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Dynamic Kinetic Resolution of L-Threonine-derived α-Bromo Esters for Asymmetric Synthesis of α-Amino Esters

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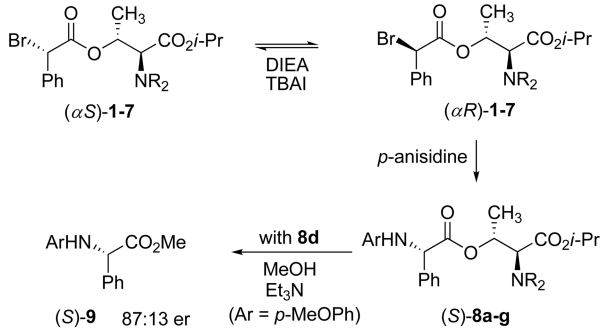
Many chiral alcohols have successfully been used as a chiral auxiliary for the dynamic resolution of α-halo esters in nucleophilic substitution.[1] L-Threonine is a proteinogenic α-amino acid that bears a chiral alcohol group. However, so far L-threonine has not been used as a chiral auxiliary for the dynamic resolution of α-halo esters. We herein report the first example of L-threonine-mediated dynamic kinetic resolution of α-bromo esters in nucleophilic substitution with various amine nucleophiles.

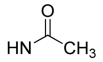
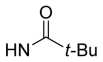
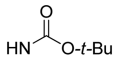
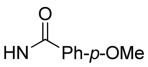
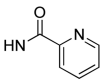
Treatment of *N*-acetyl L-threonine isopropyl ester with racemic α-bromo phenylacetic acid in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) provided α-bromo ester (α*RS*)-**1** in 70% yield with about 50:50 diastereomeric ratio (dr). When the mixture of (α*S*)-**1** and (α*R*)-**1** was treated with *p*-anisidine (1.2 equiv), tetrabutylammonium iodide (TBAI, 1.0 equiv) and diisopropylethylamine (DIEA, 1.0 equiv) in CH_2Cl_2 at room temperature for 12 h, amino ester **8a** was produced in 63% yield with 84:16 dr as shown in Table 1, entry 1. Also, six different *N*-protection groups of L-threonine were examined for the substitution with *p*-anisidine as shown in entries 2-7. The reactions of **2**, **3**, **4**, and **7** bearing *N*-pivaloyl, *N*-Boc, *N*-benzoyl, and *N*,*N*-dibenzyl groups gave slightly better drs ranging from 88:12 to 86:14, while the reactions of **5** and **6** bearing *N*-*p*-methoxybenzoyl and *N*-2-pyridinylcarbonyl groups gave lower drs compared to the reaction of **1**. The dr and yield of the substitutions in Table 1 imply that α-bromo carbon center is configurationally labile with respect to the rate of substitution and L-threonine-derived α-bromo esters (α*RS*)-**1-7** are dynamically resolved during the reaction. When *N*-benzoyl L-threonine-derived **8d** was treated with MeOH and Et_3N for 12 h, the chiral auxiliary was easily removed and *N*-aryl phenylglycinate (*S*)-**9** was obtained in 71% yield with 87:13 enantiomeric ratio (er).[2]

In order to understand the asymmetric substitution pathway, we carried out two reactions with *N*-benzoyl L-threonine-derived α-bromo ester **4** of 90:10 dr. When **4** of 90:10 dr was treated with *p*-anisidine under the same conditions, **8d** was obtained with the same stereoselectivity (87:13 dr) as in the reaction of **4** of 50:50 dr. Thus, the dr of **8d** is not dependent on the starting dr of **4**. Also, when **4** of 90:10 dr was allowed to reach thermodynamic equilibrium in the presence of DIEA for 48 h, the dr of recovered **4** was determined to be 55:45 dr. The result indicates that the thermodynamic stabilities of two epimers are almost same, ruling out dynamic thermodynamic resolution as a primary pathway.[3] These preliminary results indicate that the epimerization is sufficiently fast with respect to the rate of substitution and the primary pathway of the asymmetric induction is a dynamic kinetic resolution.[4]

