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Novel Stereoselective Synthesis of Functionalized Oxazolidinones from Chiral Aziridines†

Chan Sun Park, Min Sung Kim, Tae Bo Sim, Do Kyu Pyun,‡ Cheol Hae Lee,‡ Daeock Choi,§ and Won Koo Lee*

Department of Chemistry, Sogang University, Seoul 121-742, Korea

Jae-Won Chang and Hyun-Joon Ha*

ChemBioNex, HUFS BI, Wangsan, Yongin, Kyunggi 449-791, Korea

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Enantiomerically pure *N*-(*R*)-α-methylbenzyl-4(*R*)-(chloromethyl)oxazolidinones (4*R*)-**5a**−**k** were synthesized in one step and high yields from various aziridine-2-methanols (*S*)-**2a**−**k** by intramolecular cyclization with phosgene. The α-methylbenzyl substituent on the nitrogen was easily cleaved to give both enanatiomers of 4-(chloromethyl)oxazolidinones (*R*)-**7a** and (*S*)-**7a**. (*R*)-**7a** was used for the efficient syntheses of (L)-homophenylalaninol analogues (*S*)-**12a**−**j**. We also applied the same methodology to prepare oxazolidinones **9a**−**c** containing a heteroatom-substituted alkyl group at C-4 in high yields.

I. Introduction

α-Amino acids and their derivatives continue to attract much attention because of the biological and biochemical properties, prompting many organic chemists to develop useful and enantioselective methods for the synthesis of various structurally modified α-amino acids.[1,2] Chiral oxazolidinones are prepared from α-amino acids, and functionalized chiral oxazolidin-2-ones have been used as versatile chiral synthons in asymmetric syntheses of biologically active compounds or their synthetic intermediates.[3] They are also used as chiral auxiliaries in many important asymmetric syntheses[4] and as biologically active compounds themselves.[5] Especially, an enantiomerically pure 4-(halomethyl)oxazolidin-2-one has played a key role as an alanine or alaninol synthon in the synthesis of (−)-Slaframine,[6] nonprotein α-amino acid derivatives such as *E*- or *Z*-*β*,*γ*-unsaturated amino alcohols,[7] silicon-containing alanines,[8] and chiral *β*-amido alkylzinc iodides.[9] Also, chiral oxazolidinones functionalized at the 4- and 5-position are very useful and generally applicable in organic and medicinal chemistry

† In memory of the late Professor Henry Rapoport.

‡ Korea Research Institute of Chemical Technology.

§ Sunchon National University.

(1) (a) Williams, R. M. *Synthesis of Optically Active* α*-Amino Acids*; Pergamon Press: Oxford, 1989. (b) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539.

(2) (a) Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816. (b) Izumi, Y.; Chibata, I.; Itoh, T. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 176.

(3) (a) Bach, J.; Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee, H. J.; Smith, A. D. *Tetrahedron Lett.* **1999**, *40*, 6677. (b) O'Hagan, D.; Tavasli, M. *Tetrahedron: Asymmetry* **1999**, *10*, 1189. (c) Lohray, B. B.; Baskaran, S.; Rao, B. S.; Reddy, B. Y.; Rao, I. N. *Tetrahedron Lett.* **1999**, *40*, 4855. (d) Barbachyn, M. R.; Hutchinson, D. K.; Brickner, S. J.; Cynamon, M. H.; Kilburn, J. O.; Klemens, S. P.; Glickman, S. E.; Grega, K. C.; Hendges, S. K.; Toops, D. S.; Ford, C. W.; Zurenko, G. E. *J. Med. Chem.* **1996**, *39*, 680. (e) Brickner, S. J.; Hutchinson, D. K.; Barbachyn, M. R.; Manninen, P. R.; Ulanowicz, D. A.; Garmon, S. A.; Grega, K. C.; Hendges, S. K.; Toops, D. S.; Ford, C. W.; Zurenko, G. E. *J. Med. Chem.* **1996**, *39*, 673. (f) Grega, K. C.; Barbachyn, M. R.; Brickner, S. J.; Mizsak, S. A. *J. Org. Chem.* **1995**, *60*, 5255. (g) Seneci, P.; Caspani, M.; Ripamonti, F.; Ciabatti, R. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2345. (h) Park, C.-H.; Brittelli, D. R.; Wang, C. L.-J.; Marsh, F. D.; Gregory, W. A.; Wuonola, M. A.; McRipley, R. J.; Eberly, V. S.; Slee, A. M.; Forbes, M. *J. Med. Chem.* **1992**, *35*, 1156. (i) Gregory, W. A.; Brittelli, D. R.; Wang, C. L.-J.; Kezar, H. S.; Carlson, R. K.; Park, C.-H.; Corless, P. F.; Miller, S. J.; Rajagopalan, P.; Wuonola, M. A.; McRipley, R. J.; Eberly, V. S.; Slee, A. M.; Forbes, M. *J. Med. Chem.* **1990**, *33*, 2569. (j) Gregory, W. A.; Brittelli, D. R.; Wang, C. L.-J.; Wuonola, M. A.; McRipley, R. J.; Eustice, D. C.; Eberly, V. S.; Bartholomew, P. T.; Slee, A. M.; Forbes, M. *J. Med. Chem.* **1989**, *32*, 1673.

(4) (a) Friestad, G. K.; Qin, J. *J. Am. Chem. Soc.* **2000**, *122*, 8329. (b) Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee, H. J.; Smith A. D. *Tetrahedron: Asymmetry* **2000**, *11*, 3475. (c) Bravo, P.; Fustero, S.; Guidetti, M.; Volonterio, A.; Zanda, M. *J. Org. Chem.* **1999**, *64*, 8731−8735. (d) Bull, S. D.; Davies, S. G.; Jones, S.; Sanganee, H. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 387−398. (e) Davies, S. G.; Sanganee, H. J.; Szolcsanyi, P. *Tetrahedron* **1999**, *55*, 3337−3354. (f) Reddy, G. V.; Rao, G. V.; Iyengar, D. S. *Chem. Commun.* **1999**, 317. (g) Regan, A. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 357. (h) Gibson, C. L.; Gillon, K.; Cook, S. *Tetrahedron Lett.* **1998**, *39*, 6733. (i) Fonquerna, S.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1685. (j) Lützen, A.; Köll, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1193. (k) Lützen, A.; Köll, P. *Tetrahedron: Asymmetry* **1997**, *8*, 29. (l) Ager, D. J.; Prakash, I.; Schaad, D. R. *Aldrichim. Acta* **1997**, *30*, 3. (m) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835. (n) Köll, P.; Lützen, A. *Tetrahedron: Asymmetry* **1996**, *7*, 637. (o) Evans, D. A. *Aldrichim. Acta* **1982**, *15*, 23.

(5) (a) Jandu, K. S.; Barrett V.; Brockwell, M.; Cambridge, D.; Farrant, D. R.; Foster, C.; Giles, H.; Glen, R. C.; Hill, A. P.; Hobbs, H.; Honey, A.; Martin, G. R.; Salmon, J.; Smith, D.; Woollard, P.; Selwood, D. L. *J. Med. Chem.* **2001**, *44*, 681. (b) Iwama, S.; Segawa, M.; Fujii, S.; Ikeda, K.; Katsumura, S. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3495 (c) Brickner, S. J.; Hutchinson, D. K.; Barbachyn, M. R.; Manninen, P. R.; Ulanowicz, D. A.; Garmon, S. A.; Grega, K. C.; Hendges, S. K.; Toops, D. S.; Ford, C. W.; Zurenko, G. E. *J. Med. Chem.* **1996**, *39*, 673. (d) Barbachyn, M. R.; Hutchinson, D. K.; Brickner, S. J.; Cynamon, M. H.; Klemens, S. P.; Glickman S. E.; Grega, K. C.; Hendges, S. K.; Toops, D. S.; Ford, C. W.; Zurenko, G. E. *J. Med. Chem.* **1996**, *39*, 680.

