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Silver (I)-promoted asymmetric halohydrin reaction of chiral *N*-enoyl-2-oxazolidinones: scope and limitations

Saumen Hajra,* Ananta Karmakar and Manishabrata Bhowmick

Department of Chemistry, Indian Institute of Technology, Salua road, Kharagpur 721 302, India

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Abstract—The halohydrin reaction of chiral *N*-enoyl-2-oxazolidinones **1** by halogen (Br_2/I_2) and water were efficiently carried out in aqueous organic solvent promoted by silver(I) with high anti- and regioselectivity and moderate to good diastereoselectivities. The alkenoyl, cinnamoyl and electron-deficient cinnamoyl substrates smoothly underwent bromohydrin reaction in aqueous acetone but no iodohydrin reaction, where as electron-rich cinnamoyl substrates preferred to undergo iodohydrin reaction in aqueous acetone with moderate diastereoselectivity and enhanced diastereoselectivity was observed in aqueous THF.

1. Introduction

Carboxyhalohydrins especially α-halo-β-hydroxycarboxylic acid derivatives are versatile and useful synthetic intermediates because of their facile transformation to a variety of important compounds. These moieties are present in precursors to many biologically active compounds.[1] Carboxyhalohydrins are also good precursors for stereoselective radical reactions.[2] A potentially straightforward method for the synthesis of carboxyhalohydrins is the stereoselective halohydrin reaction of α,β-unsaturated carboxylic acid derivatives.[3] Only few reports on the asymmetric halohydrin reaction are known in literature.[4–6] Henry et al. first reported palladium(II)-catalyzed enantioselective hydroxychlorination of terminal alkenes with a metal chloride—mechanistically it is a hydroxychlorination to alkenes and there is no involvement of halonium (X^+) intermediate.[4] Sudalai et al. described $NaIO_4$ mediated oxidative enantioselective halohydrination of alkenes (encapsulated in β-cyclodextrin) using alkali metal halides with moderate enantioselectivity.[5] Barluenga et al. reported a highly diastereoselective iodohydrination of terpene derivatives using Py_2IBF_4.[6]

There are only a few methods, other than halohydrin reaction, for the stereoselective synthesis of the α-halo-β-hydroxycarboxylic acid derivatives.[7–9] Reagent controlled aldol reaction of chiral α-halogenated imide enolates with suitable aldehydes provide selectively both *anti*- and *syn*-α-halo-β-hydroxycarboxylic acid derivatives.[7] Genet et al. reported the catalytic asymmetric hydrogenation of α-chloro-β-ketocarboxylic acid esters for the enantioselective synthesis of α-chloro-β-hydroxycarboxylic acid esters.[8] Under controlled reaction conditions, epoxide ring opening of β-alkyl-α,β-epoxycarboxylic acids/derivatives provide stereoselectively α-halo-β-hydroxy-, as well as α-hydroxy-β-halocarboxylic acids/derivatives.[9] However, epoxide ring opening of the β-aryl-α,β-epoxycarboxylic acid derivatives with halides give either poor regioselectivity or selectively α-hydroxy-β-halocarboxylic acid derivatives.[9b,d]

In this paper we report in full the silver(I)-promoted asymmetric halohydrin reaction of chiral *N*-enoyl-2-oxazolidinones **1**,[10] in which high regio- and diastereoselectivities up to 82:18 of *anti*-α-halo-β-hydroxy carbonyls **3** and **4** with good yields are demonstrated.

2. Results and discussion

Initially (4*S*)-*N*-cinnamoyl-4-(1-methylethyl)-2-oxazolidinones were selected as substrates for the development of the diastereoselective halohydrin reaction. It was assumed that the β-aryl group of the three-member halonium intermediate **2** would enhance the electrophilicity towards the water nucleophile to achieve high regioselectivity (Scheme 1; R = Ar and R′ = *i*-Pr) and also these carboxyhalohydrins are very important precursors to many biologically active compounds.[1] Moreover our research group is involved in the chelation controlled stereoselective radical

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* Corresponding author. Tel.: +91 3222 283340; fax: +91 3222 255303; e-mail: shajra@chem.iitkgp.ernet.in

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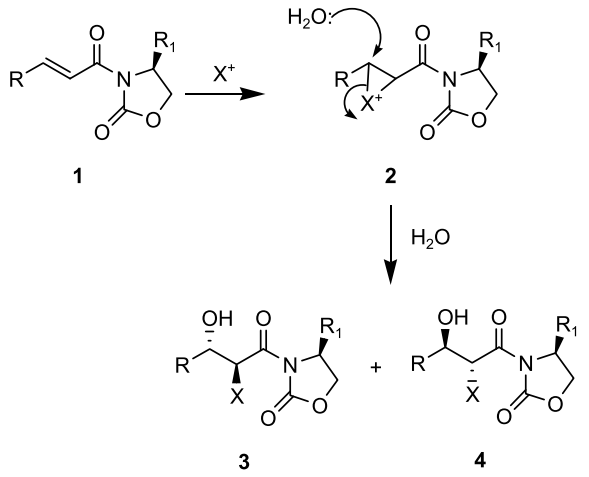


Scheme 1.

reaction of chiral β-aryl-α-halo-β-oxycarboxylic acid esters for the enantioselective synthesis of lignans.[11] However, there is no suitable method, other than the aldol reaction,[7] for the synthesis of the chiral β-aryl-α-halo-β-oxycarboxylic acid derivatives.