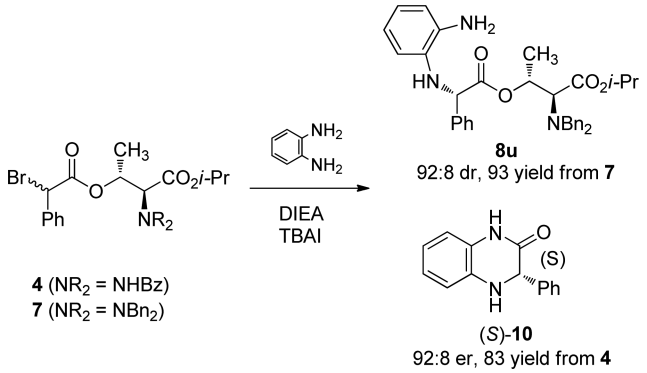
Next, the scope of the dynamic kinetic resolution has been examined with various amine nucleophiles as shown in Table 2. *N*,*N*-Dibenzyl substituted α-bromo ester **7** and *N*-benzoyl substituted α-bromo ester **4**, which gave the highest drs for the reaction with *p*-ansidine were then used to explore the scope of the substitution. The treatment of **4** with

Table 1. L-Threonine-mediated dynamic kinetic resolution



Entry[a]	Substrate	NR_2	Product	Yield[b] (%)	Dr[c]
1	**1**		**8a**	63	84:16
2	**2**		**8b**	64	87:13
3	**3**		**8c**	58	86:14
4	**4**		**8d**	62	87:13
5	**5**		**8e**	86	81:19
6	**6**		**8f**	62	80:20
7	**7**	$N(Bn)_2$	**8g**	66	88:12

[a]All reactions were carried out in CH_2Cl_2 at rt. [b]Isolated yields after 12 h. [c]The drs were determined by ^1H NMR of reaction mixture.



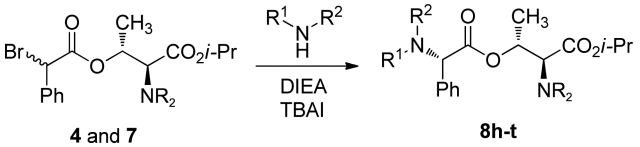
Scheme 1. Asymmetric synthesis of dihydroquinoxalinone.

benzylamine in CH_2Cl_2 for 12 h at rt gave amino ester **8h** in 73% yield with 80:20 dr. (entry 1) Under the same reaction condition, the reactions with diphenylmethyl amine and *o*-anisidine gave amino esters **8i** and **8j** with 80:20 and 81:19 drs, respectively (entries 2-3). In contrast, the reactions with secondary amines such as dibenzylamine and benzyl methylamine gave lower drs compared to the reactions with primary amines (entries 4 and 5). Pleasingly, much higher drs were observed in the reactions of **7** with both primary and secondary amines. The reactions with primary amines such as *o*-anisidine, diphenylmethyl amine, (*R*)-methylbenzylamine and benzyl amine provided amino esters **8m**-**8p** in 54-71% yields with drs ranging from 90:10 to 87:13 (entries 6-9). Among the reactions of secondary amines, high stereoselectivities were observed in the reactions with dibenzylamine, benzylmethylamine and dibutylamine to afford **8r**, **8s**, and **8t** with drs ranging from 93:7 to 91:9, whereas mild drop in stereoselectivity was seen with a cyclic secondary amine, tetrahydroisoquinoline (entries 10-13). Limited results indicate that the size of amine nucleophile may have effect on the stereoselectivity of the substitution.

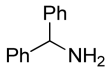
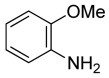
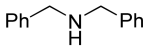
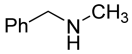
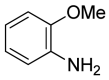
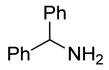
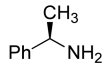
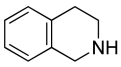
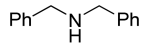
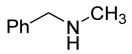
Encouraged by the high stereoselectivities in the reactions of α-bromo esters **4** and **7** with aryl amines, we also examined the substitution with 1,2-diaminobenzene for asymmetric syntheses of 3-substituted dihydroquinoxalinone as shown in Scheme 1. The heterocyclic compound possesses important biological and pharmacological properties, and accordingly there is growing interest in developing the asymmetric synthetic methods for the compound.[5] When α-bromo ester **7** was treated with 1,2-diaminobenzene, TBAI and DIEA in CH_2Cl_2 for 24 h at rt, the substitution gave **8u** in 93% yield with 92:8 dr and no spontaneous cyclization occurred. As with α-bromo esters **4**, however, the substitution and spontaneous cyclization took place to afford dihydroquinoxalinones (*S*)-**10** in 83% yield with 92:8 er.[2]

