
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1. Introduction

β-Methoxy-α-amino acids are the unusual amino acid components of many biologically active cyclic peptide and depsipeptide antibiotics such as callipeltines,[1] papuamides,[2] cyclomarins,[3] neamphamide A[4] and discokiolides.[5] There are only a few reports on asymmetric synthesis of β-methoxy-α-amino acids.[6–11] Hamada and co-workers reported the diastereoselective synthesis of all stereoisomers of β-methoxytyrosine based on Garner's aldehyde and determined the absolute stereochemistry of the residue in papuamide A.[6] A catalytic and asymmetric method for the synthesis of an *anti* disposed aromatic β-hydroxy-α-amino acid, a key intermediate for the synthesis of *anti*-β-methoxyamino acid, has also been described by the same group.[7] Recently, D'Auria et al. determined the absolute configuration of β-methoxytyrosine in callipeltin A by synthesizing all the stereoisomers of that residue.[8] Gustafson et al. described the complete stereochemistry of neamphamide A and absolute configuration of the β-methoxytyrosine residue in papuamide B.[9] Synthesis of four stereoisomers of β-methoxytyrosine from serine has also been reported by Joullié et al.[10] Boukhris and Souizi described[11] the reduction of β-alkoxy-α-oximino acid esters to β-alkoxy-α-amino esters by $NaBH_4$ in the presence of $TiCl_3$ and L-tartaric acid, but the configuration of the diastereomers and the enantioselectivities were not determined.

α-Halo-β-methoxy-carboxylic acid derivatives, similar to carboxyhalohydrins,[12] would be an important direct precursor to the β-methoxyamino acids. A potentially straight forward method for the synthesis of α-halo-β-methoxy-carboxylic acid derivatives is the regio- and stereoselective halomethoxylation reaction of α,β-unsaturated carboxylic acid derivatives.[13]

Herein, we report,[14] in detail, the silver(I)-promoted asymmetric halomethoxylation of chiral α,β-unsaturated carboxylic acid derivatives with high regio- and diastereoselectivities up to 86:14 of *anti*-α-halo-β-methoxy carbonyls. Their application to the short synthesis of both enantiomers of N-protected *syn*-β-methoxyphenylalanine and N- and O-protected *syn*-β-methoxytyrosine, unusual amino acid components of cyclomarins and neamphamide A are also described.

2. Results and discussion

Initially, (4*S*)-*N*-cinnamoyl-4-(1-methylethyl)-2-oxazolidinones[15] were selected as substrates for the development

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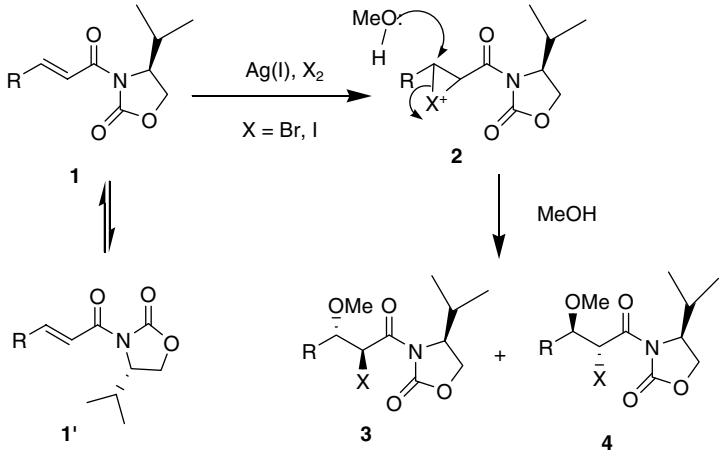


Scheme 1.

of the diastereoselective halomethoxylation reaction. It was assumed that the β-aryl group of the three membered halonium intermediate **2** would enhance electrophilicity towards the methanol nucleophile to achieve high regioselectivity (Scheme 1, R = Ar), thus affording the β-methoxyamino acid components of the biologically active natural cyclic peptide and depsipeptide antibiotics possessing a β-aryl group.[1–5] The auxiliary of choice was an oxazolidinone derived from readily available L-valine.[15a,b] It is well known that chelated *N*-cinnamoyl-2-oxazolidinone usually exists in the *s-cis-syn-dipole* conformation **1′** and unchelated one in the *s-cis-anti-dipole* conformation **1**. So, it was expected to provide different diastereoselectivity depending on the reaction conditions. Initially, it was presumed that the halomethoxylation reaction of **1** would yield **4** as the major diastereoisomer.

There are only a few reports[16] on the halomethoxylation of α,β-unsaturated carbonyls. By screening those methods we found that the combination of silver nitrate and halogen (Br_2/I_2) in methanol favours the regio- and stereoselective halomethoxylation of chiral *N*-enoyl-2-oxazolidinones **1** over aromatic electrophilic substitution. Initially, $AgNO_3$ promoted halomethoxylation of three electronically different cinnamoyl substrates **1a**–**1c**, containing (4*S*)-4-(1-methylethyl)-2-oxazolidinone as a chiral auxiliary were studied (Table 1). Therefore, a methanolic solution of substrate **1a** was treated with silver nitrate (1.2 equiv) and bromine (1.2 equiv) at rt (25 °C). Within 20 min, it gave the desired α-bromo-β-methoxycarbonyls **3a** and **4a** with a diastereomeric ratio (dr) of 67:33 in 80% yield (entry 1). A little improvement in dr, as well as yield, was obtained when the reaction was performed at 0–5 °C (entry 2). However, bromomethoxylation of **1a** in the absence of $AgNO_3$ gave a mixture of products. Among them, the desired compounds **3a**/**4a** (25%) and a non-separable mixture of diastereoisomers (dr 60:40) of dibromo compounds *anti*-(4*S*)-3-(2′,3′-dibromo-3′-phenyl-propionyl)-4-(1-methylethyl)-2-oxazolidinone (28%) were obtained.[17] The iodomethoxylation of **1a** under the same reaction conditions, using I_2 as halogen source gave <5% of the desired products, and there was no improvement even with the use of excess reagents and under different reaction conditions (entry 3). Electron-deficient cinnamoyl substrate **1b** also underwent bromomethoxylation, but no iodomethoxylation. Alternatively, substrate **1c** readily underwent the iodomethoxylation with moderate diastereoselectivity, while the bromomethoxylation reaction provided two undesired products **3′c** and **4′c** (65:35) in 41% yield (43% of **1c** was recovered) and later these two undesired compounds were characterized as diastereomers of *anti*-(4*S*)-3-[2′-bromo-3′-methoxy-3′-(3-bromo-4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone **3′c** and **4′c**, whereby the *p*-methoxy phenyl fragment had also been brominated (Fig. 1). When the same reaction was again performed with an excess of $AgNO_3$ (2.5 equiv) and Br_2 (2.5 equiv) under the same conditions, compounds **3′c** and **4′c** were obtained in 96% yield (entry 8). The halomethoxylation of **1a**–**1c** was also studied under different temperatures. It was found that at −10 °C, all three substrates **1a**–**1c**

Table 1. $AgNO_3$-promoted halomethoxylation of **1** under different reaction conditions[a]

Entry	Substrate	R	X	Ratio[b] (**3**:**4**)	Yield[c] (%)
1[d]	**1a**	Ph	Br	67:33 (65:35)	80
2	**1a**	Ph	Br	71:29 (70:30)	92
3	**1a**	Ph	I	ND	<5[e]
4	**1b**	4-$NO_2C_6H_4$	Br	65:35 (65:35)	84
5	**1b**	4-$NO_2C_6H_4$	I	—	NR
6[d]	**1c**	4-$MeOC_6H_4$	I	60:40 (62:38)	89
7	**1c**	4-$MeOC_6H_4$	I	62:38 (61:39)	94
8	**1c**	4-$MeOC_6H_4$	Br	65:35[f] (66:34)	96[g]

ND: Not determined; NR: no reaction.

[a] Halomethoxylation reactions were performed using 1.2 equiv of $AgNO_3$ and 1.2 equiv of halogen (X_2) in methanol at 0–5 °C for 30 min.

[b] Determined from the ^1H NMR spectrum of the crude reaction mixture. Ratios in the parentheses refer to the ratio of isolated **3** and **4** after column chromatography.

[c] Combined isolated yields of **3** and **4** after chromatography.

[d] Reaction at room temperature (25 °C).

[e] >90% of **1a** was recovered.

[f] Ratio of compounds **3′c** and **4′c**.

[g] Combined isolated yields of **3′c** and **4′c** after chromatography, when excess $AgNO_3$ (2.5 equiv) and Br_2 (2.5 equiv) were used.

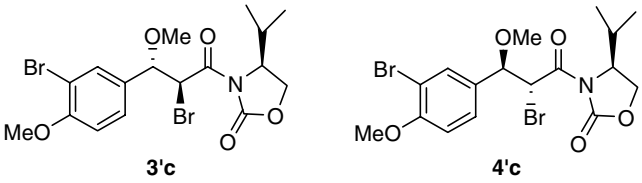


Figure 1.

smoothly underwent halomethoxylation without any appreciable change in dr and yields. However, at −20 °C, it gave poor yields with incomplete conversion and there was no reaction at −40 °C. Compounds **1a**–**1c** also responded to the halomethoxylation reaction in other non-nucleophilic solvents such as CH_2Cl_2, CH_3COCH_3, CH_3CN containing 5–20% of methanol and showed similar dr and yields, but **1a** and **1b** did not undergo any reaction in methanolic THF, whereas **1c** responded to the iodomethoxylation reaction in methanolic THF. The stereochemistry of **3** was confirmed by a single crystal X-ray analysis of compound **3c** (Fig. 2).[18]

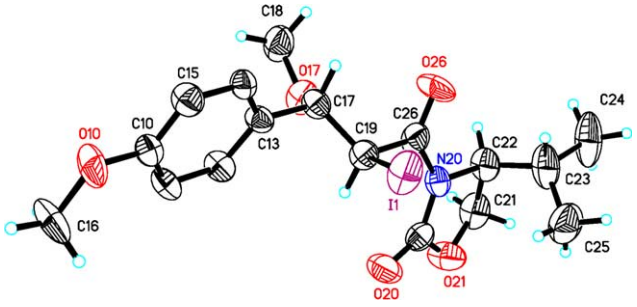
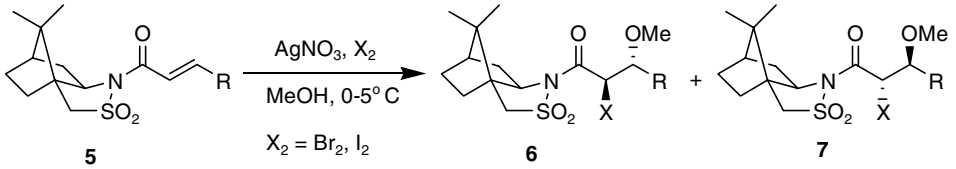


Figure 2. ORTEP diagram of **3c**.