(6) Sibi, M. P.; Christensen, J. W.; Li, B.; Renhowe, P. A. *J. Org. Chem.* **1992**, *57*, 4329.

(7) Sibi, M. P.; Renhowe, P. A. *Tetrahedron Lett.* **1990**, *35*, 7407.

(8) Sibi, M. P.; Harris, B. J.; Shay J. J.; Hajra, S. *Tetrahedron* **1998**, *54*, 7221.

(9) Duddu, R.; Eckhardt, M.; Furlong, M.; Knoess, H. P.; Berger, S.; Knochel, P. *Tetrahedron* **1994**, *50*, 2415.

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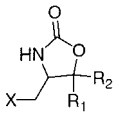
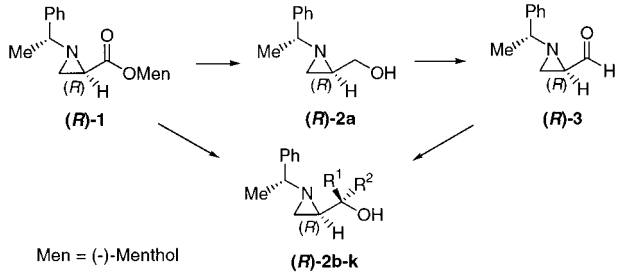


Functionalized Oxazolidin-2-one

FIGURE 1.

SCHEME 1



(Figure 1). Despite their various usefulness and general applicability, there are only a few preparative methods available from L- and D-serine,[6−8,10] *N*-sulfonylated allylic carbamates,[11] amino alcohols,[12] a chiral aziridine,[13] and allylic amine.[14] The requirement of a more efficient preparative pathway to enantiomerically pure functionalized oxazolidinones prompted us to develop a new efficient synthetic route.

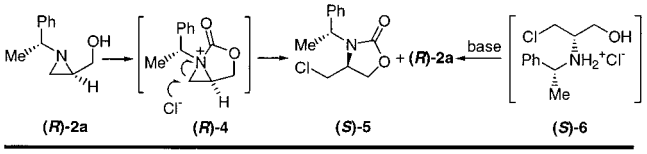
In this report we describe a novel efficient preparative pathway to enantiomerically pure functionalized oxazolidinones from aziridine-2(*S*)- and 2(*R*)-methanols.

II. Results and Discussion

Recently, we reported the preparation and elaboration of enantiomerically pure aziridine-2(*S*)- and 2(*R*)-carboxylates obtained from the reaction of optically pure α-methylbenzylamine and ethyl 2,3-dibromopropionate.[15] However, if we use the commercially available aziridine-2(*R*)-carboxylate (*R*)-**1** various aziridine-2(*R*)-methanols (*R*)-**2a**−**k** are readily available from organometallic addition to the corresponding aziridine-2(*R*)-carboxaldehyde (*R*)-**3** and directly to the aziridine-2(*R*)-carboxylate (*R*)-**1** (Scheme 1).[16]

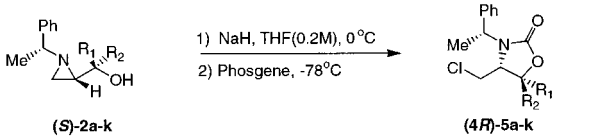
Since we observed highly regioselective nucleophilic ring opening of aziridine-2-methanols in the presence of proton or Lewis acid, we selected phosgene as the intramolecular cyclizing agent of the amino alcohol moiety to form a cyclic carbamate with regioselective ring opening of the aziridine by the chloride ion. However, the reaction of phosgene with the enantiomerically pure aziridine 2(*R*)-methanol (*R*)-**2a** provided a mixture of the oxazolidinone (*S*)-**5** through the bicyclic intermediate (*R*)-**4** and the recovered starting material (*R*)-**2a**. The recovered starting material (*R*)-**2a** might have been formed from base workup of the quaternary ammonium salt (*S*)-**6** which originated from ring opening of the aziridine-2(*R*)-methanol (*R*)-**2a** by in situ generated HCl. We varied equivalents of phosgene, bases, reaction solvents, and reaction temperatures to obtain the optimum condition for the 4(*S*)-chloromethyloxazolidin-2-one (*S*)-**5**. We found that the elimination of HCl generated in situ by treating (*R*)-**2a** with NaH and 2 equiv of phosgene in THF at − 78 to 0 °C (entry 6) provided the best result in terms of selectivity and yield (Scheme 2).

SCHEME 2



entry	phosgene (eq.)	solvent	temp.	base	yield(%) (*S*)-5	yield(%) (*R*)-2a
1	2.0	CH_2Cl_2	0 °C	-	51	40
2	1.0	CH_2Cl_2	0 °C	-	55	34
3	2.0	CH_2Cl_2	-78 °C	TEA	67	23
4	1.0	Hexane	-78 °C	-	76	12
5	2.0	Hexane	-78 °C	TEA	77	10
6	2.0	THF	-78 °C to 0 °C	NaH	89	trace

SCHEME 3

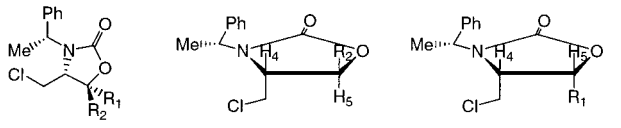


entry	R_1	R_2	yield(%)
a	H	H	89
b	Me	Me	92
c	Ph	Ph	83
d	H	Me	91
e	H	*n*-Bu	84
f	H	*t*-Bu	90
g	H	Ph	88
h	H	*p*-F-Ph	85
i	H	*m*-tolyl	90
j	H	vinyl	89
k	vinyl	H	80

We applied the optimized reaction condition to various aziridine-2(*S*)-methanols (*S*)-**2a**−**k**, which were prepared from nucleophilic additions to the corresponding aziridine-2(*S*)-carboxaldehyde, to prepare 4(*R*)-(chloromethyl)-5-substituted-2-oxazolidinones (4*R*)-**5a**−**k** in good yields in one step (Scheme 3). Even with a bulky tertiary alcohol containing diphenyl group, we obtained the corresponding oxazolidinone (4*R*)-**5c** in 83% yield (entry c). The absolute configuration at C-4 of 4,5-disubstituted 2-oxazolidinones was indirectly established by measuring the coupling constants of the two vicinal protons at C-4 and C-5. It is well-known that the coupling constant of *cis*-4,5-disubstituted 2-oxazolidinone is ∼7.5 Hz, whereas that of the *trans*-isomer is ∼4.5 Hz.[14] The coupling

(10) Sibi, M. P.; Li, B. *Tetrahedron Lett.* **1992**, *29*, 4115.
(11) Hirama, M.; Iwashita, M.; Yamazaki, Y.; Itô, S. *Tetrahedron Lett.* **1984**, *25*, 4963.
(12) Gabriele, B.; Salerno, G.; Brindisi, D.; Costa, M.; Chiusoli, G. P. *Org. Lett.* **2000**, *2*, 625
(13) Lucarini, S.; Tomasini, C. *J. Org. Chem.* **2001**, *66*, 727.
(14) Cardillo, G.; Orena, M.; Sandri, S. *J. Org. Chem.* **1986**, *51*, 713.
(15) Lim, Y.; Lee, W. K. *Tetrahedron Lett.* **1995**, *36*, 8431.
(16) Hwang, G.; Chung, J.; Lee, W. K. *J. Org. Chem.* **1996**, *61*, 6183. Both 2(*R*)- and 2(*S*)-aziridinecarboxylic acid menthol esters are available from ChemBioNex.