We conclude that *N*,*N*-dibenzyl L-threonine isopropyl ester is an effective and convenient chiral auxiliary for dynamic kinetic resolution of α-bromo esters in nucleophilic substitution with various amine nucleophiles. Also, we demonstrated that this methodology is efficient for the asymmetric preparation of 3-phenyl dihydroquinoxalinone **10** with high stereoselectivity. Simple and easy procedure in obtaining highly diastereoenriched α-amino acid derivatives suggests that the dynamic kinetic resolution approach should be further developed.

Table 2. Substitutions with various amine nucleophiles



4 and **7** → **8h-t**

Entry[a]	Substrate	Nucleophile	Product	Yield[b] (%)	Dr[c]
1	**4**		**8h**	73	80:20
2	**4**		**8i**	60	80:20
3	**4**		**8j**	85	81:19
4	**4**		**8k**	68	65:35
5	**4**		**8l**	62	71:29
6	**7**		**8m**	67	87:13
7	**7**		**8n**	67	88:12
8	**7**		**8o**	54	89:11
9	**7**		**8p**	71	90:10
10	**7**		**8q**	66	88:12
11	**7**		**8r**	73	93:7
12	**7**		**8s**	67	91:9
13	**7**		**8t**	64	92:8

[a]All reactions were carried out in CH_2Cl_2 at rt. [b]Isolated yields after 12 h. [c]The drs are determined by ^{1}H NMR of reaction mixture.

Experimental

General Procedure for the Asymmetric Nucleophilic Substitution *via* Dynamic Kinetic Resolution. To a solution of L-threonine-derived α-bromo ester (**1-7**) in CH_2Cl_2 (*ca.* 0.1 M) at rt were added DIEA (1.0 equiv), TBAI (1.0 equiv) and an amine nucleophile (1.2 equiv). After the resulting reaction mixture was stirred at room temperature for 12-24 h, the solvent was evaporated and the crude material was purified by column chromatography to give a α-amino ester. The drs of **8a-u** were determined by ^{1}H NMR

integration of hydrogens of two diastereomers and the ers of **9** and **10** were determined by CSP-HPLC.

***N*-Acetyl-*O*-(α-(*p*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8a).** 63% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.44-7.30 (m, 5H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 6.20 (d, *J* = 9.2 Hz, 1H), 5.40 (m, 1H), 4.98 (s, 1H), 4.94 (m, 1H), 4.77 (m, 1H), 3.69 (s, 3H), 2.01 (s, 1H), 1.22 (d, *J* = 6.0 Hz, 3H), 1.06 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 170.9, 170.4, 169.2, 152.7, 140.2, 137.4, 128.9, 128.5, 127.3, 127.2, 114.8, 72.2, 70.0, 61.8, 55.7, 55.4, 23.1, 21.7, 21.5, 16.4.

***N*-Pivaloyl-*O*-(α-(*p*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8b).** 64% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.45-7.26 (m, 5H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 6.15 (d, *J* = 9.2 Hz, 1H), 5.41 (m, 1H), 4.99 (m, 1H), 4.94 (s, 1H), 4.72 (m, 1H), 3.69 (s, 3H), 1.25 (m, 3H), 1.19 (s, 9H), 1.12 (m, 3H), 1.02 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 178.7, 170.8, 169.2, 152.7, 140.1, 137.6, 128.9, 128.4, 127.2, 121.9, 114.8, 72.7, 69.8, 61.8, 55.6, 55.2, 38.8, 27.4, 21.7, 21.5, 16.2.

***N*-Boc-*O*-(α-(*p*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8c).** 58% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.44-7.30 (m, 5H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 5.42 (m, 1H), 5.15 (d, *J* = 9.6 Hz, 1H), 4.93 (m, 2H), 4.50 (m, 1H), 4.38 (m, 1H), 3.69 (s, 3H), 1.50 (s, 9H), 1.24 (m, 3H), 1.08 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 170.9, 169.3, 155.8, 152.6, 140.2, 137.3, 128.9, 128.4, 127.2, 114.8, 80.2, 72.5, 69.8, 61.7, 57.2, 55.7, 28.8, 21.7, 21.5, 16.3.

