JOC *Article*

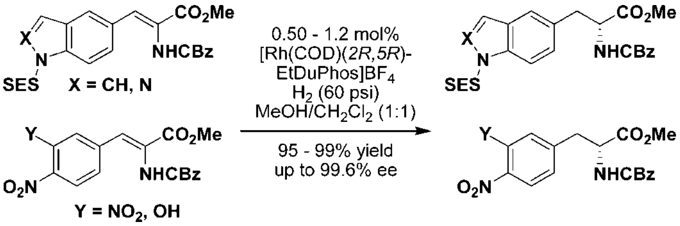
Catalytic Asymmetric Syntheses of Tyrosine Surrogates

Xiaojun Han,* Rita L. Civiello, Haiquang Fang, Dedong Wu, Qi Gao,
Prasad V. Chaturvedula, John E. Macor, and Gene M. Dubowchik

*Neuroscience Discovery Chemistry, Research & Development, Bristol-Myers Squibb Company,
5 Research Parkway, Wallingford, Connecticut 06492*

xiaojun.han@bms.com

Received July 21, 2008



Amino acid esters **5**−**11** as tyrosine mimics have been synthesized in excellent enantioselectivity (up to 99.6% ee) and in good overall chemical yields. The key step in the sequence was the Burk's [Rh(COD)(2*R*,5*R*)-Et-DuPhos]BF_4-catalyzed asymmetric hydrogenation of enamides with a variety of reactive functional groups.

Introduction

Tyrosine is one of four natural amino acids (histidine, phenylalananine, tryptophan, and tyrosine) that contain aromatic moieties. In biological systems, the uniqueness of tyrosine rests on its phenolic −OH acting as both hydrogen bond donor and acceptor and its electron-rich aromatic ring capable of engaging in $\pi-\pi$ stacking interactions. Tyrosine surrogates have been used in pharmaceutical research to improve the potency, pharmacokinetic properties and binding selectivity of target molecules.[1]

As a part of a medicinal chemistry project, we required tyrosine surrogates **1** shown in Figure 1, where various NH-containing heterocycles could be used to probe SAR as well as provide good pharmacokinetic properties. For example, the presence of the heterocyclic ring could fine-tune the electron density of the phenyl ring and potentially modulate $\pi-\pi$ stacking interactions in the active site.[2] We envisioned that these amino acid esters could be synthesized by the asymmetric hydrogenation of enamides **2**, which could be obtained by olefination of aldehydes **3** and ylide **4**.

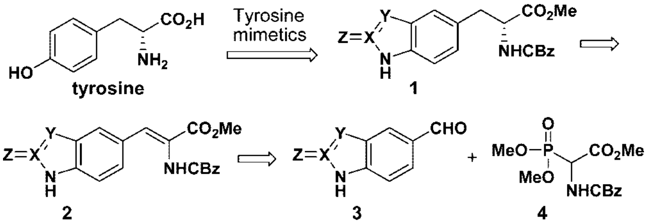


FIGURE 1. Tyrosine mimetics and their retro synthetic analysis.

The structures of the amino acid esters synthesized in this paper are shown in Figure 2. The asymmetric synthesis of indole amino acid **6b** and its cation-π interaction properties were reported.[3] A seven step racemic synthesis of free oxoindole amino acid **7** (without CBz protection) was reported in 1979.[4] Racemic amino acids **8**−**10** have been synthesized by the reaction of substituted benzyl bromides with sodioethylacetamidomalonate or its equivalent, and were used as DOPA and dopamine analogues to study their effects on dopamine β-hydroxylase and tyrosinase.[5] They have also been prepared in racemic form by nitration of 4-aminophenylalanine to study their potential as inhibitors of norepinephrine biosynthesis.[6] The

---

(1) (a) Song, Y.-L.; Peach, M.; Roller, P. P.; Qiu, S.; Wang, S.; Long, Y.-Q. *J. Med. Chem.* **2006**, *49*, 1585–1596. (b) Dolle, R. E.; Machaut, M.; Martinez-Teipel, B.; Belanger, S.; Cassel, J. A.; Stabley, G. J.; Graczky, T. M.; DeHaven, R. N. *Bioorg. Med. Med. Chem.* **2004**, *14*, 3545–3548.

(2) (a) South, C. R.; Burd, C.; Weck, M. *Acc. Chem. Res.* **2007**, *40*, 63–74. (b) Lewis, D. F. V.; Jacobs, M. N.; Dickins, M. *Drug Discovery Today* **2004**, *9*, 530–7. (c) Nose, T. *Peptide Science* **2003**, *39*, 9–12.

(3) Carlier, P. R.; Lam, P. C.-H.; Wong, D. M. *J. Org. Chem.* **2002**, *67*, 6256–6259.

(4) Atkinson, J. G.; Wasson, B. K.; Fuentes, J. J.; Girard, Y.; Rooney, C. S. *Tetrahedron Lett.* **1979**, 2857–2860.

(5) (a) Loriga, M.; Paglietti, G.; Sparatore, F.; Pinna, G.; Sisini, A. *IL Farmaco* **1992**, *47*, 439–448. (b) Schmidhammer, H.; Hohenlohe-Oehringen, K. *Sci. Pharm.* **1983**, *51*, 8–16. (c) Zenker, N.; Talaty, C. N.; Callery, P. S.; Wright, J.; Hubbard, L. S.; Johnson, E. M., Jr. *J. Heterocyclic Chem.* **1983**, *20*, 435–437.

(6) Milkowski, J. D.; Miller, F. M., Jr.; Zenker, N. *J. Med. Chem.* **1970**, *13*, 741–742.

10.1021/jo801577t CCC: $40.75

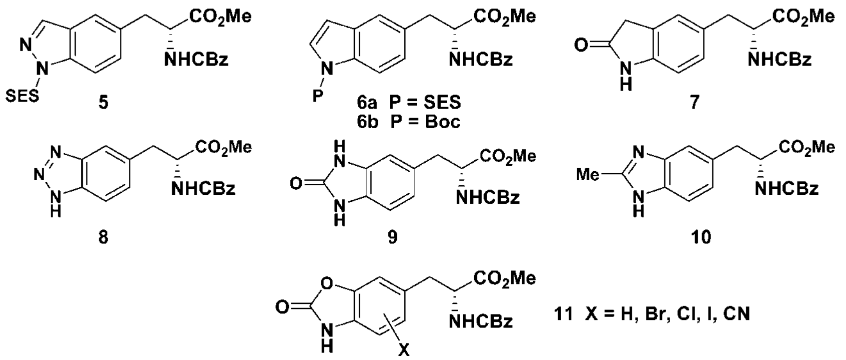
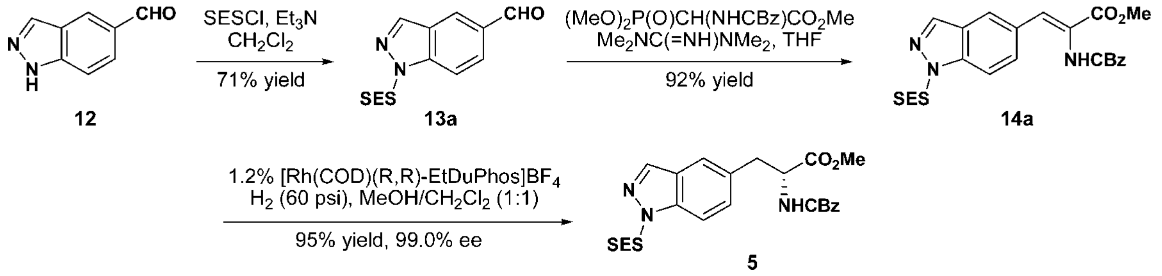
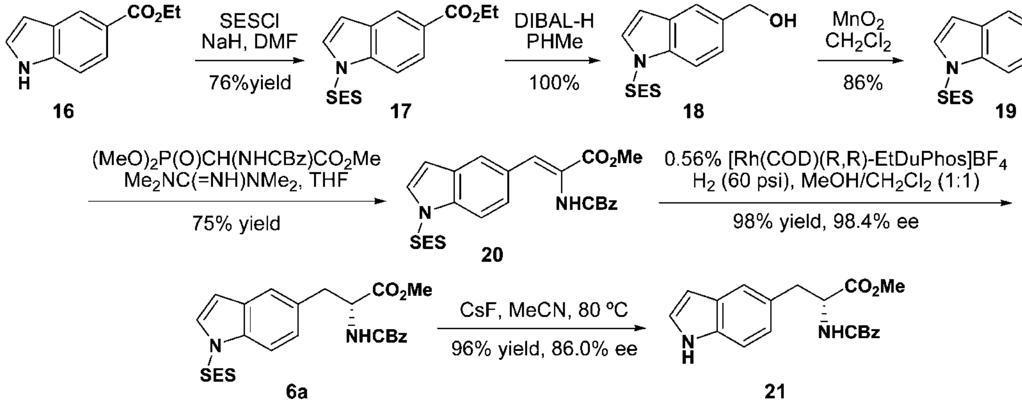


FIGURE 2. Protected amino acids described in this paper.

SCHEME 1. Synthesis of Indazole Amino Acid Ester 5



SCHEME 2. Synthesis of Amino Acid Esters 6a and 21



enantiopure amino ester **27** (Scheme 3), a common precursor to amino acid esters **8**−**10**, was prepared by enzymatic resolution.[7] Racemic amino acid esters **31** and **32** (Scheme 5), intermediates toward benzoxalone amino ester **11** (X = H) were synthesized to study their potential as α-amino-3-hydroxy-5-methyl-4-isoxazolepropanic acid (AMPA) agonist.[8] Racemic amino ester **32** was also used as a specific biomarker of pheomelanin, a melanin pigment occurring in the hair and skin of mammals to detect disease and drug usage.[9] Herein we report the asymmetric synthesis of these unnatural amino acids.

