Efficient Kinetic Resolution in the Asymmetric Hydrosilylation of Imines of 3-Substituted Indanones and 4-Substituted Tetralones

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Received August 20, 1999

Kinetic resolution of the *N*-methyl imines of 3-substituted indanones and 4-substituted tetralones could be accomplished by hydrosilylation with a chiral titanocene catalyst. *N*-Methyl imines of 4-substituted tetralones were resolved to yield, after hydrolysis of the unreacted starting materials, ketones with high ee's and the amine products with high diastereomeric and enantiomeric purity. The utility of this process was demonstrated in the synthesis of sertraline.

Introduction

A large number of bioactive and pharmaceutically interesting molecules contain an indan ring framework[1] or a tetrahydronaphthalene core.[2] Indanones or tetralones possessing chiral centers are also useful molecules as starting material for the synthesis of biologically active compounds. These products are of great current interest in the pharmaceutical industry, and therefore, their derivatives have been extensively evaluated for their biological activities.[3] There are a number of approaches to introduce chirality to the indanone and tetralone ring systems; the most general method is the preparation of chiral aryl carboxylic acids either by resolution or asymmetric synthesis followed by Friedel−Crafts cyclization onto an aromatic ring.[4] Kinetic resolution of racemic substrates has also been employed.[5,6]

We have recently reported an efficient procedure to reduce ketones[7] and imines[8] utilizing a chiral (EBTHI)-titanocene catalyst, (*R*,*R*)-(EBTHI)TiF_2 (**1**) (EBTHI = ethylenebis(tetrahydroindenyl)). Herein we wish to report our work on the application of asymmetric imine hydrosilylation to the kinetic resolution of racemic acyclic imines[9] of 3-substituted indanones and 4-substituted tetralones, including the enantio- and diastereoselective preparation of sertraline, an important antidepressant sold under the trade name Zoloft.

Results

Based on the stereochemical model of the transition state for the reduction of imines with the (EBTHI)-titanocene catalyst,[10a] we reasoned that imines could be successfully kinetically resolved.[10b,11] The two important predictions of this model are that the substituent on the nitrogen atom has the greatest influence on the stereochemical outcome of the reaction and the syn and the anti isomers of an imine react to give opposite enantiomers of the product. It seemed necessary to have a substituent on the nitrogen atom big enough to direct the facial selectivity but not so large as to slow the reduction. Therefore, the *N*-propyl imines of 3-substituted indanones were chosen as the initial substrates. These were subjected to the previously described hydrosilylation conditions using phenylsilane as the stoichiometric reductant (Table 1). The reactions proceeded smoothly at room temperature; however, it was necessary to use 2.5−5 mol % catalyst and long reaction times (1.5−3 d) in order to reach conversions that gave high ee of the ketone derived by hydrolysis of the recovered starting material. Substrates **2a** and **2b** were transformed with similar selectivity[12] to give the corresponding ketones[13] in >90% ee at ca. 60% conversion. The resolutions of **2c** (R = *n*-butyl) and **2d** (R = *tert*-butyl) were less efficient.

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(5) For enzymatic kinetic resolutions of 2-substituted indanones or tetralones, see: (a) Adam, W.; Díaz, M. T.; Fell, R. T.; Saha-Möller, C. R. *Tetrahedron*: *Asymmetry* **1996**, *7*, 2207. (b) Kajiro, H.; Mitamura, S.; Mori, A.; Hiyama, T. *Tetrahedron*: *Asymmetry* **1998**, *9*, 907. For nonenzymatic kinetic resolutions of 2-substituted tetralones, see: (c) Genêt, J. P.; Pfister, X.; Ratovelomanana-Vidal, V.; Pinel, C.; Laffitte, J. A. *Tetrahedron Lett.* **1994**, *35*, 4559. (d) Kabuto, K.; Ziffer, H. *J. Org. Chem.* **1975**, *40*, 3467. (e) Schmalz, H.-G.; Jope, H. *Tetrahedron* **1998**, *54*, 3457. (f) Sugi, K. D.; Nagata, T.; Yamada, T.; Mukaiyama, T. *Chem. Lett.* **1996**, 1081.

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(9) For an example of kinetic resolution of acylic imines, see: Lensink, C.; de Vries, J. G. *Tetrahedron*: *Asymmetry* **1993**, *4*, 215.

(10) (a) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 11703. (b) We began this project by investigating the kinetic resolution of 3-methylindanone using **1** under hydrosilylation conditons; however, the results were not promising. The recovered ketone was essentially racemic and the diastereomeric alcohol products were produced in a ∼1:1 ratio.

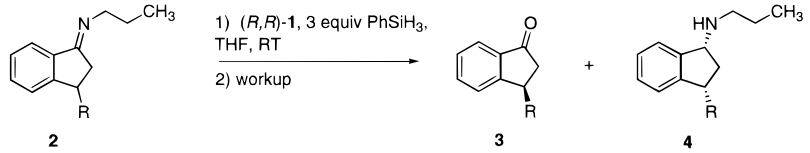
(11) For examples of highly efficient kinetic resolution processes using (EBTHI)Zr derivatives, see: Hoveyda, A. H.; Morken, J. P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1262.

(12) The selectivity factor, *s*, was calculated by the equation published in: Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

(13) The starting acyclic imines were unstable and could not be isolated by the usual separation procedure. Therefore, they were isolated as the corresponding ketones after hydrolysis with HOAc/NaOAc buffer solution or silica gel chromatography.

10.1021/jo991328h CCC: $19.00
Published on Web 01/14/2000

Table 1. Kinetic Resolution of *N*-Propyl Imines of 3-Substituted Indanones



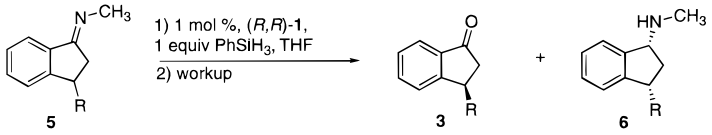
2a; R = Me
2b; R = Ph
2c; R = *n*-Bu
2d; R = *t*-Bu

$NaBH_4$ Reduction
Amine d.r =
4a 88 : 12
4b 95 : 5
4c 87 : 13
4d 95 : 5

entry	substrate	cat. (mol %)	time (h)	convn[a] (%)	recovered ketone (% ee)	*s*[b]	amine product cis (% ee)/trans (% ee)
1	**2a**[c]	2.5	72	64.5	94 (*R*)	10.3	81 (80)[d]:19
2	**2a**[c,e]	2.5	36	49	66 (*R*)	10.5	90 (82):10
3	**2b**	5	48	60	90	11.7	85 (74):15 (74)
4	**2b**[e]	5	45	58	84	10.4	86 (77.5):14 (70)
5	**2c**	5	36	54	74	9.5	87.5 (75):12.5 (53)
6	**2c**	5	42	61	86	9.1	85 (78):15 (64)
7	**2d**	5	48	60	71	5.7	96 (47):4

[a] Conversion was determined by GC with an internal standard based on consumption of starting imine substrate. See the Experimental Section for isolated yields of recovered ketone and amine product. [b] Selectivity factor.[12] [c] [Substrate] = 1.0 M. The other runs used [substrate] = 0.5 M. [d] Absolute stereochemistry was determined by X-ray analysis of the corresponding (+)-camphorsulfonic acid salt and is as shown above. [e] Toluene was used as solvent.

Table 2. Kinetic Resolution of *N*-Methyl Imines of 3-Substituted Indanones



5a; R=Me
5b; R=Ph

$NaBH_4$ Reduction
Amine product d.r =
6a 87.5 : 12.5
6b 95 : 5

entry	substrate	*T* (°C)	time (h)	convn[a] (%)	recovered ketone (% ee)	s	diastereomeric ratio of amine products (% ee)
1	**5a**	15[b]	1.5	57	92 (*R*)	17.5	93.5 (77):6.5 (42)
2		0[b]	2	55	93 (*R*)	24.5	95 (83):5 (41)
3		−20	20	51	86 (*R*)	28.8	97 (88):3 (30)
4		−30[c]	24	44	68 (*R*)	28.1	98 (94):2 (16)
5	**5b**	0	2	51	83	22.7	94.5 (89):5.5 (64)
6		0[d]	2	52	80	16.0	94.5 (84.5):5.5

[a] Conversion was determined by GC with an internal standard based on consumption of starting imine substrate. See the Experimental Section for isolated yields of recovered ketone and amine products. [b] Reactions were carried out in [substrate] = 1 M. The other runs used [substrate] = 0.5 M. [c] 2.5 mol % (*R*,*R*)-**1** and 2 equiv of $PhSiH_3$ were used. [d] Toluene was used as solvent.