Since, the chiral auxiliary (4*S*)-4-(1-methylethyl)-2-oxazolidinone gave moderate to good diastereoselectivities, we have also examined other oxazolidinone chiral auxiliaries viz (4*S*)-4-phenyl- and (4*S*)-4-(diphenylmethyl)-2-oxazolidinones.[15,19] Halomethoxylation of substrates containing different oxazolidinone chiral auxiliaries (Ph and Ph_2CH) using either Br_2 or I_2 gave complex mixtures of products. One of the undesired products was identified as a halocarbocyclized product.[17,20] This halomethoxylation reaction was further studied for the cinnamoyl substrates **5a**–**5c** containing another well-known chiral auxiliary, Oppolzer's bornane sultam.[21] $AgNO_3$-promoted halomethoxylation of **5a**–**5c** showed improved diastereoselectivity[22] (Table 2). Substrates **5a** and **5c** responded well to both bromomethoxylation and iodomethoxylation reactions. Unlike **1c**, **5c** provided only bromomethoxylated products **6c** and **7c** (entry 5), no arene bromination was observed. Bromomethoxylation reaction of **5a** gave a lower yield of a non-separable mixture of diastereomers; *Br*-**6a** and *Br*-**7a**, while the iodomethoxylation products of **5c** could not be obtained in pure form since purification by chromatography resulted in decomposition via an elimination pathway to afford **5c**. Similar to **1b**, substrate **5b** underwent only bromomethoxylation reaction (entry 3).

To assess whether the counter ion of Ag(I) salt affects the diastereoselectivity of halomethoxylation reactions, studies were carried out employing the electronically different cinnamoyl substrates **1a**–**1c** and **5a**–**5c** using AgOAc and Ag_2O instead of $AgNO_3$ as a promoter under a variety of reaction conditions (Table 3). $AgNO_3$ (Eq. 1) and AgOAc (Eq. 2) produce nitric acid and acetic acid, respectively, on reaction with a halogen in MeOH, whereas Ag_2O produces water as a by-product (Eq. 3) under the same conditions. When the halomethoxylation reactions of **1a**–**1c** were performed in the presence of AgOAc instead of $AgNO_3$, similar results were obtained with **3** being produced as the major diastereomer (entries 1–3).[23] However, in the case of Ag_2O-mediated reactions,[23] diastereoselectivities were in favour of the diastereomers **4** (entries 4–6) and more interestingly, compounds **1a** and the electron-deficient **1b** showed opposite diastereoselectivities (entries 4 and 5) compared to the $AgNO_3$ (Table 1, entries 2 and 4) or AgOAc (Table 3, entries 1 and 2) mediated reactions. When the Ag_2O-promoted halomethoxylation reactions of **1a**–**1c** were performed in the presence of either AcOH or HNO_3 as an additive,[24] diastereoselectivities (entries 7–9) similar to either $AgNO_3$ or AgOAc-promoted reactions were obtained. However, no counter ion effect on

Table 2. $AgNO_3$-promoted halomethoxylation reactions of **5**



5 **6** **7**

Entry	Substrate	R	X	Ratio (**6**:**7**)[a]	Yield (%)[b]
1	**5a**	Ph	Br	65:35	76
2	**5a**	Ph	I	77:23	95
3	**5b**	2-$NO_2C_6H_4$	Br	72:28	94
4	**5b**	2-$NO_2C_6H_4$	I	—	NR
5	**5c**	4-$MeOC_6H_4$	Br	71:29	92
6	**5c**	4-$MeOC_6H_4$	I	—	[c]

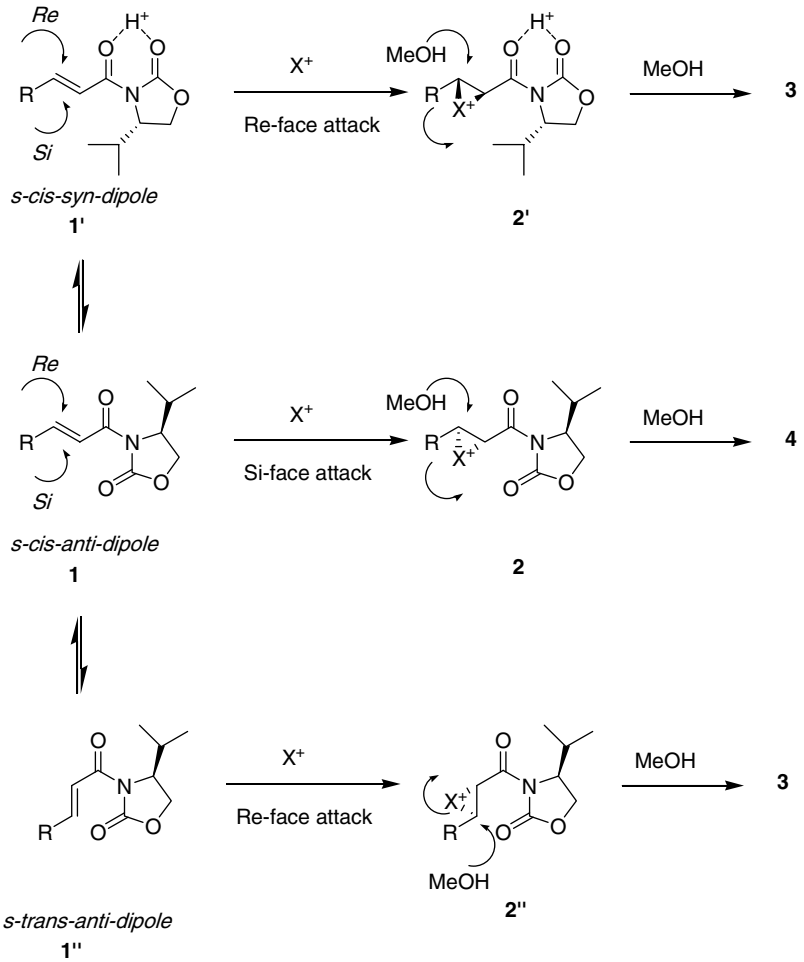
[a] Ratio of isolated **6** and **7** after column purification.
[b] Combined isolated yield of **6** and **7** after column chromatography.
[c] Compounds *I*-**6c** and *I*-**7c** could not be isolated in pure form as they decomposed during silica gel (230–400 mesh) column purification.

Table 3. AgOAc- and Ag_2O-promoted halomethoxylation reaction[a]

Entry	Substrate	Ag(I) salt	Additive	X	dr[b] (**3**:**4**)/(**6**:**7**)	Yield (%)[c]
1	**1a**	AgOAc	None	Br	70:30	86
2	**1b**	AgOAc	None	Br	63:37	92
3	**1c**	AgOAc	None	I	61:39	97
4	**1a**	Ag_2O	None	Br	27:73	89
5	**1b**	Ag_2O	None	Br	35:65	83
6	**1c**	Ag_2O	None	I	48:52	91
7	**1a**	Ag_2O	HNO_3	Br	72:28 (70:30)	79 (82)
8	**1b**	Ag_2O	HNO_3	Br	64:36 (67:33)	83 (81)
9	**1c**	Ag_2O	HNO_3	I	61:39 (62:38)	74 (78)
10	**5a**	Ag_2O	None	I	75:25	84
11	**5b**	Ag_2O	None	Br	70:30	91
12	**5c**	Ag_2O	None	Br	70:30	93

[a] Ag_2O-promoted halomethoxylation reactions were performed using 0.7 equiv of Ag_2O and 1.2 equiv of halogen (X_2) in methanol at 0–5 °C for 30 min and the AgOAc-promoted reaction was the same as $AgNO_3$ in Table 1.
[b] Determined from the ^1H NMR spectrum of the crude reaction mixture. Ratios in parentheses refer to reactions in the presence of AcOH.
[c] Combined isolated yields.

the diastereoselectivities of halomethoxylation of substrates **5a**–**5c** containing the sultam chiral auxiliary (entries 10–12) was observed. Reactions of either $AgNO_3$ or AgOAc with halogens in methanol generate acid (Eqs. 1 and 2), so it may be proposed that a H^+-chelated *s-cis-syn-dipole* conformation **1′** might be involved in these halomethoxylation reactions. The preferred attack of X^+ from the *Re-face* of conformation **1′** and subsequent (*anti*) opening of the halonium intermediate **2′** by nucleophilic attack of MeOH at the β-position yielded **3** as the major diastereomer (Scheme 2). In the Ag_2O-promoted reaction, the *Si-face* of the unchelated *s-cis-anti-dipole* conformation **1** might be involved giving **4** as a major diastereomer. This model



Scheme 2.

is supported by the Ag_2O-mediated reactions performed in the presence of either HNO_3 or AcOH as an additive (Table 3, entries 7–9). The poor diastereoselectivities of the electron-rich substrate **1c** in Ag_2O-promoted reactions (Table 3, entry 6) might be accounted for by the involvement of both the equilibrated *s-cis*- and *s-trans-anti-dipole* conformations **1** and **1″**, due to extensive conjugation of the electron donating substituent at the *p*-position with the α,β-unsaturated carbonyls.

$$AgNO_3 + X_2 + MeOH \rightarrow AgX\downarrow + MeOX + HNO_3 \quad (1)$$

$$AgOAc + X_2 + MeOH \rightarrow AgX\downarrow + MeOX + AcOH \quad (2)$$

$$Ag_2O + 2MeOH + 2X_2 \rightarrow 2AgX\downarrow + 2MeOX + H_2O \quad (3)$$

It was found that in the absence of the $AgNO_3$, bromomethoxylation of **1a** gave a mixture of bromomethoxylated products and dibromo compounds with almost no selectivity. So, Ag(I) is necessary as a X^- scavenger for the selective formation of halomethoxylated compounds. Further, the counter ion effect of Ag(I) salts on the diastereoselectivity of the halomethoxylation reaction and the effect of HNO_3 and AcOH as additives in Ag_2O promoted reactions also support the role of Ag(I) salt as a X^- scavenger but not as Lewis acid. Otherwise, compound **3** would always have the major diastereomer irrespective of the counter ion of Ag(I) salts.