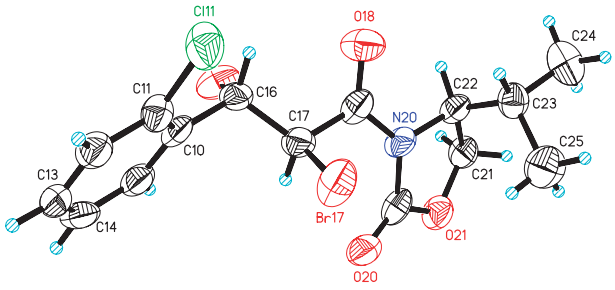
There are only a few reports for the halohydrin reactions of α,β-unsaturated carbonyls.[2d,3,12] By screening these methods, we found that halogen (Br_2/I_2) and silver nitrate ($AgNO_3$) is an effective combination for the halohydrin reaction of *N*-cinnamoyl-2-oxazolidinoes **1** over aromatic electrophilic substitutions. Halohydrin reaction of **1a** (R= Ph and R′=*i*-Pr) with Br_2 and $AgNO_3$ in aqueous acetone gave the desired carboxybromohydrine, along with a minor amount of a non-separable mixture of diastereoisomers (dr 60:40) of a dibromo compounds -*anti*-(4*S*)-3-(2′,3′-dibromo-3′-phenyl-propionyl)-4-(1-methylethyl)-2-oxazolidinone (**5a**). The formation of **5a** varied with the amount of water in the reaction media. A systematic study showed that when the acetone/water ratio was maintained between 4:1 and 6:1, it gave >95:05 of carboxybromohydrins; lower as well as higher amount of water enhanced the formation of **5a**. The compound **5a** was characterized by the ^1H and ^{13}C NMR spectra analysis and compared with the authentic dibromo compound, prepared on reaction of **1a** with Br_2 in CCl_4. It was also found that there was no reaction in 50% aqueous acetone and no appreciable change in the product distribution when the concentrations of the reaction medium were varied between 0.1 M and 0.5 M in a 4:1 (v/v) acetone/water ratio. All halohydrin reactions were performed in aqueous organic solvent (solvent: H_2O, 4:1 v/v) at 0.2 M concentration.

To establish suitable reaction conditions, initially $AgNO_3$-promoted halohydrin reactions of three electronically different cinnamoyl substrates **1a**–**1c**, containing (4*S*)-4-(1-methylethyl)-2-oxazolidinone as chiral auxiliary were studied (Table 1). When a solution of **1a** in aqueous acetone (acetone/water 4:1) was treated with $AgNO_3$ (1.2 equiv) and Br_2 (1.2 equiv) at rt (25 °C), it gave the desired carboxybromohydrin with poor diastereoselectivity (dr 52:48; entry 1) and the diastereomeric ratio was increased to 65:35 (entry 2) when the reaction was performed at 0–5 °C. The bromohydrin reaction of **1a** in aqueous acetonitrile was comparable (entry 3) with aqueous acetone. However, there was no bromohydrin reaction in aqueous DMF, DMSO and THF (entry 4). Iodohydrin reaction of **1a** under the same reaction conditions gave <5% of the desired compounds (entry 5), also there was no improvement even with the use of excess reagents and under different reaction conditions. While the bromohydrin reaction of **1b** was performed under the same reaction conditions, it gave mixture of products (entry 6). However, **1b** smoothly underwent iodohydrin reaction with 70:30 diastereoselectivity (entry 8) in aqueous acetone. There is no appreciable change in diastereomeric ratio and yield when the reaction was performed at rt (25 °C) (entry 7). Unlike **1a**, **1b** underwent iodohydrin reaction in aqueous THF with improved diastereoselectivity of 80:20 (entry 9). Bromohydrin reaction was also studied for the

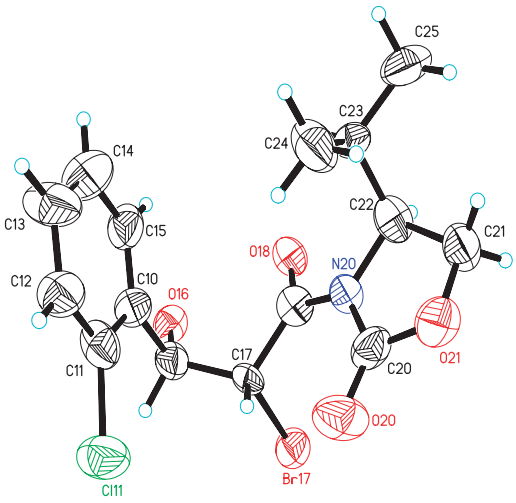
Table 1. $AgNO_3$-promoted halohydrin reactions of **1** under different reaction conditions

	Substrate	R	R_1	Solvent	X	Ratio[a] (**3**:**4**)	Yield[b] (%)
1[c]	**1a**	Ph	*i*-Pr	Acetone	Br	52:48 (55:45)	88
2	**1a**	Ph	*i*-Pr	Acetone	Br	65:35 (66:34)	92
3	**1a**	Ph	*i*-Pr	CH_3CN	Br	64: 36 (62:38)	82
4	**1a**	Ph	*i*-Pr	DMF or DMSO or THF	Br		NR
5	**1a**	Ph	*i*-Pr	Acetone or THF or CH_3CN	I	ND	<5%[d]
6	**1b**	4-$MeOC_6H_4$	*i*-Pr	Acetone	Br	ND	[e]
7[c]	**1b**	4-$MeOC_6H_4$	*i*-Pr	Acetone	I	65:35 (68:32)	86
8	**1b**	4-$MeOC_6H_4$	*i*-Pr	Acetone	I	70:30 (70:30)	89
9	**1b**	4-$MeOC_6H_4$	*i*-Pr	THF	I	80:20 (82:18)	92
10	**1c**	2-ClC_6H_4	*i*-Pr	Acetone	Br	62:38 (65:35)	91
11[c]	**1c**	2-ClC_6H_4	*i*-Pr	Acetone	Br	52:48	87
12	**1c**	2- ClC_6H_4	*i*-Pr	Acetone	I		NR
13	**1d**	Ph	Ph	Acetone	Br/I	ND	[e]
14	**1e**	Ph	Ph_2CH	Acetone	Br/I	ND	[e]
15	**1f**	4-$MeOC_6H_4$	Ph	Acetone	Br/I	ND	[e]
16	**1 g**	4-$MeOC_6H_4$	Ph_2CH	Acetone	Br/I	ND	[e]

[a] Determined from the ^1H NMR spectrum of the crude reaction mixture. Ratio in the parentheses refer to the ratio of isolated **3** and **4** after column chromatography.
[b] Combined isolated yields of **3** and **4** after chromatography.
[c] Reaction at room temperature (25 °C).
[d] >90% of **1a** was recovered.
[e] Mixture of products. ND: Not determined; NR: No reaction.



compound **3c**



compound **4c**

Figure 1. ORTEP diagram of **3c** and **4c**.

electron-deficient substrate **1c**, obtaining moderate diastereoselectivity with good yield (entry 10). Like **1a**, when the bromohydrination of **1c** was performed at rt, it also showed poor diastereoselectivity (entry 11) as well as not responding to the iodohydrin reaction (entry 12). The configurational assignments for the diastereomeric carboxyhalohydrins **3** and **4** were made by confirming the stereochemistry of **3a** and **4a** on comparison with the literature data.[7d,13] This was confirmed by the single crystal X-ray analysis[14] of **3c** and **4c** (Fig. 1), crystallized from $CHCl_3$.

