Asymmetric Rh-Catalyzed Hydrogenation of Enamides with a Chiral 1,4-Bisphosphine Bearing Diphenylphosphino Groups

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Introduction

Much effort has been devoted to the development of efficient asymmetric synthetic methods for the preparation of enantiomerically enriched compounds.[1,2] Among various methods for the enantiomerically selective synthesis of chiral organic compounds from prochiral precursors, enantioselective catalytic hydrogenation of dehydro precursors has been extensively developed.[3] In fact, asymmetric hydrogenation is one of the most practical methods in asymmetric synthesis, accounting for 70% of all procedures used on a commercial scale.[4] However, most asymmetric catalytic hydrogenation systems only hydrogenate electron-deficient olefins with high enantioselectivity and high reactivity. In contrast, electron-rich olefins, such as simple enamides[5] and enolates,[6] are generally poor substrates for asymmetric hydrogenation with most known systems. Since enamides and enolates upon asymmetric hydrogenation can be converted to enantiomerically pure amines and alcohols,[7] it would be extremely desirable to have a general and efficient method for this transformation. Recently, Burk and coworkers have reported that Rh complexes bearing the electron-rich DuPhos- and BPE-type ligands were efficient catalysts for the asymmetric hydrogenation of enamides[8] and enolates.[9] They reported that analogous Rh-chiral bisphosphines bearing diphenylphosphino groups (e.g., BINAP, DIOP, and CHIRAPHOS) led to significantly lower enantioselectivities in the reduction of enamides (<60% ee).[8]

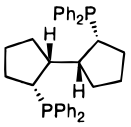

Figure 1. (*R*,*R*)-BICP.

We have been interested in elucidating the steric and electronic effects[10] of various diphenylphosphino-bearing chiral ligands in asymmetric hydrogenation processes. Recently a new chiral 1,4-bisphosphine, 2(*R*),2′(*R*)-bis-(diphenylphosphino)-1(*R*),1′(*R*)-dicyclopentane ((*R*,*R*)-BICP, Figure 1), was reported from our laboratory as an excellent ligand for the Rh-catalyzed asymmetric hydrogenation of dehydroamino acids.[11] The key feature of this new ligand is that four stereogenic centers are introduced in a conformationally rigid bicyclic backbone, which is fundamentally different from either axially dissymmetric BINAP or bisphosphines with two stereogenic centers. Herein, we describe the highly enantioselective Rh-catalyzed hydrogenation of enamides using the BICP ligand. Among the known chiral bisphosphines with diphenylphosphino groups, the BICP ligand gives the highest enantioselectivity for the rhodium-catalyzed asymmetric hydrogenation of simple enamides.

Results and Discussion

The active catalyst employed in our study was generated in situ from a cationic Rh complex, $[Rh(COD)_2]BF_4$ or $[Rh(COD)_2]OTf$, and bisphosphine BICP (1:1.2). Enamide **1a** was chosen as a model substrate to screen various reaction conditions. As shown in Table 1, the solvent had little effect on the enantioselectivities for this reaction. Under 40 psi H_2 at room temperature, reaction in nonpolar solvents such as benzene (85.2% ee, entry 1) and toluene (86.3% ee, entry 2) gave better enantioselectivities than in polar solvents (entry 3, CH_2Cl_2, 75.7% ee; entry 4, MeOH, 80.8% ee; entry 5, acetone, 77.3% ee, entry 6, DMF, 77.4% ee, entry 7, THF, 80.6% ee). A small hydrogen pressure effect was found for this asymmetric catalytic system. Higher pressure gave slightly better enantioselectivities and reactivities (e.g., 86.3% ee under 40 psi of hydrogen (entry 2) vs 80.2% ee under 14.7 psi (entry 9)). However, increasing hydrogen pressure further did not provide any improvement in the enantioselectivity. A neutral rhodium catalyst formed in situ from