We also attempted to extend our methodology for the synthesis of other haloalkoxylated carbonyl compounds (Table 4), as key intermediates for β-alkoxy-α-amino acids of potential interest for exploring the structure–activity relationship study of derived biologically active peptide and depsipeptides.[1–5] It was found that substrates **1a–1c** smoothly underwent haloalkoxylation with EtOH and $MeOCH_2CH_2OH$, however, none of the desired products were obtained using *n*-hexanol, $PhCH_2OH$, CH_2: $CHCH_2OH$, *i*-PrOH as nucleophiles.

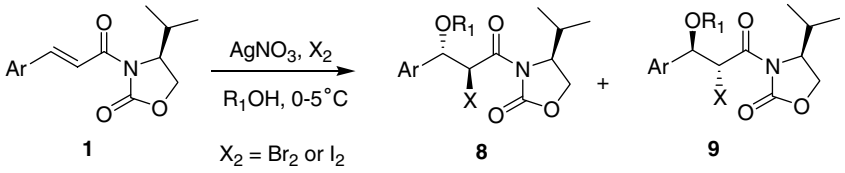
It was found that using $AgNO_3$/AgOAc as a promoter with (4*S*)-4-(1-methylethyl)-2-oxazolidinone as a chiral auxiliary or the use of any Ag(I) salt with Oppolzer's sultam chiral auxiliary provide the best combination for these types of Ag(I)-promoted halomethoxylation reactions. To investigate further the scope and limitation of this asymmetric reaction, a variety of other enoyl substrates containing (4*S*)-4-(1-methylethyl)-2-oxazolidi-

Table 5. $AgNO_3$-promoted halomethoxylation of different enoyl substrates **1**[a]

Entry	Substrate	R	X	Ratio[b] (**3**:**4**)	Yield[c] (%)
1	**1d**	2-ClC_6H_4	Br	60:40 (60:40)	91
2	**1e**	4-$BnOC_6H_4$	I	77:23 (75:25)	92
3	**1f**	3,4-$MeOC_6H_3$	I	76:24 (75:25)	91
4	**1g**	3,4,5-$MeOC_6H_2$	I	74:26 (75:25)	93
5[d]	**1h**	2-Naphthyl	I	73:27 (73:27)	88
6	**1i**	CH_3	Br	86:14[e] (85:15)	62[f]

[a] Halomethoxylation reactions were performed using 1.2 equiv of $AgNO_3$ and 1.2 equiv of halogen (X_2) in methanol at 0–5 °C for 30 min.
[b] Determined from the ^1H NMR spectrum of the crude reaction mixture. Ratios in the parentheses refer to the ratio of isolated **3** and **4** after column chromatography.
[c] Combined isolated yields of **3** and **4** after column chromatography.
[d] 30% CH_2Cl_2 used due to poor solubility of the substrate **1h** in methanol.
[e] Including 18% of the other regioisomers.
[f] Isolated yield of the major isomer **3i** only, minor isomer **4i** could not be separated from the other regioisomers.

Table 4. $AgNO_3$-promoted haloalkoxylation of **1**



1 **8** **9**

Entry	Substrate	R_1OH	X	Ratio[a] (**8**:**9**)	Yield[b] (%)
1	**1a**	EtOH	Br	70:30	89
2	**1a**	2-$MeOCH_2CH_2OH$	Br	71:29	84
3	**1b**	EtOH	Br	66:34	92
4	**1b**	2-$MeOCH_2CH_2OH$	Br	68:32	88
5	**1c**	EtOH	I	—	51[c]
6	**1c**	2-$MeOCH_2CH_2OH$	I	67:33	85
7	**1a**	*n*-Hexanol	Br	ND	[d]
8	**1a**	$PhCH_2OH$, Allyl alcohol, *i*-PrOH	Br	—	NR

NR: No reaction; ND: not determined.
[a] Ratio of isolated **8** and **9** after column purification.
[b] Combined isolated yields of **8** and **9** after column chromatography.
[c] Isolated yield of isomer **8**, due to instability of minor isomer **9** in silica gel during column chromatography.
[d] Mixture of products.

none as a chiral auxiliary were studied (Table 5). Another electron-deficient cinnamoyl substrate **1d** smoothly underwent the bromomethoxylation reaction under the same reaction conditions with moderate diastereoselectivity (entry 1). Similar to **1b**, no iodohydrin reaction was observed for **1d**. Electron-rich cinnamoyl substrates **1e**–**1g** preferred to undergo the iodomethoxylation reaction with good diastereoselectivity (entries 2–4), while the bromomethoxylation reaction of **1e**–**1g** gave a mixture of products. Substrate **1h** behaved like an electron-rich cinnamoyl substrate, that is it responded to the iodomethoxylation reaction (entry 5), whilst alkenoyl substrate **1i** underwent bromomethoxylation reaction with a good dr of 86:14 along with 18% of other regioisomers (entry 6).

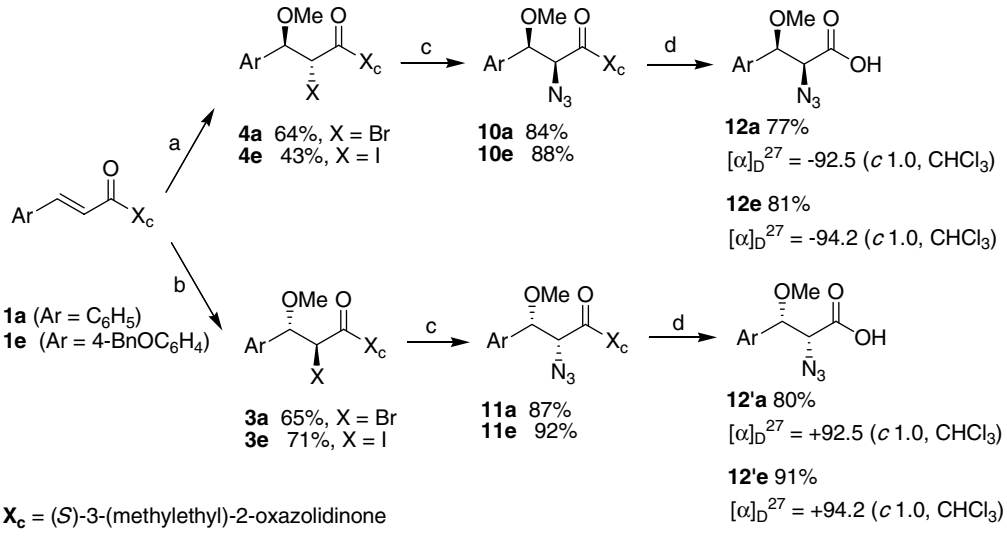
After achieving the reagent controlled reverse diastereoselectivity of the halomethoxylation reaction of oxazolidinone derived cinnamoyl substrates, the usefulness of the process was exemplified in the short synthesis of both enantiomers of N-protected *syn*-β-methoxyphenylalanine, and N- and O-protected *syn*-β-methoxytyrosine (Scheme 3). Ag_2O mediated halomethoxylation reaction of **1a** gave α-bromo-β-methoxy-carboxylic acid derivative **4a** as major product in 64% yield. Reaction of **4a** with NaN_3 in DMF at 60 °C gave *syn*-α-azido-β-methoxy-carboxylic acid derivative **10a** (84%). Subsequent removal of the chiral auxiliary by treatment with LiOH and H_2O_2 in THF at 0 °C yielded *syn*-α-azido-β-methoxy-carboxylic acid **12a** (77%). Compound **12a** can be used directly as N-protected β-methoxyphenylalanine for the synthesis of cyclomarins, as azido-carboxylic acids serve as N-protected amino acids in peptide antibiotic syntheses.[12b] In the same way, the other *syn*-enantiomer of N-protected-β-methoxyphenylalanine **12′a** was synthesized from the major isomer **3a**, obtained by $AgNO_3$-mediated bromomethoxylation reaction of **1a**. The absolute stereochemistry of the β-methoxytyrosine fragment of callipeltins[7] and papuamides[6,9] have recently been determined and found to be *anti* and the absolute stereostructure of β-methoxytyrosine residue in neamphamide A[9] is *syn*. Both enantiomers of *syn*-2-azido-3-(4-benzyloxy-phenyl)-3-methoxy-propionic acids **12e** and **12′e** were similarly synthesized from **1e**, which can directly be used as N- and O-protected β-methoxytyrosine building blocks for the synthesis of peptides.

3. Conclusion

In conclusion, we have described the Ag(I)-promoted asymmetric halomethoxylation reaction of chiral α,β-unsaturated carboxylic acid derivatives **1** and **5** with high regio- and *anti*-selectivity and moderate to good diastereoselectivity in good yields. Alkenoyl, cinnamoyl and electron-deficient cinnamoyl substrates smoothly underwent bromomethoxylation, whereas the electron-rich cinnamoyl substrates were best suited to the iodomethoxylation reaction. More interestingly for halomethoxylation of *N*-cinnamoyl-2-oxazolidinones **1**, the use of Ag_2O reverses the diastereoselectivity, with greatest stereocontrol being observed for cinnamoyl and electron-deficient cinnamoyl substrates. However, no counter ion effect for the Ag(I) salt was observed for cinnamoyl substrates containing sultam chiral auxiliary. This process has been applied to the synthesis of both enantiomers of N-protected *syn*-β-methoxyphenylalanine and N- and O-protected *syn*-β-methoxytyrosine. Thus, this methodology offers a general asymmetric method for the synthesis of *syn*-β-methoxy-α-amino acids.