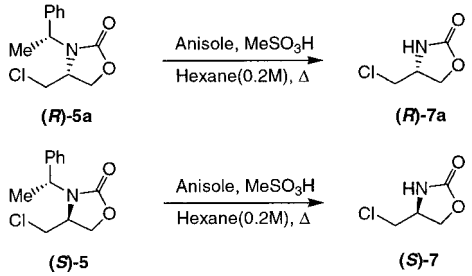
SCHEME 4



(4*R*)-5g-k | *trans*-isomer (~4.5 Hz) | *cis*-isomer (~7.5 Hz)

compound	R_1	R_2	$J_{4,5}$ (Hz)
(4*R*)-5g	H	Ph	3.0
(4*R*)-5h	H	*p*-F-Ph	3.1
(4*R*)-5i	H	*m*-tolyl	3.2
(4*R*)-5j	H	vinyl	3.5
(4*R*)-5k	vinyl	H	8.0

SCHEME 5



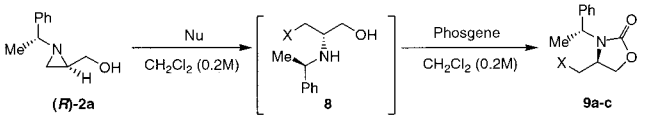
constants of (4*R*)-**5g** (3.0 Hz), (4*R*)-**5h** (3.1 Hz), and (4*R*)-**5i** (3.2 Hz) for the $J_{4,5}$ were consistent with the assigned *trans* configuration. Comparison of the coupling constants of (4*R*)-**5j** (3.5 Hz) and (4*R*)-**5k** (8.0 Hz) clearly indicates the difference between *cis*- and *trans*-4,5-disubstituted oxazolidinones (Scheme 4).

The benzyl group on the nitrogen was successfully removed by refluxing *N*-benzyl compounds [(*R*)-**5a** and (*S*)-**5**] in the presence of anisole and CH_3SO_3H in hexane to provide the free 4-(chloromethyl)oxazolidin-2-ones (*R*)-**7a** and (*S*)-**7** in almost quantitative yields (Scheme 5).[17]

We recently reported the introduction of various heteroatom nucleophiles at C-3 of the aziridine-2(*R*)-methanol (*R*)-**2a** by highly regioselective ring opening reaction with HOAc,[18] HSPh,[19] and $TMSN_3$.[20] We applied the same protocol to prepare oxazolidinones containing heteroatoms such as 4-acetyloxymethyl [(*R*)-**9a**], phenylthiomethyl [(*S*)-**9b**], and azidomethyl [(*R*)-**9c**] in high yields (Scheme 6).

Once we had enantiomerically pure 4(*R*)-(chloromethyl)-2-oxazolidinone (*R*)-**7a** in hand we utilized it for the synthesis of homophenylalanine and its analogues. The preparation of enantiomerically pure homophenylalanine has been accomplished by using alkenyl boronic acid,[21] organozinc,[22] allylic amination,[23] Rh-catalyzed asymmetric hydrogenation,[24] and Friedel−Crafts acylation.[25] Since each of the methods has room for improvement in terms of yield and stereoselectivity, we applied

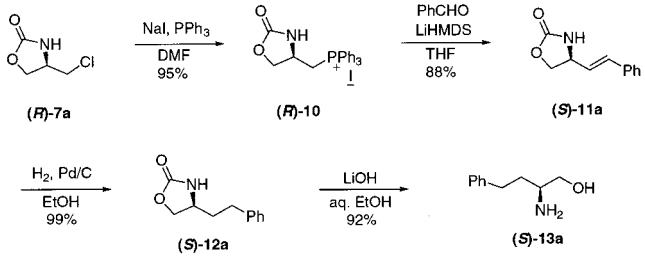
SCHEME 6



entry	Nu	X	*yield(%) of 9
a	HOAc	OAc	90
b	HSPh	SPh	93
c	$TMSN_3$	N_3	96

*Two step yield

SCHEME 7



the easily accessible 4(*R*)-(chloromethyl)-2-oxazolidinone (*R*)-**7a** for the synthesis of various aryl-substituted homophenylalaninols.

The 4(*R*)-(chloromethyl)-2-oxazolidinone (*R*)-**7a** was converted to the corresponding phosphonium salt (*R*)-**10** in 95% yield by stirring with NaI and PPh_3 in DMF at 100 °C for 24 h.[7] Treatment of the phosphonium salt with LiHMDS at −78 °C generated the ylide which was then reacted with benzaldehyde to provide the *E* alkene (*S*)-**11a** exclusively (*E*:*Z* = 99:1) in 88% yield.[7,26] The alkene (*S*)-**11a** was reduced by catalytic hydrogenation (5% Pd/C, H_2, EtOH, rt, 12 h, 99%) to give the 4(*S*)-phenylethyl-substituted oxazolidin-2-one (*S*)-**12a** which was hydrolyzed in aqueous EtOH by LiOH to provide the corresponding (L)-homophenylalaninol (*S*)-**13a** in 92% yield (Scheme 7).[27]

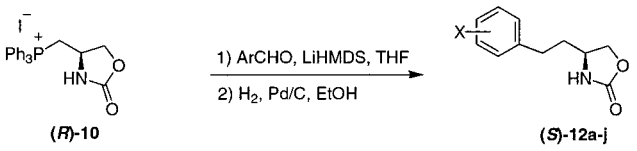
We prepared various homophenylalaninol precursors (*S*)-**12a**−**j** using this protocol with substituted benzaldehydes under the same reaction condition, and the results are summarized in Scheme 8.

IV. Conclusion

In summary, we have developed a novel methodology to prepare functionalized oxazolidin-2-ones from a com-

(17) Sugiyama, S.; Morishita, K.; Ishii, K. *Heterocycles* **2001**, *55*, 353.
(18) Choi, S.; Lee, J.; Kim, J.; Lee, W. K. *J. Org. Chem.* **1997**, *62*, 743.
(19) Bae, J.; Shin, S.; Park, C. S.; Lee, W. K. *Tetrahedron* **1999**, *55*, 10041.
(20) Shin, S.; Han, E. Y.; Park, C. S.; Lee, W. K.; Ha, H. *Tetrahedron: Asymmetry* **2000**, *11*, 3293.
(21) Petasis, N. A.; Zavialov, I. A. *J. Am. Chem. Soc.* **1997**, *119*, 445. (b) Petasis, N. A.; Zavialov, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 11798.
(22) Jackson, R. F. W.; Moore, R. J.; Dexter, C. S. *J. Org. Chem.* **1998**, *63*, 7875. (b) Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Turner, D. J. *J. Org. Chem.* **1995**, *60*, 2210. (c) Jackson, R. F. W.; Wishart, N.; Wood, A.; James, K.; Wythes, M. J. *J. Org. Chem.* **1992**, *57*, 3397.
(23) Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 6761.
(24) (a) RajanBabu, T. V.; Ayers, T. A.; Halliday, G. A.; You, K. K.; Calabrese, J. C. *J. Org. Chem.* **1997**, *62*, 6012. (b) Li, X.; Yeung, C.; Chan, A. S. C.; Lee, D.; Yang, T. *Tetrahedron: Asymmetry* **1999**, *10*, 3863.
(25) Xu, Q.; Wang, G.; Wang, X.; Wu, T.; Pan, X.; Chan, A. S. C.; Yang, T. *Tetrahedron: Asymmetry* **2000**, *11*, 2309.
(26) Sibi, M. P.; Renhowe, P. A. *Tetrahedron Lett.* **1990**, *31*, 7407.
(27) (a) Bertozzi, C. R.; Hoeprich, P. D.; Bednarski, M. D. *J. Org. Chem.* **1992**, *57*, 6092. (b) Sibi, M. P.; Li, B. *Tetrahedron Lett.* **1992**, *33*, 4115.
(28) Combret, Y.; Duflos, J.; Dupas, G.; Bourguignon, J.; Queguiner, G. *Tetrahedron: Asymmetry* **1993**, *4*, 1635.

