Investigation of substrate-selectivity pattern in the oxidation of secondary alcohols by amino acid-derived IBX derivatives

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Abstract

The chiral amino acid-derived 2-iodoxybenzamides **2a-e** were prepared and employed for investigation of their synthetic potential for the oxidation of *sec*-alcohols. The results indicate that they can readily oxidize *sec*-alcohols to the corresponding ketones in good to excellent yields, however, with lack of selectivity.

Keywords: Hypervalent iodine, oxidation, IBX amide

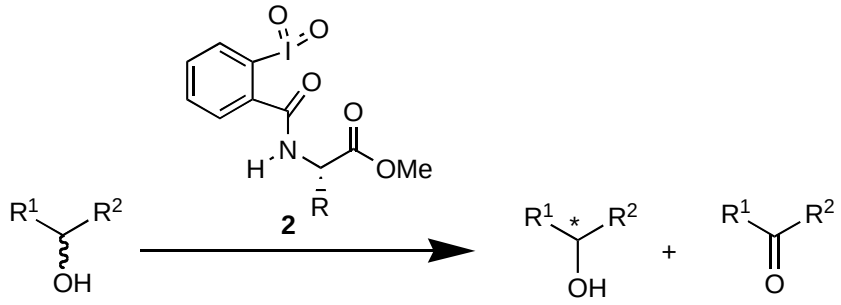
Introduction

Chiral *sec*-alcohols are of particular importance as intermediates and auxiliaries in organic synthesis and are found in a number of natural products and pharmaceuticals. As a consequence, practical access to obtain enantiomerically enriched *sec*-alcohols is still of interest to many chemists. Among current methodologies developed for this purpose, kinetic resolution of racemic *sec*-alcohols is preferably attractive due to their ease of preparation.[1] Kinetic resolutions of *sec*-alcohols have previously been accomplished through a number of strategies, i.e. acylation,[2] oxidation[3] and epoxidation.[4]

2-Iodoxybenzoic acid (IBX) has gained increasing popularity over the past decade as oxidizing reagent for conversion of alcohols to aldehydes or ketones and other synthetically useful transformations because of its mild, efficient, selective and environmentally friendly properties.[5, 6] However, due to its inherent insolubility in most common organic solvents, considerable efforts have been pushed toward the syntheses of the modified IBX reagents.[7] Recently, Zhdankin et al. reported the synthesis of novel IBX analogs deriving from amino acids, which exhibit reactivity similar to IBX.[8] They were briefly demonstrated as potentially useful reagents for oxidative kinetic resolution of secondary alcohols.

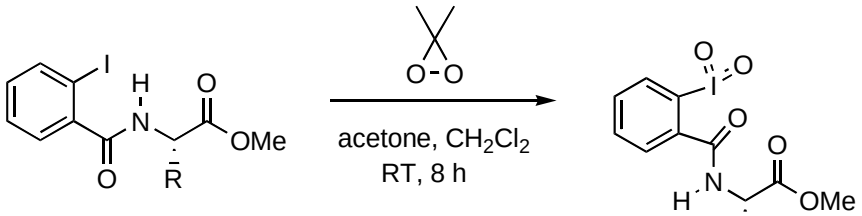
Results and Discussion

In order to probe the scope of their synthetic utilities as chiral oxidizing reagents, the present report deals with the investigation on the oxidation of various secondary alcohols using a collection of amino acid-derived IBX derivatives (Scheme 1).