Results and Discussions

I. The Synthesis of Indazole, Indole and Indolinone Amino Acid Esters (5−**7).** For the synthesis of amino acid esters **5**−**7**, the carboxylic acids were protected as methyl esters, the amino group was protected as the NHCBz derivative, and the indazole and indole NH moieties were protected as the *N*-SES (SES = trimethylsilylethanesulfuryl) functionalities. *N*-SES protection was chosen because of its stability toward normal peptide-bond forming and acidic-deprotection conditions. Its strong electron withdrawing ability was also envisioned to increase the stability of electron-rich enamides and perhaps accelerate asymmetric hydrogenation of less electron-rich enamides (*vide infra*).

The synthesis of indazole amino ester **5** is shown in Scheme 1. The reaction of aldehyde **12**[10] and SESCl[11] afforded SES-protected aldehyde **13a**. The olefination[12] of aldehyde **13a** with

---

(7) Porter, J.; Dykert, J.; Rivier, J. *Int. J. Peptide Protein Res.* **1987**, *30*, 13–21.

(8) Hill, R. A.; Wallace, L. J.; Miller, D. D.; Weinstein, D M.; Shams, G.; Tai, H.; Layer, R. T.; Illins, D.; Uretsky, N. J.; Danti, S. N. *J. Med. Chem.* **1997**, *40*, 3182–3191.

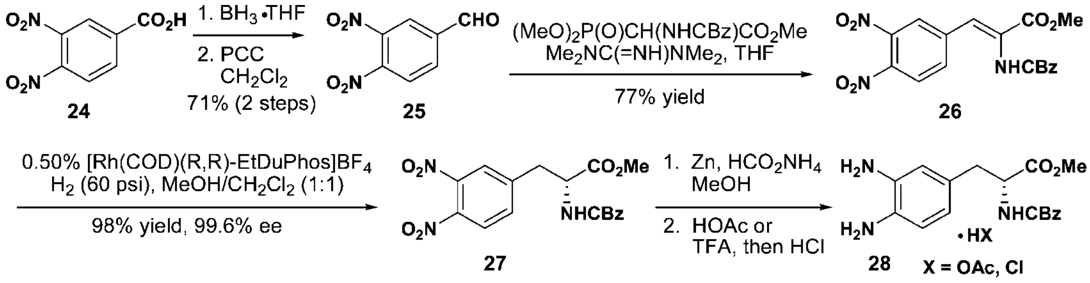
(9) (a) Patil, D. G.; Chedekel, M. R. *J. Org. Chem.* **1984**, *49*, 997–1000. (b) Wakamatsu, K.; Ito, S. *Pigment Cell Res.* **2002**, *15*, 174–183.

(10) DeLucca, G. V. US 6313110 B1.

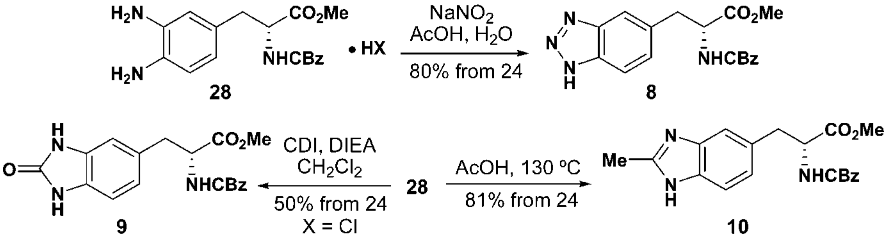
(11) (a) Weinreb, S. M.; Demko, D. M.; Lessen, T. A.; Demers, J. P. *Tetrahedron Lett.* **1986**, *27*, 2099–2102. (b) Weinreb, S. M.; Chase, C. E.; Wipf, P.; Venkatraman, S. *Org. Synth.* **1998**, *75*, 161–169. (c) Huang, J.; Widlanski, T. S. *Tetrahedron Lett.* **1992**, *33*, 2657–2660. (d) SESCl has become available from Aldrich since 2007 at $330.50/5g (CAS# 106018−85−3). The starting material to make SESCl, $Me_3SiCH_2CH_2SO_3Na$, is also available from Aldrich at $82.7/5g (CAS# 18143−40−3). In our hands, the conditions described by Widlanski[11c] were advantageous because purification was accomplished by quick silica gel filtration rather than distillation. This is especially convenient for small scale syntheses.

(12) Schmidt, U.; Griesser, H.; Leitenberger, V.; Lieberknecht, A.; Mangold, R.; Meyer, R.; Riedl, B. *Synthesis* **1992**, 487–490.

SCHEME 3. Synthesis of Amino Acid Ester 28

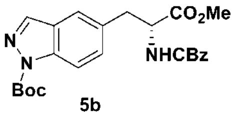


SCHEME 4. Synthesis of Amino Acid Esters 8−10

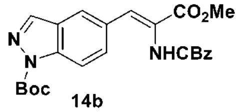


ylide **4** provided enamide **14a**. The asymmetric hydrogenation of **14a** under Burk's conditions[13] afforded amino ester **5** in 95% yield and 99.0% ee (Scheme 1).

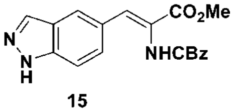
We were also interested in the catalytic enantioselective synthesis of BOC-protected indazole amino ester **5b**, since the corresponding indole amino ester **6b** has been reported.[3] Boc-protected enamide **14b** was prepared by the reaction of aldehyde **12** with Boc_2O,[14] followed by olefination.[12] It is interesting to note that **14b** did not undergo hydrogenation under the asymmetric hydrogenation conditions described above, and only a progressive loss of the Boc protecting group occurred with increasing catalyst loading. When enamide **15**, prepared by the reaction of **14b** with TMSCl,[15] was submitted to the above asymmetric hydrogenation conditions (3 mol % and 25 mol % catalyst loading), again no reaction occurred, suggesting that the free indazole NH was perhaps complexing with rhodium.[16]



5b



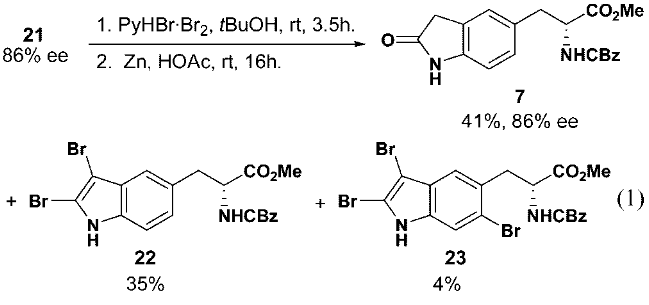
14b



15

The synthesis of indole amino ester **6a** is illustrated in Scheme 2. We were unable to obtain indole aldehyde **19** by the reaction of 1*H*-indole-5-carbaldehyde with SESCl under various conditions. Therefore, we carried out SES-protection of ester **16** with SESCl to afford **17** in 76% yield. Aldehyde **19** was obtained by sequential reaction of **17** with DIBAL-H and activated MnO_2. Enamide **20** was generated as described above. The same asymmetric hydrogenation conditions with 0.56 mol% of the catalyst converted **20** to **6a** in 98% yield and 98.4% ee. Treatment of **6a** with CsF[11a] afforded **21** in 96% yield and 86% ee. Racemization occurred to some extent in the deprotection of methyl ester **6a** [**6a** (98.4% ee) → **21** (86.0% ee)], but we did not observe any loss of chirality under identical conditions at a later stage deprotection following elaboration of both amino and acid portions of **6a** to amides.

The treatment of indole amino ester **21** with PyHBr•Br_2, followed by the removal of *t*-BuOH *in vacuo* and exposure of the residue to Zn in AcOH, afforded amino acid ester **7** in 41% yield without loss of chirality (eq 1).[17] Dibromo amino acid ester **22** (35%) along with tribromo compound **23** (4%) were also formed and their structures were determined by X-ray diffraction (see Supporting Information),[18] confirming generation of the *R* configuration. The formation of side-product **23** in which the third bromine atom was substituted at C6, instead of the more electron-rich C7 position, suggested a possible directing influence of the NHCBz group.[19]



(1)

II. The Synthesis of Benzotriazole, Benzoimidazolone, Benzoimidazole Amino Acid Esters (8−10). The amino acid esters (**8**−**10**) could be synthesized from the common diami-

---

[13] (a) Burk, M. J. *Acc. Chem. Res.* **2000**, *33*, 363–372. (b) Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125–10138. For the mechanistic study of the asymmetric hydrogenation of enamides employing Burk's catalyst, see: (c) Armstrong, S. K.; Brown, J. M.; Burk, M. J. *Tetrahedron Lett.* **1993**, *34*, 879–882. For a similar general approach for the enantioselective synthesis of aminobenzazepinone, see our prior publication: (d) Prasad, C. V. C.; Mercer, S. E.; Dubowchik, G. M.; Macor, J. E. *Tetrahedron Lett.* **2007**, *48*, 2661–2665.

[14] Grehn, L.; Ragnarsson, U. *Angew Chem, Int. Ed.* **1984**, *23*, 296–301.

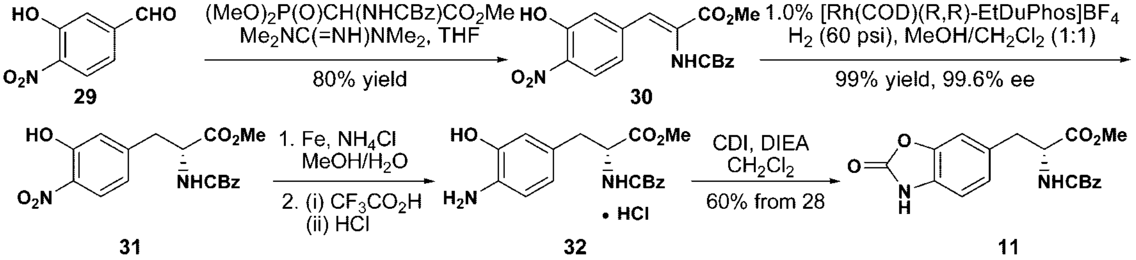
[15] Kaiser Sr, E.; Picart, F.; Kubiak, T.; Tam, J.; Merrifield, R. B. *J. Org. Chem.* **1993**, *58*, 5167–5175.