Since, the (4*S*)-4-(1-methylethyl)-2-oxazolidinone chiral auxiliary gave moderate to good diastereoselectivities, we also examined other oxazolidinone chiral auxiliaries viz (4*S*)-4-phenyl- and (4*S*)-4-(diphenylmethyl)-2-oxazolidinones.[10,15] Unfortunately, halohydrin reaction of substrates **1d**–**1e**, having different oxazolidinone chiral auxiliaries (R′=Ph, Ph_2CH) using Br_2 and/or I_2, gave mixture of products. Only 12% of an undesired compound was obtained in pure form from the bromohydrin reaction of **1d**. The same compound was obtained in 56% yield, along with minor amount (26%) of another undesired product, when **1d** was treated with $AgNO_3$ and Br_2 in dry acetone i.e. in the absence of any external nucleophile at 0–5 °C. Recently, Barluenga et al. found that phenyl group present in the terpene moiety undergoes halocarbocyclization during the iodohydrination of alkenes tethered in terpene derivatives with Py_2IBF_4.[6] Spectral analysis of the undesired compounds were found to be bromo-carbocyclized product, but the regio- and stereochemistry of the bromo-carbocylized products could not be confirmed. Our several attempts were also failed to get single crystal X-ray difraction quality crystals.[16]

To assess whether the counter anion of the Ag(I) salt affects the diastereoselctivity of the halohydrin reactions, product studies were carried out employing the electronically different cinnamoyl substrates **1a**–**1c**, using AgOAc and Ag_2O instead of $AgNO_3$ as a promoter, under a variety of reaction conditions (Table 2). $AgNO_3$ (Eq. 1) and AgOAc (Eq. 2) produce acids on reaction with a halogen in water, whereas Ag_2O does not produce any acid (Eq. 3) under the same reaction conditions. When the halohydrin reactions of **1a**-**1c** were performed in the presence of AgOAc instead of $AgNO_3$, similar results were obtained, that is, **3** was produced as the major diastereoisomer (Table 2; entries 1–3). But in the case of Ag_2O-mediated reactions, **1a** and the electron-deficient **1c** showed very poor diastereoselectivities (entries 4 and 6), whereas **1b** still showed **3b** as the

Table 2. AgOAc- and Ag_2O-promoted halohydrin reaction of **1**[a]

Entry	Substrate	Ag(I) salt	Additive	X	Ratio[b] (**3**:**4**)	Yield[c] (%)
1	**1a**	AgOAc	None	Br	65:35	94
2	**1b**	AgOAc	None	I	80:20	91
3	**1c**	AgOAc	None	Br	60:40	90
4	**1a**	Ag_2O	None	Br	50:50	97
5	**1b**	Ag_2O	None	I	65:35	88
6	**1c**	Ag_2O	None	Br	50:50	94
7	**1a**	Ag_2O	HNO_3	Br	67:33 (66:34)	96 (95)
8	**1b**	Ag_2O	HNO_3	I	79:21 (77:23)	90 (87)
9	**1c**	Ag_2O	HNO_3	Br	61:39 (62:38)	94 (91)

[a] Halohydrin reactions were performed using 0.7 equiv of Ag_2O and 1.2 equiv of halogen (X_2) in aqueous organic solvent (**1a** and **1c** in aqueous acetone and **1b** in aqueous THF) at 0–5 °C for 30 min.
[b] Determined from the ^1H NMR spectrum of the crude reaction mixture.
[c] Isolated yields: ratios in parentheses refer to the reactions in the presence of AcOH.

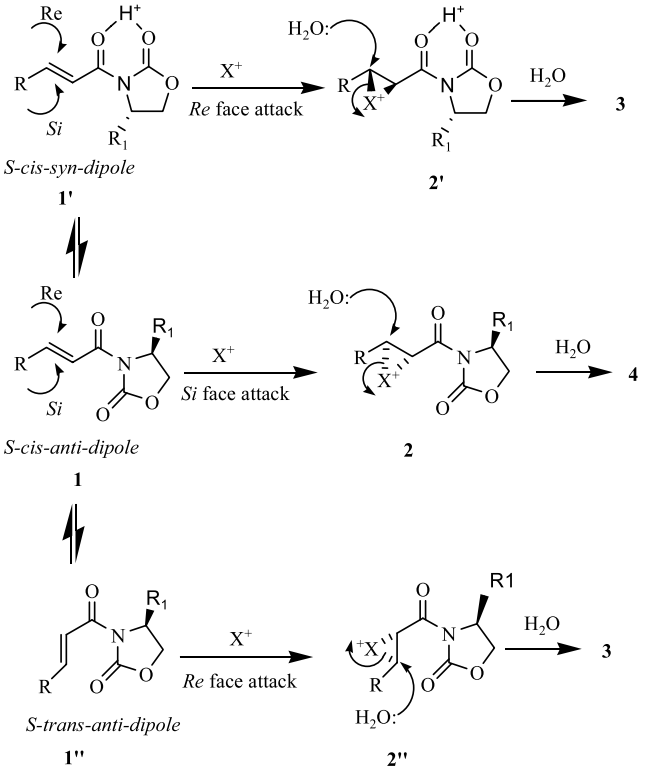
major diastereomer with dr of 65:35 (Table 2; entry 5). When the Ag_2O-promoted halohydrin reactions of **1a–1c** were performed in the presence of either HNO_3 or AcOH as an additive, these showed diastereoselectivities (Table 2; entries 7–9) similar to either $AgNO_3$- or AgOAc-promoted reactions (Table 1, entries 2, 9 and 10 and Table 2, entries 1–3).