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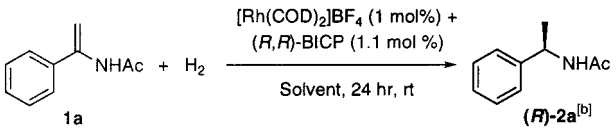
Table 1. Rhodium Catalyzed Asymmetric Hydrogenation of Enamide 1a[a]



entry	solvent	pressure (psi)	ee[c] (%)
1	benzene	40	85.2
2	toluene	40	86.3
3	CH_2Cl_2	40	75.7
4	MeOH	40	80.8
5	acetone	40	77.3
6	DMF	40	77.4
7	THF	40	80.6
8[d]	toluene	40	86.3
9	toluene	14.7	80.2
10	benzene	14.7	84.9
11[e]	toluene	40	11.4

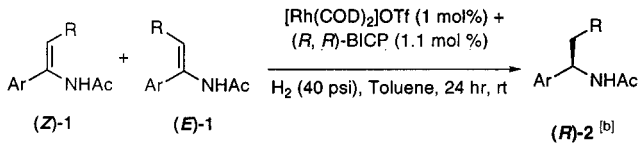
[a] The reaction was carried out at rt for 24 h. The catalyst was made in situ by stirring a solution of $[Rh(COD)_2]BF_4$ and the ligand in toluene [[substrate (0.5 mmol, 0.125 M)/[Rh]/(*R*,*R*)-BICP = 1:0.01:0.011]]. The reaction was in quantitative yield. [b] The *R* configuration was assigned by comparison of optical rotation with reported data.[8] [c] Enantiomeric excesses were determined by chiral GC using a Supelco Chiral Select 1000 column at 130 °C. [d] $[Rh(COD)_2]OTf$ was used as catalyst precursor. [e] $[Rh(COD)Cl]_2$ was used as catalyst precursor.

BICP and $[Rh(COD)Cl]_2$ was much less effective than the cationic Rh species (entry 11, 11.4% ee vs entry 8, 86.3% ee). Under similar conditions, hydrogenation of enamide **1a** proceeded with low conversion, giving only 11.4% enantiomeric excess (entry 11). Overall, the optimized conditions use the catalyst generated in situ from $[Rh(COD)_2]BF_4$ or $[Rh(COD)_2]OTf$ (1.0 mol %) and BICP (1.2 mol %), and the reaction is carried out at room temperature in toluene under 40 psi H_2.

The scope of the asymmetric hydrogenation reaction with different substrates is shown in Table 2. A series of α-aryl enamides were reduced to give the enantiomerically enriched α-arylethylamine derivatives with good enantioselectivities using the optimal reaction conditions. Only a small electronic effect of the aryl ring was observed on the enantioselectivity. For example, 4′-methylphenyl-substituted and 4′-(trifluoromethyl)phenyl-substituted enamides **1b** (entry 2) and **1d** (entry 4) gave similar results with enamide **1a** (entry 1), while 4′-methoxyphenyl-substituted enamide **1f** gave better enantioselectivity (entry 6). Increasing the steric bulk of the group on the 4′-position on the phenyl ring of the enamide gave slightly better enantioselectivities. For example, 4′-phenylphenyl-substituted enamide **1e** (entry 5) was hydrogenated in high yield with 93.0% ee compared to phenyl enamide **1a** (86.3% ee, entry 1).

An important feature of the Rh-BICP catalyst was found when we extended this hydrogenation reaction to an α-aryl enamide with a *β*-methyl group, **1h**. The catalyst system can hydrogenate this *β*-substituted enamide effectively and gave higher enantioselectivity than the corresponding terminal enamide substrate **1a**. The hydrogenation reaction was not sensitive to the geometry of the substrates, as an isomeric mixture of (*Z*)- and (*E*)-enamides with a ratio of 1:2 was reduced smoothly in 95% ee under the standard reaction conditions. The ability to reduce such *β*-substituted enamides greatly expands the utility of this hydrogenation methodology for the synthesis of various chiral amine derivatives. These

Table 2. Asymmetric Hydrogenation of Enamides by a Cationic Rhodium−(R,R)-BICP Complex[a]



entry	1[c]	Ar	R	ee[d] (%)
1	**1a**	C_6H_5	H	86.3
2	**1b**	4-Me-C_6H_4	H	86.1
3	**1c**	3-Me-C_6H_4	H	85.7
4	**1d**	4-CF_3-C_6H_4	H	86.4
5	**1e**	4-Ph-C_6H_4	H	93.0
6	**1f**	4-MeO-C_6H_4	H	91.6
7	**1g**	2-Np	H	85.2
8	**1h**	C_6H_5	CH_3	95.0
9	**1i**	C_6H_5	$CH(CH_3)_2$	93.5
10	**1j**	C_6H_5	CH_2Ph	90.5
11	**1k**	4-MeO-C_6H_4	CH_3	95.2
12	**1l**	4-CF_3-C_6H_4	CH_3	95.1
13	**1m**	2-Np	CH_3	93.6