4. Experimental

All reactions were conducted using oven-dried glassware under an atmosphere of Argon (Ar). Commercial grade reagents were used without further purification. Solvents were dried and distilled following usual protocols. Flash chromatography was carried out using Spectrochem



Scheme 3. Reagents and conditions: (a) Ag_2O, X_2, MeOH, 0–5 °C, 30 min; (b) $AgNO_3$, X_2, MeOH, 0–5 °C, 30 min; (c) NaN_3, DMF, 60 °C, 2.5–3 h; (d) LiOH, H_2O_2, THF, 0–5 °C, 2 h.

Silica gel (230–400 mesh) purchased from Spectrochem, India. TLC was performed on aluminium-backed plates coated with Silica gel 60 with F_{254} indicator (Merck).

The ^{1}H NMR spectra were measured on a Bruker-200 (200 MHz) and ^{13}C NMR spectra were measured with Bruker-200 (50 MHz) using $CDCl_3$ as a solvent. ^{1}H NMR chemical shifts are expressed in parts per million (δ) downfield to $CHCl_3$ ($\delta = 7.26$); ^{13}C NMR chemical shifts are expressed in parts per million (δ) relative to the central $CDCl_3$ resonance ($\delta = 77.0$). Coupling constants in ^{1}H NMR are expressed in Hertz. Elemental analyses were carried out on a Perkin–Elmer 2400-II. Melting points were measured using Toshniwal (India) melting point apparatus. Substrates **1** and **5** were synthesized following the literature procedures.[15,21,25]

4.1. General experimental procedure for the halomethoxylation reaction

To a well-stirred solution of the substrate **1** or **5** (1 mmol) in MeOH (20 ml), Ag(I) salt (for $AgNO_3$ 1.2 mmol and Ag_2O 0.7 mmol) and X_2 (Br_2 or I_2, 1.2 mmol) were added, respectively, at 0–5 °C and allowed to stir under argon for 20–30 min. On completion, the reaction mixture was diluted with H_2O and extracted with Et_2O at least three times. The combined organic layer was washed with water and dried over Na_2SO_4. The organic solution was filtered through a small Celite pad (otherwise locking problem or poor base line was found in the ^{1}H NMR of the crude mixture) and the filtrate was concentrated under vacuum. Flash column chromatography of the crude mixture using petroleum ether–EtOAc as eluent gave the desired halomethoxylated compounds in pure form.

4.2. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-methoxy-3′-phenylpropionyl]-4-(1-methylethyl)-2-oxazolidinone 3a

White solid, Mp 75–77 °C; $[\alpha]_D^{27} = +84.3$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.30 (m, 5H), 5.83 (d, $J = 10.0$ Hz, 1H), 4.68 (d, $J = 10.0$ Hz, 1H), 4.65–4.50 (m, 1H), 4.40–4.20 (m, 2H), 3.19 (s, 3H), 2.52–2.35 (m, 1H), 0.96 (d, $J = 4.2$ Hz, 3H), 0.93 (d, $J = 4.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.3, 153.1, 136.9, 128.8, 128.3 (4C), 83.4, 63.5, 58.5, 57.4, 44.1, 28.1, 17.7, 14.8. Anal. Calcd for $C_{16}H_{20}BrNO_4$: C, 51.90; H, 5.44; N, 3.78. Found: C, 51.87; H, 5.42; N, 3.89.

4.3. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-methoxy-3′-phenylpropionyl]-4-(1-methylethyl)-2-oxazolidinone 4a

White solid, Mp 71–73 °C; $[\alpha]_D^{27} = -4.8$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.30 (m, 5H), 5.94 (d, $J = 10.0$ Hz, 1H), 4.63 (d, $J = 10.0$ Hz, 1H), 4.60–4.50 (m, 1H), 4.50–4.20 (m, 2H), 3.16 (s, 3H), 2.52–2.30 (m, 1H), 0.97 (d, $J = 2.9$ Hz, 3H), 0.93 (d, $J = 2.9$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.7, 153.2, 136.8, 128.8, 128.3 (4C), 84.7, 63.4, 58.9, 57.2, 44.0, 28.3, 17.7, 14.5. Anal. Calcd for $C_{16}H_{20}BrNO_4$: C, 51.90; H, 5.44; N, 3.78. Found: C, 51.91; H, 5.47; N, 3.81.

4.4. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-methoxy-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3b

Gummy liquid; $[\alpha]_D^{27} = +171.35$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.86 (d, $J = 7.96$, 1H), 7.78–7.65 (m, 3H), 5.83 (d, $J = 10.0$ Hz, 1H), 5.61 (d, $J = 10.0$ Hz, 1H), 4.60–4.75 (m, 1H), 4.45–4.20 (m, 2H), 3.30 (s, 3H), 2.52–2.30 (m, 1H), 0.93 (d, $J = 5.6$ Hz, 3H), 0.88 (d, $J = 5.6$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.1, 153.8, 150.6, 132.9, 132.2, 129.4, 129.3, 123.9, 76.8, 63.5, 58.4, 58.2, 44.2, 27.9, 17.7, 14.7. Anal. Calcd for $C_{16}H_{19}BrN_2O_6$: C, 46.28; H, 4.61; N, 6.75. Found: C, 46.15; H, 4.51; N, 6.79.

4.5. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-methoxy-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4b

White solid; Mp 83–85 °C; $[\alpha]_D^{27} = +18.6$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.90–7.60 (m, 3H), 7.59–7.49 (m, 1H), 5.88 (d, $J = 9.7$ Hz, 1H), 5.59 (d, $J = 9.7$ Hz, 1H), 4.57–4.45 (m, 1H), 4.40–4.20 (m, 2H), 3.29 (s, 3H), 2.52–2.30 (m, 1H), 0.98 (d, $J = 4.6$ Hz, 3H), 0.95 (d, $J = 4.6$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.5, 153.2, 150.8, 133.0, 132.3, 129.4, 129.1, 123.8, 78.0, 63.5, 59.0, 58.0, 43.8, 28.3, 17.7, 14.5. Anal. Calcd for $C_{16}H_{19}BrN_2O_6$: C, 46.28; H, 4.61; N, 6.75. Found: C, 46.33; H, 4.68; N, 6.71.

4.6. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-methoxy-3′-(4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3c

White solid; Mp 141–143 °C; $[\alpha]_D^{27} = +22.5$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.30 (d, $J = 8.5$ Hz, 2H), 6.91 (d, $J = 8.5$ Hz, 2H), 6.01 (d, $J = 10.3$ Hz, 1H), 4.70 (d, $J = 10.3$ Hz, 1H), 4.65–4.50 (m, 1H), 4.45–4.20 (m, 2H), 3.83 (s, 3H), 3.16 (s, 3H), 2.55–2.32 (m, 1H), 0.97 (t, $J = 1.7$ Hz, 3H), 0.88 (d, $J = 1.7$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.8, 159.9, 153.1, 129.5 (3C), 113.6 (2C), 83.8, 63.3, 58.4, 57.6, 55.2, 27.9, 24.4, 17.8, 15.0. Anal. Calcd for $C_{17}H_{22}INO_5$: C, 45.65; H, 4.96; N, 3.13. Found: C, 45.46; H, 4.99; N, 3.03.

4.7. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-methoxy-3′-(4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4c

White solid; Mp 87–89 °C; $[\alpha]_D^{27} = -19.5$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.30 (d, $J = 8.6$ Hz, 2H), 6.91 (d, $J = 8.6$ Hz, 2H), 6.05 (d, $J = 10.3$ Hz, 1H), 4.65 (d, $J = 10.3$ Hz, 1H), 4.55–4.45 (m, 1H), 4.33 (t, $J = 8.8$ Hz, 1H), 4.22 (dd, $J = 9.0$, 3.3 Hz, 1H), 3.82 (s, 3H), 3.14 (s, 3H), 2.55–2.30 (m, 1H), 0.95 (d, $J = 3.8$ Hz, 3H), 0.92 (d, $J = 3.8$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 172.0, 159.9, 153.3, 129.5 (2C), 129.4, 113.5 (2C), 85.0, 63.3, 58.9, 57.3, 55.1, 28.4, 24.0, 17.7, 14.5. Anal. Calcd for $C_{17}H_{22}INO_5$: C, 45.65; H, 4.96; N, 3.13. Found: C, 45.77; H, 4.90; N, 2.99.

4.8. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-methoxy-3′-(3-bromo-4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3′c

Liquid; $[\alpha]_D^{28} = +88.9$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.58 (d, $J = 2.11$ Hz, 1H), 7.32 (dd, $J = 8.38$, 2.11 Hz, 1H), 6.91 (d, $J = 8.38$ Hz, 1H), 5.74 (d, $J = 10.07$ Hz, 1H), 4.60 (d, $J = 10.07$ Hz, 1H), 4.56–4.44 (m, 1H), 4.42–4.16 (m, 2H), 3.91 (s, 3H), 3.17 (s, 3H), 2.60–2.25 (m, 1H), 0.98 (d, $J = 4.86$ Hz, 3H), 0.92 (d, $J = 4.86$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.3, 156.0, 152.9, 132.7, 130.4, 128.4, 111.4, 111.3, 82.2, 63.4, 58.3, 57.3, 56.0, 44.0, 29.4, 28.4, 17.5 and 14.6. Anal. Calcd for $C_{21}H_{21}Br_2NO_5$: C, 42.61; H, 4.42; N, 2.92. Found: C, 42.73 H, 4.75; N, 2.78.

4.9. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-methoxy-3′-(3-bromo-4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4′c

Liquid; $[\alpha]_D^{28} = +8.4$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.60 (d, $J = 2.04$ Hz, 1H), 7.35 (dd, $J = 8.40$, 2.04 Hz, 1H), 6.91 (d, $J = 8.40$ Hz, 1H), 5.85 (d, $J = 10.09$ Hz, 1H), 4.59–4.48 (m, 2H), 4.34 (t, $J = 9.05$ Hz, 1H), 4.24 (dd, $J = 9.05$, 3.30 Hz, 1H), 3.91 (s, 3H), 3.15 (s, 3H), 2.52–2.30 (m, 1H), 0.96 (d, $J = 3.62$ Hz, 3H), 0.93 (d, $J = 3.62$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.3, 156.0, 153.2, 132.8, 130.4, 128.4, 111.4 (2C), 83.6, 63.3, 58.8, 57.1, 56.0, 29.4, 28.2, 17.5 and 14.4. Anal. Calcd for ($C_{21}H_{21}Br_2NO_5 + 1$-H_2O): C, 41.07; H, 4.66; N, 2.82. Found: C, 41.43 H, 4.76; N, 3.01.