Next, we examined *N*-methyl imines of 3-substituted indanones as substrates in the hope that the smaller nitrogen substituent would give higher turnover numbers without affecting the selectivity of the reaction. In fact, the imine hydrosilylation of substrate **5a** proceeded quickly at room temperature.[14] The reaction was thus carried out at a lower temperature employing a smaller quantity of catalyst (1 mol %) and phenylsilane (1 equiv) than used in the previous case (Table 2). When imine substrates **5a** and **5b** were subjected to the hydrosilylation conditions, the ketones derived from the unreacted imines at ~50% conversion had a high ee. Lowering the reaction temperature increased the *s* value for the process at the expense of the reaction rate. The reaction proceeded very slowly at temperatures lower than −30 °C.[15] Using phenylsilane as the silane source is important for reasonable turnover rate; the use of diphenylsilane significantly slowed the reaction.[16]

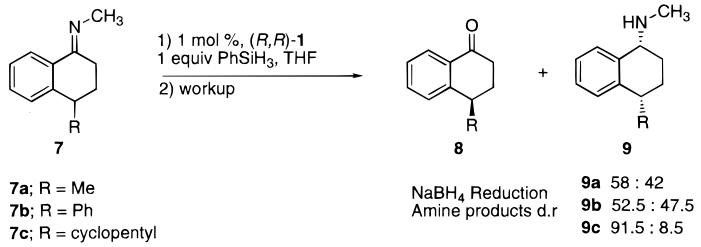
The resolution of *N*-methyl imines of 4-substituted tetralones was investigated with the same catalyst system (Table 3). Better results were achieved with tetralone substrates than with the indanone ones; the *s* values ranged from ~18 to 78 at room temperature. In addition, the amine products are formed with high diastereoselectivity and enantioselectivity. Considering the diastereomeric ratio of amine products in the $NaBH_4$ reduction of these imines (Table 3, for **7a** and **7b**), the

(14) With 2 mol % catalyst and 3 equiv $PhSiH_3$, the reaction went to completion at room temperature in 3 h. The distereomeric ratio of the amine products was 77:23 and the ee's of the products were 27% and 91% respectively.

(15) With 5 mol % catalyst and 2 equiv of $PhSiH_3$ at −45 °C there was no product formation after 15 h. When the reaction was warmed to −30 °C, it gave 19% conversion in 12 h.

(16) With diphenylsilane (3 equiv) as the silane source (2 mol % catalyst) we observed 8% conversion at room temperature in 24 h.

Table 3. Kinetic Resolution of *N*-Methyl Imines of 4-Substituted Tetralones



entry	substrate	T^a (°C)	time (h)	convn[b] (%)	recovered ketone (% ee)	s	diasteromeric ratio of amine products (% ee)
1	**7a**	rt	24	54	96 (*R*)	38.5	95 (90):5 (99)
2		13	24	54	99 (*R*)	60.8	96 (93):4 (99)
3	**7b**	rt	15	61.5	98	17.9	89 (88):11
4		13	15	53	99	80.1	95.5 (96):4.5
5	**7c**	rt	36	49	89	78.3	98 (97):2 (99)
6		13	48	44	75.5	114	98.5 (98):1.5 (99)

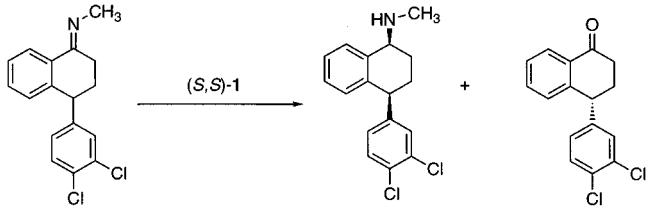
[a] rt = ~24 °C; 13 °C was the temperature in the glovebox. [b] Determined by GC with an internal standard based on consumption of starting material. Isolated yields were calculated on the basis of conversion and reported in the Experimental Section. All the reactions were carried out in [substrate] = 0.5 M with the exception of entries 1 and 2; [substrate] = 1 M (1 mmol/1 mL THF) and 0.8 M (2 mmol/2.5 mL THF) were used.

diastereoselectivity obtained in this kinetic resolution is impressive.[17]

Since the amine products are produced with high de's and high ee's in the kinetic resolution of *N*-methyl imines of tetralones, this method could be also used for asymmetric synthesis of chiral amine products. Sertraline ((+)-*cis*-(1*S*,4*S*)-1-methylamino-4-(3,4-dichlorophenyl)tetralin) (**11**), an antidepressant sold by Pfizer under the trade name Zoloft, is a competitive inhibitor of synaptosomal serotonin uptake. It is produced commercially by the resolution of the racemate with D-mandelic acid.[2a] Even though a few synthetic routes to the sertraline penultimate tetralone (*4S*)-**12**[18] and sertraline **11**[19] have been reported, a classical resolution method is still the preferred industrial means of its production. In view of the structural resemblance of sertraline precursor **10** to **7b**, we decided to synthesize sertraline using our kinetic resolution method (Table 4).

Exposing **10**[20] to a catalytic quantity of (*S*,*S*)-**1** using $PhSiH_3$ as the stoichiometric reductant led to the formation of (1*S*,4*S*)-**11** in a highly diastereo- and enantioselective manner. During the course of the reaction, the active catalytic species was slowly deactivated by the substrate **10**,[21] necessitating the use of 2.5−4 mol % of the catalyst to obtain useful conversions (~45%) in ≤24 h. Overall, sertraline could be isolated in high ee in ~40% average yield.

Table 4. Synthesis of Sertraline via Kinetic Resolution of *rac*-10



cat. (mol %)	$PhSiH_3$ (equiv)	*T* (°C)/ time (h)	conversion (%)	ee (isolated yield)[a]	ketone (% ee)
5	2	rt, 24	54.5	dr 94.5:5.5 ee 91% (48%)[b]	96
4	2	15, 13	51	dr 96:4 ee 95% (39%)	89
4[c]	3	rt, 5	47	dr 95.5:4.5 ee 94% (38%)	83.5
2.5[c]	3	rt, 24	44	dr 96.5:3.5 ee 97% (40%)	71

[a] Pure cis compound was isolated by silica gel chromatography, and this yield represents that of the cis product. [b] This sample showed a 96:4 cis and trans ratio by GC and ^{1}H NMR. [c] (*R*,*R*)-**1** was used. The absolute stereochemistry of this reaction is opposite to that shown in the diagram.

Discussion

All the imine substrates used in this work were obtained exclusively as one isomer (>95%) as judged by ^{1}H NMR. X-ray analysis of imine **10**[22] showed that the major isomer is *E* (anti) where the methyl group points away from the phenyl ring. Since the absolute stereochemistry of several of the reaction products (both recovered ketone and the major amine product) have been determined, we can comment on the origins of selectivity of the kinetic resolution process (Figure 1). Of the four possible ways for the racemic substrate to approach (*R*,*R*)-(EBTHI)Ti−H, it appears that path A is the most favorable. In this case, the *N*-methyl group is positioned in an empty quadrant and the R group is oriented away from the bulk of the catalyst. This orientation should

(17) It has been reported that similar diastereomeric mixtures of racemic amine products are often difficult to resolve.[3a]

(18) (a) Corey, E. J.; Gant, T. G. *Tetrahedron Lett.* **1994**, *35*, 5373. (b) Quallich, G. J.; Woodall, T. M. *Tetrahedron* **1992**, *48*, 10239.

(19) (a) Lautens, M.; Rovis, T. *J. Org. Chem.* **1997**, *62*, 5246. (b) Chen, C.-Y.; Reamer, R. A. *Org. Lett.* **1999**, *1*, 293.

(20) Quallich, G. J.; Williams, M. T.; Friedmann, R. C. *J. Org. Chem.* **1990**, *55*, 4971.

(21) An experiment with equal amounts of **7b** (0.5 mmol) and **10** (0.5 mmol) using 2 mol % catalyst and phenylsilane (2 equiv) was carried out. In 4 h, both substrates reached ~50% conversion, and the conversion had not increased after an additional 11 h (**7b** is one of the fast reacting substrate in Table 3).

(22) While the resolution of this crystal structure was not high, it was sufficient to show that the methyl group is in an anti position.