[a] The reaction was carried out at rt under an initial hydrogen pressure of 40 psi for 24−36 h. The catalyst was made in situ by stirring a solution of $[Rh(COD)_2]OTf$ and (*R*,*R*)-BICP in toluene [[substrate (0.5 mmol, 0.125 M)/][Rh]/(R,R)-BICP = 1:0.01:0.011]]. The reaction went in quantitative yield. [b] The *R* configuration was assigned by comparison of optical rotation with reported data.[8] [c] Enamides **1** were prepared according to literature methods[5a−c,12] or by reduction of corresponding oximes by iron powder in the presence of acetic anhydride in DMF. [d] Enantiomeric excesses were determined by chiral GC using a Supelco Chiral Select 1000 column or by Chiral HPLC with a Regis (*R*,*R*)-Whelk-O1 column.

amine derivatives are useful building blocks for biologically active compounds. Because it is currently difficult to synthesize isomerically pure enamides using existing methods,[5a−c,12] this insensitivity to the isomeric composition of enamides should be critical for the practical synthesis of chiral amines. Further study showed that a series of different *β*-substituted isomeric enamide mixtures (**1h**−**j**) and *β*-methyl-substituted enamides with various substituents on the 1-aryl group (**1k**−**l**) can be reduced in high yield with high enantioselectivities. The reaction is not sensitive to electronic effects of a substituent on the 1-aryl group. For example, the 4-methoxyphenyl-substituted species **1k** and the 4-(trifluoromethyl)phenyl analogue **1l** showed almost the same reactivities and enantioselectivities under identical hydrogenation conditions (entries 11 and 12). The enantioselectivities achieved in the Rh-BICP system are comparable to the results obtained with Burk's Rh-DuPhos catalysts, the only previously reported system that can tolerate *Z* and *E* mixtures of simple enamides.

To further expand the utility of this asymmetric enamide hydrogenation, we have examined our catalytic system with some cyclic enamides (Figure 2). The successful reduction of these cyclic enamide substrates can lead to important chiral cyclic amines[12b,13] (e.g.,

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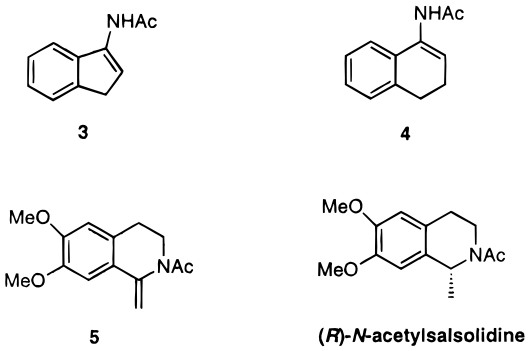

Figure 2.

tetrahydroisoquinolines[14]). Under the standard reaction conditions used for acyclic enamide substrates, hydrogenation of cyclic enamides **3** and **4** showed high reactivity, giving the corresponding *N*-acetylamine with moderate enantioselectivity (60.3% ee for **3** and 64.5% ee for **4**). Asymmetric hydrogenation of *N*-acetyl-1-methylene-1,2,3,4-tetrahydroisoquinoline **5** proceeded smoothly, affording (*R*)-(−)-*N*-acetylsalsolidine[15] in quantitative yield in 77.8% ee.

In summary, the BICP ligand is one of the best chiral diphenylphosphino ligands for the rhodium-catalyzed asymmetric hydrogenation of electron-rich olefin substrates.[16] This method provides an efficient approach to a wide range of enantiomerically enriched arylalkylamines. The key feature of this catalytic system is that the enantioselectivity of the hydrogenation reaction is not sensitive to the geometry of the starting enamides. Thus, a series of *Z*- and *E*-*β*-substituted amide isomers can be reduced in high yield and with high enantioselectivity. The mechanistic details for this reaction are not yet clear. Further study will focus on this aspect of the chemistry as well as further modification of the new ligand system to accommodate a broader range of enamide substrates.