4.10. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-methoxy-3′-(2-chlorophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3d

White solid; Mp 97–99 °C; $[\alpha]_D^{27} = +77.8$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.60–7.20 (m, 4H), 5.91 (d, $J = 9.9$ Hz, 1H), 5.41 (d, $J = 9.9$ Hz, 1H), 4.60–4.52 (m, 1H), 4.40–4.22 (m, 2H), 3.20 (s, 3H), 2.55–2.32 (m, 1H), 0.96 (d, $J = 3.8$ Hz, 3H), 0.93 (d, $J = 3.8$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.7, 153.0, 135.3, 135.0, 129.8, 129.3, 128.7, 127.3, 78.4, 63.4, 58.5, 57.6, 43.4, 28.0, 17.7, 14.7. Anal. Calcd for $C_{16}H_{19}BrClNO_4$: C, 47.49; H, 4.73; N, 3.46. Found: C, 47.28; H, 4.67; N, 3.49.

4.11. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-methoxy-3′-(2-chlorophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4d

Gummy liquid; $[\alpha]_D^{27} = +7.3$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.55 (d, $J = 7.2$ Hz, 1H), 7.45–7.20 (m, 3H), 6.01 (d, $J = 9.9$ Hz, 1H), 5.37 (d, $J = 9.9$ Hz, 1H), 4.62–4.49 (m, 1H), 4.45–4.15 (m, 2H), 3.18 (s, 3H), 2.55–2.32 (m, 1H), 0.94 (t, $J = 6.3$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.1, 153.2, 135.3, 134.9, 129.7, 129.2, 128.6, 127.3, 79.5, 63.4, 58.9, 57.3, 43.2, 28.2, 17.6, 14.4. Anal. Calcd for $C_{16}H_{19}BrClNO_4$: C, 47.49; H, 4.73; N, 3.46. Found: C, 47.54; H, 4.76; N, 3.48.

4.12. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-methoxy-3′-(4-benzyloxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3e

White solid; Mp 147–149 °C; $[\alpha]_D^{27} = +78.9$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.23 (m, 7H), 6.99 (d, $J = 8.57$ Hz, 2H), 6.02 (d, $J = 10.3$ Hz, 1H), 5.07 (s, 2H), 4.70 (d, $J = 10.3$ Hz, 1H), 4.60–4.50 (m, 1H), 4.33 (t, $J = 7.94$ Hz, 1H), 4.25 (dd, $J = 9.0$, 3.28 Hz, 1H), 3.17 (s, 3H), 2.55–2.35 (m, 1H), 0.97 (d, $J = 2.14$ Hz, 3H), 0.94 (d, $J = 2.14$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.7, 159.2, 153.1, 136.7, 129.8, 129.5 (2C), 128.5 (2C), 127.9, 127.5 (2C), 114.5 (2C), 83.7, 69.9, 63.3, 58.4, 57.6, 27.8, 24.4, 17.8, 15.0. Anal. Calcd for $C_{23}H_{26}INO_5$: C, 52.78; H, 5.01; N, 2.68. Found: C, 52.83; H, 5.13; N, 2.67.

4.13. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Iodo-3′-methoxy-3′-(4-benzyloxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4e

Gummy liquid; $[\alpha]_D^{27} = +21.8$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.25 (m, 7H), 6.99 (d, $J = 8.48$ Hz, 2H), 6.06 (d, $J = 10.2$ Hz, 1H), 5.07 (s, 2H), 4.66 (d, $J = 10.2$ Hz, 1H), 4.60–4.45 (m, 1H), 4.34 (t, $J = 8.30$ Hz, 1H), 4.23 (dd, $J = 9.01$, 3.16 Hz, 1H), 3.15 (s, 3H), 2.52–2.30 (m, 1H), 0.96 (d, $J = 3.80$ Hz, 3H), 0.92 (d, $J = 3.80$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.1, 159.2, 153.4, 136.8, 129.8, 129.6 (2C), 128.6 (2C), 128.0, 127.5 (2C), 114.5 (2C), 85.1, 70.0, 63.4, 59.0, 57.5, 28.5, 24.1, 17.8, 14.6. Anal. Calcd for $C_{23}H_{26}INO_5$: C, 52.78; H, 5.01; N, 2.68. Found: C, 52.89; H, 5.00; N, 2.54.

4.14. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-methoxy-3′-(3,4-dimethoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3f

White solid; Mp 160–162 °C; $[\alpha]_D^{27} = +75.0$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.00–6.81 (m, 3H), 6.01 (d, $J = 10.4$ Hz, 1H), 4.68 (d, $J = 10.4$ Hz, 1H), 4.62–4.50 (m, 1H), 4.40–4.21 (m, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 3.18 (s, 3H), 2.52–2.32 (m, 1H), 0.96 (d, $J = 6.8$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.7, 153.1, 149.3, 148.8, 129.9, 121.4, 110.3 (2C), 84.1, 63.3, 58.4, 57.6, 55.8, 55.7, 27.9, 24.3, 17.8, 15.0. Anal. Calcd for $C_{18}H_{24}INO_6$: C, 45.30; H, 5.07; N, 2.93. Found: C, 45.42; H, 5.11; N, 3.02.

4.15. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Iodo-3′-methoxy-3′-(3,4-dimethoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4f

Gummy liquid; $[\alpha]_D^{27} = -3.85$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.00–6.80 (m, 3H), 6.06 (d, $J = 10.2$ Hz, 1H), 4.64 (d, $J = 10.2$ Hz, 1H), 4.56–4.45 (m, 1H), 4.34 (t, $J = 8.0$ Hz, 1H), 4.23 (dd, $J = 8.9$, 3.3 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.16 (s, 3H), 2.52–2.35 (m, 1H), 0.96 (d, $J = 3.8$ Hz, 3H), 0.92 (d, $J = 3.8$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.0, 153.4, 149.3, 149.0, 129.8, 127.5, 110.3, 110.2, 85.4,

63.4, 59.0, 57.5, 55.9, 55.7, 28.4, 24.0, 17.7, 14.6. Anal. Calcd for $C_{18}H_{24}INO_6$: C, 45.30; H, 5.07; N, 2.93. Found: C, 45.47; H, 5.18; N, 3.02.

4.16. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-methoxy-3′-(3,4,5-trimethoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3g

White solid; Mp 105–107 °C; $[\alpha]_D^{27} = +86.6$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 6.75 (s, 2H), 6.02 (d, $J = 9.98$ Hz, 1H), 5.37 (d, $J = 9.98$ Hz, 1H), 4.64–4.50 (m, 1H), 4.45–4.15 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.22 (s, 3H), 2.55–2.35 (m, 1H), 0.97 (d, $J = 2.6$ Hz, 3H), 0.93 (d, $J = 2.6$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.6, 153.1, 152.9 (2C), 138.0, 133.0, 105.0 (2C), 84.4, 63.3, 60.8, 58.3, 57.8, 56.0 (2C), 27.8, 23.9, 17.8, 14.9. Anal. Calcd for $C_{19}H_{26}INO_7$: C, 44.98; H, 5.17; N, 2.76. Found: C, 45.13; H, 5.18; N, 2.72.

4.17. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Iodo-3′-methoxy-3′-(3,4,5-trimethoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4g

White solid; Mp 149–151 °C; $[\alpha]_D^{27} = -17.1$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 6.82 (s, 2H), 6.08 (d, $J = 9.72$ Hz, 1H), 5.32 (d, $J = 9.72$ Hz, 1H), 4.53–4.45 (m, 1H), 4.34 (t, $J = 8.8$ Hz, 1H), 4.22 (dd, $J = 8.99$, 2.9 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 6H), 3.21 (s, 3H), 2.52–2.32 (m, 1H), 0.94 (d, $J = 6.9$ Hz, 3H), 0.89 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.8, 153.3, 152.9 (2C), 138.0, 132.9, 105.0 (2C), 85.6, 63.3, 60.7, 58.9, 57.7, 56.0 (2C), 28.3, 23.6, 17.7, 14.5. Anal. Calcd for $C_{19}H_{26}INO_7$: C, 44.98; H, 5.17; N, 2.76. Found: C, 45.10; H, 5.23; N, 2.88.

4.18. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-methoxy-3′-(2-naphthyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 3h

White solid; Mp 177–179 °C; $[\alpha]_D^{27} = +108.6$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.95–7.82 (m, 4H), 7.60–7.45 (m, 3H) 6.15 (d, $J = 10.32$ Hz, 1H), 4.92 (d, $J = 10.32$ Hz, 1H), 4.64–4.52 (m, 1H), 4.36 (t, $J = 8.96$ Hz, 1H), 4.27 (dd, $J = 9.00$, 3.15 Hz, 1H), 3.21 (s, 3H), 2.55–2.40 (m, 1H), 0.99 (d, $J = 1.00$ Hz, 3H), 0.95 (d, $J = 1.00$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.7, 153.1, 134.8, 133.6, 132.6, 128.6, 128.4, 128.0, 127.7, 126.3, 126.2, 124.8, 84.4, 63.3, 58.4, 57.8, 27.9, 23.6, 17.8, 15.0. Anal. Calcd for $C_{20}H_{22}INO_4$: C, 51.40; H, 4.75; N, 3.00. Found: C, 51.67; H, 4.54; N, 2.98.

4.19. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Iodo-3′-methoxy-3′-(2-naphthyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 4h

White solid; Mp 94–96 °C; $[\alpha]_D^{27} = -39.5$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.95–7.80 (m, 4H), 7.60–7.45 (m, 3H), 6.20 (d, $J = 10.25$ Hz, 1H), 4.88 (d, $J = 10.25$ Hz, 1H), 4.60–4.50 (m, 1H), 4.35 (t, $J = 8.23$ Hz, 1H), 4.25 (dd, $J = 8.90$, 3.08 Hz, 1H), 3.20 (s, 3H), 2.55–2.35 (m, 1H), 0.97 (d, $J = 3.98$ Hz, 3H), 0.94 (d, $J = 3.98$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.1, 153.4, 134.7, 133.7, 132.7, 128.7, 128.5, 128.1, 127.7, 126.4, 126.2, 124.8, 89.2, 63.4, 59.1, 57.7, 28.5, 23.3, 17.8, 15.6. Anal. Calcd for $C_{20}H_{22}INO_4$: C, 51.40; H, 4.75; N, 3.00. Found: C, 51.98; H, 4.99; N, 3.04.