SCHEME 8



entry	X	yield of (*S*)-12 (%)
a	H	87
b	2-Me	84
c	4-CF_3	79
d	4-MeO	76
e	3,4,5-tri-MeO	79
f	4-CN	80
g	4-Cl	86
h	2,4-di-F	74
i	*3-NH_2	67
j	4-$N(Me)_2$	80

*Obtained from 3-Nitrobenzaldehyde

mercially available enantiomerically pure aziridine-2-carboxylate and aziridine-2-carboxaldehyde through organometallic addition followed by intramolecular cyclization of the amino alcohol moiety with regiospecific ring opening of the aziridine with phosgene. We have also developed an efficient pathway for the preparation of enantiomerically pure (L)-homophenylalaninol and its analogues using a Wittig reaction and catalytic hydrogenation from 4(*R*)-(chloromethyl)-2-oxazolidinone. Using the same protocol the (D)-homophenylalaninol analogues can be also available starting from the 4(*S*)-(chloromethyl)-2-oxazolidinone.

V. Exerimental Section

General. Flash chromatography was performed with 230−400 mesh silica gel. Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained on 200, 300, and 500 MHz spectrometers. NMR spectra were recorded in ppm (δ) related to tetramethylsilane ($\delta = 0.00$) as an internal standard unless stated otherwise and are reported as follows; chemical shift, multiplicity (br = broad, s = singlet, t = triplet, q =quartet, m = multiplet), coupling constant, and integration. Elemental analyses were performed by an elemental analyzer. Optical rotations were obtained on a digital polarimeter. Data are reported as follow: $[\alpha]^{25}_D$ (concentration g/100 mL, solvent). Solvents and liquid reagents were transferred using hypodermic syringes. All other reagents and solvents used were reagent grade. All glassware was dried in an oven at 150 °C prior to use. Methylene chloride and triethylamine were dried over calcium hydride prior to use. Small and medium scale purifications were performed by flash chromatography.

Preparation of 4(*S*)-(Chloromethyl)-3-(1′(*R*)-α-methylbenzyl)oxazolidin-2-one (*S*)-5. To a solution of [1-(1′(*R*)-α-methylbenzyl)aziridin-2(*R*)-yl]methanol (*R*)-**2a** (100 mg, 0.564 mmol) in 2.82 mL of THF under nitrogen atmosphere was added a 60% oil dispersion of NaH (68 mg, 1.693 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C and then cooled to −78 °C. To the mixture was slowly added phosgene solution (0.60 mL, 1.13 mmol, 1.89 M in toluene) at −78 °C. The mixture was stirred for 2 h at −78 °C then quenched with water and warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a white solid which was purified by silica gel flash chromatography with 15% EtOAc/hexane to give 119 mg (88%) of (*S*)-**5** as a white solid. mp = 83−84 °C; $[\alpha]^{28}_D$ = −13.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.32 (m, 5H), 5.21 (q, *J* = 7.3 Hz, 1H), 4.36−4.19 (m, 2H), 3.68−3.64 (m, 1H), 3.52 (dd, *J* = 3.5, 11.7 Hz, 1H), 3.48 (dd, *J* = 6.8, 11.2 Hz, 1H), 1.68 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 138.4, 128.9, 128.2, 127.2, 65.6, 54.5, 52.6, 45.1, 18.5. Anal. Calcd for $C_{12}H_{14}ClNO_2$: C, 60.13; H, 5.89; N, 5.84. Found: C, 60.14; H, 5.88; N, 5.89.

(4*R*)-5a. $[\alpha]^{29}_D$ = +104.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.30 (m, 5H), 5.17 (q, *J* = 7.1 Hz, 1H), 4.35 (t, *J* = 8.7 Hz, 1H), 4.20 (dd, *J* = 4.4, 9.1 Hz, 1H), 4.09−4.04 (m, 1H), 2.97 (dd, *J* = 3.4, 11.3 Hz, 1H), 2.93 (dd, *J* = 8.1, 11.3 Hz, 1H), 1.70 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 140.4, 128.7, 128.1, 126.9, 65.9, 54.0, 51.5, 44.2, 16.1. Anal. Calcd for $C_{12}H_{14}ClNO_2$: C, 60.13; H, 5.89; N, 5.84. Found: C, 60.08; H, 5.92; N, 5.83.

(4*R*)-5b. mp = 72−74 °C; $[\alpha]^{28}_D$ = +46.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.21 (m, 5H), 5.08 (q, *J* = 7.1 Hz, 1H), 3.55 (dd, *J* = 2.8, 8.7 Hz, 1H), 3.01 (dd, *J* = 2.8, 12.0 Hz, 1H), 2.89 (dd, *J* = 8.7, 12.0 Hz, 1H), 1.62 (d, *J* = 7.2 Hz, 3H), 1.39 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 140.6, 128.6, 127.9, 126.8, 79.9, 63.0, 51.6, 40.7, 28.8, 21.0, 16.3. Anal. Calcd for $C_{14}H_{18}ClNO_2$: C, 62.80; H, 6.78; N, 5.23. Found: C, 62.82; H, 6.82; N, 5.30.

(4*R*)-5c. mp = 209−210 °C; $[\alpha]^{26}_D$ = −171.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.14 (m, 15H), 4.98 (q, *J* = 6.8 Hz, 1H), 4.50 (dd, *J* = 4.4, 4.9 Hz, 1H), 2.92 (m, 2H), 1.51 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 142.5, 140.3, 137.5, 128.7, 128.6, 128.6, 128.4, 128.13, 128.12, 128.0, 127.1, 126.6, 125.7, 86.9, 63.4, 53.6, 42.8, 17.8. Anal. Calcd for $C_{24}H_{22}ClNO_2$: C, 73.56; H, 5.66; N, 3.57. Found: C, 73.59; H, 5.76; N, 3.44.

(4*R*)-5d. mp = 75−76 °C; $[\alpha]^{26}_D$ = −34.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.14 (m, 5H), 5.24 (q, *J* = 7.1 Hz, 1H), 4.39 (qd, *J* = 3.5, 6.3 Hz, 1H), 3.45 (m, *J* = 3.6 Hz, 1H), 2.83 (dd, *J* = 8.4, 11.2 Hz, 1H), 2.79 (dd, *J* = 3.7, 11.2 Hz, 1H), 1.61 (d, *J* = 7.1 Hz, 3H), 1.32 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 140.6, 128.8, 128.2, 127.0, 74.3, 60.6, 51.4, 43.9, 21.3, 16.2. Anal. Calcd for $C_{13}H_{16}ClNO_2$: C, 61.54; H, 6.36; N, 5.52. Found: C, 61.56; H, 6.43; N, 5.54.