$$AgNO_3 + X_2 + H_2O \rightarrow AgX\downarrow + HOX + HNO_3 \quad (1)$$

$$AgOAc + X_2 + H_2O \rightarrow AgX\downarrow + HOX + AcOH \quad (2)$$

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

Unchelated *N*-cinnamoyl-2-oxazolidinone usually exists in the *S-cis-anti-dipole* conformation **1**,[17] so it was also expected to give carboxyhalohydrin **4** as a major diastereoisomer for the above halohydrin reactions, but that was not observed. So it might be concluded here that in either $AgNO_3$ or AgOAc promoted reactions, the H^+-chelated *S-cis-syn-dipole* conformation **1′** might be involved in the halohydrin reaction. The preferred attack of X^+ from the *Re*-face of conformation **1′** and subsequent opening of the halonium intermediate **2′** by *anti*-nucleophilic attack of H_2O at the β-position yielded **3** as the major diastereoisomer (Scheme 2). The poor diastereoselectivities of the cinnamoyl- and electron-deficient cinnamoyl substrates **1a** and **1c** in Ag_2O-promoted reactions i.e. under unchelated conditions (Table 2; entries 4 and 6) might be accounted for by the involvement of both the equilibrated *S-cis-* and *S-trans-anti-dipole* conformations **1** and **1″**. The iodohydrination of electron-rich cinnamoyl substrate **1b** promoted by Ag_2O, that is, under unchelated conditions still showed carboxyhalohydrin **3b** a major diastereoisomer. This could be due to the extensive conjugation of the electron-donating substituent at the *p*-position with the α,β-unsaturated carbonyls, equilibrium might be shifted more towards the unchelated *S-trans-anti-dipole* conformation **1″** and involve the *Re*-face of *S-trans-anti-dipole* conformation **1″**, providing **3b** as the major diastereoisomer. This was supported by the Ag_2O-mediated reactions performed in the presence of either HNO_3 or AcOH as an additive (Table 2; entries 7–9).



Scheme 2.

It was found that either $AgNO_3$ or AgOAc as a promoter and (4*S*)-4-(1-methylethyl)-2-oxazolidinone as a chiral auxiliary are a better combination for the Ag(I)-promoted halohydrin reaction. So, to generalize this asymmetric halohydrin reaction, the reaction was further studied for a variety of enoyl substrates containing (4*S*)-4-(1-methylethyl)-2-oxazolidinone as a chiral auxiliary (Table 3). Substrate **1h** possessing strong electron-withdrawing substituents, for example, $-NO_2$ group on the aromatic ring, smoothly underwent bromohydrin reaction in aqueous acetone under the same reaction conditions with moderate diastereoselectivity (entry 1). Similar to **1c**, no iodohydrin reaction was observed for **1h**. Substrate **1i** with an electron-donating substituent on the aromatic ring efficiently underwent iodohydrin reaction under the same reaction conditions in aqueous acetone with moderate diastereoselectivity (entry 2). Like **1b**, the iodohydrin reaction of **1i** in aqueous THF provided improved diastereoselectivity (entry 3). Another two electron-rich cinnamoyl substrates **1j** and **1k** also responded to the iodohydrin reaction in aqueous THF with dr of 82:18 and 78:22, respectively (entries 4 and 5). However, due to instability of the minor isomers **4j** and **4k** in silica-gel during column chromatography, they could not

Table 3. $AgNO_3$-promoted halohydrin reaction of different substrates **1**

	Substrate	R	Solvent	X	Ratio[a] (**3**:**4**)	Yield[b] (%)
1	**1 h**	2-$NO_2C_6H_4$	Acetone	Br	60:40	86
2	**1i**	4-$BnOC_6H_4$	Acetone	I	64:36	91
3	**1i**	4-$BnOC_6H_4$	THF	I	80:20	92
4	**1j**	3, 4-$MeOC_6H_3$	THF	I	82:18	77[c]
5	**1k**	4-BnO-3-$MeOC_6H_3$	THF	I	78:22	74[c]
6	**1 l**	3, 5-Br-4-$BnOC_6H_2$	Acetone	Br	65:35	87
7	**1m**	2-naphthyl	Acetone	I	68:32	88
8	**1n**	CH_3	Acetone	Br	62:38[d]	86[e]

[a] Determined from the ^1H NMR spectrum of the crude reaction mixture.
[b] Combined isolated yields of **3** and **4** after chromatography otherwise it is noted.
[c] Isolated yield of the isomer **3**.
[d] Along with 15% of other regio-isomers
[e] Combined isolated yield of **3n**, **4n** and the other regio-isomers.

be obtained in pure form. While the bromohydrin reaction of **1i–1k** were performed under the same reaction conditions; these gave a mixture of products. We have also studied the halohydrin reaction of electronically different cinnamoyl substrates, where **1l** behaved like an electron-deficient cinnamoyl substrate, that is, responded to the bromohydrin reaction in aqueous acetone (entry 6) but no iodohydrin reaction. On the other hand, **1m** acted as an electron-rich cinnamoyl substrate and smoothly underwent iodohydrin reaction in aqueous acetone (entry 7), whereas bromohydrin reaction gave mixture of products. We have also studied the halohydrin reaction of alkenoyl substrate **1n**. This responded to the bromohydrin reaction with moderate diastereoselectivity (entry 8), along with 15% of other regio-isomers, minor isomer **4n** was always obtained as a non-separable mixture with regio-isomers.

3. Conclusion

In conclusion, we have described Ag(I)-promoted asymmetric halohydrin reaction of chiral *N*-enoyl-2-oxazolidinones **1** with high regio- and *anti*-selectivity and moderate to good diastereoselectivity in good yields. Alkenoyl, cinnamoyl and electron-deficient cinnamoyl substrates smoothly undergo bromohydrin reactions but no iodohydrin reactions, whereas electron-rich cinnamoyl substrates prefer to undergo iodohydrin reactions. $AgNO_3$ and AgOAc are found to be better promoters than Ag_2O for promoting diastreoselectivity. It was found that the acids produced on reactions of $AgNO_3$ and AgOAc with halogen in aqueous media were responsible for the involvement of the H^+-chelated *S-cis-syn-dipole* conformation and provided better diastereoselectivity for the halohydrin reactions of *N*-enol-2-oxazolidinoes. It was also found that the oxazolidinone chiral auxiliary should contain alkyl substituents, more specifically non-nucleophilic substituents; otherwise that would act as a competitive nucleophile. This methodology, that is, the direct use of halogen and water promoted by Ag(I), offers an alternative method for the asymmetric synthesis of carboxyhalohydrins, that is, *anti*-α-halo-β-hydroxycarboxylic acid derivatives. We are currently applying the concept of halohydrin reaction to other halonucleophilic (X^+ Nu^-) addition reactions for the asymmetric 1,2-hetero-bifunctionalization of alkenes.