Scheme 1

The chiral 2-iodoxybenzamides **2a-e** were prepared from the readily available 2-iodobenzamides **3** according to the previously reported procedure using dimethyldioxirane oxidation.[8] The 2-iodoxybenzamides **2a-e** were obtained in the range 30-70% (Scheme 2). It should be noted that 2-iodoxybenzamides **2a-c** were previously synthesized.[8a]



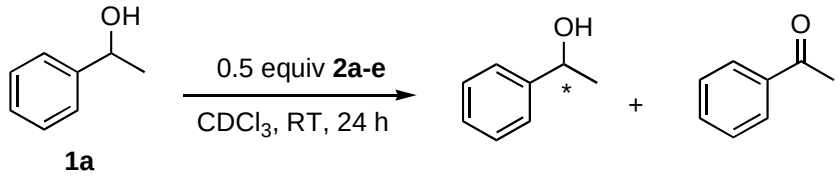
2a; R = CH_3, 73%
2b; R = CH_2Ph, 33%
2c; R = $CH_2CH(CH_3)_2$, 71%
2d; R = $CH(CH_3)_2$, 26%
2e; R = Ph, 61%

Scheme 2

The oxidation of racemic secondary alcohols was allowed to proceed to the maximum of 50% conversion by using 0.5 equivalent of the respective oxidant. The reaction mixture was purified by column chromatography on silica gel and the enantiomeric excesses of the unreacted alcohols were determined by analytical HPLC on a chiral column. In initial investigation, we

studied the oxidation of racemic 1-phenyl-1-ethanol. The results are summarized in Table 1. 1-Phenyl-1-ethanol was efficiently converted to acetophenone, after 24 h at room temperature, in good yields. Of the various chiral 2-iodoxybenzamides **2a-e** tested, low to modest of selectivities were obtained.

Table 1. Oxidation of racemic 1-Phenyl-1-ethanol



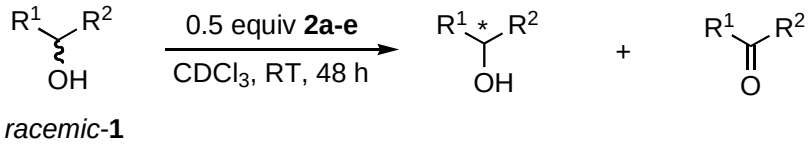
1a

Entry	Oxidant	Ketone (%)	ee (%)
1	**2a**	96	6
2	**2b**	Quant.	5[b]
3	**2c**	Quant.	1
4	**2d**	Quant.	2
5	**2e**	[a]	2

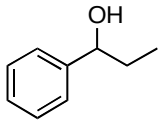
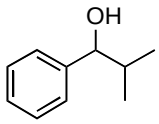
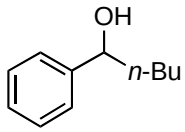
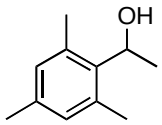
[a]Not determined due to the presence of inseparable side-product.
[b]According to the previously reported data, 9%ee was observed as determined by GC.[8a]

The substrate-selectivity pattern of the oxidation using chiral amino acid-derived 2-iodoxybenzamides was evaluated (Table 2). The results indicated that 2-iodoxybenzamides **2a-e** readily oxidized benzylic secondary alcohols to the corresponding ketones in variable yields as a function of oxidizing reagent or alcohol substrate employed. The oxidation of the substrates carrying a group larger than methyl group at the carbinol carbon was found to be sluggish and required longer reaction time (48 h) in order to achieve good conversion. Even though all the chiral 2-iodoxybenzamides attempted led to satisfying yields of ketones (50-98%), the remaining alcohols, in all cases, are nearly racemic. As far as the instrumental error is concerned, the enantiomeric purities in the range 1-7 could be a consequence of experimental errors from analytical chiral HPLC analysis. The selectivity was found to be insensitive to the increase in steric encumbrance of either the alcohol substrates or chiral reagents employed. The 2-iodoxybenzamides **2a**, **2c** and **2d** derived from amino acid containing aliphatic α-substituent gave no to low selectivity (Table 2, entries 1, 3, 4). Modest selectivities were obtained, in some cases, when (*S*)-phenylalanine- or (*R*)-phenylglycine-derived 2-iodoxybenzamide was used as oxidizing reagent (Table 2, entries 2, 5, 7 and 17).