(4*R*)-5e. mp = 93 °C; $[\alpha]^{26}_D$ = +28.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.21 (m, 5H), 5.12 (q, *J* = 7.2 Hz, 1H), 4.26 (m, 1H), 3.49 (m, 1H), 2.83 (dd, *J* = 8.5, 11.2 Hz, 1H), 2.78 (dd, *J* = 3.4, 11.3 Hz, 1H), 1.60 (d, *J* = 7.1 Hz, 3H), 1.64−1.50 (m, 3H), 1.42−1.25 (m, 3H), 0.84 (t, *J* = 7.0, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 140.6, 128.8, 128.2, 127.0, 77.8, 59.0, 51.5, 44.2, 35.1, 26.3, 22.3, 16.2, 13.8; HRMS Calcd for $C_{16}H_{22}ClNO_2$ 295.133907, found 295.133095.

(4*R*)-5f. mp = 120−121 °C; $[\alpha]^{27}_D$ = +18.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.23 (m, 5H), 5.10 (q, *J* = 7.1 Hz, 1H), 3.90 (d, *J* = 3.4 Hz, 1H), 3.69 (m, 1H), 2.85−2.84 (m, 2H), 1.62 (d, *J* = 7.1 Hz, 3H), 0.86 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 140.6, 128.7, 128.2, 127.2, 84.3, 55.0, 51.8, 45.1, 34.4, 24.5, 16.3; HRMS Calcd for $C_{16}H_{22}ClNO_2$: 295.133194, found: 295.133907.

(4*R*)-5g. mp = 92 °C; $[\alpha]^{26}_D$ = −33.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.18 (m, 10H), 5.28 (d, *J* = 3.0 Hz, 1H), 5.16 (q, *J* = 7.1 Hz, 1H), 3.70 (m, 1H), 2.98 (dd, *J* = 8.6, 11.4 Hz,1H), 2.85 (dd, *J* = 3.0, 11.4 Hz, 3H), 1.48 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 140.2, 138.9, 129.0, 128.9, 128.8, 128.4, 127.2, 125.0, 78.0, 62.2, 51.7, 44.0, 16.3. Anal. Calcd for $C_{18}H_{18}ClNO_2$: C, 68.46; H, 5.75; N, 4.44. Found: C, 68.44; H, 5.78; N, 4.43.

(4*R*)-5h. mp = 81−82 °C; $[\alpha]^{26}_D$ = −29.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.00 (m, 9H), 5.26 (d, *J* = 3.1 Hz, 1H), 5.16 (q, *J* = 7.1 Hz, 1H), 3.66 (m, 1H), 2.88 (dd, *J* = 8.9, 11.5 Hz, 1H), 2.84 (dd, *J* = 3.1, 11.4 Hz, 1H), 1.49 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 161.9, 157.1,

140.1, 134.8, 128.9, 128.5, 127.1, 127.0, 126.9, 116.1, 115.9, 77.4, 62.2, 51.8, 43.8, 16.3. Anal. Calcd for $C_{18}H_{17}ClFNO_2$: C, 64.77; H, 5.13; N, 4.20. Found: C, 64.75; H, 5.20; N, 4.21.

(4*R*)-5i. mp = 67−68 °C; $[\alpha]^{26}_D = -36.2°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.02 (m, 9H), 5.24 (d, J = 3.2 Hz, 1H), 5.14 (q, J = 7.1 Hz, 1H), 3.71 (m, 1H), 2.99 (dd, J = 8.5, 11.4 Hz, 1H), 2.87 (dd, J = 3.0, 11.4 Hz, 1H), 2.29 (s, 3H), 1.50 (J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 149.6, 140.2, 138.9, 138.8, 129.5, 128.8, 128.4, 127.2, 125.6, 122.1, 78.0, 62.2, 51.8, 44.0, 21.4, 16.3. Anal. Calcd for $C_{19}H_{20}ClNO_2$: C, 69.19; H, 6.11; N, 4.25. Found: C, 69.18; H, 6.17; N, 4.25.

(4*R*)-5j. mp = 81−82 °C; $[\alpha]^{26}_D = +17.8°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.23 (m, 5H), 5.80−5.74 (m, 1H), 5.39 (ddd, J = 0.8, 1.4, 16.5 Hz, 1H), 5.25 (dt, J = 0.9, 10.5 Hz,1H), 5.11 (q, J = 7.1 Hz, 1H), 4.73−4.71 (m, 1H), 3.57 (dt, J = 3.3, 8.5 Hz, 1H), 2.89 (dd, J = 8.5, 11.4 Hz, 1H), 2.8 (dd, J = 3.2, 11.4 Hz, 1H), 1.57 (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 140.3, 134.3, 128.8, 128.3, 127.1, 118.1, 77.5, 59.5, 51.6, 43.7, 16.2. Anal. Calcd for $C_{14}H_{16}ClNO_2$: C, 63.28; H, 6.07; N, 5.27. Found: C, 63.26; H, 6.14; N, 5.16.

(4*R*)-5k. mp = 96 °C; $[\alpha]^{27}_D = +66.8°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.23 (m, 5H), 5.99−5.92 (m, 1H), 5.47 (dt, J = 1.2, 17.2 Hz,1H), 5.37 (dt, J = 1.1, 10.6 Hz, 1H), 5.07 (q, J = 7.1 Hz, 1H), 4.92 (m, 1H), 3.97 (td, J = 2.6, 7.8 Hz, 1H), 2.99 (dd, J = 2.6, 11.8, 1H), 2.87 (dd, J = 7.8, 11.8 Hz, 1H), 1.66 (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 140.5, 129.7, 128.8, 128.2, 127.0, 121.2, 77.4, 58.1, 52.3, 40.8, 16.9; HRMS Calcd for $C_{14}H_{16}ClNO_2$: 265.086234, found: 265.086970.

Preparation of 4(*R*)-(Chloromethyl)oxazolidin-2-one (*R*)-7a. To a solution 4(*R*)-(Chloromethyl)-3-[1′(*R*)-α-methylbenzyl]oxazolidin-2-one (4*R*)-**5a** (70 mg, 0.29 mmol) in 1.5 mL of hexane under nitrogen atmosphere were added methanesulfonic acid (95 μL, 1.48 mmol) and anisole (79 μL, 0.73 mmol). The mixture was refluxed for 4 h and then cooled to room temperature. The reaction was quenched by 4 mL of saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product which was purified by silica gel flash chromatography with 15% EtOAc/hexane to give 39 mg (99%) of (*R*)-**7a** as a white solid. mp = 44−45 °C; $[\alpha]^{25}_D = +18.3°$ (*c* 10.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (s, HNCO), 4.53 (t, J = 8.7 Hz, 1H), 4.27 (dd, J = 4.6, 9.2 Hz, 1H), 4.19−4.14 (m, 1H), 3.60 (dd, J = 5.3, 11.3 Hz, 1H), 3.57 (dd, J = 6.2, 11.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 67.9, 53.2, 45.6. Anal. Calcd for $C_4H_6ClNO_2$: C, 35.44; H, 4.46; N, 10.33. Found: C, 35.45; H, 4.53; N, 10.28.

(*S*)-7. mp = 44−45 °C; $[\alpha]^{25}_D = -18.2°$ (*c* 10.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (s, HNCO), 4.53 (t, J = 8.7 Hz, 1H), 4.27 (dd, J = 4.6, 9.2 Hz, 1H), 4.19−4.14 (m, 1H), 3.60 (dd, J = 5.3, 11.3 Hz, 1H), 3.57 (dd, J = 6.2, 11.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 67.9, 53.2, 45.6. Anal. Calcd for $C_4H_6ClNO_2$: C, 35.44; H, 4.46; N, 10.33. Found: C, 35.48; H, 4.53; N, 10.29.