4. Experimental

The ^1H NMR spectra were measured on a Bruker-200 (200 MHz) and Bruker-500 (500 MHz) using $CDCl_3$ as solvent. The ^{13}C NMR spectra were measured with Bruker-200 (50 MHz) and Bruker-500 (125 MHz) using $CDCl_3$ as solvent. ^1H 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 ^1H NMR are in Hz. IR spectra were recorded using Thermo Nicolet FT-IR spectroscopy. Elemental analyses were carried out using Perkin–Elmer 2400-II and mass spectra were analyzed by Waters LCT mass spectrometer.

Commercial grade reagents were used without further purification. Solvents are used after distillation following usual protocols. For the halohydrin reaction distilled water is used. Flash chromatography was carried out using Acme silica gel (230–400 mesh). Substrates **1** were synthesized following the literature procedures.[10,18]

4.1. General experimental procedure for the halohydrin reaction

To a solution of the substrate **1** (1 mmol) in aqueous organic solvent (20 ml; acetone or THF; organic solvent/H_2O 4:1) Ag(I) (for $AgNO_3$ and AgOAc 1.2 mmol and Ag_2O (0.7 mmol) and halogen (Br_2 or I_2, 1.2 mmol) were added, respectively, at 0–5 °C and allowed to stir for 20–30 min. The reaction mixture was extracted with Et_2O at least three times, washed with water, dried over Na_2SO_4. The organic solution was filtered through a small cellite pad (otherwise locking problem or poor base line was found in the ^1H 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 desired carboxyhalohydrins in pure form.

4.1.1. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[3′-Hydroxy-2′-iodo-3′-(4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3b). Gummy liquid, $[\alpha]_D^{21}$ +88.4° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3459 (br, OH), 2963, 2837, 1778, 1694, 1612, 1586, 1515, 1484, 1463, 1387, 1303, 1250, 1205, 1178, 1142, 1103, 1022, 971, 835, 789, 768, 728, 694, 565 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (d, $J=8.6$ Hz, 2H), 6.89 (d, $J=8.6$ Hz, 2H), 6.13 (d, $J=7.9$ Hz, 1H), 5.15 (d, $J=7.9$ Hz, 1H), 4.47 (m, 1H), 4.30–4.20 (m, 2H), 3.80 (s, 3H), 3.40 (br s, 1H), 2.5–2.33 (m, 1H), 0.95 (t, $J=6.3$ Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.9, 159.7, 152.9, 131.7, 128.3 (2C), 113.9 (2C), 75.4, 63.4, 58.2, 55.2, 27.9, 25.0, 17.7, 15.0. Anal. Calcd for $C_{16}H_{20}INO_5$: C, 44.36; H, 4.65; N, 3.23. Found: C, 44.18; H, 4.45; N, 2.92%.

4.1.2. *anti*-(4*S*, 2′*R*, 3′*R*)-3-[3′-Hydroxy-2′-iodo-3′-(4-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (4b). Gummy liquid; $[\alpha]_D^{22}$ +8.6° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3473 (br OH), 2962, 2929, 1777, 1697, 1611, 1514, 1485, 1463, 1386, 1303, 1250, 1202, 1177, 1120, 1030, 972, 830, 789, 769, 694, 562 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (d, $J=8.7$ Hz, 2H), 6.87 (d, $J=8.7$ Hz, 2H), 6.18 (d, $J=7.0$ Hz, 1H), 5.10 (d, $J=7.0$ Hz, 1H), 4.49–4.11 (m, 3H), 3.79 (s, 3H), 2.37–2.12 (m, 1H), 0.85 (d, $J=7.0$ Hz, 3H), 0.65 (d, $J=7.0$ Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.2, 159.7, 153.0, 131.6, 128.0 (2C), 113.9 (2C), 75.8, 63.4, 59.0, 55.3, 28.5, 23.8, 17.8, 14.3. Anal. Calcd for $C_{16}H_{20}INO_5$: C, 44.36; H, 4.65; N, 3.23. Found: C, 44.54; H, 4.86; N, 3.02%.

4.1.3. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[2′-Bromo-3′-hydroxy-3′-(2-chlorophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3c). Mp 108–109 °C; $[\alpha]_D^{22}$ +69.9° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3450 (br OH), 2964, 2920, 2849, 1782, 1702, 1464, 1439, 1386, 1302, 1203, 1120, 1049, 1024, 971, 763, 717, 686, 636, 599, 465 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.55–7.51 (m, 1H), 7.42–7.24 (m, 3H), 6.12 (d, $J=7.3$ Hz, 1H), 5.66 (br d, 1H), 4.44 (m, 1H), 4.23 (m, 2H), 3.72 (br s, 1H), 2.5–2.3 (m, 1H), 0.93 (d, $J=7.0$ Hz, 6H); ^{13}C NMR

(50 MHz, $CDCl_3$) δ 169.0, 152.7, 136.5, 133.4, 129.8, 129.7, 128.4, 127.2, 71.7, 63.5, 58.3, 43.1, 28.0, 17.8, 14.8. Anal. Calcd for $C_{15}H_{17}BrClNO_4$: C, 46.12; H, 4.39; N, 3.59. Found: C, 46.08; H, 4.18; N, 3.59%.

4.1.4. *anti*-(4*S*, 2′*R*, 3′*R*)-3-[2′-Bromo-3′-hydroxy-3′-(2-chlorophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (4c). Mp 123–124 °C; $[\alpha]_D^{21}$ −6.4° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3455 (br OH), 2964, 2926, 1779, 1703, 1676, 1593, 1483, 1465, 1438, 1385, 1301, 1201, 1120, 1049, 1023, 973, 755, 718, 684, 669, 632, 464 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.60–7.45 (m, 1H), 7.40–7.20 (m, 3H), 6.22 (d, J=6.5 Hz, 1H), 5.58 (d, J=6.5 Hz, 1H), 4.42 (m, 1H), 4.33–4.14 (m, 2H), 2.30–2.15 (m, 1H), 0.86 (d, J=7.0 Hz, 3H), 0.60 (d, J=7.0 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.1, 152.8, 136.5, 133.2, 129.7, 129.6, 128.2, 127.1, 72.3, 63.4, 58.9, 42.0, 28.3, 17.7, 14.3. Anal. Calcd for $C_{15}H_{17}BrClNO_4$: C, 46.12; H, 4.39; N, 3.59. Found: C, 46.34; H, 4.24; N, 3.54%.