***N*-Benzoyl-*O*-(α-(*p*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8d).** 62% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.55-7.26 (m, 10H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 5.49 (m, 1H), 5.02-4.95 (m, 3H), 4.57 (m, 1H), 3.68 (s, 3H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.15 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 171.0, 169.1, 167.6, 152.7, 140.2, 137.6, 133.7, 132.0, 128.9, 128.7, 128.4, 127.3, 127.2, 114.9, 114.7, 72.7, 70.1, 61.9, 55.9, 55.7, 21.8, 21.6, 16.6.

***N*-(*p*-Methoxybenzoyl)-*O*-(α-(*p*-methoxyanilino)phenyl acetyl)-L-threonine Isopropyl Ester (8e).** 86% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.69 (d, *J* = 8.8 Hz, 2H), 7.48-7.26 (m, 5H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 5.47 (m, 1H), 5.02-4.94 (m, 3H), 4.59 (br, 1H), 3.85 (s, 3H), 3.68 (s, 3H), 1.25 (m, 3H), 1.15 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 178.7, 170.8, 169.2, 152.7, 140.1, 137.6, 129.9, 128.9, 128.4, 127.8, 127.2, 121.9, 114.8, 114.7, 72.7, 69.8, 61.8, 55.6, 55.2, 21.7, 21.5, 16.2.

***N*-(2-pyridinylcarbonyl)-*O*-(α-(*p*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8f).** 62% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 8.67 (m, 2H), 8.18 (m, 1H), 7.86 (m, 1H), 7.50-7.26 (m, 5H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 5.54 (m, 1H), 5.05-4.92 (m, 3H), 4.57 (m, 1H), 3.69 (s, 3H), 1.24 (d, *J* = 6.0 Hz, 3H), 1.10 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 170.9, 168.8, 164.7, 152.6, 148.4, 140.2, 140.0, 139.9, 137.4, 128.8, 128.3, 127.2, 126.6, 122.5, 116.4, 114.9, 72.3, 70.0, 61.8, 55.7, 55.6, 21.7, 21.5, 16.5.

***N,N*-Dibenzyl-*O*-(α-(*p*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8g).** 66% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.38-7.21 (m, 15H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.50 (d, *J* = 8.8 Hz, 2H), 5.43 (m, 1H), 5.10 (m, 1H), 4.98 (d, *J* = 5.6 Hz, 1H), 4.70 (d, *J* = 6.0 Hz, 1H), 4.03 (d, *J* = 13.6 Hz, 2H), 3.69 (s, 3H), 3.59 (d, *J* = 13.6 Hz, 2H), 3.36 (d, *J* = 7.6 Hz, 1H), 1.31 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 171.1, 169.3, 152.5, 140.3, 139.3, 137.8, 129.0, 128.8, 128.4, 128.1, 127.2, 114.9, 114.7, 70.2, 68.5, 64.7, 61.9, 55.7, 55.4, 22.3, 22.0, 17.0.

***N,N*-Dibenzyl-*O*-(α-(*o*-methoxyanilino)phenylacetyl)-L-threonine Isopropyl Ester (8m).** 67% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.40-7.23 (m, 15H), 6.78-6.32 (m, 4H), 5.55 (d, *J* = 5.2 Hz, 1H), 5.45 (m, 1H), 5.11 (m, 1H), 5.04 (d, *J* = 5.2 Hz, 1H), 4.03 (d, *J* = 13.6 Hz, 2H), 3.82 (s, 3H), 3.61 (d, *J* = 13.6 Hz, 2H), 3.36 (d, *J* = 7.2 Hz, 1H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 170.9, 169.3, 147.1, 139.5, 139.3, 137.7, 136.1, 129.1, 128.9, 128.8, 128.7, 128.3, 128.1, 127.6, 127.2, 127.0, 121.0, 117.2, 110.7, 109.5, 70.3, 68.4, 64.7, 61.0, 55.4, 55.3, 22.3, 22.0, 17.0.