Preparation of Acetic Acid 2-Oxo-3-[1′(*R*)-α-methylbenzyl]oxazolidin-4(*R*)-yl Methyl Ester (*R*)-9a. To a solution 1-[(1′(*R*)-α-methylbenzyl)-aziridin-2(*R*)-yl]-methanol (*R*)-**2a** (240 mg, 1.35 mmol) in 6.77 mL of methylene chloride was added acetic acid (0.40 mL, 6.77 mmol). The mixture was stirred under a nitrogen atmosphere for 14 h at room temperature and then was quenched with 10 mL of saturated aqueous $NaHCO_3$ solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 10 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a yellow oil. To the solution of crude product in 6.80 mL of THF was slowly added phosgene solution (1.43 mL, 2.71 mmol, 1.89 M in toluene) at −78 °C. The mixture was stirred under a nitrogen atmosphere for 2 h at −78 °C and then quenched with water and warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a white solid which was purified by silica gel flash chromatography with 15% EtOAc/hexane to give 321 mg (90%) of (*R*)-**9a** as a white solid. mp = 64−66 °C; $[\alpha]^{25}_D = +25.3°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.21 (m, 5H), 5.10 (q, J = 7.2 Hz, 1H), 4.14 (t, J = 8.9 Hz, 1H), 4.03−3.99 (m, 2H), 3.93 (dd, J = 5.5, 11.7 Hz, 1H), 3.55 (m, 1H), 1.96 (s, 3H), 1.57 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 157.8, 138.6, 128.7, 127.9, 127.1, 65.0, 63.7, 52.54, 52.52, 20.4, 18.1. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.84; H, 6.63; N, 5.33.

Preparation of 3-[1′(*R*)-α-methylbenzyl]-4(*S*)-(phenylsulfanylmethyl)oxazolidin-2-one (*S*)-9b. To a solution 1-[(1′(*R*)-α-methylbenzyl)aziridin-2(*R*)-yl]methanol (*R*)-**2a** (150 mg, 0.846 mmol) in 4.20 mL of methylene chloride was added thiophenol (0.26 mL, 2.54 mmol). The mixture was stirred under a nitrogen atmosphere for 2 h at room temperature and then was quenched by 5 mL of saturated aqueous NaOH solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 10 mL). The combined extracts were dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a yellow oil. To the solution of crude product in 4.2 mL of THF was slowly added phosgene solution (0.90 mL, 1.69 mmol, 1.89 M in toluene) at −78 °C. The mixture was stirred under a nitrogen atmosphere for 2 h at −78 °C then quenched with water and warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a white solid which was purified by silica gel flash chromatography with 15% EtOAc/hexane to give 247 mg (93%) of (*S*)-**9b** as a white solid. mp = 58−59 °C; $[\alpha]^{24}_D = -65.4°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21−6.88 (m, 10H), 5.08 (q, J = 7.1 Hz, 1H), 4.12 (t, J = 8.7 Hz, 1H), 4.05 (dd, J = 5.1, 9.0 Hz, 1H), 3.46−3.41 (m, 1H), 3.13 (dd, J = 3.1, 13.6 Hz, 1H), 2.64 (dd, J = 10.5, 13.6 Hz, 1H), 1.57 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 138.1, 133.6, 129.2, 129.0, 128.7, 127.9, 127.2, 126.5, 66.7, 53.0, 52.3, 37.0, 18.7; HRMS Calcd for $C_{18}H_{19}NO_2S$: 313.113651, found: 313.113780.

Preparation of 4(*R*)-Azidomethyl-3-[1′(*R*)-α-methylbenzyl]oxazolidin-2-one (*R*)-9c. To a solution 1-[(1′(*R*)-α-methylbenzyl)aziridin-2(*R*)-yl]methanol (*R*)-**2a** (150 mg, 0.846 mmol) in 4.20 mL of methylene chloride was added azidotrimethylsilane (0.34 mL, 2.54 mmol). The mixture was stirred under a nitrogen atmosphere for 3 h at room temperature and then was quenched by 2 mL of 1 N H_2SO_4 solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 10 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a yellow oil. To the solution of the crude product in 4.20 mL of THF was slowly added phosgene solution (0.90 mL, 1.69 mmol, 1.89 M in toluene) at −78 °C. The mixture was stirred under a nitrogen atmosphere for 2 h at −78 °C. The reaction was quenched with water and warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). The combined extract was dried over $MgSO_4$, and the solvent was evaporated to give the crude product as a white solid which was purified by silica gel flash chromatography with 15% EtOAc/hexane to give 200 mg (96%) of (*R*)-**9c** as a colorless oil. $[\alpha]^{26}_D = -52.0°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.19 (m, 15H), 5.13 (q, J = 7.2 Hz, 1H), 4.08 (t, J = 8.9 Hz, 1H), 3.96 (dd, J = 4.5, 9.0 Hz, 1H), 3.46 (m, 1H), 3.34 (dd, J = 5.3, 12.8 Hz, 1H), 3.31 (dd, J = 3.8, 12.7 Hz, 1H), 1.58 (d, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 138.5, 128.5, 127.7, 126.8, 65.0, 53.0, 52.7, 52.5, 18.2. Anal. Calcd for $C_{12}H_{14}N_4O_2$: C, 58.53; H, 5.73; N, 22.75. Found: C, 58.55; H, 5.81; N, 22.74.

Preparation of [(4*R*)-2-Oxo-1,3-oxazolidin-4-yl]triphenylphosphonium Iodide (*R*)-10. To a solution of (*R*)-**7a** (56 mg, 0.41 mmol) in 2 mL of DMF was added NaI (93 mg, 0.61

mmol) and PPh_3 (1.0 g, 4.13 mmol). The reaction mixture was heated at 100 °C for 24 h and then cooled to room temperature. To the mixture was added ethyl ether to remove excess triphenylphosphine followed by washing with THF to afford a white solid (190 mg, 95%). mp 88−89 °C; $[\alpha]^{25}_D$ −11.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (D_2O, 200 MHz) δ 7.91−7.70 (m, 15H), 4.54−5.44 (m, 1H), 4.38 (t, J = 9.0 Hz, 1H), 4.03 (dd, J = 4.7, 9.0 Hz, 1H), 3.92 (dd, J = 6.1, 13.3 Hz, 1H), 3.81 (d, J = 6.1, 13.8 Hz, 1H); ^{13}C NMR (D_2O, 50 MHz) δ 157.6, 135.1, 133.4-(d), 130.3(d), 116.5(d), 68.9, 47.2, 27.8; HRMS(EI) calcd for $C_{22}H_{21}NO_2P$: 362.1309, found: 362.1310.

(4*S*)-4-[(*E*)-2-Phenylethenyl]-1,3-oxazolidin-2-one (*S*)-11a. To a suspension of (*R*)-**10** (120 mg, 0.24 mmol) in 2 mL of dry THF was added LiHMDS (1.0 M in THF, 0.52 mL) at −78 °C. The reaction mixture was stirred for 1 h at the same temperature and quenched with benzaldehyde (20.8 μL, 0.20 mmol). The resulting mixture was stirred for 2 h at room temperature and then quenched with 1 mL of sat. aqueous NH_4Cl. The mixture was extracted with EtOAc (3 × 3 mL). The combined organic extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica gel flash chromatography (EtOAc/*n*-hexane = 1/1) provided 34 mg (88%) of (*S*)-**11a** as white crystals. mp 139−140 °C; $[\alpha]^{25}_D$ −17.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.37−7.28 (m, 5H), 6.60 (d, J = 15.9 Hz, 1H), 6.12 (dd, J = 7.5, 15.9 Hz, 1H), 5.95 (br, 1H), 4.59 (dd, J = 1.8, 4.2 Hz, 2H), 4.13 (dt, J = 10.5, 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.7, 135.3, 133.6, 128.6, 128.3, 126.6, 126.4, 70.1, 55.0; HRMS(EI) calcd for $C_{11}H_{11}NO_2$: 189.0789, found: 189.0785.