Experimental Section

General Methods. All reactions and manipulations were performed in a nitrogen-filled glovebox or using standard Schlenk techniques. Toluene, benzene and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl under nitrogen. Methylene chloride was distilled from CaH_2. Methanol was distilled from Mg under nitrogen. The chiral BICP ligand was prepared as previously described.[11] All the enamide substrates were prepared following reported procedures or by reduction of the corresponding oxime by iron in the presence of acetic anhydride in DMF.[5a−c,12] GC analysis was carried out on Helwett-Packard 5890 and 6890 gas chromatographs using a chiral capillary column: Chiral Select 1000 column [dimensions, 15 m × 0.25 mm (i.d.); Carrier gas, He (1 mL/min)]. HPLC analysis was carried out on a Waters 600 chromatograph with an (*R*,*R*)-Poly Whelk-01 column from Regis Technologies, Inc. [particle size, 5.0 mm; column dimensions, 25 cm (length) × 0.46 cm (i.d.); column temperature, 25 °C].

General Procedure for Asymmetric Hydrogenation. To a solution of $[Rh(COD)_2]BF_4$ (5.0 mg, 0.012 mmol) in toluene (10 mL) in a glovebox was added (*R*,*R*)-BICP (0.15 mL of 0.1 M solution in toluene, 0.015 mmol). After the mixture was stirred for 30 min, substrate enamide (1.2 mmol) was added. The hydrogenation was performed at room temperature under 40 psi of hydrogen for 24 h. After the hydrogen was released, the reaction mixture was passed through a short silica gel column to remove the catalyst. The enantiomeric excess was measured by capillary GC or HPLC directly without any further purification. The absolute configuration of the products was determined by comparing the observed rotation with the reported value.[8]

Characterization of Substrates. ***N*-Acetyl-1-phenylenthenamine (1a):**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.13 (br, 3H), 5.09 (s, 1H), 5.88 (s, 1H), 6.85 (br, 1H), 7.43−7.21 (m, 5H). ***N*-Acetyl-1-(4-methylphenyl)enthenamine (1b):**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.36 (s, 3H), 5.05 (s, 1H), 5.83 (s, 1H), 6.80 (br, 1H), 7.17 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 7.53 Hz, 2H). ***N*-Acetyl-1-(3-methylphenyl)enthenamine (1c):**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.37 (s, 3H), 5.06 (s, 1H), 5.85 (s, 1H), 6.89 (br, 1H), 7.27−7.15 (m, 4H). ***N*-Acetyl-1-[4-(trifluoromethyl)phenyl]enthenamine (1d):**[8] ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.11 (s, 3H), 5.16 (s, 1H), 5.82 (s, 1H), 6.98 (br, 1H), 7.50−7.64 (m, 4H). ***N*-Acetyl-1-(4-phenylphenyl)-enthenamine (1e):** ^{1}H NMR (360 MHz, acetone-d_6) δ 2.35 (s, 3H), 5.27 (s, 1H), 6.09 (s, 1H), 7.60−7.91 (m, 9 H), 8.80 (br, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 24.6, 101.9, 128.05, 128.1, 128.8, 130.2, 139.0, 141.6, 142.2, 142.9, 170.1; MS *m*/*z* 237, 221, 180, 152, 78, 63, 43; HRMS calcd for $C_{16}H_{15}NO$ (M^+) 237.1154, found 237.1143. ***N*-Acetyl-1-(4-methoxyphenyl)enthenamine (1f):**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.13 (s, 3H), 3.82 (s, 3H), 5.01 (s, 1H), 5.77 (s, 1H), 6.75 (br, 1H), 6.89 (d, J = 8.80 Hz, 2H), 7.35 (d, J = 8.50 Hz, 2H); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.11 (s, 3H), 5.16 (s, 1H), 5.82 (s, 1H), 6.98 (br, 1H), 7.50−7.64 (m, 4H). ***N*-Acetyl-1-(2-naphthyl)ethenamine (1g):**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.15 (s, 3H), 5.24 (s, 1H), 5.94 (s, 1H), 7.03 (br, 1H), 7.49−7.55 (m, 3H), 7.80−7.87 (m, 4H). ***N*-Acetyl-1-phenylpropenamine (1h):**[8] *Z*−*E* isomers (1:2.05), ^{1}H NMR (360 MHz, $CDCl_3$) δ (major isomer) 1.70 (d, J = 7.34 Hz, 3H), 2.18 (s, 3H), 5.95 (q, J = 6.94 Hz, 1 H), 6.59 (br, 1H), 7.25−7.45 (m, 5H); δ (minor isomer) 1.86 (d, J = 7.02 Hz, 3H), 2.05 (s, 3H), 6.05 (q, J = 7.00 Hz, 1 H), 6.65 (br, 1H). ***N*-Acetyl-1-phenyl-3-methylbutenamine (1i):**[8] *Z*−*E* isomers (1.53:1), ^{1}H NMR (360 MHz, $CDCl_3$) δ (major isomer) 1.08 (d, J = 6.63 Hz, 6H), 2.17 (s, 3H), 2.53−2.65 (m, 1H), 5.71 (d, J = 9.64 Hz, 1H), 6.58 (br, 1H), 7.25−7.45 (m, 5H); δ (minor isomer) 1.70 (s, 3H), 2.80 (m, 1H), 5.77 (d, J = 9.70 Hz, 1H), 5.65 (br, 1H). ***N*-Acetyl-1,3-diphenylpropenamine (1j):**[8] *Z*−*E* isomer (2.61:1): ^{1}H NMR (360 MHz, $CDCl_3$) δ (major isomer) 1.81 (s, 6H), 3.52 (d, J = 7.06 Hz, 2H), 6.00 (t, J = 7.07 Hz, 1H), 6.69 (br, 1H), 7.21−7.48 (m, 10H); δ (minor isomer) 1.81 (s, 3H), 3.60 (d, J = 7.33 Hz, 2H), 6.16 (m, 1H).