[16] Adamczyk, M.; Akireddy, S. R.; Reddy, R. E. *Org. Lett.* **2001**, *3*, 3157–3159.

[17] Marfat, A.; Carta, M. P. *Tetrahedron Lett.* **1987**, *28*, 4027–4030.

[18] Full crystallographic data have been deposited to the Cambridge Crystallographic Data Center (CCDC reference number 694858). Copies of the data can be obtained free of charge via the internet at http://www.ccdc.cam.ac.uk.

SCHEME 5. Synthesis of Amino Acid Ester 11



nophenyl intermediate **28** (Scheme 3). 3,4-Dinitrobenzoic acid **24** was converted to its aldehyde **25**[20] by sequential reactions with BH_3•THF[21] and PCC.[22] The reaction of aldehyde **25** with ylide **4** afforded the pure (*Z*)-isomer enamide **26** in 77% yield after crystallization from EtOAc and flash chromatography on silica gel using CH_2Cl_2 as eluent. We found these two purification steps were necessary in preparation for the rapid and highly enantioselective hydrogenation reaction (**26** → **27**). The asymmetric hydrogenation of enamide **26** with 0.5 mol% of the catalyst provided amino ester **27** in 98% yield and 99.6% ee. The two nitro groups were cleanly reduced to give **28** using Zn and HCO_2NH_4.[23] Diamine **28** was stored either as an acetate salt or as a hydrochloride salt.

Diamine **28** was converted into amino acid esters **8**−**10** as shown in Scheme 4. Benzotriazole amino ester **8** was obtained in 80% yield and 99.6% ee (two steps, from **27**) by the reaction of **28** (X = OAc) with $NaNO_2$.[5] The reaction of diamine **28** (X = Cl) and carbonyl diimidazole afforded benzoimidazolone amino ester **9** in 50% yield (2 steps, from **27**).[5] The ee of amino ester **9** was not determined. Finally, 2-methylbenzimidazole amino ester **10** was obtained in 81% yield and 97.6% ee (2 steps, from **27**) by heating diamine **28** (X = OAc) in AcOH at reflux for 4 h.[5]

III. The Synthesis of Benzoxalone Amino Acid Esters (11, 11a-e and 33). The olefination of aldehyde **29** with ylide **4** afforded enamide **30** in 80% yield (Scheme 5). Asymmetric hydrogenation of enamide **30** with Burk's catalyst produced amino ester **31** in 99% yield and 99.6% ee. Reduction of the nitro group in **31** was accomplished by treatment with Fe and NH_4Cl.[24] Aminophenol **32** was first converted to a CF_3CO_2H salt, then an HCl salt.[25] Aminophenol **32**•HCl was reacted with CDI in the presence of Et_3N to produce amino acid ester **11** (60% yield from **31**).

We were also interested in obtaining amino acid esters with aromatic halogen substitutents for SAR studies, since it has been shown that halogens may impart favorable biological and pharmacokinetic properties. Equally important, the halogen substituent could be used for transition metal (such as Pd) catalyzed coupling reactions to provide more complex unnatural amino acid ester analogues. Among the various classes of amino acid esters we have synthesized (indazole **5**, indole **6**, indolinone **7**; benzotriazole **8**, benzoimidazolone **9**, benzoimidazole **10**; and benzoxalone **11**) we believed benzoxalone **11** would be the easiest substrate to study in direct halogenation reactions to form 6-X and 7-X substituted amino acids for our medicinal chemistry project needs.[26] Indeed, after some experimentation, we were able to prepare 6 and 7- Cl and Br, and 7-I substituted benoxalones (**11a**−**e**) (Scheme 6). Using typical conditions for electrophilic halogenation of electron rich aromatics, the reaction of **11** with NCS or NBS in AcOH for 16 h at 100 °C produced 6-Cl- and 6-Br-substituted benzoxalones **11a** and **11b** in 32% and 34% yield, respectively. After trying different halogenation conditions, it was discovered that bromobenzoxalone **11c** could be obtained in an 80% yield by the reaction of **11** with NBS in the presence of silica gel at rt for 6 h in CH_2Cl_2. Bromination of electron-rich aromatics using $NBS/SiO_2/CH_2Cl_2$ was first reported by Kende.[27] No reaction occurred with NCS under the same conditions. However, when this reaction was run in dichloroethane at 90 °C for 16 h in the presence of silica gel, 7-chlorobenzoxalone **11d** and 6-chlorobenzoxalone **11a** were formed in 10% and 19% yield, respectively. In the presence of silica gel, the reaction of **11** with I_2 or NIS in either CH_2Cl_2 or $(CH_2Cl)_2$ at rt or at reflux gave no desired product. Benzoxalone **11e** was obtained in 40% yield by the reaction of **11** with IPy_2BF_4[28] in dichloroethane at 90 °C for 6 h in the presence of silica gel. The structures of halogenated benzoxalones **11a-e** were determined primarily by NMR analysis. Chemical shifts were assigned by ^1H, ^{13}C, DEPT, COSY, HMQC, and HMBC. The connectivity of key protons and carbons were determined by HMQC and HMBC. These halogenated compounds could indeed be used as the substrates for palladium-catalyzed coupling reactions.[29] For example, the reaction of **11c** with $Zn(CN)_2$ [10% $Pd(PPh_3)_4$, DMF, 80 °C, 3 h] afforded nitrile **33** in 90% yield.[30]

Conclusion

In conclusion, we have achieved the asymmetric synthesis of tyrosine mimetics, in which the phenol in the amino acid has been replaced by indazole, indole, indolinone, benzotriazole, benzoimidazolone, benzoimidazole, and benzoxalone, to afford

---

(19) Barluenga, J.; Alvarez-Gutierrez, J. M.; Ballesteros, A.; Gonzalez, J. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1281–1283.

(20) Goldstein, H.; Voegeli, R. *Helv. Chim. Acta* **1941**, *26*, 1125–1128.

(21) Kende, A. S.; Fludzinski, P. *Org. Synth., Coll.* **1990**, *7*, 221–223.

(22) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2650.

(23) Gowda, D. C.; Mahesh, B.; Gowda, S. *Ind. J. Chem., Sec. B: Org. Chem.* **2001**, *40B*, 75–77, A variety of reduction conditions were screened for this transformation. Only the employed conditions gave a clean reaction.

(24) (a) Ramadas, K.; Srinivasan, N. *Synth. Commun.* **1992**, *22*, 3189–3195. Fe/NH_4Cl was first reported by Shih to reduce aromatic nitro compounds: (b) Shih, Y.-T. *Huaxue Xuebao* **1956**, *22*, 352–355.

(25) Aminophenol **32**•HCl was better than **32**•TFA for both storage and the reaction of **32** with CDI in the presence of DIEA to form **11**. HCl was not added directly to the reaction mixture of **31** due to the concern that hydrogen formed by the reaction of Fe and aq. HCl could remove CBz group.

(26) The reaction of indazole **5** with NBS under various conditions produced mainly 3-Br-substituted indazole, while the reactions of **6**−**10** with NBS gave multi-component mixtures.

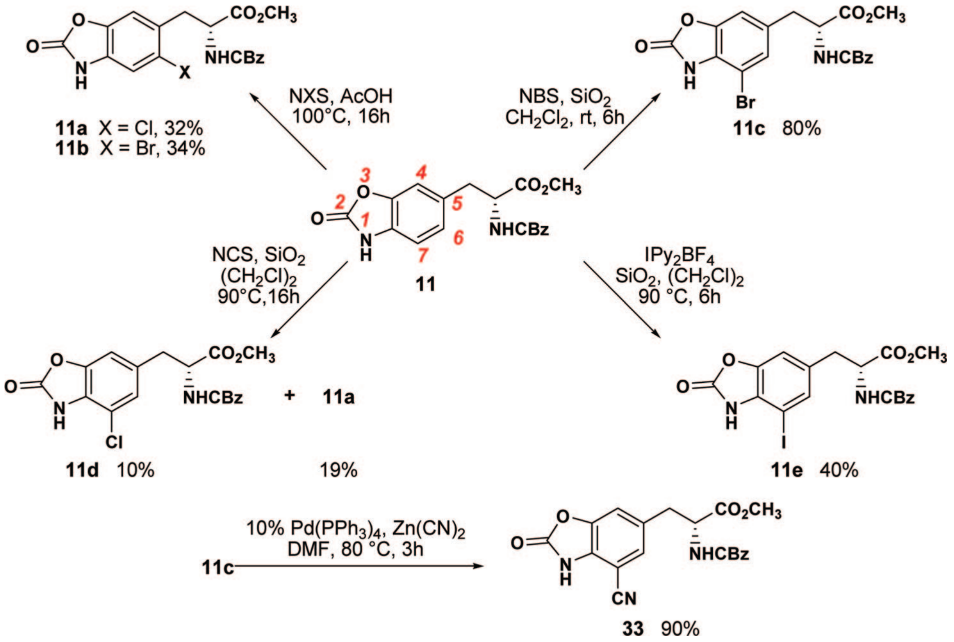
(27) Kende, A. S.; Deng, W.-P.; Zhong, M.; Guo, X.-C. *Org. Lett.* **2003**, *5*, 1785–1788.

(28) IPy_2BF_4: A review: (a) Barluenga, J. *Pure Appl. Chem.* **1999**, *71*, 431–436. Iodination of aromatic compounds: (b) Barluenga, J.; Gonzalez, J. M.; Garcia-Martin, M. A.; Campos, P. J.; Asensio, G. *J. Org. Chem.* **1993**, *58*, 2058–2060.

(29) Hartz, R. A.; Nanda, K. K.; Ingalls, C. L. *Tetrahedron Lett.* **2005**, *46*, 1683–1686.

(30) Tschaen, D. M.; Desmond, R.; King, A. O.; Fortin, M. C.; Pipik, B.; King, S.; Verhoeven, T. R. *Synth. Commun.* **1994**, *24*, 887–890.