Table 2. Oxidation of racemic secondary benzylic alcohols with chiral amino acid-derived 2-iodoxybenzamides



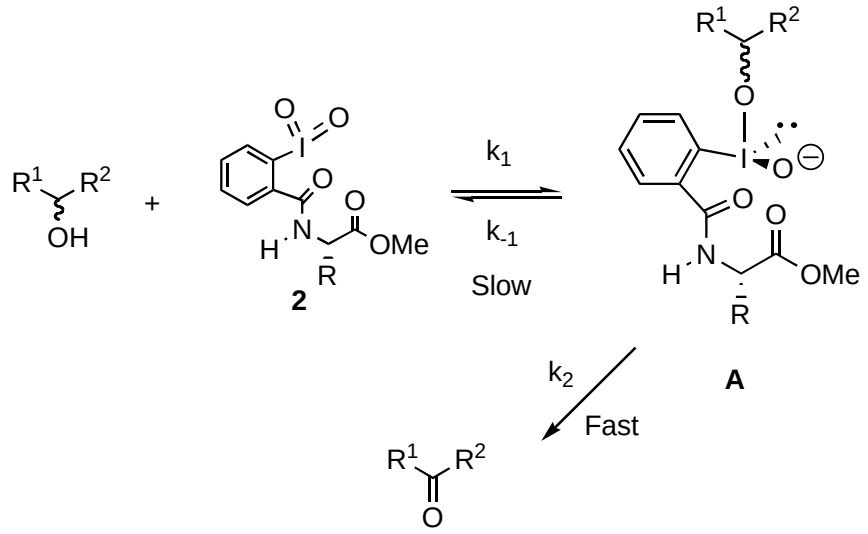
racemic-**1**

Entry	Alcohol	Oxidant	Ketone (%)	ee (%)
1	 **1b**	**2a**	54	0
2		**2b**	78	5
3		**2c**	88	1
4		**2d**	56	2
5		**2e**	[a]	7
6	 **1c**	**2a**	50	1
7		**2b**	91	7
8		**2c**	91	2
9		**2d**	74	1.5
10		**2e**	[a]	1
11	 **1d**	**2a**	75	1
12		**2b**	98	3
13		**2c**	71	2
14		**2d**	74	0
15		**2e**	[a]	2
16	 **1e**	**2a**	89	4
17		**2b**	89	5
18		**2c**	71	1.5
19		**2d**	87	2
20		**2e**	76	3

[a]Not determined due to the presence of inseparable side-product.

The relatively low enantioselectivity observed in the oxidation of *rac*-*sec*-alcohols with amino acid-derived 2-iodoxybenzamides is in agreement with previously reported data on asymmetric reactions of other hypervalent iodine reagents. A number of chiral hypervalent iodines compounds, particularly organo-iodine (III) compounds, have been previously synthesized.[9] Some of these reagents have been used in an effort to effect a variety of asymmetric oxidations with variable enantioselectivities (none to moderate %ee), i.e. phenolic oxidation,[9k] sulfide oxidation[9e] and oxygenation of olefins.[9j] The lack of chirality induction was

arisen from a fast conversion to achiral reactive species.[9k] In our oxidation, low enantioselection was believed to stem from a pre-equilibrium step between alcohol and 2-iodoxybenzamide derivative, leading to alkoxyiodinane oxide **A**, followed by a fast disproportionation to carbonyl compound and IBA derivative through a reductive elimination of the intermediate **A**.[10] Thus, once the intermediate **A** was formed from either enantiomer of the alcohol substrate, it rapidly collapses to the corresponding carbonyl compound (Scheme 3).