4.20. *anti*-(4*S*,2′*S*,3′*S*)-3-(2′-Bromo-3′-methoxy-butionyl)-4-(1-methylethyl)-2-oxazolidinone 3i

Gummy liquid; $[\alpha]_D^{27} = +60.6$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 5.52 (d, $J = 9.30$ Hz, 1H), 4.53–4.42 (m, 1H), 4.36–4.20 (m, 2H), 3.95–3.83 (m, 1H), 3.33 (s, 3H), 2.52–2.30 (m, 1H), 1.39 (d, $J = 6.2$ Hz, 3H), 0.94 (d, $J = 1.5$ Hz, 3H), 0.91 (d, $J = 1.5$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.2, 153.0, 76.6, 63.3, 58.4, 57.5, 44.8, 27.9, 17.7, 16.3, 14.7. Anal. Calcd for $C_{11}H_{18}BrNO_4$: C, 42.87; H, 5.89; N, 4.55. Found: C, 42.98; H, 6.00; N, 4.67.

4.21. *anti*-(2*R*,2′*R*,3′*R*)-*N*-[2′-Iodo-3′-methoxy-3′-phenyl-propionyl]-bornanesultam 6a

White solid; Mp 154–156 °C; $[\alpha]_D^{27} = -102.2$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.25 (m, 5H), 5.07 (d, $J = 9.68$ Hz, 1H), 4.70 (d, $J = 9.68$ Hz, 1H), 4.09–4.00 (m, 1H), 3.50 (s, 2H), 3.19 (s, 3H), 2.20–2.05 (m, 2H), 2.00–1.85 (m, 3H), 1.60–1.30 (m, 2H), 1.88 (s, 3H), 0.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.4, 137.6, 128.8, 128.4 (2C), 128.2 (2C), 84.2, 64.9, 57.9, 52.8, 48.7, 47.8, 44.3, 37.2, 32.7, 26.4, 25.8, 20.6, 19.8. Anal. Calcd for $C_{20}H_{26}INO_4S$: C, 47.72; H, 5.21; N, 2.78. Found: C, 47.90 H, 5.34; N, 2.75.

4.22. *anti*-(2*R*,2′*S*,3′*S*)-*N*-[2′-Iodo-3′-methoxy-3′-phenyl-propionyl]-bornanesultam 7a

White solid; Mp 163–165 °C; $[\alpha]_D^{27} = -7.0$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.45–7.27 (m, 5H), 5.05 (d, $J = 9.74$ Hz, 1H), 4.64 (d, $J = 9.74$ Hz, 1H), 4.00–3.85 (m, 1H), 3.60–3.40 (m, 2H), 3.14 (s, 3H), 2.30–2.10 (m, 2H), 2.07–1.80 (m, 3H), 1.55–1.25 (m, 2H), 1.21 (s, 3H), 0.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.1, 137.1, 128.9, 128.3 (2C), 128.2 (2C), 87.0, 65.6, 57.5, 52.7, 48.6, 47.8, 44.6, 38.0, 32.7, 26.3, 25.6, 20.4, 19.9. Anal. Calcd for $C_{20}H_{26}INO_4S$: C, 47.72; H, 5.21; N, 2.78. Found: C, 48.03 H, 5.42; N, 2.77.

4.23. *anti*-(2*R*,2′*R*,3′*R*)-*N*-[2′-Bromo-3′-methoxy-3′-phenyl-propionyl]-bornanesultam *Br*-6a and *anti*-(2*R*,2′*S*,3′*S*)-*N*-[2′-bromo-3′-methoxy-3′-phenyl-propionyl]-bornanesultam *Br*-7a

Non-separable mixture of diastereomers (65:35); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.25 (m, 5H), 4.93 (d, $J = 9.60$ Hz, 0.65H), 4.85 (d, $J = 9.60$ Hz, 0.35H), 4.67 (d, $J = 9.70$ Hz, 0.65H), 4.58 (d, $J = 9.70$ Hz, 0.35H), 4.10–3.90 (m, 1H), 3.60–3.45 (m, 2H), 3.20 (s, 1.95H), 3.13 (s, 1.05H), 2.30–2.05 (m, 2H), 2.04–1.75 (m, 3H), 1.60–1.25 (m, 2H), 1.21 (s, 1.05H), 1.16 (s, 1.95H), 0.93 (s, 1.05H), 0.91 (s, 1.95H). ^{13}C NMR ($CDCl_3$, 50 MHz): major δ 166.7, 136.9, 128.7, 128.2

(2C), 128.1 (2C), 83.0, 64.8, 57.6, 52.7, 47.7, 45.9, 44.4, 37.7, 32.5, 26.3 (2C), 20.5, 19.7. Minor δ 166.9, 136.7, 128.8, 128.2 (2C), 128.1 (2C), 85.7, 65.2, 57.1, 48.6, 48.5, 46.5, 44.5, 37.5, 31.7, 29.5 (2C), 20.3, 19.8.

4.24. *anti*-(2*R*,2′*R*,3′*R*)-*N*-[2′-Bromo-3′-methoxy-3′-(2-nitrophenyl)-propionyl]-bornanesultam 6b

Liquid; $[\alpha]_D^{27} = -109.1$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.95–7.40 (m, 4H), 5.61 (d, $J = 9.14$ Hz, 1H), 4.91 (d, $J = 9.14$ Hz, 1H), 3.98 (dd, $J = 7.23$, 5.44 Hz, 1H), 3.50 (d, $J = 1.62$ Hz, 2H), 3.32 (s, 3H), 2.20–2.00 (m, 2H), 2.00–1.80 (m, 3H), 1.55–1.25 (m, 2H), 1.14 (s, 3H), 0.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 165.8, 150.5, 133.2, 129.6 (2C), 124.0 (2C), 64.9, 58.4, 52.8, 48.7, 47.8, 45.7, 44.4, 37.5, 32.6, 29.6, 26.3, 20.6, 19.8. Anal. Calcd for $C_{20}H_{25}BrN_2O_6S$: C, 47.91; H, 5.03; N, 5.59. Found: C, 48.21; H, 5.23; N, 5.67.

4.25. *anti*-(2*R*,2′*S*,3′*S*)-*N*-[2′-Bromo-3′-methoxy-3′-(2-nitrophenyl)-propionyl]-bornanesultam 7b

Liquid; $[\alpha]_D^{27} = +56.2$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.98–7.40 (m, 4H), 5.52 (d, $J = 8.88$ Hz, 1H), 4.95 (d, $J = 8.88$ Hz, 1H), 4.05–3.90 (m, 1H), 3.50 (d, $J = 4.16$ Hz, 2H), 3.29 (s, 3H), 2.18–2.06 (m, 2H), 2.05–1.85 (m, 3H), 1.55–1.35 (m, 2H), 1.13 (s, 3H), 0.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 165.9, 150.6, 133.2, 129.6 (2C), 124.0 (2C), 65.4, 58.2, 52.8, 48.7, 47.8, 46.1, 44.6, 37.9, 32.7, 29.6, 26.3, 20.4, 19.9. Anal. Calcd for $C_{20}H_{25}BrN_2O_6S$: C, 47.91; H, 5.03; N, 5.59. Found: C, 48.22; H, 5.08; N, 5.34.

4.26. *anti*-(2*R*,2′*R*,3′*R*)-*N*-[2′-Bromo-3′-methoxy-3′-(4-methoxyphenyl)-propionyl]-bornanesultam 6c

Liquid; $[\alpha]_D^{27} = -90.3$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.33 (d, $J = 8.69$ Hz, 2H), 6.90 (d, $J = 8.69$ Hz, 2H), 4.83 (d, $J = 9.79$ Hz, 1H), 4.62 (d, $J = 9.79$ Hz, 1H), 4.07–3.90 (m, 1H), 3.81 (s, 3H), 3.48 (s, 2H), 3.18 (s, 3H), 2.25–2.05 (m, 2H), 2.04–1.80 (m, 3H), 1.55–1.25 (m, 2H), 1.17 (s, 3H), 0.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 166.8, 159.8, 129.4 (2C), 128.9, 113.6 (2C), 82.6, 64.8, 57.4, 55.1, 52.8, 48.6, 47.7, 46.3, 44.4, 37.5, 32.6, 26.3, 20.6, 19.8. Anal. Calcd for $C_{21}H_{28}BrNO_5S$: C, 51.85; H, 5.80; N, 2.88. Found: C, 51.73 H, 5.75; N, 2.68.

4.27. *anti*-(2*R*,2′*S*,3′*S*)-*N*-[2′-Bromo-3′-methoxy-3′-(4-methoxyphenyl)-propionyl]-bornanesultam 7c

Liquid; $[\alpha]_D^{27} = +19.3$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.33 (d, $J = 8.61$ Hz, 2H), 6.90 (d, $J = 8.61$ Hz, 2H), 4.91 (d, $J = 9.46$ Hz, 1H), 4.53 (d, $J = 9.46$ Hz, 1H), 4.10–3.85 (m, 1H), 3.81 (s, 3H), 3.60–3.40 (s, 2H), 3.11 (s, 3H), 2.25–2.02 (m, 2H), 2.00–1.75 (m, 3H), 1.55–1.25 (m, 2H), 1.21 (s, 3H), 0.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.2, 159.9, 129.4 (2C), 128.7, 113.6 (2C), 85.4, 65.3, 57.0, 55.1, 52.8, 48.6, 47.7, 46.9, 44.6, 37.8, 32.7, 26.3, 20.4, 19.9. Anal. Calcd for $C_{21}H_{28}BrNO_5S$: C, 51.85; H, 5.80; N, 2.88. Found: C, 51.88; H, 5.94; N, 3.01.