***N*-Acetyl-1-(3-methoxyphenyl)propenamine(1k):** *Z*−*E* isomer (1.8:1), ^{1}H NMR (360 MHz, $CDCl_3$) δ (major isomer) 1.69 (d, J = 7.43 Hz, 3H), 2.18 (s, 3H), 3.80 (s, 1H), 5.84 (q, J = 7.00 Hz, 1H), 6.56 (br, 1H), 6.83−6.94 (m, 2H), 7.26−7.37 (m, 2H); δ (minor isomer) 1.75 (d, 3H), 1.74 (s, 3H), 3.82 (s, 3H), 5.91 (q, 1H), 6.60 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major isomer) 14.0, 23.1, 55.3, 113.7, 119.1, 126.6, 130.1, 130.9, 133.9, 159.2, 169.1; δ (minor isomer) 13.6, 20.5, 55.4, 114.2, 120.3, 126.7, 130.3, 130.8, 135.3, 159.7, 173.8; MS *m*/*z* 205, 190, 162, 134, 119, 91, 77, 43; HRMS calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1103, found 205.1095.

***N*-Acetyl-1-[4-(trifluoromethyl)phenyl]propenamine (1l):** *Z*−*E* isomer (3.28:1), ^{1}H NMR (360 MHz, $CDCl_3$) δ (major isomer) 1.80 (d, J = 6.92 Hz, 3H), 2.18 (s, 3H), 6.00 (q, J = 7.00 Hz, 1H), 6.70 (br, 1H), 7.45−7.60 (m, 4H); δ (minor isomer) 1.89 (d, J = 6.79 Hz, 3H), 1.80 (s, 3H), 6.18 (m, 1H), 6.70 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major isomer) 14.0, 23.1, 55.3, 113.7, 119.1, 126.6, 130.1, 130.9, 133.9, 159.2, 169.1; δ (minor isomer) 13.6, 20.5, 55.4, 114.2, 120.3, 126.7, 130.3, 130.8, 135.3,

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159.7, 173.8; MS *m*/*z* 243, 200, 172, 132, 56, 43; HRMS calcd for $C_{12}H_{12}F_3NO$ (M^+) 243.0871, found 243.0864.