4.1.5. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[2′-Bromo-3′-hydroxy-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3h). Mp 155–156 °C; $[\alpha]_D^{23}$ +113.6° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3381 (br OH), 2965, 1748, 1707, 1529, 1488, 1403, 1393, 1364, 1300, 1281, 1227, 1217, 1143, 1119, 1043, 1018, 972, 853, 780, 749, 719, 674, 608, 504 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.95 (dd, J=8.0, 0.9 Hz, 1H), 7.85–7.60 (m, 2H), 7.57–7.45 (m, 1H), 6.08 (d, J=8.0 Hz, 1H), 5.93 (d, J=8.0 Hz, 1H), 4.49 (m, 1H), 4.35–4.18 (m, 2H), 3.75 (br s, 1H), 2.50–2.33 (m, 1H), 0.94 (d, J=7.0 Hz, 3H), 0.92 (d, J=7.0 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.4, 152.8, 149.1, 133.7, 133.3, 129.4, 129.3, 124.6, 69.6, 63.6, 58.3, 43.8, 28.0, 17.7, 14.7. Anal. Calcd for $C_{15}H_{17}BrN_2O_6$: C, 44.90; H, 4.27; N, 6.98. Found: C, 44.60; H, 4.03; N, 6.73%.

4.1.6. *anti*-(4*S*, 2′*R*, 3′*R*)-3-[2′-Bromo-3′-hydroxy-3′-(2-nitrophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (4h). Gummy liquid; $[\alpha]_D^{22}$ −39.1° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3453 (br OH), 2964, 2927, 2876, 1779, 1704, 1608, 1580, 1529, 1485, 1464, 1386, 1351, 1300, 1203, 1142, 1120, 1052, 1020, 972, 853, 786, 750, 713, 672 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.97 (dd, J=8.0, 0.9 Hz, 1H), 7.87–7.60 (m, 2H), 7.57–7.42 (m, 1H), 6.16 (d, J=7.4 Hz, 1H), 5.90 (d, J=7.4 Hz, 1H), 4.43 (m, 2H), 4.40–4.15 (m, 2H), 2.48–2.15 (m, 1H), 0.89 (d, J=7.0 Hz, 3H), 0.71 (d, J=7.0 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.6, 152.9, 148.9, 134.1, 133.4, 129.3, 129.0, 124.8, 70.6, 63.6, 59.1, 42.6, 24.4, 17.7, 14.5. Anal. Calcd for $C_{15}H_{17}BrN_2O_6$: C, 44.90; H, 4.27; N, 6.98. Found: C, 44.67; H, 4.13; N, 6.73%.

4.1.7. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[3′-Hydroxy-2′-iodo-3′-(4-benzyloxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3i). Mp 163–164 °C; $[\alpha]_D^{22}$ +63.0° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3465 (br OH), 3033, 2959, 2921, 2874, 1768, 1678, 1608, 1515, 1487, 1455, 1429, 1388, 1366, 1329, 1307, 1247, 1221, 1206, 1178, 1119, 1101, 1078, 1049, 1021, 1003, 970, 922, 857, 841, 821, 800, 760, 749, 729, 702, 694, 626, 562, 509, 490 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.50–7.25 (m, 7H), 6.97 (d, J=8.7 Hz, 2H), 6.13 (d, J=7.9 Hz, 1H), 5.16 (d, J=7.9 Hz, 1H), 5.06 (s, 2H), 4.52–4.38 (m, 1H), 4.33–4.18 (m, 2H), 3.44 (br s, 1H), 2.51–2.30 (m, 1H), 0.96 (quasi t, J=5.90, 6.8 Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.0, 159.0, 152.9, 136.8, 131.9, 128.5 (2C), 128.3 (2C), 128.0, 127.4 (2C), 114.9 (2C), 75.5, 70.1, 63.0, 58.2, 28.0, 24.9, 17.8, 15.1. Anal. Calcd for $C_{22}H_{24}INO_5$: C, 51.88; H, 4.75; N, 2.75. Found: C, 51.99; H, 4.79; N, 2.67%.

4.1.8. *anti*-(4*S*, 2′*R*, 3′*R*)-3-[3′-Hydroxy-2′-iodo-3′-(4-benzyloxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (4i). Gummy liquid, $[\alpha]_D^{23}$ +8.6° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3459 (br OH), 2962, 2925, 1777, 1695, 1609, 1512, 1485, 1463, 1454, 1384, 1302, 1202, 1175, 1120, 1020, 829, 738, 697, 624, 558 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.48–7.25 (m, 7H), 6.96 (d, J=8.7 Hz, 2H), 6.19 (d, J=7.0 Hz, 1H), 5.13–5.05 (m, 3H), 4.51–4.08 (m, 3H), 3.63 (br d, J=7.0 Hz, 1H), 2.32–2.15 (m, 1H), 0.84 (d, J=7.0 Hz, 3H), 0.64 (d, J=7.0 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.1, 158.9, 153.0, 136.8, 131.9, 128.5 (2C), 128.0 (2C), 127.9, 127.3 (2C), 114.9 (2C), 75.8, 70.0, 63.4, 58.9, 28.4, 23.7, 17.7, 14.3. Anal. Calcd for $C_{22}H_{24}INO_5$: C, 51.88; H, 4.75; N, 2.75. Found: C, 51.93; H, 4.57; N, 2.75%.

4.1.9. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[3′-Hydroxy-2′-iodo-3′-(3,4-dimethoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3j). Mp 164–165 °C; $[\alpha]_D^{23}$ +54.6° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3473 (br OH), 3024, 2964, 1761, 1702, 1607, 1591, 1517, 1484, 1465, 1448, 1438, 1421, 1388, 1365, 1332, 1298, 1262, 1236, 1218, 1201, 1160, 1137, 1119, 1105, 1071, 1052, 1024, 1002, 969, 889, 835, 761, 700, 655, 618, 576 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.10–6.70 (m, 3H), 6.17 (d, J=7.6 Hz, 1H), 5.13 (d, J=7.6 Hz, 1H), 4.45 (m, 1H), 4.25 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 2.51–2.30 (m, 1H), 0.95 (t, J=6.5 Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.0, 152.8, 149.0, 148.9, 131.9, 119.4, 110.9, 109.8, 75.6, 63.3, 58.1, 55.9, 55.8, 27.8, 24.6, 17.8, 15.0. Anal. Calcd for $C_{17}H_{22}INO_6$: C, 44.07; H, 4.79; N, 3.02. Found: C, 44.11; H, 4.77; N, 2.85%.