(*S*)-11b. 86% yield, mp 82−83 °C; $[\alpha]^{25}_D$ −19.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.43−7.37 (m, 1H), 7.25−7.11 (m, 3H), 6.82 (d, J = 15.6 Hz, 1H), 6.12 (br, 1H), 6.02 (dd, J = 7.1, 15.6 Hz, 1H), 4.64−4.51 (m, 2H), 4.13 (dt, J = 8.7, 11.5 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.7, 135.6, 134.4, 131.4, 130.3, 128.2, 127.7, 126.1, 125.7, 70.1, 55.2, 19.6; HRMS(EI) calcd for $C_{12}H_{13}NO_2$: 203.0946, found: 203.0947.

(*S*)-11c. 80% yield, mp 117−118 °C; $[\alpha]^{25}_D$ −12.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.68−7.39 (m, 4H), 6.62 (d, J = 15.6 Hz, 1H), 6.21 (dd, J = 7.1, 15.7 Hz, 1H), 6.01 (br, 1H), 4.63−4.50 (m, 2H), 4.13 (dt, J = 9.5, 11.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.6, 138.9, 132.0, 131.9, 129.2, 128.5, 128.2, 126.8, 125.6, 69.9, 54.7, 28.8; HRMS(EI) calcd for $C_{12}H_{10}NO_2F_3$: 257.0663, found: 257.0661.

(*S*)-11d. 78% yield, mp 121−122 °C; $[\alpha]^{25}_D$ −14.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.30 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 6.9 Hz, 2H), 6.54 (d, J = 15.6 Hz, 1H), 5.98 (dd, J = 7.7, 15.6 Hz, 1H), 5.63 (br, 1H), 4.62−4.51 (m, 2H), 4.12-(dt, J = 6.3, 12.4 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.7, 150.8, 133.2, 128.1, 127.9, 124.1, 114.0, 72.2, 55.2, 28.8; HRMS(EI) calcd for $C_{12}H_{13}NO_3$: 219.0895, found: 219.0892.

(*S*)-11e. 82% yield, $[\alpha]^{25}_D$ −14.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.53−7.40 (m, 2H), 6.51 (d, J = 16.0 Hz, 1H), 6.05 (dd, J = 7.5, 16.0 Hz, 1H), 5.87 (br, 1H), 4.63−4.47 (m, 2H), 4.14 (dt, J = 6.2, 10.0 Hz, 1H), 3.86 (s, 6H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.4, 153.1, 133.1, 131.7, 131.1, 128.4, 126.1, 69.9, 60.7, 55.9, 54.8; HRMS(EI) calcd for $C_{14}H_{17}NO_5$: 279.1106, found: 279.1106.

(*S*)-11f. 81% yield, mp 147−148 °C; $[\alpha]^{25}_D$ −1.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.58−7.26 (m, 4H), 6.63 (br, 1H), 6.48 (d, J = 15.8 Hz, 1H), 6.13 (dd, J = 6.5, 15.7 Hz, 1H), 4.46−4.43 (m, 2H), 4.05−3.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.3, 139.9, 132.2, 131.7, 131.1, 128.4, 127.0, 118.5, 69.5, 54.4; HRMS(EI) calcd for $C_{12}H_{10}N_2O_2$: 214.0742, found: 214.0745.

(*S*)-11g. 87% yield, mp 96−97 °C; $[\alpha]^{25}_D$ −22.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.35−7.26 (m, 4H), 6.56 (d, J = 15.8 Hz, 1H), 6.25 (br, 1H), 6.10 (dd, J = 7.1, 15.7 Hz, 1H), 4.63−4.49 (m, 2H), 4.12 (dt, J = 9.7, 11.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.7, 133.9, 132.3, 128.8, 128.2, 127.8, 127.1, 70.0, 54.9; HRMS(EI) calcd for $C_{11}H_{10}NO_2Cl$: 223.0400, found 223.0395.

(*S*)-11h. 75% yield, $[\alpha]^{25}_D$ −21.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.43−7.31 (m, 1H), 6.88−6.71 (m,2H), 6.65 (d, J = 16.0 Hz, 1H), 6.14 (dd, J = 7.5, 16.0 Hz, 1H), 6.02 (br, 1H), 4.64−4.47 (m, 2H), 4.12 (dt, J = 8.3, 11.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.6, 128.7, 125.3, 111.8, 111.4, 104.5, 104.1, 103.8, 70.0, 55.2; HRMS(EI) calcd for $C_{11}H_9NO_2F_2$: 225.0601, found: 225.0599.

(*S*)-11i. 79% yield, mp 125−126 °C; $[\alpha]^{25}_D$ +0.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.20−8.10 (m, 1H), 7.73−7.40 (m, 3H), 6.67 (d, J = 16.0 Hz, 1H), 6.30 (dd, J = 7.1, 16.0 Hz, 1H), 6.07 (br, 1H), 4.67−4.54 (m, 2H), 4.17 (dt, J = 10.3, 11.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.3, 137.2, 133.3, 132.3, 131.2, 130.7, 129.5, 128.2, 122.6, 69.6, 54.4; HRMS(EI) calcd for $C_{11}H_{10}N_2O_4$: 234.0640, found: 234.0642.

(*S*)-11j. 81% yield, mp 199−200 °C; $[\alpha]^{25}_D$ −12.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.19 (d, J = 9.5 Hz, 2H), 6.60 (d, J = 8.7 Hz, 2H), 6.43 (d, J = 15.8 Hz, 1H), 5.98 (br, 1H), 5.82 (dd, J = 7.5, 15.6 Hz, 1H), 4.55−4.38 (m, 2H), 4.08−4.05 (m, 1H), 2.90 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.7, 150.8, 133.2, 128.1, 127.9, 124.1, 114.0, 72.2, 55.2, 28.8; HRMS-(EI) calcd for $C_{12}H_{13}NO_3$: 219.0895, found: 219.0892.

(4*S*)-4-(2-Phenylethyl)-1,3-oxazolidin-2-one (*S*)-12a. To a solution of (*S*)-**11a** (30 mg, 0.15 mmol) in 3 mL of EtOH was added 15 mg of 5% Pd/C. The mixture was stirred under a balloon pressure of hydrogen for 10 h at room temperature. The reaction mixture was filtered and concentrated under reduced pressure. Purification by silica gel flash chromatography (EtOAc/*n*-hexane = 1/1) provided 30 mg (99%) of (*S*)-**12a** as white crystals. mp 96−97 °C; $[\alpha]^{25}_D$ −32.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.35−7.15 (m, 5H), 6.12 (br, 1H), 4.45 (t, J = 8.3 Hz, 1H), 4.01 (dd, J = 6.2, 8.3 Hz, 1H), 3.86 (quintet, J = 6.5 Hz, 1H), 2.68 (dt, J = 2.9, 7.9 Hz, 2H), 1.98−1.85 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.3, 140.2, 128.3, 128.1, 126.0, 70.0, 51.8, 36.7, 31.3; HRMS(EI) calcd for $C_{11}H_{13}NO_2$: 191.0946, found: 191.0948.