Scheme 3

Conclusions

In conclusion, the preliminary study on the oxidation of *rac*-*sec*-alcohols employing chiral amino acid-derived 2-iodoxybenzamides was carried out. The phenylglycine- and phenylalanine-derived iodoxybenzamides **2e** and **2b** exhibited promising results in that the modified structures of these reagents may find practical use as selective oxidizing reagents. The oxidation was proposed to take place via the mechanism previously described by Santagostino and co-workers.[11] Studies are in progress in the modification of the oxidizing reagent structure in order to improve the enantioselectivity

Experimental Section

General Procedures. Melting points (uncorrected) were measured on an Electrothermal 9100 apparatus. ^{1}H NMR spectra were recorded on a Bruker DPX-300 (300 MHz) spectrometer. ^{13}C NMR spectra were obtained from a Bruker Advance-300 (75 MHz) spectrometer. NMR data are reported as follow: ^{1}H NMR chemical shifts, measured in parts per million (ppm) down field

from TMS (δ), multiplicity, observed coupling constant (*J*) in Hertz (Hz), Proton count. Multiplicities are reported as singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), and multiplet (m). ^{13}C NMR chemical shifts are reported in ppm with residual non-deuterated solvent peak as the internal standard. The IR spectra were recorded on either a Jasco A-302 or a Perkin Elmer 683 infrared spectrometer. HPLC was performed on an Agilent system using chiral stationary phases with detection by UV. Microanalyses were carried out with a Perkin Elmer Elemental Analyzer 2400 CHN. Unless otherwise noted, all reactions were performed under Ar atmosphere in oven-dried glassware cooled in a dessiccator before use. Solvents and reagents were purified as follows: dichloromethane (CH_2Cl_2) and acetone were distilled from P_2O_5 and were stored over activated molecular sieves (4 Å). Flash column chromatography was performed with Merck silica gel 60 (Art. 7734). Preparatory layer chromatography (PLC) was performed using Merck silica gel 60 PF_{254} (Art. 7747). Analytical TLC was performed with Merck silica gel 60 PF_{254} (Art. 5554) with 0.2 mm thickness. All chemicals were purchased from Fluka, Aldrich and Acros organics and were used without prior purification.

General procedure A for preparation of amino acid methyl ester hydrochloride salts

Thionyl chloride (1.5 equiv) was added dropwise to a stirred 0 ^oC suspension of amino acid in methanol (ca. 2.0 M) at such a rate that the reaction mixture slightly refluxed. After the refluxing ceased, the mixture was brought to reflux (oil bath at 70 ^oC) for an additional 2 h. Methanol was removed (aspirator followed by vacuum) to give a crude amino acid methyl ester hydrochloride salt, which was used without further purification in the following *N*-acylation reaction.

General procedure B for prepartion of *N*-(2-iodobenzoyl) amino acid methyl ester[8a]

To a stirred mixture of 2-iodobenzoic acid (1.0 equiv) and a catalytic amount of N,N-dimethylformamide in dry CH_2Cl_2 (ca. 2.0 M), thionyl chloride (4.0 equiv) was added at room temperature and the reaction mixture was brought to reflux (oil bath at 50 ^oC) for 2 h. After cooling to room temperature, the CH_2Cl_2 was removed (aspirator). The resulting residue was dissolved in dry toluene (2-3 mL) and the toluene and residual thionyl chloride were removed (aspirator) to give 2-iodobenzoyl chloride, which was used without further purification in the next step. To a stirred mixture of amino acid methyl ester hydrochloride salt and triethylamine (5.0 equiv) in dry CH_2Cl_2 (ca. 0.33 M) at 0 ^oC, the 2-iodobenzoyl chloride in dry CH_2Cl_2 (ca. 2.0 M) was added dropwise using a pasture pipet. The reaction mixture was stirred at room temperature for an additional 2 h before the mixture was quenched with water (20 mL). Layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x10 mL). The combined CH_2Cl_2 extracts were washed with 2.0 M HCl (20 mL), 5% NaOH (20 mL), brine (20 mL), and were then dried over anhydrous Na_2SO_4, and concentrated (aspiratior then *vacuo*). Pure materials were obtained by column chromatography or crystallization.