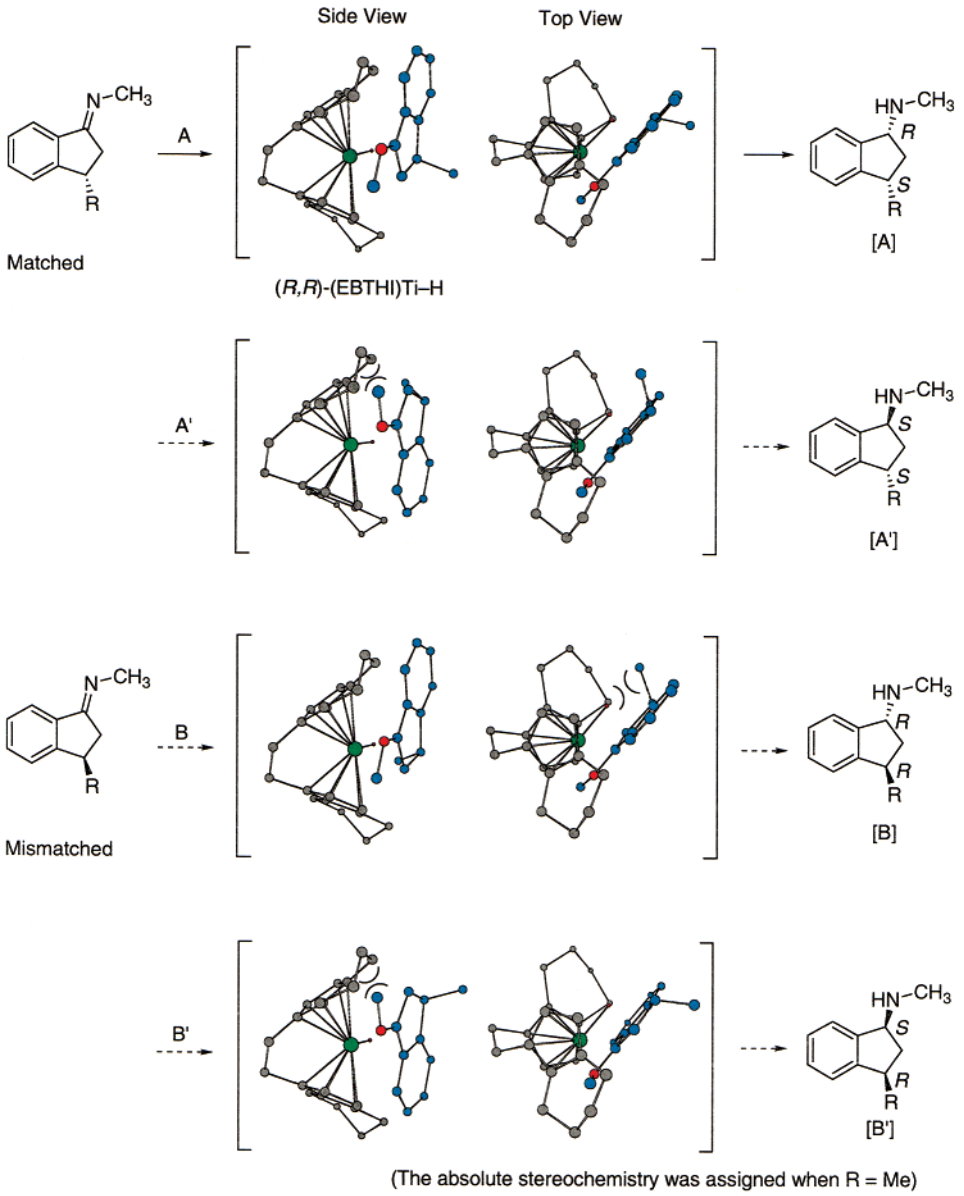


Figure 1.

minimize steric interactions with the ligand framework to yield the major amine product with the observed absolute and relative configuration. The high ee's and de's of the amine products at ~50% conversion in the kinetic resolution of *N*-methyl imines of 4-substituted tetralones reflect the fact that path A predominates over the other pathways.

Unlike in cases of simple kinetic resolution where one enantiomer reacts faster than the other enantiomer with no creation of a new chiral center, the mathematical relationships correlating the relative amounts and the enantiomeric excesses of reaction products and recovered starting material are complex in instances in which kinetic resolution is combined with the creation of an asymmetric center. Horeau and Guetté described a relationship that correlates the ee's of the two diastereomeric products and the diastereomeric ratio in cases where complete conversion occurred.[23] This equation shows that the diastereomeric ratio is equal to the inverse ratio of the ee's of the diastereomers. Our data are in good agreement with that predicted by their equation. At complete conversion the values are as follows: 77/23 = 3.35 for the diastereomeric ratio and 91/27 = 3.37 for the inverse ratio of the ee's.[14] In cases of partial conversion, the mathematical equations dealing with analogous relationships have been discussed by Kagan.[24] These equations are useful to calculate or to refine data not easily measured and to check the self-consistency of a set of data coming from a kinetic resolution. We have applied these equations to the data from the experiments described in Table 2 for which we could obtain all the information[25] necessary to check the consistency. The theoretical value of the ee of recovered starting material is in good agreement with the experimental value.[26] In the case of the data in Table 3, we have not determined the absolute configuration of the minor amine product, which was produced as a single enantiomer. However, applying Kagan's equation[27] with both possible sign conventions of the ee of the minor amine product gave quite different calculated diastereomeric ratios of the

(23) Guetté, J.-P.; Horeau, A. *Bull. Soc. Chim. Fr.* **1967**, 1747.

amine products. The calculated diastereomeric ratio is very similar to the observed ratio only when the absolute stereochemistry of the minor amine product is assumed to be the one (e.g., 1*R*,4*R* for **9a**) obtained by path B (Figure 1).

We can also draw useful information about the diastereoselectivity of the process creating a new asymmetric center in each enantiomer.[28] For example, with the data for **5a** (Table 2, entry 2), the estimated diastereomeric product ratio ([A]/[A′]) of the matched imine enantiomer is 59:1 and that of the mismatched one is 2.3:1([B′]/[B]) (Figure 1). For the tetralone substrate (Table 3, entry 1), the estimated diastereomeric product ratio of the matched imine enantiomer is $>10^4$:1 and that of the mismatched one is 0.95:1. This means that if we had enantiomerically pure 4-substituted tetralone, we could transform it to the corresponding *cis*-*N*-methylamine product with very high diastereoselectivity (>99% de). Combining previously reported asymmetric syntheses of tetralone (*4S*)-**12**,[18] the imine hydrosilylation reaction using the (EBTHI)titanocene catalyst could provide sertraline very efficiently.

In summary, we have achieved the efficient kinetic resolution of imine derivatives of indanones and tetralones having a substituent at a position remote from the reaction center. The amine product was formed with high diastereoselectivity using **1** under hydrosilylation conditions. We have also applied this methodology to the enantiomeric synthesis of sertraline.

Experimental Section

General Methods. THF and diethyl ether were distilled under argon from sodium benzophenone ketyl. Toluene was distilled under nitrogen from molten sodium. Phenylsilane and pyrrolidine were stored under argon in Schlenk tubes and were manipulated under an argon atmosphere.

Ketones were prepared according to known literature procedures except for 3-methyl-1-indanone,[29] 3-phenyl-1-indanone, and 4-methyl-1-tetralone, which were available from Aldrich. 3-*n*-Butyl-1-indanone was prepared by conjugation addition[30] of *n*-butylcuprate to ethyl *trans*-cinnamate in the presence of TMSCl and HMPA, followed by hydrolysis of the ester (NaOH), transformation to the acid chloride (oxalyl chloride, catalytic DMF, benzene), and Friedel−Crafts cyclization of the acid chloride with $AlCl_3$ in refluxing benzene. 3-*tert*-Butyl-1-indanone was prepared by the Friedel−Crafts cyclization of *β*-*tert*-butylhydrocinnamic acid.[31] 4-Phenyl-1-tetralone was prepared from *γ*-phenyl-*γ*-butyrolactone using triflic acid following a reported procedure.[20] 4-Cyclopentyl-1-tetralone was prepared by following the literature procedure[3b] starting from commercially available α-phenylcyclopentaneacetic acid instead of α-phenylcyclohexylacetic acid, and the Friedel−Crafts cyclization was carried out with $ClSO_3H$ in CH_2Cl_2[32] instead of the original reaction conditions utilizing $(CF_3CO)_2O$ in refluxing benzene. 4-(3,4-Dichlorophenyl)-1-tetralone was prepared by the literature procedure.[20]