***N,N*-Dibenzyl-*O*-(α-(diphenylmethylamino)phenyl acetyl)-L-threonine isopropyl ester (8n).** 67% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.49-7.17 (m, 25H), 5.60 (s, 1H), 5.45 (m, 1H), 5.11 (m, 1H), 4.81 (s, 1H), 3.95 (d, *J* = 13.6 Hz, 2H), 3.51 (d, *J* = 13.6 Hz, 2H), 3.26 (d, *J* = 6.4 Hz, 1H), 1.33 (d, *J* = 6.4 Hz, 3H), 1.24 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 172.4, 169.3, 143.3, 139.3, 129.2, 128.8, 128.7, 128.6, 128.3, 127.8, 127.7, 127.6, 127.5, 127.2, 69.4, 68.4, 64.8, 64.2, 63.0, 55.4, 22.4, 22.1, 17.1.

***N,N*-Dibenzyl-*O*-(α-((*R*)-phenethylamino)phenyl acetyl)-L-threonine Isopropyl Ester (8o).** 54% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.31-7.15 (m, 20H), 5.38 (m, 1H), 5.08 (m, 1H), 4.19 (s, 1H), 3.93 (d, *J* = 13.6 Hz, 2H), 3.57 (m, 1H), 3.49 (d, *J* = 13.6 Hz, 2H), 3.22 (d, *J* = 8.0 Hz, 1H), 1.36 (d, *J* = 6.4 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.21 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 171.9, 169.2, 139.3, 129.0, 128.7, 128.5, 128.2, 127.9, 127.7, 127.2, 127.0, 126.8, 69.1, 68.2, 64.7, 62.6, 55.2, 54.3, 24.7, 22.2, 22.0, 17.0.

***N,N*-Dibenzyl-*O*-(α-(benzylamino)phenylacetyl)-L-threonine Isopropyl Ester (8p).** 71% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.24-7.14 (m, 20H), 5.36 (m, 1H), 5.01 (m, 1H), 4.28 (s, 1H), 3.92 (d, *J* = 13.6 Hz, 2H), 3.69 (m, 2H), 3.48 (d, *J* = 13.6 Hz, 2H), 3.22 (d, *J* = 7.2 Hz, 1H), 2.32 (br, 1H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H), 0.92 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) 172.2, 169.4, 139.7, 139.4, 138.1, 129.1, 128.7, 128.6, 128.3, 128.0, 127.6, 127.2, 127.1, 69.7, 68.4,

64.7, 64.6, 55.5, 51.3, 22.3, 22.1, 17.2.

***N,N*-Dibenzyl-*O*-(α-(3,4-dihydro-2(1*H*)-isoquinolinyl) phenylacetyl)-L-threonine Isopropyl Ester (8q).** 66% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.28-6.88 (m, 19H), 5.44 (m, 1H), 5.06 (m, 1H), 4.14 (s, 1H), 4.08 (d, *J* = 13.6 Hz, 2H), 3.75-3.62 (m, 4H), 3.34 (d, *J* = 6.8 Hz, 1H), 2.84-2.79 (m, 4H), 1.32 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) 170.7, 169.5, 139.4, 136.0, 134.4, 134.3, 129.0, 128.8, 128.7, 128.6, 128.3, 128.2, 127.1, 126.7, 126.2, 125.6, 73.8, 69.9, 68.3, 64.6, 55.5, 53.4, 48.5, 28.9, 22.2, 22.0, 17.0.

***N,N*-Dibenzyl-*O*-(α-(dibenzylamino)phenylacetyl)-L-threonine Isopropyl Ester (8r).** 73% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.28-7.16 (m, 25H), 5.58 (m, 1H), 5.11 (m, 1H), 4.59 (s, 1H), 3.95 (d, *J* = 13.6 Hz, 2H), 3.88 (d, *J* = 13.6 Hz, 2H), 3.66 (d, *J* = 13.6 Hz, 2H), 3.58 (d, *J* = 13.6 Hz, 2H), 3.30 (d, *J* = 6.4 Hz, 1H), 1.32 (d, *J* = 6.4 Hz, 3H), 1.24 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 171.5, 169.6, 139.6, 139.4, 139.3, 136.2, 129.1, 128.9, 128.3, 128.2, 127.0, 69.8, 68.3, 66.1, 64.5, 55.7, 54.0, 22.3, 22.0, 17.5.