SCHEME 6. Synthesis of Amino Acid Esters 11a−e and 33



unnatural amino acid esters **5−11** in good overall chemical yields and extremely high enantioselectivities (up to 99.6% ee). The key steps involved an olefination to form enamides and subsequent asymmetric hydrogenation using Burk's Rhodium complex of EtDuphos. The success of these reactions highlight the robustness of Burk's catalyst and provide easy access to these amino acid esters for pharmaceutical use in the synthesis of novel analogs. The reaction sequence employed here should be useful for making other unnatural amino acids esters of either enantiomeric configuration.

Experimental Section

2-Trimethylsilanyl-ethanesulfonyl chloride, SESCl [the Modified Procedure].[11c] Sulfuryl chloride (SO_2Cl_2, 43 mL, 539 mmol) was added over 3 min to a clear solution of PPh_3 (129 g, 490 mmol) in CH_2Cl_2(200 mL) stirred at 0 °C in a flame-dried three-neck round-bottom flask. After 5 min, the ice−water bath was removed and $TMSCH_2CH_2SO_3Na$ (50 g, 245 mmol) was added in portions over 10 min. The resulting white suspension was stirred at rt for 16 h and then filtered through a pad of Celite. The filtrate was concentrated to ca. 50 mL. EtOAc/hexanes (1:3, 1000 mL) and Celite (40 g) were added. The mixture was stirred at room temperature for 15 min and filtered through a pad of Celite. The filtrate was concentrated and the residue was subjected to flash column chromatography using EtOAc/hexanes (1:3) as the eluent to give the title compound as a light tan liquid (41.9 g, 85% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.61−3.57 (m, 2H), 1.32−1.27 (m, 2H), 0.10 (s, 9H). The prepared SESCl was stored under N_2 in a freezer for two months without significant decomposition (<5%).

1-(2-Trimethylsilanyl-ethanesulfonyl)-1*H*-indazole-5-carbaldehyde (13a). To a solution of 1*H*-indazole-5-carbaldehyde (10.0 g, 68.4 mmol) and Et_3N (28.6 mL, 205 mmol) in CH_2Cl_2 (300 mL) was added freshly prepared SESCl (20.6 g, 103 mmol). The reaction mixture was stirred at rt for 18 h and then washed with water (400 mL). The organic layer was separated, dried over $MgSO_4$ and filtered. The filtrate was concentrated and subjected to flash column chromatography (gradient; 1:7 EtOAc/hexanes to 1:4 EtOAc/hexanes) to afford the title compound as a white solid (15.1 g, 71% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.10 (s, 1H), 8.40 (s, 1H), 8.30 (s, 1H), 8.21 (d, $J = 8.8$ Hz, 1H), 8.07 (dd, $J = 8.8$, 1.5 Hz, 1H), 3.46−3.40 (m, 2H), 0.88−0.82 (m, 2H), −0.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 190.9, 143.7, 141.3, 133.1, 129.0, 125.6, 125.2, 113.8, 51.4, 9.8, −2.1; HRMS $(M - H)^-$; calcd for $C_{13}H_{17}N_2O_3SiS$: 309.0729, found 309.0721.

2-Benzyloxycarbonylamino-3-[1-(2-trimethylsilanyl-ethanesulfonyl)-1*H*-indazol-5-yl]-acrylic Acid Methyl Ester (14a). 1,1,3,3-Tetramethylguanidine (0.68 mL, 5.43 mmol) was added to a solution of *N*-(benzyloxycarbonyl)-α-phosphonoglycine trimethyl ester (1.88 g, 5.69 mmol) in THF (40 mL). After stirring at rt for 15 min, the mixture was cooled to −78 °C and a solution of **13a** (1.6 g, 5.17 mmol) in THF (15 mL) was added slowly. The resulting reaction mixture was stirred at −78 °C for 2 h and then allowed to warm to rt over 3 h. The solvents were removed *in vacuo* and the residue was subjected to flash chromatography using CH_2Cl_2/hexanes (2:3) containing 1% Et_3N as eluent to afford the title compound as a 95:5 Z/E mixture (determined by the integration of $-C\underline{H}{=}C(CO_2Me)(NHCBz)$, 2.45 g, 92% yield). For the Z isomer: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16 (s. 1H), 7.98 (d, $J = 8.8$ Hz, 1H), 7.86 (s, 1H), 7.67 (d, $J = 8.8$ Hz, 1H), 7.46 (s, 1H), 7.34−7.27 (m, 5H), 6.55 (bs, 1H), 5.09 (s, 2H), 3.83 (s, 3H), 3.41−3.35 (m, 2H), 0.91−0.85 (m, 2H), −0.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.7, 153.7, 140.9, 135.9, 130.8, 130.7, 130.1, 128.6, 128.5, 128.3, 125.4, 124.2, 123.0, 113.1, 67.7, 52.9, 51.2, 9.8, −2.0; HRMS $(M + NH_4)^+$ calcd for $C_{24}H_{33}N_4O_6SiS$: 533.1890, found 533.1893.

(*R*)-2-Benzyloxycarbonylamino-3-[1-(2-trimethylsilanyl-ethanesulfonyl)-1*H*-indazol-5-yl]-propionic Acid Methyl Ester (5). In a flame-dried 500 mL Parr hydrogenation bottle, a solution of **14a** (860 mg, 1.67 mmol) in MeOH (20 mL) and CH_2Cl_2 (20 mL) was degassed by a flow of N_2 for 30 min. (−)-1,2-bis((2*R*,5*R*)-2,5-diethylphospholano)benzene(cyclooctadiene) rhodium (I) tetrafluoroborate (13 mg, 0.020 mmol, 1.2 mol%, weighed into a small vial under N_2 atmosphere in a glovebag) was quickly added to the reaction mixture. The reaction mixture was purged with 5 vacuum/H_2 cycles, and then agitated for 2 h at 60 psi H_2. Prior to its removal from the Parr hydrogenation apparatus, the reaction mixture was purged with 3 vacuum/N_2 cycles. The solvent was evaporated and the residue was subjected to flash chromatography using EtOAc/hexanes (gradient, 1:4 to1:2) as eluent to afford the title compound as a white solid (817 mg, 95% yield and 99.0% *ee*). The *ee* was determined by HPLC analysis (Chiracel-OD column, 4.6 × 250 mm, 10 μm; 80% hexane/20% ethanol @1.0 mL/min for 20 min; $\lambda = 213$ nm; $t_R = 13.9$ min for the *R*-enantiomer and $t_R = 11.2$

min for *S*-enantiomer). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.17 (s, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.47 (s, 1H), 7.35−7.25 (m, 6H), 5.29−5.24 (m, 1H), 5.08 (dd, *J* = 19.0, 12.1 Hz, 2H), 4.73−4.67 (m, 1H), 3.73 (s, 3H), 3.38−3.32 (m, 2H), 3.29 (dd, *J* = 14.2, 5.6 Hz, 1H), 3.19 (dd, *J* = 13.9, 5.6 Hz, 1H), 0.91−0.85 (m, 2H), −0.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 155.6, 140.4, 140.3, 136.2, 131.9, 130.8, 128.6, 128.4, 128.2, 125.5, 121.6, 113.2, 67.2, 55.0, 52.6, 51.1, 38.0, 9.7, −2.0; HRMS $(M + NH_4)^+$ calcd for $C_{24}H_{35}N_4O_6SiS$: 535.2047, found 535.2051.

***tert*-Butyl 5-formyl-1H-indazole-1-carboxylate (13b).** A solution of $(BOC)_2O$ (388 mg, 1.78 mmol) in CH_2Cl_2 (2 mL) was added dropwise at rt to a solution of 1*H*-indazole-5-carbaldehyde (273 mg, 1.87 mmol), DMAP (114 mg, 0.94 mmol), and Et_3N (260 ul, 1.87 mmol) in CH_2Cl_2 (10 mL). The resulting bright-yellow solution was stirred at rt for 16 h. The solvents were removed *in vacuo* and the residue was subjected to flash column chromatography using EtOAc/hexanes (1:1) containing 1% Et_3N as eluent to afford the title compound as a brownish yellow liquid (414 mg, 90% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.08 (s, 1H), 8.38 (s, 1H), 8.34 (s, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 1.71 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.8, 149.0, 142.5, 140.6, 133.0, 128.3, 126.4, 125.8, 115.3, 85.7, 27.8; HRMS $(M + H)^+$ calcd for $C_{13}H_{15}N_2O_3$: 247.1083, found 247.1089.

(*Z*)-*tert*-Butyl 5-(2-(Benzyloxycarbonylamino)-3-methoxy-3-oxoprop-1-enyl)-1*H*-indazole-1-carboxylate (14b). Compound **14b** was prepared from **13b** (416 mg, 1.69 mmol) according to the procedure described for the preparation of **14a**. Purification by flash chromatography using EtOAc/hexanes (1:2) as eluent gave the title compound (550 mg, 72% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (s, 1H), 7.98 (m, 2H), 7.72 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.34 (s, 1H), 7.22 (br s, 5H), 5.00 (s, 2H), 3.65 (s, 3H), 1.57 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 207.0, 166.1, 155.0, 149.2, 140.1, 139.7, 132.6, 130.7, 129.7, 128.9, 128.5, 128.3, 126.5, 125.8, 123.5, 114.7, 85.3, 67.2, 52.6, 27.9; HRMS $(M + H)^+$ calcd for $C_{24}H_{26}N_3O_6$: 452.1822, found 452.1826.

(*Z*)-Methyl 2-(benzyloxycarbonylamino)-3-(1*H*-indazol-5-yl)acrylate (15). A 4 M solution of phenol in CH_2Cl_2 (6 mL) and a 4 M solution of chlorotrimethylsilane in CH_2Cl_2 (2 mL) were mixed together and then passed through a plug of sodium carbonate. The TMS-phenol solution in CH_2Cl_2 was added to a solution of **14b** (1.0 g, 2.2 mmol) in CH_2Cl_2 (2 mL) and the reaction mixture was stirred at rt until disappearance of the starting material was complete. The solvent was removed *in vacuo* and the residue was subjected to flash column chromatography using EtOAc/hexanes containing 1% Et_3N (1:1, then 3:1) as eluent to give the title compound (600 mg, 77% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.02 (s, 1H), 7.90 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.51 (s, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.35−7.27 (m, 5H), 5.11 (s, 2H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.0, 154.0, 134.0, 135.8, 133.0, 129.7, 128.6, 128.3, 127.0, 123.6, 122.9, 120.7, 115.4, 110.0, 67.6, 52.8, 28.6; HRMS $(M + H)^+$, calcd $C_{19}H_{18}N_3O_4$: 352.1297, found 352.1304.