(3-Methyl-indan-1-ylidene)propylamine (2a): General Procedure for the Preparation of *N*-Propylimines. 3-Methyl-1-indanone (1.80 g, 12.4 mmol) was placed in a dry Schlenk flask under argon. Anhydrous ether (60 mL) was added, and the reaction flask was cooled to −35 °C. *N*-Propylamine (5.0 mL, 62 mmol) was introduced via syringe, followed by the addition of $TiCl_4$ (0.75 mL, 6.6 mmol). The reaction mixture was allowed to warm to room temperature slowly and stirred overnight. The reaction mixture was filtered through a pad of Celite, thoroughly washed with ether, and concentrated. The product was purified by Kugelrohr distillation to give the title product as a yellow oil in 95% yield. It was stored in a N_2-filled glovebox.[33] In cases where the imine product was a solid, the crude product was dried under vacuum and washed under Ar with a small amount of cold pentane or hexane to remove colored impurities: ^{1}H NMR (300 MHz, $CDCl_3$) 7.78 (d, J = 7.69 Hz, 1H), 7.42−7.25 (m, 3H), 3.41 (t, J = 7.19 Hz, 2H), 3.44−3.33 (m, 1H), 2.99 (ddd, J = 0.64, 8.15, 17.86 Hz, 1H), 2.23 (ddd, J = 1.12, 4.05, 17.84 Hz, 1H), 1.76 (sext, J = 7.30 Hz, 2H), 1.34 (d, J = 7.05 Hz, 3H), 0.99 (t, J = 7.37 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.84, 154.33, 139.38, 131.15, 127.20, 124.44, 122.17, 56.01, 37.55, 35.28, 24.34, 22.05, 12.47; IR (neat) 1656 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{13}H_{17}N_1$ 187.1361, found 187.1365.

(3-Phenylindan-1-ylidene)propylamine (2b). Using the general procedure, the title compound was prepared as a white solid (the isolated yield was not determined): mp 70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.88 (dd, J = 2.53, 6.68 Hz, 1H), 7.39−7.20 (m, 5H), 7.14−7.11 (m, 3H), 4.50 (dd, J = 4.32, 8.89 Hz, 1H), 3.43 (t, J = 7.17 Hz, 2H), 3.30 (dd, J = 8.64, 18.10 Hz, 1H), 2.67 (dd, J = 4.40, 18.10 Hz, 1H), 1.78 (qt, J = 7.17, 7.23 Hz, 2H), 0.99 (t, J = 7.23 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.54, 152.43, 145.41, 139.97, 131.54, 128.95, 127.85, 127.72, 126.85, 126.12, 122.26, 56.04, 47.02, 39.37, 24.27, 12.41; IR (neat) 1656 cm^{-1}. Anal. Calcd for $C_{18}H_{19}N_1$: C, 86.70; H, 7.68. Found: C, 86.47; H, 7.65.

(3-*n*-Butylindan-1-ylidene)propylamine (2c). Using the general procedure, the title compound was prepared as a yellow oil in 92% yield: ^{1}H NMR (500 MHz, $CDCl_3$) 7.79 (d, J = 7.63 Hz, 1H), 7.40−7.26 (m, 4H), 3.43 (t, J = 7.17 Hz, 2H), 3.29−3.25 (m, 1H), 2.90 (dd, J = 8.09, 17.85 Hz, 1H), 2.34 (dd, J = 3.81, 17.85 Hz, 1H), 1.87−1.84 (m, 1H), 1.81−1.73 (m, 2H), 1.47−1.32 (m, 5H), 1.00 (t, J = 7.32 Hz, 3H), 0.92 (t, J = 7.17 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 173.05, 153.45, 139.84,

(24) (a) El-Baba, S.; Poulin, J.-C.; Kagan, H. B. *Tetrahedron* **1984**, *40*, 4275. (b) Kagan, H. B.; Fiaud, J. C. In *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Ed.; John Wiley & Sons: New York, 1988; Vol. 18; p 249.

$$X_2/X_3 = x = (C(Y_1 - Y_3) - Y_1)/(C(Y_2 - Y_1) + Y_1) \quad (1)$$

$$Y_1 = C(xY_2 + Y_3)/((C - 1)(1 + x)) \quad (2)$$

$$Y_2 = ((C - 1)/C) \times (1 + 1/x)Y_1 - Y_3/x \quad (3)$$

$$Y_3 = ((C - 1)/C) \times (1 + x)Y_1 - xY_2 \quad (4)$$

$$a = x(1 + Y_2)/(1 + Y_3) = [RS']/[RR'] \quad (5)$$

$$b = x(1 - Y_2)/(1 - Y_3) = [SR']/[SS'] \quad (6)$$

Y_1: ee of *R*,*S* after kinetic resolution = $(R - S)/(R + S) > 0$. Y_2 and Y_3: ee of diastereomers. $Y_2 = (RS' - SR')/(RS' + SR')$, $Y_3 = (RR' - SS')/(RR' + SS')$. X_1, X_2, and X_3 represent the fractional amounts after partial conversion of 1 mol of a compound. *C*: fractional conversion of one mole of the initial mixture. The asymmetric centers created are labeled *R*′ or *S*′. The stereochemical assignment of the equations in the original paper has been modified to that of Figure 1 (R = Me).

(25) The ee's of the minor *trans*-amine products were determined for **6a** and **6b**. For the imines of indanones **5a** and **5b**, the higher the conversion, the lower the ee of the *cis*-amine and the higher the ee of the *trans*-amine. From this information, the absolute configuration of the minor amine product of **6a** was determined as 1*R*,3*R*; see Figure 1.

(26) Experimental/*calculated* ee value of recovered ketone according to eq 2.[24] For data in Table 2: **3a**, 92/*91.8*, 93/*93.9*, 86/*87.9*; **3b**, 83/*83.9*. For data in Table 3: **8a**, 96/*94.5*, 99/*100*; **8c**, 89/*89.4*, 75.5/*74*.

(27) Equation 1 in ref 24 was used.

(28) Equations 5 and 6 in ref 24 were used.

(29) One-step synthesis from crotonic acid and $AlCl_3$ in benzene, see: Koelsch, C. F.; Hochmann, H.; Le Claire, C. D. *J. Am. Chem. Soc.* **1943**, *65*, 59.

(30) Yamamoto, K.; Ogura, H.; Jukuta, J.; Inoue, H.; Hamada, K.; Sugiyama, Y.; Yamada, S. *J. Org. Chem.* **1998**, *63*, 4449.

(31) Wotiz, J. H.; Matthews, J. S.; Greenfield, H. *J. Am. Chem. Soc.* **1953**, *75*, 6342.

(32) The Friedel−Crafts cyclization proceeded smoothly (1−2 h) at room temperature under these conditions,[18a] yielding the cyclized product in good yield (84%), while under the conditions originally reported[3b] the cyclization did not proceed to completion.

(33) The imines of 3-substituted indanones are very sensitive to air and moisture, especially if they are liquids. Therefore, as soon as they were purified by Kugelrohr distillation, the products were transferred to a glovebox. All of the prepared imines were stored in a −40 °C freezer in a glovebox.

131.07, 127.29, 124.80, 122.30, 55.98, 40.69, 36.48, 35.23, 29.91, 24.32, 23.05, 14.27, 12.42; IR (neat) 1656 cm^{-1}. Anal. Calcd for $C_{16}H_{23}N_1$: C, 83.79; H, 10.11. Found: C, 83.63; H, 10.18.

(3-*tert*-Butylindan-1-ylidene)propylamine (2d). Using the general procedure, the title compound was prepared as a colorless oil in 89% yield: ^{1}H NMR (300 MHz, $CDCl_3$) 7.81 (d, J = 7.61 Hz, 1H), 7.44 (br d, J = 7.65 Hz, 1H), 7.37−7.26 (m, 2H), 3.49−3.39 (m, 2H), 3.14 (dd, J = 2.51, 7.86 Hz, 1H), 2.70 (dd, J = 1.74, 17.46 Hz, 1H), 2.60 (dd, J = 7.85, 17.46 Hz, 1H), 1.84−1.74 (m, 2H), 1.01 (t, J = 7.42 Hz, 3H), 0.92 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) 173.38, 150.78, 141.01, 130.24, 127.40, 127.25, 122.15, 55.87, 51.55, 34.93, 32.63, 27.81; IR (neat) 1657 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{23}N_1$ 229.1831, found 229.1834.