(*S*)-12b. 98% yield, $[\alpha]^{25}_D$ −19.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.14−7.07 (m, 4H), 6.43 (br, 1H), 4.46 (t, J = 8.1 Hz, 1H), 4.00 (dd, J = 6.3, 8.1 Hz, 1H), 3.89 (m, 1H), 2.64 (dt, J = 4.5, 7.3 Hz, 2H), 2.28 (s, 3H), 1.85 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.1, 138.4, 135.6, 130.4, 128.7, 126.4, 126.1, 70.1,52.3, 35.6, 29.0, 19.1; HRMS(EI) calcd for $C_{12}H_{15}NO_2$: 205.1102, found: 205.1096.

(*S*)-12c. 99% yield, mp 70−71 °C; $[\alpha]^{25}_D$ −23.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.54 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 7.7 Hz, 2H), 6.94 (br, 1H), 4.48 (t, J = 8.5 Hz, 1H), 4.03 (dd, J = 6.1, 8.5 Hz, 1H), 3.87 (m, 1H), 2.75 (q, J = 7.7 Hz, 2H), 1.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.3, 144.4, 131.9, 128.6, 128.2, 125.4, 70.0, 51.8, 36.6, 31.3; HRMS-(EI) calcd for $C_{12}H_{12}NO_2F_3$: 259.0820, found: 259.0821.

(*S*)-12d. 98% yield, mp 77−78 °C; $[\alpha]^{25}_D$ −32.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.06 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 6.37 (br, 1H), 4.41 (t, J = 8.3 Hz, 1H), 3.97 (dd, J = 6.3, 8.3 Hz, 1H), 3.82 (m, 1H), 3.76 (s, 3H), 2.60 (dt, J = 3.3, 6.9 Hz, 2H), 1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.1, 158.0, 132.1, 129.1, 114.0, 70.1, 55.2, 52.0, 37.0, 30.7; HRMS(EI) calcd for $C_{12}H_{15}NO_3$: 221.1051, found: 221.1054.

(*S*)-12e. 96% yield, $[\alpha]^{25}_D$ −15.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.67−7.40 (m, 2H), 6.56 (br, 1H), 4.44 (t, J = 8.3 Hz, 1H), 4.00 (dd, J = 6.1, 8.3 Hz, 1H), 3.87 (m, 1H), 3.81 (s, 6H), 3.79 (s, 3H), 2.58 (dt, J = 6.3, 10.9 Hz, 2H), 1.94−1.81 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.1, 153.1, 136.0, 131.8, 128.5, 70.0, 60.7, 55.9, 36.9, 31.8; HRMS (EI) calcd for $C_{14}H_{19}NO_5$: 281.1263, found: 281.1268.

(*S*)-12f. 99% yield, mp 86−87 °C; $[\alpha]^{25}_D$ −32.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.43 (d, J = 8.6 Hz, 2H), 7.27 (d, J = 8.6 Hz, 2H), 7.04 (br, 1H), 4.47 (t, J = 8.5 Hz, 1H), 4.02 (dd, J = 6.1, 8.5 Hz, 1H), 3.85 (m, 1H), 2.72 (m, 2H), 1.89 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.8, 146.1, 131.8,

129.0, 118.7, 109.9, 69.7, 51.6, 36.3, 31.4; HRMS (EI) calcd for $C_{12}H_{12}N_2O_2$: 216.0898, found: 216.0892.

(*S*)-12g. 99% yield, mp 76−77 °C; $[\alpha]^{25}_D$ −22.1 (c1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.26 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.2 Hz, 2H), 6.78 (br, 1H), 4.45 (dt, J = 2.4, 8.5 Hz, 1H), 4.01 (dd, J = 6.1, 8.5 Hz, 1H), 3.86 (m, 1H), 2.61 (dt, J = 7.0, 13.6 Hz, 2H), 1.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.2, 138.7, 132.0, 129.6, 128.2, 70.0, 51.8, 36.8, 30.8; HRMS (EI) calcd for $C_{11}H_{12}NO_2Cl$: 225.0556, found: 225.0554.

(*S*)-12h. 99% yield, $[\alpha]^{25}_D$ −32.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.13 (m, 1H), 6.80 (m, 2H), 6.56 (br, 1H), 4.49 (t, J = 8.5 Hz, 1H), 4.04 (dd, J = 6.1, 8.5 Hz, 1H), 3.85 (m, 1H), 2.66 (m, 2H), 1.87 (dq, J = 2.9, 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.1, 150.9, 131.0, 128.3, 122.7, 111.4, 103.8, 70.0, 51.5, 35.6, 24.5; HRMS (EI) calcd for $C_{11}H_{11}NO_2F_2$: 227.0757, found: 227.0757.

(*S*)-12i. 85% yield, $[\alpha]^{25}_D$ −16.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.08 (t, J = 7.8 Hz, 1H), 6.57−6.50 (m, 3H), 5.87 (br, 1H), 4.44 (t, J = 8.3 Hz, 1H), 3.99 (dd, J = 6.3, 8.3 Hz, 1H), 3.84 (m, 1H), 3.69 (br, 2H), 2.58 (t, J = 8.2 Hz, 2H), 1.94−1.82 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.6, 146.7, 141.3, 129.6, 118.4, 114.9, 113.2, 70.1, 52.0, 36.6, 31.8. HRMS (EI) calcd for $C_{11}H_{14}N_2O_2$: 206.1055, found: 206.1059.

(*S*)-12j. 99% yield, mp 163−164 °C; $[\alpha]^{25}_D$ −12.7° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.03 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 8.5 Hz, 2H), 6.05 (br, 1H), 4.42 (t, J = 8.1 Hz, 1H), 3.98 (dd, J = 6.5, 8.1 Hz, 1H), 3.84 (m, 1H), 2.91 (s, 6H), 2.58 (t, J = 7.3 Hz, 2H), 1.88 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.9, 149.2, 128.8, 127.9, 112.9, 70.2, 52.1, 40.6, 37.1, 30.6; HRMS (EI) calcd for $C_{13}H_{18}N_2O_2$: 234.1368, found: 234.1367.

(2*S*)-2-Amino-4-phenyl-1-butanol (*S*)-13a. To a solution of (*S*)-**12a** (30 mg, 0.16 mmol) in 4 mL of 30% aqueous EtOH was added LiOH (200 mg, 4.81 mmol). The mixture was refluxed for 2 h and cooled to room temperature. The reaction mixture was concentrated to 2 mL and then extracted with EtOAc (5 ×5 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica gel flash chromatography (EtOAc/MeOH = 2/3) provided 24 mg (92%) of (*S*)-**13a** as white crystals. mp 78−79 °C; $[\alpha]^{25}_D$ −4.5° (*c* 0.8, CH_3OH); ^{1}H NMR (CD_3OD, 200 MHz) δ 7.31−7.12 (m, 5H), 3.59 (dd, J = 7.0, 9.9 Hz, 1H), 3.37 (dd, J = 7.0, 10.9 Hz, 1H), 2.80 (m, 1H), 2.71 (dt, J = 6.4, 9.3 Hz, 2H), 1.86−1.55 (m, 2H); ^{13}C NMR (CD_3OD, 50 MHz) δ 144.2, 130.2, 127.7, 68.1, 54.3, 37.2, 34.2; HRMS (EI) calcd for $C_{10}H_{15}NO$: 165.1153, found: 165.1149.

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