1-(2-Trimethylsilanyl-ethanesulfonyl)-1*H*-indole-5-carboxylic Acid Ethyl Ester (17). A solution of 1*H*-Indole-5-carboxylic acid ethyl ester **16** (10.31 g, 58.8 mmol) in DMF (50 mL) was added dropwise at 0 °C to a mixture of NaH (1.83 g, 76.4 mmol) in DMF (150 mL). After stirring at 0 °C for 30 min, a solution of SESCl (17.7 g, 88.2 mmol) in DMF (100 mL) was added slowly at 0 °C. The mixture was stirred for 2 h, quenched with saturated aqueous NH_4Cl (200 mL) and extracted with EtOAc (300 mL). The organic layer was separated and the aqueous layer was extracted with additional EtOAc (2 × 150 mL). The combined organic extracts were washed with brine (3 × 150 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated and the resulting residue was subjected to flash column chromatography using CH_2Cl_2/hexanes (2:3) as eluent to afford the title compound as a white solid (15.8 g, 76% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.36 (d, *J* = 1.5 Hz, 1H), 8.03 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.50 (d, *J* = 3.5 Hz, 1H), 6.75 (d, *J* = 3.5 Hz, 1H), 3.94 (s, 3H), 3.21 - 3.18 (m, 2H), 0.84 - 0.80 (m, 2H), −0.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.3, 137.7, 130.3, 128.3, 125.9, 125.5, 124.0, 112.8, 108.3, 52.2, 51.2, 10.1, −2.1; HRMS $(M - H)^-$, calcd for $C_{16}H_{22}NO_4SSi$ 352.1039, found 352.1043.

[1-(2-Trimethylsilanyl-ethanesulfonyl)-1*H*-indol-5-yl]-methanol (18). DIBAL-H (82.9 mL, 1 M in toluene, 82.9 mmol) was added slowly to a solution of **17** (8.81 g, 25.9 mmol) in toluene (200 mL) at 0 °C. After stirring at 0 °C for 45 min, the reaction was quenched by the addition of MeOH (26 mL), finely ground $Na_2SO_4 \bullet 10H_2O$ (194 g) and Celite (26 mL). The mixture was warmed to rt over 1 h and filtered through a pad of Celite. The solvents were removed *in vacuo* to afford the title compound as a viscous liquid, which solidified upon standing to give a white solid (8.08 g, 100% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.87 (d, *J* = 8.5 Hz, 1H), 7.62 (s, 1H), 7.44 (d, *J* = 3.7 Hz, 1H), 7.35 (dd, *J* = 8.6, 1.5 Hz, 1H), 6.66 (d, *J* = 3.7 Hz, 1H), 4.79 (s, 2H), 3.18−3.14 (m, 2H), 1.73 (s, 1H), 0.85−0.82 (m, 2H), −0.06 (s, 9H); HRMS $(M + Na)^+$ calcd for $C_{14}H_{21}NNaO_3SSi$ 324.0909, found 324.0915.

1-(2-Trimethylsilanyl-ethanesulfonyl)-1*H*-indole-5-carbaldehyde (19). A solution of **18** (2.1 g, 6.74 mmol) in CH_2Cl_2 (30 mL) was added at 0 °C to a mixture of activated MnO_2 (22 g, azeotropically dried with toluene twice) and CH_2Cl_2 (70 mL) in a 500 mL round-bottom flask. The reaction mixture was stirred at 0 °C for 30 min and filtered through a pad of Celite. The solvents were removed *in vacuo* to afford the title compound as a white solid (1.8 g, 86% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.06 (s, 1H), 8.15 (s, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.87 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.54 (d, *J* = 3.4 Hz, 1H), 6.80 (d, *J* = 3.6 Hz, 1H), 3.24 - 3.20 (m, 2H), 0.86 - 0.82 (m, 2H), −0.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.9, 138.5, 132.3, 130.7, 128.8, 125.3, 125.1, 113.6, 108.4, 51.4, 10.2, −2.1; HRMS $(M - H)^-$ calcd for $C_{14}H_{18}NO_3SSi$ 308.0777, found 308.0782.

2-Benzyloxycarbonylamino-3-[1-(2-trimethylsilanyl-ethanesulfonyl)-1*H*-indol-5-yl]-acrylic Acid Methyl Ester (20). Compound **20** was prepared from **19** (1.6 g, 5.17 mmol) according to the procedure described for the preparation of **14a**. Purification by flash chromatography using CH_2Cl_2/hexanes (2:3) containing 1% Et_3N as eluent afforded the title compound (1.9 g, 75% yield) as a 92:8 Z/E mixture (determined by the integration of $CO_2\underline{CH_3}$, for Z isomer it was at 3.79 ppm and E isomer 3.65 ppm). For the Z isomer: ^{1}H NMR (CD_3CN, 500 MHz) δ 7.96 (s, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 3.7 Hz, 1H), 7.51 (s, 1H), 7.43 - 7.35 (m, 5H), 7.67 (d, *J* = 3.7 Hz, 1H), 5.16 (s, 2H), 3.79 (s, 3H), 3.42 - 3.38 (m, 2H), 0.87 - 0.83 (m, 2H), −0.04 (s, 9H); ^{13}C NMR (126 MHz, ACETONITRILE-d_3) δ ppm 166.27, 155.00, 135.80, 133.79, 131.11, 129.06, 128.91, 128.66, 128.47, 128.22, 126.67, 124.86, 124.01, 118.01, 113.61, 108.09, 67.12, 52.48, 51.25, 10.11, −2.74; HRMS $(M + NH_4)^+$ calcd for $C_{25}H_{34}N_3O_6SSi$ 532.1938, found 532.1940.

(*R*)-2-Benzyloxycarbonylamino-3-[1-(2-trimethylsilanyl-ethanesulfonyl)-1*H*-indol-5-yl]-propionic Acid Methyl Ester (6a). Compound **6a** was prepared according to the procedure described for the preparation of **5**: [3.21 g of **20**, 23 mg (0.56 mol %) of $[Rh(COD)L]BF_4$, L = (*R*,*R*)-Et-DuPhos, MeOH (60 mL), CH_2Cl_2 (60 mL), H_2 (60 psi), rt, 2 h]. Purification by flash chromatography using EtOAc/hexanes (1:3) as eluent gave the title compound as an off-white foamy solid (3.15 g, 98% yield, 98.4% *ee*). The *ee* was determined by HPLC analysis (Chiralcel-OD column, 4.6 × 250 mm, 10 μm; 80% hexane/20% EtOH @ 1.0 mL/min. for 14 min; λ = 214 nm; t_R = 9.7 min for *R*- and 7.6 min for *S*-enantiomer). ^{1}H NMR (CD_3OD, 500 MHz) δ 7.82 (d, *J* = 8.5 Hz, 1H), 7.52 (d, *J* = 3.5 Hz, 1H), 7.50 (s, 1H), 7.32−7.26 (m, 6H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 4.0 Hz, 1H), 5.05 (d, *J* = 12.5 Hz, 1H), 5.01 (d, *J* = 12.5 Hz, 1H), 4.51 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.72 (s, 3H), 3.35 - 3.32 (m, 2H), 3.28 (dd, *J* = 14.0, 5.2 Hz, 1H), 3.06 (dd, *J* = 14.0, 9.4 Hz, 1H), 0.75 - 0.72 (m, 2H); ^{13}C NMR (CD_3OD, 125 MHz) δ 172.9, 157.3, 137.2, 134.6, 132.4, 131.2, 128.5, 128.0, 127.7, 127.6, 125.9, 122.1, 113.0, 107.6, 66.5, 56.3, 51.8, 50.4, 37.5, 10.1, −3.2; HRMS $(M + NH_4)^+$ Calc for $C_{25}H_{36}N_3O_6SSi$ 534.2094, found 534.2100.

2-Benzyloxycarbonylamino-3-(1*H*-indol-5-yl)-propionic Acid Methyl Ester (21). CsF (2.11 g, 13.9 mmol) was added to a solution of **6a** (715 mg, 1.39 mmol) in CH_3CN (50 mL). The resulting suspension was heated at 80 °C for 3 h. After cooling to rt, the solvent was removed *in vacuo* and the residue was subjected to flash chromatography using CH_2Cl_2/MeOH/Et_3N (93:5:2) as eluent to afford the title compound as a tan viscous oil (470 mg, 96% yield, 86.0% *ee*). The *ee* was determined by HPLC analysis (Chiralpak-AD column, 4.6 × 250 mm, 10 μm; A = EtOH, B = 0.05% diethylamine/hexane, 85%B @ 1.0 mL/min for 30 min; λ = 223 nm; t_R = 23.7 min for *R*- and 21.9 min for *S*-enantiomer). ^{1}H NMR (CD_3OD, 500 MHz) δ 7.39 (s, 1H), 7.36 - 7.26 (m, 7H), 7.22 (d, J = 3.0 Hz, 1H), 6.97 (dd, J = 7.8, 1.5 Hz, 1H), 6.40 - 6.39 (m, 1H), 5.06 (d, J = 12.5 Hz, 1H), 5.02 (d, J = 12.5 Hz, 1H), 4.48 (dd, J = 8.5, 6.0 Hz, 1H), 3.70 (s, 3H), 3.21 (dd, J = 14.0, 6.0 Hz, 1H), 3.02 (dd, J = 14.0, 8.75 Hz, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 173.4, 157.4, 137.1, 135.8, 128.7, 128.5, 128.0, 127.7, 127.3, 125.1, 122.7, 120.8, 111.4, 101.4, 66.6, 56.7, 51.8, 38.0; HRMS $(M + H)^+$ Calc. for $C_{20}H_{21}N_2O_4$ 353.1501, found 353.1508.