***N*-(2-Iodobenzoyl)-(*S*)-alanine-OMe (3a).** Following the general procedure B, 2-iodobenzoic acid (2.48 g, 10.0 mmol) was coupled with (*S*)-alanine methyl ester hydrochloride salt (10.0 mmol). After column chromatography on silica gel (15x3.5 cm, 7:3 *n*-hexane/ethyl acetate

eluent), *N*-(2-iodobenzoyl)-(*S*)-alanine-OMe (2.39 g, 72%) was obtained as a pale yellow solid: mp 129.9-130.3 °C (Lit 130-131 °C)[8a], analytical TLC on silica gel, 1:1 *n*-hexane/ethyl acetate, R_f = 0.30. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.88 (1H, d, J = 7.9 Hz) 7.45-7.36 (2H, m) 7.14-7.09 (1H, m) 6.41 (1H, br d, J = 7.2 Hz) 4.82 (1H, dq, J = 7.2, 7.1 Hz) 3.80 (3H, s) 1.56 (3H, d, J = 7.1 Hz).

***N*-(2-Iodobenzoyl)-(*S*)-phenylalanine-OMe (3b).** Following the general procedure B, 2-iodobenzoic acid (4.96 g, 20.0 mmol) was coupled with (*S*)-phenylalanine methyl ester hydrochloride salt (20.0 mmol). After crystallization from ethyl acetate/*n*-hexane, *N*-(2-iodobenzoyl)-(*S*)-phenylalanine-OMe (6.21 g, 76%) was obtained as a pale yellow needle: mp 98.8-99.2 °C (Lit 98-99 °C)[8a], analytical TLC on silica gel, 1:1 *n*-hexane/ethyl acetate, R_f = 0.38. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.88 (1H, d, J = 7.9 Hz) 7.39-7.20 (7H, m) 7.11 (1H, t, J = 7.4 Hz) 6.32 (1H, br d, J = 7.0 Hz) 5.11 (1H, ddd, J = 7.0, 5.8, 5.7 Hz) 3.79 (3H, s) 3.35 (1H, dd, ABX, J = 13.9, 5.8 Hz) 3.25 (1H, dd, ABX, J = 13.9, 5.7 Hz).

***N*-(2-Iodobenzoyl)-(*S*)-leucine-OMe (3c).** Following the general procedure B, 2-iodobenzoic acid (4.96 g, 20.0 mmol) was coupled with (*S*)-leucine methyl ester hydrochloride salt (20.0 mmol). After column chromatography on silica gel (18x4.5 cm, 8:2 to 7:3 *n*-hexane/ethyl acetate as eluent), *N*-(2-iodobenzoyl)-(*S*)-leucine-OMe (6.40 g, 85%) was obtained as a white solid: mp 73.8-74.6 °C (Lit 71-73 °C)[8a], analytical TLC on silica gel, 1:1 *n*-hexane/ethyl acetate, R_f = 0.45. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.87 (1H, d, J = 8.0 Hz) 7.43-7.35 (2H, m) 7.13-7.07 (1H, m) 6.25 (1H, br d, J = 8.5 Hz) 4.86 (1H, ddd, J = 8.5, 8.5, 5.4 Hz) 3.77 (3H, s) 1.91-1.62 (3H, m) 1.02 (3H, d, J = 6.3 Hz) 0.98 (3H, d, J = 6.4 Hz).