Methyl(3-methylindan-1-ylidene)amine (5a): General Procedure for the Preparation for *N*-Methylimines. 3-Methyl-1-indanone (2 g, 13.7 mmol) was placed in a dry Schlenk flask under argon. Anhydrous ether (45 mL) was added, and the reaction flask was cooled to −35 °C. Condensed methylamine (2.0 mL, 68 mmol) was introduced via cannula, followed by the addition of $TiCl_4$ (0.83 mL, 7.5 mmol). The reaction mixture was allowed to warm to room temperature slowly and stirred overnight. The reaction mixture was filtered through a pad of Celite and washed with ether. The combined filtrates were concentrated, and the product was purified by Kugelrohr distillation to give the title product as a pale pink oil in 91% yield: ^{1}H NMR (300 MHz, $CDCl_3$) 7.75 (d, J = 7.66 Hz, 1H), 7.44−7.26 (m, 3H), 3.42−3.32 (m, 1H), 3.33 (s, 3H), 3.00 (dd, J = 8.15, 18.10 Hz, 1H), 2.24 (dd, J = 5.38, 18.10 Hz, 1H), 1.36 (d, J = 7.17 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 175.12, 154.53, 139.28, 131.32, 127.36, 124.57, 121.95, 41.02, 37.27, 35.20, 22.02; IR (neat) 1659 cm^{-1}; HRMS (EI) m/z calcd for $C_{11}H_{13}N_1$ 159.1048, found 159.1050.

Methyl(3-phenylindan-1-ylidene)amine (5b). Using the general procedure, the title compound was prepared as a white solid in 88% yield: mp 96−97 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.83 (br d, J = 6.60 Hz, 1H), 7.39−7.20 (m, 5H), 7.13−7.10 (m, 3H), 4.52 (dd, J = 4.12, 8.61 Hz, 1H), 3.34 (s, 3H), 3.30 (dd, J = 8.70, 18.59 Hz, 1H), 2.65 (dd, J = 4.03, 17.58 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 174.57, 152.47, 145.25, 139.75, 131.61, 128.92, 127.82, 127.77, 126.85, 126.16, 121.91, 46.95, 41.15, 39.19; IR (neat) 1657 cm^{-1}. Anal. Calcd for $C_{16}H_{15}N_1$: C, 86.84; H, 6.83. Found: C, 86.85; H, 6.94.

Methyl(4-methyl-3,4-dihydro-2*H*-naphthalen-1-ylidene)amine (7a). Using the general procedure, the title compound was prepared as a colorless oil in 98% yield: ^{1}H NMR (300 MHz, $CDCl_3$) 8.09 (dd, J = 2.01, 7.78 Hz, 1H), 7.32 (dt, J = 1.50, 7.33 Hz, 1H), 7.23 (dt, J = 0.9, 7.51 Hz, 2H), 3.32 (s, 3H), 2.97−2.91 (m, 1H), 2.71−2.49 (m, 2H), 2.10−2.00 (m, 1H), 1.81−1.70 (m, 1H), 1.32 (d, J = 6.96 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 166.71, 145.12, 134.12, 129.95, 126.86, 126.46, 125.53, 38.68, 33.00, 29.77, 24.97, 20.82; IR (neat) 1630 cm^{-1}. Anal. Calcd for $C_{12}H_{15}N_1$: C, 83.19; H, 8.73. Found: C, 83.01; H, 8.71.

Methyl(4-phenyl-3,4-dihydro-2*H*-naphthalen-1-ylidene)-amine (7b). Using the general procedure, the title compound was prepared as a white solid in 96% yield: mp 69−70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.21−8.18 (m, 1H), 7.32−7.20 (m, 5H), 7.09−7.06 (m, 2H), 6.94−6.91 (m, 1H), 4.20 (dd, J = 4.44, 6.82 Hz, 1H), 3.31 (s, 3H), 2.53 (br t, J = 6.50 Hz, 2H), 2.30 (dtd, J = 4.40, 6.89, 13.05 Hz, 1H), 2.18 (qd, J = 6.55, 13.10 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 166.42, 144.21, 142.13, 135.12, 130.05, 129.15, 128.70, 128.60, 127.05, 126.57, 125.47, 45.18, 38.80, 30.78, 24.97; IR (neat) 1625 cm^{-1}. Anal. Calcd for $C_{17}H_{17}N_1$: C, 86.77; H, 7.28. Found: C, 86.67; H, 7.23.

(4-Cyclopentyl-3,4-dihydro-2*H*-naphthalen-1-ylidene)-methylamine (7c). Using the general procedure, the title compound was prepared as a white solid in 97% yield: mp 61 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.03 (dd, J = 1.88, 7.28 Hz, 1H), 7.29−7.21 (m, 2H), 7.12 (br d, J = 6.41 Hz, 1H), 3.31 (s, 3H), 2.60−2.50 (m, 3H), 2.18−2.09 (m, 1H), 1.98−1.76 (m, 3H), 1.71−1.54 (m, 3H), 1.46−1.38 (m, 2H), 1.33−1.24 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 166.94, 144.62, 134.11, 129.26, 128.65, 126.70, 125.72, 44.70, 43.67, 38.79, 32.43, 31.47, 25.80, 25.28, 25.10, 24.00; IR (neat) 1629 cm^{-1}. Anal. Calcd for $C_{16}H_{21}N_1$: C, 84.53; H, 9.31. Found: C, 84.42; H, 9.34.

(4-(3,4-Dichlorophenyl)-3,4-dihydro-2*H*-naphthalen-1-ylidene)methylamine (10). Using the general procedure, the title compound was prepared as a white solid in 91% yield: mp 145−146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 8.25 (br s, 1H), 7.37−7.27 (m, 3H), 7.20 (d, J = 1.83 Hz, 1H), 6.92−6.89 (m, 2H), 4.17 (dd, J = 4.62, 6.55 Hz, 1H), 3.34 (s, 3H), 2.61−2.45 (m, 2H), 2.35−2.25 (m, 1H), 2.19−2.08 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 165.77, 144.54, 140.76, 134.97, 132.69, 130.64, 130.57, 130.52, 130.32, 128.95, 128.07, 127.53, 125.79, 44.40, 38.81, 30.58, 24.72; IR (neat) 1625 cm^{-1}. Anal. Calcd for $C_{17}H_{15}N_1Cl_2$: C, 67.12; H, 4.97. Found: C, 66.85; H, 5.03.

General Procedure for the Kinetic Resolution. To a solution of (*R*,*R*)-**1** (3.5 mg, 0.01 mmol) in anhydrous THF (1 mL) were added sequentially phenylsilane (12 μL, 0.1 mmol), pyrrolidine (8 μL, 0.1 mmol), and MeOH (4 μL, 0.1 mmol) under an atmosphere of argon in a resealable Schlenk tube. The reaction mixture was then heated at 60 °C until the color of the solution turned from yellow to green. The Schlenk tube was removed from the oil bath and cooled to room temperature. In a glovebox, the imine substrate (1 mmol) and internal standard (dodecane or tetradecane) were added to a flask fitted with a septum. The imine substrate was dissolved in THF (1 mL) and was added to the activated catalyst via pipet in a glovebox (Table 3). The Schlenk tube was sealed, removed from the glovebox, and allowed to stir for an indicated amount of time. For low-temperature (0 °C or below) reactions, the substrate in THF was transferred via cannula to the Schlenk flask containing a solution of the activated catalyst with the aid of a Schlenk line (Table 2). The Schlenk tube was resealed was allowed to stir for an indicated amount of time.

Workup: Procedure A.[34] The reaction mixture was diluted with either pentane or hexane (10 mL) and was added slowly to a NaOAc/HOAc buffer solution[35] (10 mL) with vigorous stirring (**Caution**: bubbling!). The biphasic mixture was stirred for 5−12 h. At this point, the organic layer containing ketone from hydrolysis of the unreacted imine was separated, ether (10 mL) was added, and the combined organic layers were washed with brine. The organic layer was dried over $MgSO_4$ and concentrated. Chromatography gave ketone in >95% purity as judged by ^{1}H NMR and GC. The aqueous layer containing the amine products was basified with 2 N NaOH and was extracted with ether (3 × 15 mL). The combined organic layers were dried over Na_2SO_4 and purified by chromatography. **Procedure B (The Preferred Method for Imines of Tetralones).** The reaction mixture was diluted with ether (10 mL) and was added to a 1 N NaOH solution (10 mL) with vigorous stirring (**Caution**: bubbling!). The reaction mixture was stirred for 10−30 min until the bubbling stopped, and the aqueous layer was extracted with ether (3 × 20 mL). The combined ether extracts were dried over Na_2SO_4 and concentrated. Both ketone and amine products were purified by silica gel chromatography. After elution of ketone substrate from the unreacted imine with hexane and ether, the polarity of the eluant was increased to elute the amine products[36] (CH_2Cl_2/MeOH/triethylamine (or ammonium hydroxide solution) = 10:1:0.1). The isolated products were >95% pure as judged by GC and ^{1}H NMR. The absolute configuration of the product was determined by optical rotation in the cases where it had previously been determined. The ee was determined by GC analysis using a Chiraldex BPH (20 m length, 0.25 mm ID) or GTA column (20 m length, 0.25 mm ID) or

(34) This procedure was mostly used for experiments with more unstable indanone imines.