2-Benzyloxycarbonylamino-3-(2-oxo-2,3-dihydro-1*H*-indol-5-yl)-propionic Acid Methyl Ester (7) and 2-Benzyloxycarbonylamino-3-(2,3-dibromo-1*H*-indol-5-yl)-propionic Acid Methyl Ester (22). $PyHBr_3$ (1.28 g, 4.02 mmol) was added in portions over 30 min to a stirred solution of **21** (0.47 g, 1.34 mmol) in *t*-BuOH (10 mL) at rt. After stirring at rt for 3.5 h, *t*-BuOH was removed *in vacuo* and the residue was extracted with EtOAc, washing with brine twice. The combined organic extracts were dried over Na_2SO_4 and filtered. The filtrate was concentrated and the resulting residue was azeotropically dried with anhydrous EtOH. AcOH (10 mL) and Zn powder (0.88 g, 13.4 mmol) were added and the mixture was stirred overnight at rt. After AcOH was removed *in vacuo*, the residue was subjected to flash column chromatography using EtOAc/hexanes (1:3, then 3:2) as eluent to afford the title compound **7** as a white solid (202 mg, 41% yield) and compound **22** (238 mg, 35% yield) along with **23** (31 mg, 4% yield) as a tan solid. For compound **7**: The *ee* was determined by HPLC analysis (Chiralpak-AD column, 4.6 × 250 mm, 10 μm; A = IPA, B = 0.05% diethylamine/heptane, 70% B @ 1.0 mL/min for 22 min; λ = 251 nm; t_R = 17.6 min for *R*- and 14.7 min for *S*-enantiomer). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.03 (s, 1H), 7.36−7.31 (m, 5H), 6.94 (s, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 7.5 Hz, 1H), 5.26 (d, J = 8.0 Hz, 1H), 5.11 (d, J = 12.0 Hz, 1H), 5.05 (d, J = 12.5 Hz, 1H), 4.61 (dd, J = 13.5, 6.0 hz, 1H), 3.72 (s, 3H), 3.45 (s, 2H), 3.10 (dd, J = 14.0, 5.5 Hz, 1H), 3.00 (dd, J = 14.0, 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.7, 172.2, 155.7, 141.7, 136.3, 129.8, 128.9, 128.6, 128.3, 128.2, 125.8, 125.6, 109.8, 67.1, 55.1, 52.5, 38.0, 36.; HRMS $(M + H)^+$ Calc. for $C_{20}H_{21}N_2O_5$ 369.1450, found 369.1454. For compound **22**: ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 11.15 (s, 1H), 7.35 (br s, 2H), 7.30 (br s, 4H), 7.16−7.15 (m, 1H), 6.68−6.67 (m, 1H), 5.03 (s, 2H), 4.56 (s, 1H), 3.71 (s, 3H), 3.32−3.29 (m, 1H), 3.16−3.12 (m, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 172.6, 156.4, 137.6, 135.7, 130.2, 128.7, 128.13, 128.04, 127.76, 124.9, 119.0, 111.8, 110.7, 92.7, 66.3, 56.5, 51.9, 38.0; HRMS $(M + Na)^+$ Calc for $C_{20}H_{18}Br_2N_2NaO_4$ 530.9531, found 530.9535.

3,4-Dinitro-benzaldehyde (25). BH_3•THF (1 M in THF, 800 mL, 800 mmol) was added at −20 °C over 45 min to a solution of 3,4-dinitrobenzoic acid **24** (93.5 g, 441 mmol) in THF (300 mL). After stirring at −20 °C for 1 h, the mixture was warmed to rt and stirring was continued overnight. The mixture was quenched by the addition of 32 mL of 1:1 HOAc/H_2O. The solvents were removed *in vacuo* and the residue was poured into 1000 mL of ice-cold saturated aqueous $NaHCO_3$ with vigorous stirring over 15 min. The mixture was extracted with EtOAc (3 × 500 mL) and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. After filtration, the solvent was removed to afford (3,4-dinitrophenyl)-methanol as a light yellow solid (100% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.91(d, J = 8.0 Hz, 1H), 7.89 (s, 1H), 7.71 (dd, J = 8.5, 1.0 Hz, 1H), 4.87 (s, 2H), 2.30 (s, 1H).

A solution of (3,4-dinitro-phenyl)-methanol (95.3 g, 481 mmol) in CH_2Cl_2 (500 mL) was added all at once to a suspension of PCC (156 g, 722 mmol) in CH_2Cl_2 (900 mL). After stirring at rt for 1.5 h, 1.5 L of diethyl ether was added. The supernatant was decanted from the black gum and the insoluble residue was washed thoroughly with CH_2Cl_2 (3 × 250 mL). The combined organic mixtures were filtered through a pad of Florisil to afford a light bright-yellow clear solution. The solvents were removed *in vacuo* and the residue was subjected to flash column chromatography using CH_2Cl_2 as eluent to afford the title compound as a yellow solid (52.7 g, 71% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.45 (d, J = 1.5 Hz, 1H), 8.28 (dd, J = 8.1, 1.5 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 187.7, 139.2, 134.2, 126.2, 125.7.

2-Benzyloxycarbonylamino-3-(3,4-dinitro-phenyl)-acrylic Acid Methyl Ester (26). Compound **26** was prepared from 3,4-dinitrobenzaldehyde **25** (61.4 g, 313 mmol) according to the procedure described for the preparation of **14a**. Once the reaction reached completion, the solvents were removed *in vacuo*. The yellow residue was dissolved in 4.5 L of EtOAc, washed with 1.5 L of 1N H_2SO_4, H_2O twice, brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under vacuum and the residue was recrystallized from EtOAc (20 g crude product/100 mL of EtOAc). The yellow crystals were collected and further purified by flash column chromatography using CH_2Cl_2 as eluent. The title compound was obtained as yellow crystals (96.7 g, 77% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85 (d, J = 1.5 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.62 (dd, J = 8.5, 1.5 Hz, 1H), 7.35−7.34 (m, 3H), 7.34 (br s, 2H), 7.23 (s, 1H), 6.95 (br s, 1H), 5.07 (s, 2H), 3.90 (s, 3H);); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 164.8, 154.0, 142.1, 140.6, 139.8, 136.1, 134.5, 130.4, 128.3, 128.0, 127.7, 125.8, 125.6, 125.0, 66.3, 52.6.

(*R*)-2-Benzyloxycarbonylamino-3-(3,4-dinitro-phenyl)-propionic Acid Methyl Ester (27). Compound **27** was prepared according to the procedure described for the preparation of **5**: [3.61 g of **26**, 29.7 mg (0.50 mol %) of [Rh(COD)L]BF_4, L = (*R*,*R*)-Et-DuPhos, MeOH (50 mL), CH_2Cl_2 (50 mL), H_2 (60 psi), rt, 2 h]. The residue was purified by flash column chromatography using EtOAc/hexanes (1:1) as eluent to afford the title compound as a light tan gummy solid (3.56 g, 98% yield and 99.6% *ee*). The *ee* was determined by HPLC analysis (Chiralpak AD column, 4.6 × 250 mm, 10 μm; A = EtOH, B = hexane; 40% B @ 1.0 mL/min for 14 min; λ = 208 nm; t_R = 10.9 min for *R* enatiomer and 6.9 min for *S* enatiomer). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.80 (d, J = 8.0 Hz, 1H), 7.63 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.38 - 7.31 (m, 5H), 5.37 (d, J = 6.0 Hz, 1H), 5.13−5.05 (m, 2H), 4.68 (d, J = 6.0 Hz, 1H), 3.71 (s, 3H), 3.36 (dd, J = 13.5, 5.0 Hz, 1H), 3.17 (dd, J = 13.5, 6.0 Hz, 1H);); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 171.4, 155.8, 145.7, 141.9, 140.3, 136.7, 134.9, 128.2, 127.7, 127.4, 126.0, 125.4, 65.4, 54.2, 52.1, 35.5.

(*R*)-2-Benzyloxycarbonylamino-3-(3,4-diamino-phenyl)-propionic Acid Methyl Ester (28). To a suspension of **27** (1.45 g, 3.6 mmol) and Zn power (1.41 g, 21.6 mmol) in MeOH (50 mL, degassed with a flow of N_2 for 2 h), HCO_2NH_4 (2.27 g, 36 mmol) was added in portions at 0 °C. After stirring at rt overnight, the solvents were removed. Toluene (30 mL, degassed) and EtOAc (30 mL, degassed) were added, followed by HOAc (3 mL), diluting further with these solvents until all organic solids had dissolved. Then, the mixture was washed with H_2O, brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* to afford **28**•HOAc as a reddish gummy solid (1.23 g, 85% yield). HRMS $(M + H)^+$ calcd for $C_{18}H_{22}N_3O_4$ 344.1610, found 344.1616.

3-(1*H*-Benzotriazol-5-yl)-2-benzyloxycarbonylamino-propionic Acid Methyl Ester (8). To a solution of **28**•HOAc (2.68 g, 6.65 mmol) in AcOH (30 mL) and H_2O (40 mL), was added a solution of $NaNO_2$ (0.46 g, 6.65 mmol) in H_2O (8 mL) dropwise at rt. After stirring at rt for 20 min, the mixture was cooled to 0 °C and conc. NH_3•H_2O was added to adjust the pH to 11. The mixture was extracted with EtOAc twice in the presence of solid NaCl. The organic extracts were dried over Na_2SO_4 and filtered. The solvents were removed *in vacuo* and the residue was subjected to flash column chromatography using EtOAc/hexanes (6:4) as eluent to afford the title compound as a tan solid (2.12 g, 94% yield). ^1H NMR (CD_3OD, 500 MHz) δ 7.75 (d, $J = 8.5$ Hz, 1H), 7.58 (s, 1H), 7.31−7.25 (m, 5H), 7.18 (d, $J = 8.5$ Hz, 1H), 5.39 (d, $J = 8.0$ Hz, 1H), 5.10 (d, $J = 12.0$ Hz, 1H), 5.05 (d, $J = 12.0$ Hz, 1H), 4.74 (dd, $J = 13.5$, 6.0 Hz, 1H), 3.73 (s, 3H), 3.34 (dd, $J = 14.0$, 5.5 Hz,1H), 3.22 (dd, $J = 13.5$, 6.0 Hz, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 172.1, 156.0, 136.1, 128.6, 128.3, 128.1, 67.2, 55.2, 52.7, 38.5; HRMS $(M + H)^+$ calcd for $C_{18}H_{19}N_4O_4$ 355.1406, found 355.1410.