***N*-Acetyl-1-(2-naphthyl)propenamine (1m):**[8] *Z*−*E* isomers, ^{1}H NMR (360 MHz, $CDCl_3$) δ (major isomer) 1.82 (d, J = 6.97 Hz, 3H), 2.23 (s, 3H), 6.11 (q, J = 6.95 Hz, 1 H), 6.92 (br, 1H), 7.46−7.86 (m, 7H); δ (minor isomer) 1.92 (d, J = 6.96 Hz, 3H), 1.86 (s, 3H), 6.23 (q, J = 6.99 Hz, 1 H), 6.80 (br, 1H).

1-(*N*-Acetylamido)indene (3). To a solution of oxime of 1-indanone (2.64 g 20 mmol) and acetic anhydride (15 mL) in DMF (50 mL) was added iron powder (10.0 g), and then the reaction was initiated by adding few drops of chlorotrimethylsilane under nitrogen. After the reaction mixture was stirred at room temperature for 4 h, TLC showed that the reaction was complete. The reaction mixture was diluted with ether, and solid was filtered off through a short column of Celite. The filtrate was concentrated, and the residue was purified by flash chromatography on silica gel. Recrystallization from CH_2Cl_2−hexanes afforded pure enamide **3**: 2.5 g, 72.2% yield. ^{1}H NMR (360 MHz, acetone-d_6) δ 2.13 (s, 3H), 3.37 (m, 2H), 6.85 (m, 1H), 7.21−7.27 (m, 2H), 7.45−7.47 (m, 1H), 7.60 (d, J = 7.36 Hz, 1H), 9.10 (br, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 23.7, 36.8, 114.5, 118.1, 124.7, 125.9, 126.7, 137.6, 141.1, 143.6, 169.2; MS *m*/*z* 173, 132, 103, 77, 43; HRMS calcd for $C_{11}H_{11}NO$ (M^+) 173.0841, found 173.0832.

***N*-(3,4-Dihydro-1-naphthyl)acetamide (4):** ^{1}H NMR (360 MHz, acetone-d_6) δ 1.98 (s, 3H), 2.20 (m, 2H), 2.64 (m, 2H), 6.32 (m, 1H), 7.07 (m, 3H), 7.22 (m, 1H), 8.53 (br, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 22.9, 23.8, 28.4, 118.7, 122.6, 127.1, 128.1, 128.4, 133.6, 137.6, 169.6. HRMS calcd for $C_{12}H_{13}NO$ (M^+) 187.0997, found 187.0993.