(35) Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3082.

(36) Many of the minor amine products produced from the kinetic resolution are more polar than the major amine products assumed to be the cis isomer. Therefore, special care must be taken in order to isolate the minor amine products during chromatography. Thus, the diastereomeric ratio of amine products was determined on the crude reaction mixture. The ee of the products was often determined after transformation of the crude mixture of amines to proper derivatives for chiral analysis.

HPLC analysis using a Chiralcel OJ or OD column. The major enantiomer of each compound indicated below reflects the major enantiomer of the reaction products with (*R*,*R*)-**1** except in the case of sertraline where (*S*,*S*)-**1** was used. The ^{1}H NMR analysis of the amine products reported below is that of the major amine product.

3-Methyl-1-indanone (3a). This was isolated in 73% yield[37] based on 49% conversion (Table 1, entry 2). The ee was measured by chiral GC on a BPH column (90 °C isothermal, 1.0 mL/min, 25.6 min, 26.9 min (major, *R*)): ^{1}H NMR (300 MHz, $CDCl_3$) 7.73 (d, J = 7.79 Hz, 1H), 7.62 (ddd, J = 1.18, 7.21, 7.70 Hz, 1H), 7.51 (qd, J = 0.92, 7.82 Hz, 1H), 7.38 (ddt, J = 0.62, 0.93, 7.42 Hz, 1H), 3.45 (dquint, J = 3.50, 7.21 Hz, 1H), 2.95 (dd, J = 7.50, 19.07 Hz, 1H), 2.29 (dd, J = 3.42, 19.07 Hz, 1H), 1.42 (d, J = 7.17 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 206.50, 160.04, 136.51, 134.87, 127.52, 125.41, 123.56, 45.60, 33.07, 21.65; IR (neat) 1710 cm^{-1}; $[\alpha]_D$ −6.67° (for a sample of 91.6% ee) (*c* 1.05, EtOH) (lit.[4] $[\alpha]_D$ 10.1° (*c* 3, EtOH), 100% ee (*S*)).

(3-Methylindan-1-yl)propylamine (4a). This was isolated in 69% yield based on 49% conversion (Table 1, entry 2). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (120 °C isothermal, 1.0 mL/min, cis isomer, 12.6 min (major (1*R*,3*S*)), 13.5 min;, trans isomer, not separated): ^{1}H NMR (300 MHz, $CDCl_3$) 7.36−7.31 (m, 1H), 7.26−7.17 (m, 3H), 4.19 (dd, J = 7.09, 8.89 Hz, 1H), 3.08−2.98 (m, 1H), 2.78−2.64 (m, 3H), 1.66−1.39 (m, 3H), 1.34 (d, J = 6.68 Hz, 3H), 1.36−1.26 (m, 1H), 0.96 (t, J = 7.42 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 147.95, 145.81, 127.42, 126.52, 123.60, 123.27, 62.17, 49.54, 44.20, 36.86, 23.99, 19.89, 12.11; IR (neat) 3304 cm^{-1}. Anal. Calcd for $C_{13}H_{19}N_1$: C, 82.48; H, 10.12. Found: C, 82.63; H, 9.74.

3-Phenyl-1-indanone (3b). This was isolated in 81% yield based on 58% conversion (Table 1, entry 4). The ee was measured by chiral HPLC on a OJ column (10% *i*-PrOH/90% hexanes, 0.5 mL/min, 19.75 min, 25.00 min (major)): ^{1}H NMR (300 MHz, $CDCl_3$) 7.81 (dd, J = 0.50, 7.69 Hz, 1H), 7.57 (dt, J = 1.28, 7.46 Hz, 1H), 7.42 (t, J = 7.40 Hz, 1H), 7.34−7.22 (m, 4H), 7.14−7.11 (m, 2H), 4.58 (dd, J = 3.84, 7.97 Hz, 1H), 3.24 (dd, J = 7.97, 19.23 Hz, 1H), 2.70 (dd, J = 3.85, 19.32 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 205.93, 158.05, 143.88, 136.99, 135.18, 129.07, 128.03, 127.78, 127.14, 127.04, 123.57, 47.01, 44.66; IR (neat) 1710 cm^{-1}; $[\alpha]_D$ 61.2° (for a sample of 90% ee) (*c* 2.50, EtOH). Anal. Calcd for $C_{15}H_{12}O_1$: C, 86.51; H, 5.81. Found: C, 86.26; H, 5.89.

(3-Phenylindan-1-yl)propylamine (4b). This was isolated in 76% yield based on 58% conversion (Table 1, entry 4). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (140 °C for 40 min, ramp of 0.5 °C/min to 150 °C and then isothermal for 30 min; major isomer, 82.11 min (major), 83.37 min; minor isomer, 78.44 min (major), 80.03 min): ^{1}H NMR (300 MHz, $CDCl_3$) 7.42 (d, J = 7.66 Hz, 1H), 7.35−7.15 (m, 7H), 6.91 (d, J = 7.50 Hz, 1H), 4.31 (dd, J = 7.25, 8.72 Hz, 1H), 4.17 (dd, J = 7.50, 10.11 Hz, 1H), 2.93 (td, J = 6.68, 12.23 Hz, 1H), 2.73 (t, J = 7.01 Hz, 2H), 1.79 (ddd, J = 9.08, 10.30, 11.98 Hz, 1H), 1.64−1.51 (m, 3H), 0.95 (t, J = 7.48 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 146.20, 145.96, 144.77, 128.67, 128.54, 127.60, 126.92, 126.62, 125.07, 123.63, 62.23, 49.38, 49.13, 45.82, 23.93, 12.09; IR (neat) 3308 cm^{-1}. Anal. Calcd for $C_{18}H_{21}N_1$: C, 86.01; H, 8.42. Found: C, 86.34; H, 8.29.

3-*n*-Butyl-1-indanone (3c). This was isolated in 92% yield based on 54% conversion (Table 1, entry 5). The ee was measured by chiral GC on a BPH column with the corresponding alcohols after reduction with $NaBH_4$ (110 °C, isothermal, 1.0 mL/min; major alcohol, 95.24 min (major), 99.24 min; minor alchol, 86.91 min (major), 91.20 min): ^{1}H NMR (300 MHz, $CDCl_3$) 7.73 (d, J = 7.66 Hz, 1H), 7.60 (dt, J = 1.14, 7.17 Hz, 1H), 7.51 (br d, J = 6.68 Hz, 1H), 7.37 (br t, J = 7.58 Hz, 1H), 3.38−3.32 (m, 1H), 2.86 (dd, J = 7.50, 19.07 Hz, 1H), 2.37 (dd, J = 3.26, 19.07 Hz, 1H), 1.94−1.89 (m, 1H), 1.60−1.31 (m, 5H), 0.92 (t, J = 6.85 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 206.64, 159.22, 137.01, 134.79, 127.64, 125.81, 123.72, 43.36, 38.46, 36.05, 29.94, 22.96, 14.18; IR (neat) 1711 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{13}H_{16}O_1$ 188.1201, found 188.1205.

(3-*n*-Butylindan-1-yl)propylamine (4c). This was isolated in 64% yield based on 54% conversion (Table 1, entry 5). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (110 °C isothermal, 1.0 mL/min; major isomer, 90.16 min (major), 92.87 min; minor isomer, 77.30 min (major), 80.30 min): ^{1}H NMR (300 MHz, $CDCl_3$) 7.37−7.32 (m, 1H), 7.23−7.16 (m, 3H), 4.18 (t, J = 7.78 Hz, 1H), 3.01−2.90 (m, 1H), 2.77−2.63 (m, 3H), 2.05−1.97 (m, 1H), 1.66−1.47 (m, 3H), 1.46−1.28 (m, 6H), 0.96 (t, J = 7.33 Hz, 3H), 0.96−0.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 147.10, 145.75, 127.32, 126.55, 123.71, 123.48, 62.13, 49.51, 42.33, 41.56, 34.97, 30.11, 24.00, 23.22, 14.43, 12.21; IR (neat) 3311 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{16}H_{25}N_1$ 231.1987, found 231.1982.