(*R*)-2-Benzyloxycarbonylamino-3-(2-oxo-2,3-dihydro-1*H*-benzoimidazol-5-yl)-propionic Acid Methyl Ester (9). To a solution of **28**•2HCl (600 mg, 1.44 mmol) in THF (125 mL) was added Et_3N (320 mg, 3.17 mmol). A fine precipitate was observed. *N*,*N*′-Carbonyldiimidazole (280 mg, 1.73 mmol) was added all at once and the reaction mixture was stirred overnight at rt. After filtration to remove the fine precipitate, the filtrate was concentrated and subjected to flash column chromatography using MeOH/CH_2Cl_2 (1:12) as eluent to give the title compound (313 mg, 59% yield). ^1H NMR (CD_3OD, 300 MHz) δ 7.28 (m, 5H), 6.94−6.85 (m, 3H), 5.01 (dd, $J = 20.3$, 12.6 Hz, 2H), 4.44 (dd, $J = 9.1$, 5.5 Hz, 1H), 3.68 (s, 3H), 3.15 (dd, $J = 13.5$, 5.5 Hz, 1H), 2.92 (dd, $J = 13.5$, 9.1 Hz, 1H); ^{13}C NMR (CD_3OD, 75 MHz) δ 174.0, 158.4, 158.2, 138.2, 131.7, 131.0, 129.8, 129.4, 129.0. 128.7, 123.6, 111.1, 110.2, 67.6, 57.4, 52.7, 38.8; HRMS $(M + H)^+$ Calc for $C_{19}H_{20}N_3O_5$ 370.1403, found 370.1408.

(*R*)-2-Benzyloxycarbonylamino-3-(2-methyl-1*H*-benzoimidazol-5-yl)-propionic acid methyl ester (10). A solution of **28**•HOAc (640 mg) in AcOH (8 mL) was heated at 130 °C for 4 h. The mixture was poured into H_2O and cooled to 0 °C. After the pH was adjusted to 8 by adding solid $NaHCO_3$ in portions, the aqueous mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with H_2O, brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated to afford the title compound as a brown foamy solid (554 mg, 95% yield). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.39 (d, $J = 8.5$ Hz, 1H), 7.35 (s, 1H), 7.26 - 7.22 (m, 5H), 7.06 (d, $J = 8.0$ Hz, 1H), 5.03 (d, $J = 12.5$ Hz, 1H), 4.99 (d, $J = 13.0$ hz, 1H), 4.51 (dd, $J = 8.5$, 5.5 Hz, 1H), 3.70 (s, 3H), 3.27 (dd, $J = 13.5$, 5.0 Hz, 1H), 3.03 (dd, $J = 14.0$, 9.0 Hz, 1H), 2.55 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.0, 157.4, 152.2, 137.2, 131.2, 128.4, 127.9, 127.6, 123.5, 66.5, 56.5, 51.7, 37.9, 13.3; HRMS $(M + H)^+$ Calc for $C_{20}H_{22}N_3O_4$ 368.1610, found 368.1616.

2-Benzyloxycarbonylamino-3-(3-hydroxy-4-nitro-phenyl)-acrylic Acid Methyl Ester (30). Compound **30** was prepared using 3-hydroxy-4-nitrobenzaldehyde **29** (14.1 g, 84.2 mmol) according to the method described for the preparation of **14a**. Once the reaction had reached completion, the solvents were removed *in vacuo*. The yellow residue was dissolved in 1.5 L of EtOAc, washed with 1N H_2SO_4 (500 and 250 mL), H_2O twice, brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* and the resulting residue was recrystallized from EtOAc. The yellow crystals were collected and further purified by flash column chromatography using CH_2Cl_2 as eluent to afford the title compound as pale-yellow crystals (25.1 g, 80% yield). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.93 (d, $J = 9.0$ Hz, 1H), 7.32 (br s, sH), 7.28 (br s, 2H), 7.17 (s, 1H), 7.16 (d, $J = 2.0$ Hz, 1H), 7.01 (dd, $J = 9.0$, 2.0 Hz, 1H), 6.74 (br s, 1H), 5.06 (s, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.0, 154.9, 152.8, 144.0, 135.5, 132.9, 128.6, 128.5, 128.2, 127.2, 125.8, 125.1, 120.6, 120.2, 68.0, 53.3; HRMS $(M + H)^+$ Calc for $C_{18}H_{17}N_2O_7$ 373.1036, found 373.1044.

(*R*)-2-Benzyloxycarbonylamino-3-(3-hydroxy-4-nitro-phenyl)-propionic Acid Methyl Ester (31). Compound **31** was prepared according to the procedure described for the preparation of compound **5**: [6.0 g of **30**, 106 mg (1.0 mol %) of [Rh(COD)L]BF_4, L = (*R*,*R*)-Et-DuPhos, MeOH (60 mL), CH_2Cl_2 (60 mL), H_2 (60 psi), rt, 4 h]. The residue was purified by flash chromatography using straight CH_2Cl_2 as eluent to afford the title compound as an off yellow solid (5.94 g, 99% yield and 99.6% *ee*). The *ee* was determined by HPLC analysis (Chiralpak AD column, 4.6 × 250 mm, 10 μm; A = EtOH, B = heptane; 40% B @ 1.0 mL/min for 20 min; λ = 282nm; t_R = 14.8 min for *R*-enantiomer and 9.7 min for *S*-enantiomer). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.97 (d, $J = 9.0$ Hz, 1H), 7.36−7.30 (m, 5H), 6.90 (s, 1H), 6.71 (d, $J = 8.5$ Hz, 1H), 5.29 (d, $J = 7.0$ Hz, 1H), 5.11 (d, $J = 12.5$ Hz, 1H), 5.07 (d, $J = 12.0$ Hz, 1H), 4.68 (dd, $J = 13.0$, 6.0 Hz, 1H), 3.74 (s, 3H), 3.20 (dd, $J = 13.5$, 5.0 Hz, 1H), 3.05 (dd, $J = 13.5$, 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.3, 155.6, 155.0, 147.3, 136.1, 132.7, 128.6, 128.4, 128.2, 125.3, 121.5, 120.5, 67.3, 54.3, 52.8, 38.4. HRMS $(M + H)^+$ Calc for $C_{18}H_{19}N_2O_7$ 375.1192, found 375.1194.

(*R*)-methyl 3-(4-amino-3-hydroxyphenyl)-2-(benzyloxycarbonylamino)propanoate Hydrochloride (32). Fe (3.7 g, 66.4 mmol) and NH_4Cl (5.9 g, 111 mmol) were added at 0 °C to a solution of **31** (2.07 g, 5.53 mmol) in a mixture of MeOH (degassed, 200 mL) and H_2O (degassed, 200 mL). After stirring at rt for 48 h, CF_3CO_2H (7 mL) was added, swirling until the mixture was a clear dark-red solution containing unreacted Fe powder. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was extracted with EtOAc (2 × 150 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4, and filtered. HCl (4.2 mL, 4 M in dioxane) was added to the filtrate. The solvents were removed *in vacuo* to afford **32**•HCl as a tan foamy solid (80% yield). ^1H NMR (CD_3OD, 500 MHz) δ 7.34−7.28 (m, 5H), 7.20 (d, $J = 8.0$ hz, 1H), 6.88 (s, 1H), 6.78 (d, $J = 7.5$ Hz, 1H), 5.05−5.00 (m, 2H), 4.42 (dd, $J = 8.5$, 5.0 Hz, 1H), 3.70 (s, 3H), 3.65 (s, 1H), 3.33 (br s, 2H), 3.11 (dd, $J = 14.0$, 5.0 hz, 1H), 2.90 (dd, $J = 13.5$, 9.0 Hz, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 172.5, 157.4, 151.2, 140.2, 137.0, 128.5, 128.0, 127.7, 123.8, 120.9, 117.0, 116.9, 67.2, 55.7, 52.0, 37.2; HRMS $(M + H)^+$ Calc for $C_{18}H_{21}N_2O_5$ 345.1450, found 345.1454.

(*R*)-2-Benzyloxycarbonylamino-3-(2-oxo-2,3-dihydro-benzooxazol-6-yl)-propionic Acid Methyl Ester (11). To a solution of **32**•HCl (1.17 g, 3.07 mmol) and *i*PrNEt$_2$ (1.60 mL, 9.21 mmol) in CH_2Cl_2 (85 mL) at 0 °C, was added a solution of *N*,*N*′-carbonyldiimidazole (498 mg, 3.07 mmol) in CH_2Cl_2 (15 mL). After stirring at 0 °C for 4 h, the solvents were removed *in vacuo* and the residue was subjected to flash column chromatography using EtOAc/hexanes (1:1) as eluent to afford the title compound as a white solid (579 mg, 51% yield). ^1H NMR ($CDCl_3$, 500 MHz) δ 9.07 (s, 1H), 7.37−7.29 (m, 5H), 6.96 (s, 1H), 6.90 (d, $J = 8.0$ Hz, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 5.36 (d, $J = 8.0$ Hz, 1H), 5.11 (d, $J = 12.0$ Hz, 1H), 5.07 (d, $J = 12.5$ Hz, 1H), 4.65 (dd, $J = 13.5$, 5.5 Hz, 1H), 3.74 (s, 3H), 3.17 (dd, $J = 14.0$, 5.5 Hz, 1H), 3.07 (dd, $J = 14.0$, 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.9, 155.7, 155.5, 144.1, 136.2, 130.8, 128.6, 128.42, 128.38, 128.2, 125.1, 111.1, 109.8, 67.2, 55.1, 52.6, 38.3; HRMS $(M + H)^+$ calcd for $C_{19}H_{19}N_2O_6$ 371.1243, found 371.1246.