4.28. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-ethoxy-3′-phenyl-propionyl]-4-(1-methylethyl)-2-oxazolidinone *EO*-8a

White solid; Mp 81–83 °C; $[\alpha]_D^{27} = +0.7$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.65–7.20 (m, 5H), 5.81 (d, $J = 10.04$ Hz, 1H), 4.76 (d, $J = 10.04$ Hz, 1H), 4.63–4.48 (m, 1H), 4.45–4.15 (m, 2H), 3.35 (q, $J = 7.00$ Hz, 2H), 2.60–2.30 (m, 1H), 1.05 (t, $J = 7.00$ Hz, 3H), 0.96 (d, $J = 4.0$ Hz, 3H), 0.93 (d, $J = 4.0$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.6, 153.1, 137.5, 128.6, 128.2 (2C), 128.1 (2C), 82.5, 65.1, 63.3, 58.7, 44.0, 28.2, 17.7, 14.9, 14.7. Anal. Calcd for $C_{17}H_{22}BrNO_4$: C, 53.14; H, 5.77; N, 3.65. Found: C, 53.79; H, 5.73; N, 3.82.

4.29. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-ethoxy-3′-phenyl-propionyl]-4-(1-methylethyl)-2-oxazolidinone *EO*-9a

White solid; Mp 91–93 °C; $[\alpha]_D^{27} = +94.5$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.55–7.25 (m, 5H), 5.87 (d, $J = 10.11$ Hz, 1H), 4.75 (d, $J = 10.11$ Hz, 1H), 4.60–4.45 (m, 1H), 4.34 (t, $J = 8.96$ Hz, 1H), 4.24 (dd, $J = 9.00$, 3.33 Hz, 1H), 3.33 (q, $J = 7.08$ Hz, 2H), 2.55–2.30 (m, 1H), 1.03 (t, $J = 7.08$ Hz, 3H), 0.97 (d, $J = 2.4$ Hz, 3H), 0.94 (d, $J = 2.4$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.2, 153.1, 137.7, 128.6, 128.3 (2C), 128.2 (2C), 81.6, 65.2, 63.4, 58.5, 44.6, 28.2, 17.7, 15.0, 14.8. Anal. Calcd for $C_{17}H_{22}BrNO_4$: C, 53.14; H, 5.77; N, 3.65. Found: C, 53.45; H, 5.86; N, 3.72.

4.30. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-(2-methoxy-ethoxy)-3′-phenyl-propionyl]-4-(1-methylethyl)-2-oxazolidinone *MOE*-8a

White solid; Mp 77–79 °C; $[\alpha]_D^{27} = +99.8$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.70–7.27 (m, 5H), 5.81 (d, $J = 9.97$ Hz, 1H), 4.77 (d, $J = 9.97$ Hz, 1H), 4.58–4.45 (m, 1H), 4.32 (t, $J = 8.00$ Hz, 1H), 4.23 (dd, $J = 9.07$, 3.24 Hz, 1H), 3.55–3.00 (m, 4H), 3.24 (s, 3H), 2.60–2.25 (m, 1H), 0.94 (d, $J = 4.25$ Hz, 3H), 0.91 (d, $J = 4.25$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.1, 153.1, 137.1, 128.7, 128.3 (2C), 128.2 (2C), 82.2, 71.3, 68.7, 63.5, 58.6, 58.5, 44.3, 28.2, 17.7, 14.8. Anal. Calcd for $C_{18}H_{24}BrNO_5$: C, 52.18; H, 5.14; N, 3.38. Found: C, 52.35; H, 5.11; N, 3.51.

4.31. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-(2-methoxy-ethoxy)-3′-phenyl-propionyl]-4-(1-methylethyl)-2-oxazolidinone *MOE*-9a

Gummy liquid; $[\alpha]_D^{27} = -4.7$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.60–7.25 (m, 5H), 5.85 (d, $J = 10.02$ Hz, 1H), 4.82 (d, $J = 10.02$ Hz, 1H), 4.60–4.50 (m, 1H), 4.34 (t, $J = 7.98$ Hz, 1H), 4.27 (dd, $J = 7.98$, 3.36 Hz, 1H), 3.50–3.30 (m, 4H), 3.23 (s, 3H), 2.55–2.32 (m, 1H), 0.97 (d, $J = 3.17$ Hz, 3H), 0.94 (d, $J = 3.17$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.9, 153.4, 135.5, 128.6, 128.3 (2C), 128.2 (2C), 83.0, 71.5, 69.0, 63.8, 59.0, 58.8, 44.1, 28.6, 17.9, 14.8. Anal. Calcd for $C_{18}H_{24}BrNO_5$: C, 52.18; H, 5.14; N, 3.38. Found: C, 52.15; H, 5.23; N, 3.39.

4.32. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-ethoxy-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone *EO*-8b

Gummy liquid; $[\alpha]_D^{27} = +101.4$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.85–7.40 (m, 4H), 5.80 (d, $J = 9.73$ Hz, 1H), 5.66 (d, $J = 9.73$ Hz, 1H), 4.60–4.45 (m, 1H), 4.34 (t, $J = 9.27$ Hz, 1H), 4.24 (dd, $J = 8.57$, 1.95 Hz, 1H), 3.60–3.30 (m, 2H), 2.52–2.30 (m, 1H), 1.07 (t, $J = 6.93$ Hz, 3H), 0.90 (t, $J = 6.60$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.1, 152.9, 150.5, 133.1, 132.9, 129.5, 129.3, 123.8, 75.2, 66.3, 63.5, 58.4, 44.6, 28.0, 17.7, 15.0, 14.7. Anal. Calcd for $C_{17}H_{21}BrN_2O_6$: C, 47.57; H, 4.93; N, 6.93. Found: C, 47.50; H, 4.95; N, 6.88.

4.33. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-ethoxy-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone *EO*-9b

Gummy liquid; $[\alpha]_D^{27} = -92.7$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.85–7.40 (m, 4H), 5.84 (d, $J = 10.08$ Hz, 1H), 5.68 (d, $J = 10.08$ Hz, 1H), 4.57–4.45 (m, 1H), 4.34 (t, $J = 7.91$ Hz, 1H), 4.24 (dd, $J = 9.02$, 3.30 Hz, 1H), 3.60–3.35 (m, 2H), 2.60–2.30 (m, 1H), 1.06 (t, $J = 7.13$ Hz, 3H), 0.96 (d, $J = 4.16$ Hz, 3H), 0.93 (d, $J = 4.16$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.6, 153.2, 150.7, 133.0, 132.9, 129.4 (2C), 123.8, 76.3, 66.2, 63.5, 58.9, 43.8, 28.3, 17.8, 14.9, 14.8. Anal. Calcd for $C_{17}H_{21}BrN_2O_6$: C, 47.57; H, 4.93; N, 6.93. Found: C, 47.77; H, 4.89; N, 6.99.

4.34. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Bromo-3′-(2-methoxy-ethoxy)-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone *MOE*-8b

Gummy liquid; $[\alpha]_D^{27} = +147.3$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.95–7.35 (m, 4H), 5.82 (d, $J = 10.00$ Hz, 1H), 5.75 (d, $J = 10.00$ Hz, 1H), 4.60–4.45 (m, 1H), 4.34 (t, $J = 7.98$ Hz, 1H), 4.24 (dd, $J = 8.90$, 3.14 Hz, 1H), 3.75–3.45 (m, 4H), 3.20 (s, 3H), 2.65–2.30 (m, 1H), 0.94 (d, $J = 5.36$ Hz, 3H), 0.90 (d, $J = 5.36$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.0, 153.1, 150.4, 133.0, 132.8, 129.5, 129.3, 123.8, 75.5, 71.2, 69.7, 63.5, 58.5 (2C), 44.6, 28.0, 17.7, 14.7. Anal. Calcd for $C_{18}H_{23}BrN_2O_7$: C, 47.07; H, 5.05; N, 6.10. Found: C, 47.32; H, 4.98; N, 6.11.

4.35. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Bromo-3′-(2-methoxy-ethoxy)-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone *MOE*-9b

Gummy liquid; $[\alpha]_D^{27} = -89.9$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.95–7.35 (m, 4H), 5.80 (s, 2H), 4.62–4.45 (m, 1H), 4.33 (t, $J = 8.00$ Hz, 1H), 4.24 (dd, $J = 8.90$, 3.27 Hz, 1H), 3.80–3.50 (m, 4H), 3.20 (s, 3H), 2.65–2.30 (m, 1H), 0.96 (d, $J = 4.92$ Hz, 3H), 0.93 (d, $J = 4.92$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.3, 153.1, 150.6, 133.0, 132.8, 129.3 (2C), 123.8, 76.3, 71.2, 69.8, 63.5, 58.9, 58.5, 43.6, 28.3, 17.8, 14.6. Anal. Calcd for $C_{18}H_{23}BrN_2O_7$: C, 47.07; H, 5.05; N, 6.10. Found: C, 47.23; H, 5.15; N, 6.18.

4.36. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-ethoxy-3′-(4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone *EO*-8c

Gummy liquid; $[\alpha]_D^{27} = +89.8$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.28 (d, $J = 8.67$ Hz, 2H), 6.87 (d, $J = 8.67$ Hz, 2H), 5.95 (d, $J = 10.30$ Hz, 1H), 4.76 (d, $J = 10.30$ Hz, 1H), 4.60–4.45 (m, 1H), 4.32 (t, $J = 7.98$ Hz, 1H), 4.23 (dd, $J = 9.07$, 3.28 Hz, 1H), 3.80 (s, 3H), 3.31 (dq, $J = 6.94$, 3.18 Hz, 2H), 2.60–2.30 (m, 1H), 1.00 (t, $J = 6.94$ Hz, 3H), 0.95 (d, $J = 1.69$ Hz, 3H), 0.91 (d, $J = 1.69$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.7, 159.7, 153.1, 130.3, 129.4 (2C), 113.5 (2C), 81.8, 65.3, 63.3, 58.4, 55.1, 27.9, 25.0, 17.8, 15.0 (2C). Anal. Calcd for $C_{18}H_{24}INO_5$: C, 46.87; H, 5.24; N, 3.04. Found: C, 47.01; H, 5.19; N, 3.12.