Characterization of Products. *N*-Acetyl-1-phenylethylamine:[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.47 (d, J = 6.93 Hz, 3H), 1.95 (s, 3H), 5.08 (m, 1H), 6.05 (br, 1H), 7.21−7.33 (m, 5H). ***N*-Acetyl-1-(2-naphthyl)ethylamine:**[8] ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.57 (d, J = 6.90 Hz, 3H), 2.00 (s, 3H), 5.26−5.33 (m, 1H), 6.00 (br, 1H), 7.40−7.51 (m, 3H), 7.75−7.83 (m, 4H). ***N*-Acetyl-1-[4-(trifluoromethyl)phenyl]ethylamine:**[8] ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.49 (d, J = 6.98 Hz, 3H), 2.00 (s, 3H), 5.16 (m, 1H), 5.76 (br, 1H), 7.42 (d, J = 8.16 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H). ***N*-Acetyl-1-(4-phenylphenyl)ethylamine:** ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.53 (d, J = 6.90 Hz, 3H), 2.01 (s, 3H), 5.18 (m, 1H), 5.67 (br, 1H), 7.32−7.46 (m, 5H), 7.55−7.58 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 23.5, 48.5, 126.6, 127.1, 127.3, 127.4, 128.8, 140.4, 140.7, 142.1, 169.1; MS *m*/*z*: 239, 224, 196, 182, 165, 155, 120, 77, 43; HRMS calcd for $C_{16}H_{17}NO$ (M^+) 239.1310, found 239.1303. ***N*-Acetyl-1-tolylethylamine:**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.45 (d, J = 6.94 Hz, 3H), 1.94 (s, 3H), 2.34 (s, 3H), 5.04 (m, 1H), 6.06 (br, 1H), 7.12 (d, J = 8.08 Hz, 2H), 7.23 (d, J = 8.10 Hz, 2H). ***N*-Acetyl-1-(3-methylphenyl)ethylamine:**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.47 (d, J = 6.88 Hz, 3H), 1.97 (s, 3H), 2.35 (s, 3H), 5.08 (m, 1H), 5.77 (br, 1H), 7.0.07−7.11 (m, 3H), 7.23−7.26 (m, 1H). ***N*-Acetyl-1-(4-methoxyphenyl)ethylamine:**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.47 (m, 3H), 1.96 (s, 3H), 2.03 (s, 3H), 5.08 (m, 1H), 5.07 (br, 1H), 6.84−6.88 (m, 2H), 7.22−7.26 (m, 2H). ***N*-Acetyl-1-phenylpropylamine:**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, J = 7.41 Hz, 3H), 1.84 (m, 2H), 1.98 (s, 3H), 4.88 (m, 1H), 5.68 (br, 1H), 7.23−7.36 (m, 5H). ***N*-Acetyl-1-(2-naphthyl)propylamine:**[8] ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J = 7.41 hz, 3H), 1.87−1.97 (m, 2H), 2.00 (s, 3H), 5.04 (m, 1H), 5.84 (br, 1H), 7.26−7.47 (m, 3H), 7.73 (s, 1H), 7.80−7.83 (m, 3H). ***N*-Acetyl-1-phenyl-3-methylbutylamine:**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.91−0.95 (m, 6 H), 1.50−1.71 (m, 3H), 2.04 (s, 3H), 5.04 (m, 1H), 5.63 (br, 1H), 7.23−7.35 (m, 5H). ***N*-Acetyl-1,3-diphenylpropylamine:**[8] ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.95 (s, 3 H), 2.13−2.19 (m, 2H), 2.57−2.60 (m, 2H), 5.03 (m, 1H), 5.80 (br, 1H), 7.14−7.35 (m, 10 H). ***N*-Acetyl-1-(4-methoxyphenyl)propylamine:** ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.85 (t, J = 7.40 Hz, 3H), 1.73−1.88 (m, 2H), 2.04 (s, 3 H), 3.78 (s, 3H), 4.82 (m, 1H), 5.95 (d, J = 8.08 Hz, 1H), 6.83−6.87 (m, 2 H), 7.17−7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.7, 23.4, 28.9, 54.4, 55.2, 114.0, 127.8, 134.2, 158.7, 169.1; HRMS calcd for $C_{12}H_{17}NO_2$ (M^+) 207.1259, found 207.1249. ***N*-Acetyl-1-[4-(trifluoromethyl)-phenyl]propylamine:** ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.86 (t, J = 7.43 Hz, 3H), 1.73 (m, 2H), 1.93 (s, 3 H), 4.83 (m, 1H), 6.75 (d, J = 7.92 Hz, 1H), 7.34 (d, J = 8.26 Hz, 2H), 7.52 (d, J = 8.11 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.6, 23.0, 29.0, 54.8, 119.6−129.8 (m), 146.7, 169.8; HRMS calcd for $C_{12}H_{14}F_3NO$ (M^+) 245.1027, found 245.1025. **1-(*N*-Acetylamido)indane:** ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.82 (m, 1H), 2.03 (s, 3H), 2.59 (m, 1H), 2.86−2.98 (m, 2 H), 5.47 (m, 1H), 5.70 (br, 1H), 7.22−7.30 (m, 4H). ***N*-(1,2,3,4-Tetrahydro-1-naphthyl)acetamide:** ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.81 (s, 3H), 1.90−2.05 (m, 4H), 2.75−2.79 (m, 2H), 5.17 (m, 1H), 5.71 (br, 1H), 7.08−7.29 (m, 4H).