(*R*)-Methyl 2-(benzyloxycarbonylamino)-3-(5-chloro-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)propanoate (11a). A mixture of benzoxalone **11** (700 mg, 1.89 mmol), NCS (315 mg, 2.36 mmol) and AcOH (20 mL) was heated at 100 °C for 16 h. The solvents were removed *in vacuo* and the residue was subjected to flash chromatography using EtOAc/hexanes (4:6, then 1:1) as eluent to afford the title compound as an off-white solid (242 mg, 32% yield). ^1H NMR (CD_3COCD_3, 500 MHz) δ 10.47 (s, 1H), 7.36−7.28 (m, 6H), 7.20 (s, 1H), 6.80 (d, $J = 8.5$ Hz, 1H), 5.05 (d, $J = 12.5$ Hz, 1H), 5.00 (d, $J = 12.5$ Hz, 1H), 4.65−4.60 (m, 1H), 3.73 (s, 3H), 3.43 (dd, $J = 14.0$, 5.0 Hz, 1H), 3.08 (dd, $J = 14.0$, 10.5 Hz, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 172.2, 156.5, 154.5, 143.1, 137.5, 130.8, 129.0, 128.9, 128.7, 128.2, 128.0, 112.8, 110.9, 66.3, 54.3, 52.1, 35.8; HRMS $(M + H)^+$ calcd for $C_{19}H_{18}ClN_2O_6$ 405.0853, found 405.0858.

(*R*)-Methyl 2-(benzyloxycarbonylamino)-3-(5-bromo-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)propanoate (11b). A mixture of benzoxalone **11** (1070 mg, 2.89 mmol), NBS (643 mg, 3.61 mmol) and AcOH (30 mL) was heated at 100 °C for 16 h. The solvents were removed *in vacuo* and the residue was subjected to flash chromatography using EtOAc/hexanes (4:6, then 1:1) as eluent to afford the title compound as a light-yellow solid (446 mg, 34% yield). ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 10.46 (s, 1H), 7.36−7.28 (m, 7H), 6.82 (d, $J = 8.5$ Hz, 1H), 5.05 (d, $J = 12.5$ Hz, 1H), 5.00 (d, $J = 12.5$ Hz, 1H), 4.67−4.62 (m, 1H), 3.73 (s, 3H), 3.43 (dd, $J = 14.0$, 5.0 Hz, 1H), 3.10 (dd, $J = 14.0$, 10.5 Hz, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 172.2, 156.4, 154.2, 143.7, 137.6, 131.1, 130.6, 128.7, 128.2, 128.0, 118.2, 113.9, 112.9, 66.2, 54.3, 52.1, 38.3; HRMS $(M + H)^+$ calcd for $C_{19}H_{18}BrN_2O_6$ 449.0348, found 449.0356.

(*S*)-Methyl 2-(Benzyloxycarbonylamino)-3-(4-bromo-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)propanoate (11c). In a flame-dried 250 mL round-bottom flask, benzoxalone **11** (418 mg, 1.13 mmol) and NBS (221 mg, 1.24 mmol) were stirred in anhydrous CH_2Cl_2 (70 mL). Once the mixture became a clear solution, SiO_2 (2.5 g, silica gel 60, 230−240 mesh ASTM, EMD) was added and the resulting mixture was stirred at rt for 4 h. The solvents were removed *in vacuo* and the residue was subjected to flash chromatography using EtOAc/hexanes (2:3) as eluent to afford the title compound as a light-yellow solid (408 mg, 80% yield). ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 10.71 (s, 1H), 7.35−7.28 (m, 6H), 7.21 (s, 1H), 6.75 (d, $J = 7.5$ Hz, 1H), 5.06 (d, 12.5 Hz, 1H), 5.02 (d, $J = 12.5$ Hz, 1H), 4.56−4.51 (m, 1H), 3.73 (s, 3H), 3.26 (dd, $J = 14.0$, 5.0 Hz, 1H), 3.03 (dd, $J = 14.0$, 10.0 Hz, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 172.2, 156.4, 153.8, 144.4, 137.6, 133.7, 129.8, 128.7, 128.2, 128.0, 127.8, 110.1, 100.9, 66.3, 55.9, 52.0, 37.3; HRMS $(M + H)^+$ calcd for $C_{19}H_{18}BrN_2O_6$ 449.0348, found 449.0354.

(*R*)-Methyl 2-(benzyloxycarbonylamino)-3-(4-chloro-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)propanoate (11d) and (11a). In a flame-dried 50 mL sealed tube, benzoxalone **11** (373 mg, 1.01 mmol) and NCS (168 mg, 1.26 mmol) were stirred in $ClCH_2CH_2Cl$ (20 mL). Once the mixture became a clear solution, SiO_2 (3.73 g) was added and the tube was sealed. After heating at 90 °C for 16 h, the solvents were removed *in vacuo* and the residue was subjected to flash chromatography using EtOAc/hexanes (1:2) as eluent to afford both compound **11d** (40 mg, 10% yield) and compound **11a** (78 mg, 19% yield) as off-white solids. For compound **11d**: ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 7.37−7.27 (m, 5H), 7.18 (d, $J = 1.0$ Hz, 1H), 7.16 (s, 1H), 6.76 (d, $J = 8.5$ hz, 1H), 5.06 (d, $J = 12.5$ Hz, 1H), 5.02 (d, $J = 12.5$ Hz, 1H), 4.55−4.51 (m, 1H), 3.72 (s, 3H), 3.26 (dd, $J = 14.0$, 5.0 Hz, 1H), 3.04 (dd, $J = 14.0$, 9.5 Hz, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 172.2, 156.4, 154.0, 144.8, 137.6, 133.3, 128.7, 128.2, 128.0, 127.9, 125.0, 66.3, 55.9, 52.0, 37.3; HRMS $(M + H)^+$ calcd for $C_{19}H_{18}ClN_2O_6$ 405.0853, found 405.0858.

(*R*)-Methyl 2-(benzyloxycarbonylamino)-3-(4-iodo-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)propanoate (11e). In a flame-dried 50 mL sealed tube, benzoxalone **11** (324 mg, 0.876 mmol) and IPy_2BF_4 (409 mg, 1.1 mmol) were stirred in $ClCH_2CH_2Cl$ (20 mL). Once the mixture became a clear solution, SiO_2 (3.24 g) was added and the tube was sealed. After heating at 90 °C for 5 h, the solvents were removed and the residue was subjected to flash chromatography using EtOAc/hexanes (1:2) as eluent to afford the title compound as a light-yellow solid (175 mg, 40% yield). ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 10.47 (s, 1H), 7.46 (s, 1H), 7.37−7.29 (m, 5H), 7.22 (s, 1H), 6.74 (d, $J = 8.5$ Hz, 1H), 5.07 (d, $J = 12.5$ Hz, 1H), 5.02 (d, $J = 12.5$ Hz, 1H), 4.54−4.49 (m, 1H), 3.72 (s, 3H), 3.23 (dd, $J = 14.0$, 5.0 Hz, 1H), 3.01 (dd, $J = 14.0$, 9.5 Hz, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 172.2, 156.4, 153.4, 143.3, 137.6, 134.1, 133.64, 133.60, 128.7, 128.2, 128.0, 110.7, 71.1, 66.3, 56.0, 52.0, 37.1; HRMS $(M + H)^+$ calcd for $C_{19}H_{18}IN_2O_6$ 497.0210, found 497.0214.

(*S*)-Methyl 2-(Benzyloxycarbonylamino)-3-(4-cyano-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)propanoate (33). Bromide **11c** (200 mg, 0.45 mmol), $Zn(CN)_2$ (58 mg, 0.50 mmol), and $Pd(PPh_3)_4$ (104 mg, 0.09 mmol) were weighed into a 100 mL Schlenck flask and the flask was evacuated and filled with N_2 (3 times). DMF (10 mL, degassed by passing a stream of N_2 through it for 30 min) was transferred *via* cannula into the flask and the reaction mixture was again purged with 5 vacuum/N_2 cycles. After heating at 80 °C for 3 h, the solvents were removed *in vacuo* and the residue was subjected to flash chromatography using EtOAc/hexanes (2:3) as eluent to afford the title compound as a white solid (160 mg, 90% yield). ^{1}H NMR (CD_3COCD_3, 500 MHz) δ 10.27 (s, 1H), 7.31 (br s, 4H), 7.29−7.26 (m, 1H), 7.19 (s, 1H), 7.13 (s, 1H), 5.73 (d, $J = 7.9$ Hz, 1H), 5.14−5.10 (m, 2H), 4.75−4.70 (m, 1H), 3.79 (s, 3H), 3.24 - 3.20 (m, 1H), 3.05−3.00 (m, 1H); ^{13}C NMR (CD_3COCD_3, 125 MHz) δ 171.9, 156.1, 153.7, 144.1, 136.0, 132.2, 131.8, 128.7, 128.4, 128.1, 127.3, 115.5, 114.7, 93.5, 67.5, 55.0, 53.1, 38.2, 31.6; HRMS $(M + H)^+$ calcd for $C_{20}H_{18}N_3O_6$ 396.1196, found 396.1200.

Acknowledgment. Dedicated to Professor E. J. Corey on the occasion of his 80th birthday. We thank Dr. Jeffrey Campbell for his helpful discussion regarding the preparation of SESCl, Daniel R. Schroeder for 2D NMR studies, Edward S. Kozlowski for *ee* determinations, Pan Li and Marie D'Andrea for providing HRMS data.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all new compounds, HPLC traces for all *ee* determinations and ORTEP drawings of compounds **22** and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801577T