3-*tert*-Butyl-1-indanone (3d). This was isolated in 72% yield based on 60% conversion (Table 1, entry 7). The ee was measured by chiral GC on a BPH column (120 °C isothermal, 1.0 mL/min, 20.62 min, 21.94 min (major)): ^{1}H NMR (300 MHz, $CDCl_3$) 7.74 (d, J = 7.47 Hz, 1H), 7.60−7.53 (m, 2H), 7.41−7.36 (m, 1H), 3.24 (dd, J = 2.13, 7.20 Hz, 1H), 2.70 (dd, J = 7.27, 19.35 Hz, 1H), 2.61 (dd, J = 1.64, 19.42 Hz, 1H), 0.94 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) 207.00, 156.49, 137.97, 133.92, 128.11, 127.74, 123.54, 49.48, 41.30, 34.71, 27.87; IR (neat) 1713 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{13}H_{16}O_1$ 188.1201, found 188.1207.

(3-*tert*-Butylindan-1-yl)propylamine (4d). This was isolated in 82% yield based on 60% conversion (Table 1, entry 7). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (130 °C isothermal, 1.0 mL/min; major isomer, 25.17 min (major), 27.11 min; minor isomer, not separated): ^{1}H NMR (300 MHz, $CDCl_3$) 7.46−7.43 (m, 1H), 7.38−7.35 (m, 1H), 7.23−7.15 (m, 2H), 4.08 (t, J = 7.91 Hz, 1H), 2.92 (dd, J = 7.66 Hz, 1H), 2.79−2.69 (m, 2H), 2.48 (td, J = 7.25, 12.23 Hz, 1H), 1.76 (br s, 1H), 1.63−1.45 (m, 3H), 1.05 (s, 9H), 0.97 (t, J = 7.42 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 147.09, 144.78, 126.92, 126.39, 125.80, 123.92, 61.18, 53.32, 49.60, 37.47, 33.39, 28.66, 24.01, 12.16; IR (neat) 3311 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{16}H_{25}N_1$ 231.1987, found 231.1984.

3-Methyl-1-indanone (3a). This was isolated in 84% yield based on 55% conversion (Table 2, entry 2).

Methyl(3-methyl-indan-1-yl)amine (6a). This was isolated in 87% yield based on 55% conversion (Table 2, entry 2). The ee was measured by chiral GC on a GTA column with the corresponding trifluoroacetamide derivative (110 °C isothermal, 1.0 mL/min; major isomer, 36.30 min (major), 38.19 min; minor isomer, 31.66 min (major), 33.92 min): ^{1}H NMR (300 MHz, $CDCl_3$) 7.35−7.30 (m, 1H), 7.27−7.18 (m, 3H), 4.13 (dd, J = 7.51, 8.61 Hz, 1H), 3.09−3.01 (m, 1H), 2.71 (td, J = 7.05, 12.14 Hz, 1H), 2.55 (s, 3H), 1.43 (br s, 1H), 1.35 (d, J = 6.84 Hz, 3H), 1.37−1.24 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 147.91, 145.13, 127.47, 126.49, 123.60, 123.25, 63.66, 43.39, 36.85, 34.04, 20.06; IR (neat) 3311 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{11}H_{15}N_1$ 161.1204, found 161.1201.

3-Phenyl-1-indanone (3b). This was isolated in 81% yield based on 52% conversion (Table 2, entry 6).

Methyl(3-phenyl-indan-1-yl)amine (6b). This was isolated in 81% yield based on 52% conversion (Table 2, entry 6). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (150 °C isothermal, 1.0 mL/min; major isomer, 67.15 min, 70.10 min (major); minor isomer, 58.38 min (major), 59.72 min)): ^{1}H NMR (300 MHz, $CDCl_3$) 7.42 (d, J = 7.24 Hz, 1H), 7.35−7.21 (m, 7H), 6.92 (d, J = 7.42 Hz, 1H), 4.25 (dd, J = 7.05, 8.71 Hz, 1H), 4.19 (dd, J = 7.60, 10.03 Hz, 1H), 2.96 (td, J = 7.01, 12.36 Hz, 1H), 2.56 (s, 3H), 1.77 (ddd, J = 9.43, 10.07, 12.36 Hz, 1H), 1.58 (br s, 1H),; ^{13}C NMR (75 MHz, $CDCl_3$) 146.25, 145.47, 144.71, 128.68, 128.50, 127.69, 126.94, 126.64, 125.10, 123.66, 63.72, 49.07, 45.12, 33.95; IR (neat) 3319 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{16}H_{17}N_1$ 223.1361, found 223.1356.

(37) The maximum yield is 100% when the amount of (1 − % conversion/100) × (initial mol of the starting imine substrate) is recovered for ketone substrate and (% conversion/100) × (initial mol of the starting imine substrate) for amine products.

4-Methyl-1-tetralone (8a). This was isolated in 90% yield based on 54% conversion (Table 3, entry 2). The ee was measured by chiral GC on a GTA column (105 °C isothermal, 1.0 mL/min, 42.68 min (major (4*R*)), 48.52 min): ^{1}H NMR (300 MHz, $CDCl_3$) 8.03 (dd, J = 1.47, 7.82 Hz, 1H), 7.51 (ddd, J = 1.47, 7.41, 7.58 Hz, 1H), 7.35−7.28 (m, 2H), 3.10 (dq, J = 4.56, 7.01 Hz, 1H), 2.81 (ddd, J = 4.60, 8.68, 17.40 Hz, 1H), 2.61 (ddd, J = 4.85, 8.60, 17.40 Hz, 1H), 2.26 (tdd, J = 4.64, 8.64, 13.36 Hz, 1H), 1.97−1.86 (m, 1H), 1.41 (d, J = 7.01 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 198.56, 149.05, 133.77, 131.94, 127.57, 127.36, 126.65, 36.57, 33.04, 30.77, 20.97; IR (neat) 1684 cm^{-1}; $[\alpha]_D$ 21.6° (for a sample of 99% ee) (*c* 1.99, MeOH) (lit.[6] $[\alpha]_D$ −7° (*c* 2.5, MeOH), 23% ee (*S*)). Anal. Calcd for $C_{11}H_{12}O_1$: C, 82.46; H, 7.55. Found: C, 82.39; H, 7.38.

***N*-Methyl-4-methyl-1,2,3,4-tetrahydro-1-naphthylamine (9a).** This was isolated in 92% yield based on 54% conversion (Table 3, entry 2). The ee was measured by chiral GC on a GTA column with the corresponding trifluoroacetamide derivative (110 °C isothermal, 1.0 mL/min; major isomer, 65.68 min (major), 68.20 min; minor isomer, 71.91 min (major), 74.63 min): ^{1}H NMR (300 MHz, $CDCl_3$) 7.34−7.31 (m, 1H), 7.27−7.13 (m, 3H), 3.64 (t, J = 4.81 Hz, 1H), 2.88−2.81 (m, 1H), 2.50 (s, 3H), 1.97−1.78 (m, 3H), 1.72−1.60 (m, 2H), 1.33 (d, J = 7.01 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 142.44, 138.72, 128.80, 127.83, 127.06, 125.82, 57.73, 34.21, 32.90, 27.66, 25.84, 22.51; IR (neat) 3315 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{12}H_{17}N_1$ 175.1361, found 175.1356.

4-Phenyl-1-tetralone (8b). This was isolated in 85% yield based on 53% conversion (Table 3, entry 4). The ee was measured by chiral HPLC on an OJ column (10% *i*-PrOH/90% hexanes, 1.0 mL/min, 9.74 min, 18.96 min (major)): ^{1}H NMR (300 MHz, $CDCl_3$) 8.12 (dd, J = 1.63, 7.66 Hz, 1H), 7.44 (dt, J = 1.55, 7.46 Hz, 1H), 7.39−7.23 (m, 4H), 7.13−7.09 (m, 2H), 6.99 (br d, J = 7.66 Hz, 1H), 4.31 (dd, J = 4.64, 7.90 Hz, 1H), 2.74 (ddd, J = 4.64, 7.98, 17.11 Hz, 1H), 2.63 (ddd, J = 4.48, 9.13, 17.11 Hz, 1H), 2.53−2.43 (m, 1H), 2.37−2.25 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 198.25, 146.41, 143.82, 133.79, 132.93, 129.71, 128.80, 128.76, 127.25, 127.21, 126.95, 45.53, 36.99, 32.09; IR (neat) 1682 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_1$: C, 85.45; H, 6.35. Found: C, 86.27; H, 6.46.