Determination of Enantiomeric Excesses. Chiral capillary GC column: β-DEX-390 column. Dimensions: 15 m × 0.25 mm (i.d.). Carrier gas: He (1 mL/min). The racemic products were obtained by hydrogenation of substrates with an achiral catalyst. The following is the retention time for the racemic products. ***N*-Acetyl-1-phenylethylamine** (capillary GC, 130 °C, isothermal) (*S*) t_1 = 27.6 min, (*R*) t_2 = 29.3 min. ***N*-Acetyl-1-[4-(trifluoromethyl)phenyl]ethylamine** (capillary GC, 150 °C, isothermal) (*S*) t_1 = 14.0 min, (*R*) t_2 = 14.8 min. ***N*-Acetyl-1-tolylethylamine** (capillary GC, 140 °C, isothermal) (*S*) t_1 = 27.8 min, (*R*) t_2 = 28.9 min. ***N*-Acetyl-1-(3-methylphenyl)-ethylamine** (capillary GC, 140 °C, isothermal) (*S*) t_1 = 23.4 min, (*R*) t_2 = 24.6 min. ***N*-Acetyl-1-(4-methoxyphenyl)ethylamine** (capillary GC, 140 °C for 60 min then 20 °C/min to 180 °C, gradient) (*S*) t_1 = 62.8 min, (*R*) t_2 = 63.2 min. ***N*-Acetyl-1-phenylpropylamine** (capillary GC, 135 °C, isothermal) *S*) t_1 = 26.0 min, (*R*) t_2 = 27.1 min. ***N*-Acetyl-1-phenyl-3-methylbutylamine** (capillary GC, 145 °C, isothermal) (*S*) t_1 = 26.2 min, (*R*) t_2 = 27.1 min. ***N*-Acetyl-1-[4-(trifluoromethyl)phenyl]-propylamine** (capillary GC, 150 °C, isothermal) (*S*) t_1 = 17.7 min, (*R*) t_2 = 18.5 min. **1-(*N*-Acetylamido)indane** (capillary GC, 160 °C, isothermal) (*S*) t_1 = 17.9 min, (*R*) t_2 = 18.7 min. ***N*-(1,2,3,4-Tetrahydro-1-naphthyl)acetamide** (capillary GC, 180 °C, isothermal) (*S*) t_1 = 10.1 min, (*R*) t_2 = 11.4 min. ***N*-Acetyl-1-phenylbutylamine** (capillary GC, 150 °C isothermal) (*S*) t_1 = 14.8 min, (*R*) t_2 = 15.4 min. ***N*-Acetyl-1-(2-furyl)-ethylamine** (capillary GC, 140 °C, isothermal) (*S*) t_1 = 5.7 min, (*R*) t_2 = 5.9 min. ***N*-Acetyl-1-(2-thienyl)ethylamine** (capillary GC, 140 °C, isothermal) (*S*) t_1 = 16.0 min, (*R*) t_2 = 16.7 min.

Chiral HPLC Column: (*R*,*R*)-Poly Whelk-0 from Regis Technologies, Inc. Particle size: 5.0 μm. Column dimensions: 25 cm (length) × 0.46 cm (i.d.). Column temperature: 25 °C. ***N*-Acetyl-1-(2-Naphthyl)ethylamine** (HPLC, 1.0 mL/min, 2-PrOH/hexane = 1), (*S*) t_1 = 10.2 min, (*R*) t_2 = 60.7 min. ***N*-Acetyl-1-(1-naphthyl)ethylamine** (HPLC, 1.0 mL/min, 2-PrOH/hexane = 1), (*S*) t_1 = 9.4 min, (*R*) t_2 = 29.9 min. ***N*-Acetyl-1-(4-phenylphenyl)ethylamine** (HPLC, 1.0 mL/min, 2-PrOH/hexane = 1), (*S*) t_1 = 8.6 min, (*R*) t_2 = 18.5 min. ***N*-Acetyl-1-(2-naphthyl)propylamine** (HPLC, 1.0 mL/min, 2-PrOH/hexane = 1), (*S*) t_1 = 9.6 min, (*R*) t_2 = 39.8 min. ***N*-Acetyl-1,3-diphenylpropylamine** (HPLC, 1.0 mL/min, 2-PrOH/hexane = 7:3), (*S*) t_1 = 9.2 min, (*R*) t_2 = 13.5 min. ***N*-Acetyl-1-(4-methoxyphenyl)propylamine** (HPLC, 1.0 mL/min, 2-PrOH/hexane = 7:3), (*S*) t_1 = 10.7 min, (*R*) t_2 = 22.8 min.

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Supporting Information Available: Spectroscopic data of new compounds (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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