4.1.10. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[3′-Hydroxy-2′-iodo-3′-(4-benzyloxy-3-methoxyphenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3k). Gummy liquid: $[\alpha]_D^{23}$ +64.3° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3455 (br OH), 2963, 2929, 2875, 1778, 1694, 1594, 1514, 1485, 1463, 1454, 1422, 1386, 1303, 1262, 1203, 1141, 1102, 1020, 971, 912, 857, 804, 767, 734, 697, 648, 617, 563, 456 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.50–725 (m, 7H), 6.94 (s, 1H), 6.87 (m, 2H), 6.15 (d, J=7.6 Hz, 1H), 5.14 (m, 3H), 4.48–4.35 (m, 1H), 4.29–4.16 (m, 2H), 3.90 (s, 3H), 3.57 (br s, 1H), 2.50–2.31 (m, 1H), 0.94 (t, J=6.6 Hz, 6H), ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.9, 152.7, 149.5, 148.1, 136.8, 132.4, 128.4 (2C), 127.4, 127.1 (2C), 119.2, 113.5, 110.3, 75.6, 70.8, 63.2, 58.0, 55.9, 27.7, 24.5, 17.7, 14.9. Anal. Calcd for $C_{23}H_{26}INO_6$: C, 51.22; H, 4.86; N, 2.60. Found: C, 51.06; H, 4.91; N, 2.68%.

4.1.11. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[2′-Bromo-3′-hydroxy-3′-(4-benzyloxy-3, 5-dibromophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3l). Mp 170–171 °C; $[\alpha]_D^{22}$ +45.6° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3448 (br OH), 2960, 2922, 2853, 1781, 1700, 1645, 1456, 1380, 1256, 1200, 1116, 1047, 742, 701, 620, 532 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.65–7.55 (m, 4H), 7.51–7.32 (m, 3H), 5.74 (d, J=8.3 Hz, 1H), 5.12 (d, J=8.3 Hz, 1H), 5.03 (s, 2H), 4.50

(m, 1H), 4.42–4.18 (m, 2H), 2.67 (br s, 1H), 2.52–2.25 (m, 1H), 0.99 (d, $J=7.1$ Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.7, 152.9, 152.8, 137.8, 136.0, 131.6 (2C), 128.4 (5C), 118.5 (2C), 74.6, 73.3, 63.6, 58.3, 44.6, 28.0, 17.7, 14.7. Anal. Calcd for $C_{22}H_{22}Br_3NO_5$: C, 42.61; H, 3.58; N, 2.26. Found: C, 42.86; H, 3.42; N, 2.19%.

4.1.12. *anti*-(4*S*, 2′*R*, 3′*R*)-3-[2′-Bromo-3′-hydroxy-3′-(4-benzyloxy-3, 5-dibromophenyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (4l). Gummy liquid, $[\alpha]_D^{22}$ +6.88° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3473 (br OH), 3064, 3032, 2963, 2926, 2874, 1781, 1705, 1548, 1497, 1485, 1455, 1386, 1303, 1256, 1202, 1141, 1105, 1053, 1019, 970, 914, 875, 740, 697, 632, 537 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.65–7.45 (m, 4H), 7.44–7.33 (m, 3H), 5.87 (d, $J=7.4$ Hz, 1H), 5.09 (d, $J=7.4$ Hz, 1H), 5.03 (s, 2H), 4.45 (m, 1H), 4.40–4.19 (m, 2H), 2.42–2.18 (m, 1H), 0.84 (d, $J=6.9$ Hz, 3H), 0.75 (d, $J=6.9$ Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.8, 153.0, 152.8, 137.9, 135.9, 131.4 (2C), 128.4 (5C), 118.6 (2C), 74.6, 73.8, 63.6, 59.0, 43.9, 28.4, 17.7, 14.4.. Anal. Calcd for $C_{22}H_{22}Br_3NO_5$: C, 42.61; H, 3.58; N, 2.26. Found: C, 42.45; H, 3.52; N, 2.08%.

4.1.13. *anti*-(4*S*, 2′*S*, 3′*S*)-3-[3′-Hydroxy-2′-iodo-3′-(2-naphthyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (3m). Mp 90–91 °C; $[\alpha]_D^{22}$ +118.3° (*c* 0.8, $CHCl_3$); FTIR (KBr) 3444 (br OH), 2963, 2925, 1779, 1693, 1601, 1386, 1304, 1202, 1142, 1122, 1049, 1019, 819, 749, 694, 479 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.90–7.75 (m, 4H), 7.55–7.45 (m, 3H), 6.30 (d, $J=7.6$ Hz, 1H), 5.33 (d, $J=7.6$ Hz, 1H), 4.41 (m, 1H), 4.19 (m, 2H), 2.49–2.28 (m, 1H), 0.94 (t, $J=7.5$ Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.0, 152.8, 136.8, 133.3, 133.0, 128.5, 128.2, 127.6, 126.6, 126.3 (2C), 124.2, 76.1, 63.4, 58.1, 27.9, 24.2, 17.7, 15.0. Anal. Calcd for $C_{19}H_{20}INO_4$: C, 50.35; H, 4.45; N, 3.09. Found: C, 50.40; H, 4.42; N, 3.02%.

4.1.14. *anti*-(4*S*, 2′*R*, 3′*R*)-3-[3′-Hydroxy-2′-iodo-3′-(2-naphthyl)-propionyl]-4-(1-methylethyl)-2-oxazolidinone (4m). Gummy liquid, $[\alpha]_D^{22}$ +14.4° (*c* 0.5, $CHCl_3$); FTIR (KBr) 3458 (br OH), 2963, 1777, 1694, 1601, 1463, 1385, 1303, 1272, 1199, 1120, 1056, 1019, 819, 750, 693, 479 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.90–7.78 (m, 4H), 7.55–7.45 (m, 3H), 6.35 (d, $J=6.7$ Hz, 1H), 5.29 (d, $J=6.7$ Hz, 1H), 4.42–4.08 (m, 3H), 3.90 (br s, 1H), 2.19–1.95 (m, 1H), 0.76 (d, $J=7.0$ Hz, 3H), 0.37 (d, $J=7.0$ Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.1, 152.9, 136.6, 133.2, 133.0, 128.4, 128.0, 127.5, 126.2 (2C), 126.1, 124.0, 76.2, 63.3, 58.8, 28.3, 22.8, 17.6, 13.9. Anal. Calcd for $C_{19}H_{20}INO_4$: C, 50.35; H, 4.45; N, 3.09. Found: C, 50.26; H, 4.26; N, 3.03%.