***N*-(2-Iodobenzoyl)-(*S*)-valine-OMe (3d).** Following the general procedure B, 2-iodobenzoic acid (4.96 g, 20.0 mmol) was coupled with (*S*)-valine methyl ester hydrochloride salt (20.0 mmol). After crystallization from ethyl acetate/*n*-hexane, *N*-(2-iodobenzoyl)-(*S*)-valine-OMe (6.65 g, 92%) was obtained as a white solid: mp 112.7-113.2 °C, analytical TLC on silica gel, 1:1 *n*-hexane/ethyl acetate, R_f = 0.45. IR (KBr, cm^{-1}): 3276, N-H; 1737, C=O (ester); 1644, C=O (amide). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.89 (1H, d, J = 7.9 Hz) 7.44-7.37 (2H, m) 7.15-7.09 (1H, m) 6.30 (1H, br d, J = 8.9 Hz) 4.78 (1H, dd, J = 8.9, 4.1 Hz) 3.79 (3H, s) 2.38-2.99 (1H, m) 1.08 (3H, d, J = 6.6 Hz) 1.00 (3H, d, J = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 172.04, 168.92, 141.75, 139.95, 131.22, 128.31, 128.09, 92.21, 57.48, 52.22, 31.46, 19.06, 17.94.

***N*-(2-Iodobenzoyl)-(*S*)-phenylglycine-OMe (3e).** Following the general procedure B, 2-iodobenzoic acid (4.96 g, 20.0 mmol) was coupled with (*S*)-phenylglycine methyl ester hydrochloride salt (10.0 mmol). After crystallization from ethyl acetate/*n*-hexane, *N*-(2-iodobenzoyl)-(*S*)-phenylglycine-OMe (3.50 g, 89%) was obtained as a white needle: mp 155.4-155.9 °C, analytical TLC on silica gel, 1:1 *n*-hexane/ethyl acetate, R_f = 0.55. IR (KBr, cm^{-1}): 3308, N-H; 1749, C=O (ester); 1647, C=O (amide). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.80 (1H, d, J = 7.6 Hz) 7.41-7.29 (7H, m) 7.06-7.02 (1H, m) 6.75 (1H, br d, J = 7.2 Hz) 5.17 (1H, d, J = 7.2 Hz) 3.70 (3H, s) 2.38-2.99 (1H, m) 1.08 (3H, d, J = 6.6 Hz) 1.00 (3H, d, J = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 170.97, 168.23, 140.98, 140.03, 136.00, 131.38, 128.95, 128.64,

128.53, 128.08, 127.45, 92.29, 56.83, 52.89. Anal. calcd for C16H14INO3: C, 48.63; H, 3.57; N, 3.54. Found: C, 48.92; H, 3.57; N, 3.51.

Preparation of dimethyldioxirane. A 500 mL three-necked round-bottomed flask containing a mixture of water (40 ml), acetone (26 mL, 0.354 mol), sodium bicarbonate (24 g), and a magnetic stirring bar, was equipped with an addition funnel for solid containing potassium monoperoxy sulfate (50 g, 0.082 mol), and a receiving flask, cooled by means of dry ice-acetone. While applying a slight vacuum (ca.180 Torr, water aspirator), the potassium monoperoxy sulfate was added in one portion, stirring vigorously at room temperature. The yellow dimethyldioxirane-acetone solution (15 mL, 0.1 M) was collected in the receiving flask.

General procedure C for preparation of amino acid-derived IBX amide[8a]

A freshly prepared 0.1 M solution of dimethyldioxirane in acetone (30.0 mL, 3.0 mmol) was added to a stirred solution of *N*-(2-iodobenzoyl) amino acid methyl ester (1.0 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C. The reaction mixture was further stirred at room temperature for an additional 8 h, then the resulting white microcrystalline precipitate was collected by filtration, washed with ether (2x5 mL) and CH_2Cl_2 (2x5 mL), and dried in vacuum to afford analytically pure amino acid -derived IBX amide.