4.37. *anti*-(4*S*,2′*S*,3′*S*)-3-[2′-Iodo-3′-(2-methoxy-ethoxy)-3′-(4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone *MOE*-8c

Gummy liquid; $[\alpha]_D^{27} = +86.1$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.30 (d, $J = 8.71$ Hz, 2H), 6.88 (d, $J = 8.71$ Hz, 2H), 5.96 (d, $J = 10.35$ Hz, 1H), 4.81 (d, $J = 10.36$ Hz, 1H), 4.58–4.45 (m, 1H), 4.32 (t, $J = 8.91$ Hz, 1H), 4.23 (dd, $J = 8.91$, 3.00 Hz, 1H), 3.80 (s, 3H), 3.55–3.20 (m, 4H), 3.24 (s, 3H), 2.55–2.30 (m, 1H), 0.94 (d, $J = 6.83$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.5, 159.8, 153.1, 129.8, 129.5 (2C), 113.5 (2C), 82.5, 71.4, 68.8, 63.4, 58.5, 58.4, 55.1, 27.9, 24.9, 17.8, 15.0. Anal. Calcd for $C_{19}H_{26}INO_6$: C, 46.45; H, 5.33; N, 2.85. Found: C, 46.78; H, 5.32; N, 2.90.

4.38. *anti*-(4*S*,2′*R*,3′*R*)-3-[2′-Iodo-3′-(2-methoxy-ethoxy)-3′-(3,4-dimethoxyphenyl)-propionyl]-4-(1-methyl-ethyl)-2-oxazolidinone *MOE*-9c

Gummy liquid; $[\alpha]_D^{27} = -12.95$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.33 (d, $J = 8.58$ Hz, 2H), 6.89 (d, $J = 8.58$ Hz, 2H), 5.99 (d, $J = 10.37$ Hz, 1H), 4.83 (d, $J = 10.37$ Hz, 1H), 4.58–4.45 (m, 1H), 4.29 (t, $J = 7.45$ Hz, 1H), 4.23 (dd, $J = 8.99$, 3.18 Hz, 1H), 3.81 (s, 3H), 3.60–3.20 (m, 4H), 3.23 (s, 3H), 2.55–2.30 (m, 1H), 0.95 (d, $J = 3.53$ Hz, 3H), 0.92 (d, $J = 3.53$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.9, 159.8, 153.2, 129.7 (2C), 129.6, 113.5 (2C), 83.3, 71.4, 68.9, 63.3, 58.9, 58.6, 55.2, 28.3, 24.1, 17.9, 14.7. Anal. Calcd for $C_{19}H_{26}INO_6$: C, 46.45; H, 5.33; N, 2.85. Found: C, 46.67; H, 5.37; N, 2.98.

4.39. *syn*-(4*S*,2′*S*,3′*R*)-3-[2′-Azido-3′-methoxy-3′-phenyl-propionyl]-4-(1-methylethyl)-2-oxazolidinone 10a

Gummy liquid; $[\alpha]_D^{27} = +48.75$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.22 (m, 5H), 5.42 (d, $J = 7.18$ Hz, 1H), 4.61 (d, $J = 7.18$ Hz, 1H), 4.15–3.90 (m, 2H), 3.76 (t, $J = 9.20$ Hz, 1H), 4.18 (dd, $J = 9.14$, 3.54 Hz, 1H), 3.31 (s, 3H), 2.45–2.25 (m, 1H), 0.84 (t, $J = 8.12$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.9, 153.0, 136.3, 128.6, 128.4 (2C), 127.4 (2C), 88.7, 64.1, 63.5, 58.8, 57.0, 28.2, 17.7, 14.4. Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 58.01; H, 6.12; N, 16.78.

4.40. *syn*-(4*S*,2′*R*,3′*S*)-3-[2′-Azido-3′-methoxy-3′-phenyl-propionyl]-4-(1-methylethyl)-2-oxazolidinone 11a

Gummy liquid; $[\alpha]_D^{27} = +44.3$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.23 (m, 5H), 5.15 (d, $J = 4.85$ Hz, 1H), 4.86 (d, $J = 4.85$ Hz, 1H), 4.55–4.40 (m, 1H), 4.31 (t, $J = 8.42$ Hz, 1H), 4.18 (dd, $J = 9.14$, 3.54 Hz, 1H), 3.26 (s, 3H), 2.30–2.10 (m, 1H), 0.80 (d, $J = 9.16$ Hz, 3H), 0.63 (d, $J = 9.16$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.0, 153.5, 136.5, 128.5 (2C), 128.3, 127.3 (2C), 83.6, 64.7, 63.8, 58.2, 57.1, 28.2, 17.5, 14.4. Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.92; H, 6.25; N, 16.98.

4.41. *syn*-(2*S*,3*R*)-2-Azido-3-methoxy-3-phenyl-propionic acid 12a

Liquid; $[\alpha]_D^{27} = -92.5$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.20 (m, 5H), 4.83 (d, $J = 3.96$ Hz, 1H), 3.92 (d, $J = 3.96$ Hz, 1H), 3.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 173.1, 136.4, 128.7 (3C), 127.0 (2C), 83.5, 66.8, 57.6. Anal. Calcd for $C_{10}H_{11}N_3O_3$: C, 54.29; H, 5.01; N, 19.00. Found: C, 54.38 H, 5.04; N, 18.98.

4.42. *syn*-(2*R*,3*S*)-2-Azido-3-methoxy-3-phenyl-propionic acid 12′a

Liquid; $[\alpha]_D^{27} = +92.5$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.20 (m, 5H), 4.83 (d, $J = 3.96$ Hz, 1H), 3.92 (d, $J = 3.96$ Hz, 1H), 3.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 173.1, 136.4, 128.7 (3C), 127.0 (2C), 83.5, 66.8, 57.6. Anal. Calcd for $C_{10}H_{11}N_3O_3$: C, 54.29; H, 5.01; N, 19.00. Found: C, 54.23 H, 5.12; N, 18.90.

4.43. *syn*-(4*S*,2′*S*,3′*R*)-3-[2′-Azido-3′-methoxy-3′-(4-benzyloxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 10e

Gummy liquid; $[\alpha]_D^{27} = +21.5$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.20 (m, 7H), 6.97 (d, $J = 8.69$ Hz, 2H), 5.41 (d, $J = 7.32$ Hz, 1H), 5.07 (s, 2H), 4.55 (d, $J = 7.32$ Hz, 1H), 4.10–3.95 (m, 2H), 3.70 (t, $J = 9.18$ Hz, 1H), 3.28 (s, 3H), 2.45–2.15 (m, 1H), 0.83 (t, $J = 7.12$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.1, 159.0, 153.1, 136.6, 128.8 (2C), 128.6 (3C), 128.0, 127.4 (2C), 114.7 (2C), 83.6, 69.9, 64.1, 63.5, 58.9, 56.9, 28.3, 17.8, 14.5. Anal. Calcd for $C_{23}H_{26}N_4O_5$: C, 63.00; H, 5.98; N, 12.78. Found: C, 63.14 H, 5.89; N, 12.90.

4.44. *syn*-(4*S*,2′*R*,3′*S*)-3-[2′-Azido-3′-methoxy-3′-(4-benzyloxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone 11e

Gummy liquid; $[\alpha]_D^{27} = +87.6$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.55–7.20 (m, 7H), 6.98 (d, $J = 8.42$ Hz, 2H), 5.18 (d, $J = 5.05$ Hz, 1H), 5.05 (s, 2H), 4.81 (d, $J = 5.05$ Hz, 1H), 4.57–4.40 (m, 1H), 4.31 (t, $J = 8.60$ Hz, 1H), 4.19 (dd, $J = 9.11$, 3.29 Hz, 1H), 3.26 (s, 3H), 2.30–2.05 (m, 1H), 0.85 (d, $J = 6.80$ Hz, 3H), 0.62 (d, $J = 6.80$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.0, 158.9, 153.4, 136.7, 128.7 (2C), 128.5 (3C), 127.9, 127.3 (2C), 114.7 (2C), 83.2, 69.8, 64.6, 63.7, 58.1, 56.8, 28.2, 17.5, 14.3. Anal. Calcd for $C_{23}H_{26}N_4O_5$: C, 63.00; H, 5.98; N, 12.78. Found: C, 63.43; H, 6.11; N, 12.87.

4.45. *syn*-(2*S*,3*R*)-2-Azido-3-(4-benzyloxyphenyl)-3-methoxy-propionic acid 12e

White solid; Mp 162–164 °C; $[\alpha]_D^{27} = -94.2$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.20 (m, 7H), 6.99 (d, $J = 8.61$ Hz, 2H), 5.05 (s, 2H), 4.74 (d, $J = 4.19$ Hz, 1H), 3.90 (d, $J = 4.19$ Hz, 1H), 3.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 173.6, 159.1, 136.6, 128.5 (3C), 128.4 (2C), 128.0, 127.4 (2C), 114.9 (2C), 83.0, 69.9, 66.9, 57.3. Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.38; H, 5.23; N, 12.84. Found: C, 62.33 H, 5.34; N, 12.65.

4.46. *syn*-(2*R*,3*S*)-2-Azido-3-(4-benzyloxyphenyl)-3-methoxy-propionic acid 12′e

White solid; Mp 92–94 °C; $[\alpha]_D^{27} = +94.2$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50–7.20 (m, 7H), 6.99 (d, $J = 8.61$ Hz, 2H), 5.05 (s, 2H), 4.74 (d, $J = 4.19$ Hz, 1H), 3.90 (d, $J = 4.19$ Hz, 1H), 3.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 173.6, 159.1, 136.6, 128.5 (3C), 128.4 (2C), 128.0, 127.4 (2C), 114.9 (2C), 83.0, 69.9, 66.9, 57.3. Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.38; H, 5.23; N, 12.84. Found: C, 62.34 H, 5.49; N, 12.76.

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24. Hydromethoxylated product is also a possible side product by electrophilic addition of MeOH during Ag_2O promoted reaction in the presence of HNO_3. However, no such product was observed by the ^1H NMR spectrum analysis of the crude reaction mixture. It might be because of very fast halomethoxylation reaction (takes only ~20 min) compared to the hydromethoxylation reaction.
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