***N,N*-Dibenzyl-*O*-(α-(benzylmethylamino)phenylacetyl) -L-threonine Isopropyl Ester (8s).** 67% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) δ 7.42-7.20 (m, 20H), 5.45 (m, 1H), 4.98 (m, 1H), 4.23 (s, 1H), 4.10 (d, *J* = 13.6 Hz, 2H), 3.67 (d, *J* = 13.6 Hz, 2H), 3.60 (d, *J* = 13.6 Hz, 1H), 3.51 (d, *J* = 13.6 Hz, 1H), 3.34 (d, *J* = 6.4 Hz, 1H), 2.20 (s, 3H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.13 (d, *J* = 6.4 Hz, 3H), 1.06 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) 171.0, 169.5, 139.5, 139.0, 136.5, 129.0, 128.9, 128.8, 128.5, 128.3, 128.1, 127.1, 127.0, 73.1, 70.1, 68.2, 64.5, 58.7, 55.5, 39.4, 22.2, 21.9, 17.1.

***N,N*-Dibenzyl-*O*-(α-(dibutylamino)phenylacetyl)-L-threonine Isopropyl Ester (8t).** 64% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.34-7.18 (m, 15H), 5.49 (m, 1H), 5.04 (m, 1H), 4.52 (s, 1H), 4.07 (d, *J* = 13.6 Hz, 2H), 3.68 (d, *J* = 13.6 Hz, 2H), 3.35 (d, *J* = 6.4 Hz, 1H), 2.25 (m, 4H), 1.40-1.10 (m, 17H), 0.80 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 171.7, 169.6, 139.5, 137.4, 129.0, 128.3, 128.2, 127.7, 127.1, 70.0, 69.5, 68.2, 64.6, 55.6, 50.5, 29.8, 22.2, 22.0, 20.4, 17.3, 14.1.

***N,N*-Dibenzyl-*O*-(α-(*o*-aminoanilino)phenylacetyl)-L-threonine Isopropyl Ester (8u).** 93% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, major epimer) 7.34-7.21 (m, 15H), 6.71-6.44 (m, 4H), 5.44 (m, 1H), 5.09 (m, 1H), 5.02 (d, *J* = 13.6 Hz, 1H), 4.63 (br, 1H), 4.03 (d, *J* = 13.6 Hz, 2H), 3.61 (d, *J* = 13.6 Hz, 2H), 3.40 (br, 2H), 3.36 (d, *J* = 6.8 Hz, 1H), 1.32 (d, *J* = 6.4 Hz, 3H), 1.19 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, major epimer) δ 171.2, 169.3, 139.3, 129.2, 129.0, 128.7, 128.6, 128.3, 127.2, 127.1, 120.5, 119.6, 116.9, 113.5, 70.4, 68.4, 64.6, 61.5, 55.4, 22.2, 22.0, 17.0.

***N*-(*p*-Methoxphenyl)phenylglycine Methyl Ester (9).** 71% yield from **8d**; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48-7.25 (m, 5H), 6.69 (d, *J* = 8.9 Hz, 2H), 6.52 (d, *J* = 8.9 Hz, 2H), 5.00 (s, 1H), 4.67 (br, 1H), 3.72 (s, 3H), 3.67 (s, 3H).[1c] Chiral HPLC: 87:13 er, t_R (*S*)-major enantiomer, 76.2 min; t_R (*R*)-minor enantiomer, 66.3 min (Chiralcel OJ-H column; 20% 2-propanol in hexane; 0.5 mL/min).

3-Phenyl-3,4-dihydro-1,4-quinoxalin-2-one (10). 83% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95 (br, 1H), 7.43-6.70 (m, 9H), 5.08 (s, 1H), 4.28 (br, 1H).[1e] Chiral HPLC: 92:8 er, t_R (*S*)-major enantiomer, 45.0 min; t_R (*R*)-minor enantiomer, 40.1 min (Chiralcel OJ-H column; 20% 2-propanol in hexane; 0.5 mL/min).

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References and Notes

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