(*S*)-Alanine-IBX amide (2a). According to the general procedure C, *N*-(2-Iodobenzoyl)-(*S*)-alanine-OMe (**2a**) (0.33 g, 1 mmol) was employed to produce (*S*)-alanine-IBX amide (0.2678 g, 73%): mp 151.6-152.0 °C (dec.) (Lit 153 °C dec)[8a]. $[\alpha]^{28}_D$ -45 (*c* 0.027, CH_3CN), Lit $[\alpha]^{rt}_D$ -48 (*c* 0.0010, CH_3CN)[8a]. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 9.60 (1H, d, J = 7.2 Hz) 8.31 (1H, d, J = 7.2 Hz) 8.30 (1H, d, J = 7.4 Hz) 7.94 (1H, t, J = 7.6 Hz) 7.75 (1H, t, J = 7.3 Hz) 4.64 (1H, qd, J = 7.3, 7.2 Hz) 3.67 (3H, s) 1.47 (3H, d, 7.3 Hz).

(*S*)-Phenylalanine-IBX amide (2b). According to the general procedure C, *N*-(2-Iodobenzoyl)-(*S*)-phenylalanine-OMe (**3b**) (0.41 g, 1 mmol) was employed to produce (*S*)-phenylalanine-IBX-amide (0.1452 g, 33%): mp 150.1-151.2 °C (dec.) (Lit 156 °C dec)[8a]. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 9.66 (1H, br d, J = 7.6 Hz) 8.27 (1H, d, J = 7.6 Hz) 8.25 (1H, d, J = 7.6 Hz) 7.94 (1H, t, J = 7.6 Hz) 7.75 (1H, dd, J = 7.6 Hz) 7.32-7.15 (5H, m) 4.78-4.68 (1H, br) 3.66 (3H, s) 3.26-3.11 (2H, m).

(*S*)-Leucine-IBX amide (2c). According to the general procedure C, *N*-(2-Iodobenzoyl)-(*S*)-leucine-OMe (**3c**) (0.3752 g, 1 mmol) was employed to produce (*S*)-leucine-IBX amide (0.2892 g, 71%): mp 160.7-161.1 °C (dec.) (Lit 170 °C dec)[8a]. ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 9.52 (1H, d, J = 7.7 Hz) 8.31 (1H, d, J = 7.8 Hz) 8.29 (1H, d, J = 7.3 Hz) 7.96 (1H, t, J = 7.7 Hz) 7.77 (1H, t, J = 7.4 Hz) 4.63-4.57 (1H, m) 3.67 (3H, s) 1.88-1.82 (1H, m) 1.66-1.63 (2H, m) 0.92 (3H, d, J = 5.8 Hz) 0.88 (3H, d, J = 5.9 Hz).

(*S*)-Valine-IBX amide (2d). According to the general procedure C, *N*-(2-Iodobenzoyl)-(*S*)-valine-OMe (**3d**) (0.3622 g, 1 mmol) was employed to produce (*S*)-valine-IBX amide (0.1036 g, 26%): mp 153.8-154.0 °C (dec.). $[\alpha]^{28}_D$ -41 (*c* 0.021, CH_3CN). IR (KBr, cm^{-1}): 3422, 3237, N-H; 1746, C=O (ester); 1617, C=O (amide). ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 9.40 (1H, d, J =

7.9 Hz) 8.40 (1H, d, J = 7.6 Hz) 8.28 (1H, d, J = 7.3 Hz) 7.95 (1H, t, J = 7.3 Hz) 7.76 (1H, t, J = 7.5 Hz) 4.38 (1H, dd, J = 7.9, 7.9 Hz) 3.67 (3H, s) 2.30-2.19 (2H, m) 0.99 (3H, d, J = 6.6 Hz) 0.95 (3H, d, J = 6.7). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ 171.43, 166.61, 149.39, 133.24, 131.37, 128.06, 127.85, 123.19, 59.23, 52.00, 29.64, 19.12. Molecular ion calcd. for $C_{13}H_{16}INO_5$ (M^+): 393.0073; found (ESI) 393.0071.