***N*-Methyl-4-phenyl-1,2,3,4-tetrahydro-1-naphthylamine (9b).** This was isolated in 86% yield based on 53% conversion (Table 3, entry 4). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (150 °C isothermal, 1.0 mL/min; major isomer, 90.30 min, 94.39 min (major); minor isomer, not separated)): ^{1}H NMR (300 MHz, $CDCl_3$) 7.36 (d, J = 7.82 Hz, 1H), 7.31−7.01 (m, 7H), 6.83 (d, J = 7.17 Hz, 1H), 4.01 (dd, J = 5.58, 8.79 Hz, 1H), 3.73 (t, J = 3.73 Hz, 1H), 2.54 (s, 3H), 2.15−1.98 (m, 1H), 1.89−1.79 (m, 1H), 1.60 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 147.09, 140.14, 139.01, 130.23, 129.16, 129.00, 128.49, 127.26, 126.36, 126.26, 57.56, 46.26, 34.22, 28.87, 25.85; IR (neat) 3345 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{17}H_{19}N_1$ 237.1518, found 237.1523.

4-Cyclopentyl-1-tetralone (8c). This was isolated in 86% yield based on 44% conversion (Table 3, entry 6). The ee was measured by chiral GC on a BPH column (150 °C isothermal, 1.0 mL/min, 30.39 min (major), 32.59 min): mp 56−58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.01 (dd, J = 1.39, 7.74 Hz, 1H), 7.45 (dt, J = 1.39, 7.46 Hz, 1H), 7.31 (dt, J = 1.14, 7.58 Hz, 1H), 7.26 (br d, J = 7.82 Hz, 1H), 2.87−2.55 (m, 4H), 2.24−2.18 (m, 2H), 2.05−1.87 (m, 2H), 1.74−1.42 (m, 4H), 1.38−1.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 198.80, 148.57, 133.05, 131.99, 129.18, 127.55, 126.88, 44.22, 44.20, 34.53, 32.48, 31.63, 26.80, 25.31, 25.02; IR (neat) 1677 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_1$: C, 84.07; H, 8.47. Found: C, 83.98; H, 8.50.

***N*-Methyl-4-cyclopentyl-1,2,3,4-tetrahydro-1-naphthylamine (9c).** This was isolated in 86% yield based on 44% conversion (Table 3, entry 6). The ee was measured by chiral GC on a BPH column with the corresponding trifluoroacetamide derivative (130 °C for 40 min, ramp of 0.2 °C/min to 150 °C and then isothermal for 5 min; major isomer, 117.66 min, 124.63 min (major); minor isomer, 124.41 min (major), 127.01 min): ^{1}H NMR (300 MHz, $CDCl_3$) 7.36−7.33 (m, 1H), 7.24−7.12 (m, 3H), 3.71 (t, J = 6.11 Hz, 1H), 2.67−2.61 (m, 1H), 2.49 (s, 3H), 2.25−2.16 (m, 1H), 1.94−1.36 (m, 12H), 1.24−1.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 141.97, 139.04, 129.02, 128.64, 126.39, 125.95, 57.73, 45.10, 42.52, 33.80, 31.90, 29.66, 25.66, 25.10, 23.40; IR (neat) 3328 cm^{-1}. Anal. Calcd for $C_{16}H_{23}N_1$: C, 83.79; H, 10.11. Found: C, 83.59; H, 10.01.

Kinetic Resolution of *rac*-10 (Table 4, First Entry). To a solution of (*S*,*S*)-(EBTHI)TiF_2 (8.7 mg, 0.025 mmol) in anhydrous THF (1 mL) were sequentially added phenylsilane (12 μL, 0.1 mmol), pyrrolidine (8 μL, 0.1 mmol), and MeOH (4 μL, 0.1 mmol) under an atmosphere of argon in a resealable Schlenk tube. The reaction mixture was then heated at 60 °C until the color of the solution turned from yellow to green. The Schlenk tube was removed from the oil bath and cooled to room temperature. Imine substrate **10** (152 mg, 0.5 mmol) and dodecane (0.11 mL) were added to a flask fitted with a septum in a glovebox. The mixture was then dissolved in THF (1.5 mL)[38] and was added to the active catalyst via pipet in the glovebox. The reaction tube was sealed and stirred at room temperature for 24 h. The workup procedure B gave the corresponding ketone (56 mg, 0.19 mmol) and the amine products (73 mg, 0.24 mmol, 96:4 = cis/trans).

4-(3,4-Dichlorophenyl)-1-tetralone (12). The ee was measured by chiral HPLC on a OD column (10% *i*-PrOH/90% hexanes, 0.7 mL/min, 10.77 min, 12.02 min (major, (*R*)): mp 84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.13 (dd, J = 1.63, 7.82 Hz, 1H), 7.48 (dt, J = 1.71, 7.46 Hz, 1H), 7.40 (d, J = 8.31 Hz, 1H), 7.38 (t, J = 8.30 Hz, 1H), 7.23 (d, J = 2.12 Hz, 1H), 6.97−6.93 (m, 2H), 4.28 (dd, J = 4.48, 8.23 Hz, 1H), 2.72 (ddd, J = 4.81, 7.66, 17.27 Hz, 1H), 2.63 (ddd, J = 4.72, 8.80, 17.28 Hz, 1H), 2.52−2.42 (m, 1H), 2.32−2.20 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 197.51, 145.00, 144.14, 134.04, 132.93, 132.84, 131.12, 130.77, 130.68, 129.45, 128.12, 127.71, 127.55, 44.77, 36.79, 31.93; IR (neat) 1677 cm^{-1}; $[\alpha]_D$ −63.0° (for a sample of 96.3% ee) (*c* 1.0, acetone) (lit.[18b] $[\alpha]_D$ 55.7° (*c* 1.01, acetone), 84% ee (*S*)). Anal. Calcd for $C_{16}H_{12}O_1Cl_2$: C, 66.00; H, 4.15. Found: C, 65.88; H, 4.27.

***N*-Methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthylamine (11).** The ee was measured by chiral HPLC on a OD column with the corresponding 1-naphthoylamide derivative (10% *i*-PrOH/ 90% hexanes, 0.6 mL/min; cis isomer, 27.16 min, 30.41 min (major, (1*S*,4*S*)); trans isomer, 22.24 min, 38.52 min): mp 59−61 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.35 (dd, J = 1.14, 7.66 Hz, 1H), 7.34 (d, J = 8.31 Hz, 1H), 7.25 (d, J = 2.12 Hz, 1H), 7.20 (ddt, J = 0.81, 1.46, 7.58 Hz, 1H), 7.11 (dt, J = 1.47, 7.50 Hz, 1H), 6.97 (dd, J = 2.12, 8.15 Hz, 1H), 6.79 (d, J = 7.66 Hz, 1H), 3.98 (dd, J = 5.46, 9.37 Hz, 1H), 3.73 (t, J = 4.16 Hz, 1H), 2.54 (s, 3H), 2.09−1.96 (m, 3H), 1.87−1.75 (m, 1H), 1.64 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 147.46, 139.09, 138.88, 132.40, 130.86, 130.46, 130.20, 129.98, 129.43, 128.45, 127.51, 126.79, 57.48, 45.60, 34.42, 28.63, 25.76; IR (neat) 3346 cm^{-1}. Anal. Calcd for $C_{17}H_{17}N_1Cl_2$: C, 66.68; H, 5.60. Found: C, 66.62; H, 5.63.

The major amine product (1*R*,4*R*) from the resolution with (*R*,*R*)-**1** was converted to the corresponding HCl salt and its absolute stereochemistry was determined by optical rotation: $[\alpha]_D$ −32.5° (*c* 0.77, MeOH) (from the amine of 91.5% ee) (lit.[3a] $[\alpha]_D$ −37.2° (*c* 2, MeOH), 100% ee (1*R*,4*R*)).

Acknowledgment. This research was generously supported by the National Institutes of Health (GM-46059). Additional unrestricted support from Pfizer, Merck, and Novartis is gratefully acknowledged.

JO991328H

(38) The imine substrate (0.5 mmol) showed lower solubility than those of the other imine substrates in this work and was not completely soluble in 1.5 mL of THF. However, after its addition to the activated catalyst via pipet and the mixture became homogeneous (0.5 mmol substrate/ 2.5 mL solvent in total).