4.1.15. *anti*-(4*S*, 2′*S*, 3′*S*)-3-(2′-Bromo-3′-hydroxy-butionyl)-4-(1-methylethyl)-2-oxazolidinone (3n). Gummy liquid, $[\alpha]_D^{22}$ +60.7° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3442 (br OH), 1783, 1708, 1389, 1333, 1215, 1117, 1028, 772, 714 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.43 (d, $J=8.3$ Hz, 1H); 4.40 (m, 1H); 4.31–4.18 (m, 5H); 3.58 (br s, 1H), 2.39–2.27 (m, 1H); 1.40 (d, $J=6.3$ Hz, 3H); 0.87 (d, $J=7.0$ Hz, 3H); 0.83 (d, $J=7.0$ Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.5, 153.8, 69.6, 64.2, 59.7, 47.0, 29.0, 20.5, 18.3, 15.1. MS (*m*/*z*) for $C_{10}H_{16}BrNO_4$: calculated $(M+H)^+$ 294.024, found 294.015 $(M+H)^+$, 296.013 $(M+H+2)^+$. Anal. Calcd for $C_{10}H_{16}BrNO_4$: C, 40.83; H, 5.48; N, 4.76. Found: C, 40.48; H, 5.31; N, 4.75%.

4.1.16. *anti*-(4*S*, 2′*R*, 3′*R*)-3-(2′-Bromo-3′-hydroxy-butionyl)-4-(1-methylethyl)-2-oxazolidinone (4n). Oily liquid, $[\alpha]_D^{22}$ +18.4° (*c* 1.0, $CHCl_3$); FTIR (KBr) 3445 (br OH), 1773, 1702, 1377, 1318, 1200, 1104, 1012, 767, 708, 655 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.35 (d, $J=8.6$ Hz, 1H); 4.45 (m, 1H); 4.30–4.17 (m, 5H); 2.70 (br S, 1H), 2.37–2.27 (m, 1H); 1.39 (d, $J=6.3$ Hz, 3H); 0.87 (dd, $J=2.4$, 6.9 Hz, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.6, 153.4, 68.8, 64.0, 58.7, 46.8, 28.5, 20.4, 18.2, 15.2. Anal. Calcd for $C_{10}H_{16}BrNO_4$: C, 40.83; H, 5.48; N, 4.76. Found: C, 40.46; H, 5.17; N, 4.86%.

4.1.17. *anti*-(4*S*)-3-(2′,3′-Dibromo-3′-phenyl-propionyl)-4-(1-methylethyl)-2-oxazolidinone (5a). Non-seperable mixture of diastereomers (60:40); light yellow solid, mp 76–80 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.60–7.26 (m, 5H), 6.58 (d, $J=11.6$ Hz, 1H), 5.51 (d, $J=11.6$ Hz, 1H), 4.65–4.50 (m, 1H), 4.47–4.20 (m, 2H), 2.60– 2.40 (m, 1H), 0.98 (d, $J=6.8$ Hz, 1.8H), 0.97 (d,, $J=6.9$ Hz, 2.4H), 0.95 (d, $J=6.8$ Hz, 1.8H). ^{13}C NMR (125 MHz, $CDCl_3$): major δ 167.6, 153.6, 138.0, 129.9, 129.4 (2C), 128.8 (2C), 64.1, 58.9, 50.6, 44.3, 28.5, 18.2, 15.3. minor δ 167.8, 153.5, 137.9, 129.8, 129.3 (2C), 128.7 (2C), 63.9, 59.5, 51.2, 43.9, 28.7, 18.3, 15.2.

4.2. Bromocarbocyclized product

4.2.1. Major compound. White amorphous solid, mp 156–158 °C. FTIR (KBr) 1760, 1706, 1450, 1382, 1304, 1187, 1109, 1008, 750, 693, 589, 532, 485 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.40–7.20 (m, 9H); 6.01 (d, $J=7.4$ Hz, 1H); 4.45 (dd, $J=8.8$, 3.4 Hz, 1H); 5.08 (d, $J=7.4$ Hz, 1H); 4.74 (t, $J=8.7$ Hz, 1H); 4.25 (dd, $J=8.8$, 3.4 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.8, 152.5, 138.6, 137.7, 129.0 (3C), 128.3 (3C), 126.6 (2C), 125.2 (2C), 75.0, 69.9, 57.7, 44.1. MS (ESI; *m*/*z*) for $C_{18}H_{14}BrNO_3$ calculated $(M+H)^+$ 372.024, found 371.996 $(M+H)^+$, 373.995 $(M+H+2)^+$. Anal. Calcd for $(C_{18}H_{14}BrNO_3+1H_2O)$: C, 55.40; H, 4.13; N, 3.59. Found: C, 55.53; H, 4.04; N, 3.75%.

4.2.2. Minor compound. White amorphous solid, mp 151–153 °C, FTIR (KBr) 1777, 1696, 1460, 1399, 1338, 1224, 1130, 1076, 1040,766, 685, 604, 523 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.60–7.20 (m, 9H); 5.91 (d, $J=8.2$ Hz, 1H); 5.44 (dd, $J=8.6$, 4 Hz, 1H); 5.12 (d, $J=8.2$ Hz, 1H); 4.68 (t, $J=9$ Hz, 1H); 4.26 (dd, $J=8.6$, 4 Hz, 1H) ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.9, 153.1, 139.4, 138.1, 129.7 (2C), 129.4, 129.2, 129.0 (2C), 127.6 (2C), 126.1 (2C), 75.2, 70.5, 58.1, 45.5. Anal. Calcd for $(C_{18}H_{14}BrNO_3 +1H_2O)$: C, 55.40; H, 4.13; N, 3.59. Found: C, 55.38; H, 3.98; N, 3.75%.

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