(*S*)-Phenylglycine-IBX amide (2e). According to the general procedure C, *N*-(2-Iodobenzoyl)-(*S*)-phenylglycine-OMe (**3e**) (0.3952 g, 1 mmol) was employed to produce (*S*)-phenylglycine-IBX amide (0.2596 g, 61%): mp 139.7-140.5 ^{o}C (dec.). $[\alpha]^{28}_{D}$ +56 (*c* 0.018, CH_3CN). IR (KBr, cm^{-1}): 3405, 3229, N-H; 1741, C=O (ester); 1618, C=O (amide). ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 10.00 (1H, d, J = 7.2 Hz) 8.40 (1H, d, J = 7.6 Hz) 8.29 (1H, d, J = 7.7 Hz) 7.95 (1H, t, J = 7.4 Hz) 7.74 (1H, t, J = 7.6 Hz) 7.50 (2H, d, J = 7.2 Hz) 7.41-7.37 (3H, m) 5.80 (1H, d, J = 7.0 Hz) 3.69 (3H, s). ^{13}C NMR (75 MHz, DMSO-d_6, ppm) δ 170.31, 166.18, 149.46, 135.56, 133.37, 131.38, 128.70, 128.54, 128.38, 128.01, 127.91, 123.20, 57,16, 52.64. Molecular ion calcd. for $C_{16}H_{14}INO_5$ (M^+): 426.9917; found (ESI) 426.9914.

General procedure D for oxidation of racemic secondary alcohols with amino acid-derived IBX amide[8a]

Alcohol (2.0 equiv, based on oxidant) was added to a suspension mixture of the respective amino acid-derived IBX amide in $CDCl_3$ (2.0 mL). The flask was flushed with Ar, sealed with rubber septum and stirred at RT (for reaction time see details in each reaction) . The mixture was then passed through a pad of silica gel (3 cm) suspended in a pasteur pipet, and eluted with $CDCl_3$ (2.5 mL) to remove the spent oxidant. The solvent was removed, and the ^{1}H NMR was recorded to determine the conversion (% yield). The residue was purified by column chromatography on silica gel (3:2 *n*-hexane/CH_2Cl_2 as eluent). The enantiomeric excess (%ee) of the remaining alcohol was determined by analytical HPLC on chiral column.

Oxidation of 1-phenyl-1-ethanol (1a). 1-Phenyl-1-ethanol (20 mg, 163.7 μmol) was reacted with reagent **2a-2e** according to the general procedure D for 24 h.

Oxidation of 1-phenyl-1-propanol (1b). 1-Phenyl-1-propanol (20 mg, 146.8 μmol) was reacted with reagent **2a-2e** according to the general procedure D for 48 h.

Oxidation of phenyl isopropyl carbinol (1c). Phenyl isopropyl carbinol (20 mg, 133 μmol) was reacted with reagent **2a-2e** according to the general procedure D for 48 h.

Oxidation of phenyl *n*-butyl carbinol (1d). Phenyl *n*-butyl carbinol (20 mg, 121.8 μmol) was reacted with reagent **2a-2e** according to the general procedure D for 48 h.

Oxidation of mesityl methyl carbinol (1e). Mesityl methyl carbinol (20 mg, 121.8 μmol) was reacted with reagent **2a-2e** according to the general procedure D for 48 h.

HPLC analysis. HPLC analysis for enantiomeric excess determination was performed on an Agilent technologies HP-1100 system on chiral column using HPLC grade isopropanol (IPA) and hexane with rate at 1 mL/min

Table 3

Alcohol	Column	Reaction time (min)
1a	CHIRALCEL OD-H 3% IPA/Hexane	10.1 and 13.1
1b	CHIRALCEL OD-H 3% IPA/Hexane	16.0 and 23.5
1c	CHIRALCEL OD-H 3% IPA/Hexane	13.4 and 16.7
1d	CHIRALCEL OD-H 3% IPA/Hexane	14.7 and 19.6
1e	CHIRALCEL OD-H 3% IPA/Hexane	15.0 and 16.5

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