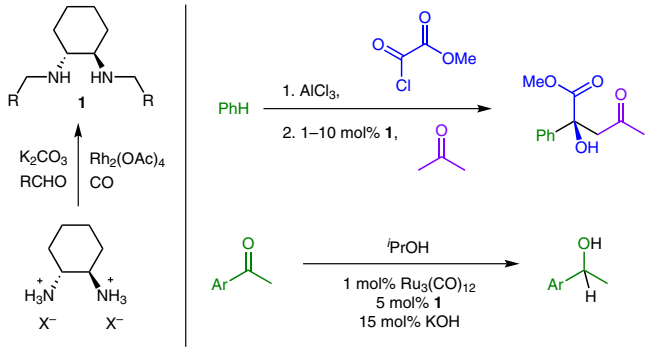
Synlett A. A. Tsygankov et al. Letter

Synthesis of N,N′-Dialkylated Cyclohexane-1,2-diamines and Their Application as Asymmetric Ligands and Organocatalysts for the Synthesis of Alcohols

Alexey A. Tsygankov[a]
Man-Seog Chun[b]
Alexandra D. Samoylova[a]
Seongyeon Kwon[b]
Yuliya M. Kreschenova[a]
Suhyeon Kim[b]
Euijin Shin[b]
Jinho Oh[b]
Tatyana V. Strelkova[c]
Valerii S. Kolesov[c]
Fedor I. Zubkov[d]
Sergei E. Semenov[a]
Ivan V. Fedyanin[c]
Denis Chusov*[a,c,d]

[a] Moscow Chemical Lyceum, Tamozhenniy proezd 4, Moscow, Russian Federation
[b] Korea Science Academy of KAIST, 105-47, Baegyanggwanmun-ro, Busanjin-gu, 47162 Busan, Republic of Korea
[c] A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Vavilova str. 28, 119991 Moscow, Russian Federation
Chusov@ineos.ac.ru
[d] Peoples Friendship University of Russia, Dept Organic Chemistry, 6 Miklukho-Maklaya St, Moscow 117198, Russian Federation



11 diamines were tested. Yields 67–98%. 72:28 to 87.5:12.5 e.r.

Received: 05.10.2016
Accepted after revision: 29.11.2016
Published online: 15.12.2016
DOI: 10.1055/s-0036-1588382; Art ID: st-2016-b0664-l

Abstract A series of N,N′-dialkylated derivatives of (1*R*,2*R*)-cyclohexane-1,2-diamine were synthesized, and a new approach to the one-pot preparation of this type of amine was demonstrated. The prepared diamines were used as organocatalysts for the two-step synthesis of α-hydroxy γ-keto esters from arenes, chlorooxoacetates, and ketones; they were also used as chiral ligands for Meervein–Ponndorf–Verley reductions and Henry reactions.

Key words aldol reaction, organocatalysis, asymmetric catalysis, hydroxy acids, diamines, Meervein–Ponndorf–Verley reaction, Henry reaction

Asymmetric organocatalysis has become the main focus of research in asymmetric synthesis since the pioneering work of List et al.,[1] who explored aldol reactions catalyzed by a simple organic molecule, L-proline. The aldol reaction is one of the most important C–C bond-formation reactions,[2,3] and consequently many asymmetric variants of this reaction have been developed.[4]

Chiral tertiary alcohols are valuable as synthetic intermediates in pharmaceutical chemistry, and therefore metal-free approaches to their synthesis are highly desirable; however, organocatalytic syntheses of this type of compound have not been well studied. In this context, we became interested in the development of an enantioselective method for the preparation of chiral tertiary alcohols through aldol-type chemistry.

Mandelic acid has a long history of use as an antibacterial agent, especially for the treatment of urinary tract infections.[5] It is also used as an oral antibiotic and as a component of chemical face peels, along with other α-hydroxy acids. Likewise, many derivatives of mandelic acid are known to be pharmaceutically important compounds, e.g. the vasodilator cyclandelate and the anticholinergic homatropine.

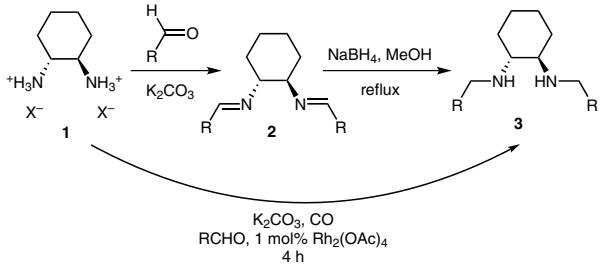
These considerations prompted our choice of mandelic acid analogues with a chiral quaternary carbon center as synthetic targets. Methods for the synthesis of this type of molecule through organocatalytic asymmetric aldol reactions are rare, and most require 20–50 mol% of the catalyst; in only a few instances can the catalytic loading be reduced to 10–15 mol%.[6]

Here, we report a convenient synthesis of aldol-reaction organocatalysts that were found to be active at loadings as low as 1–10 mol%. For the synthesis of catalysts **3a–k**, we started from an inexpensive and readily available mixture of *cis*- and *trans*-cyclohexane-1,2-diamine. Many derivatives of cyclohexanediamine have been used as chiral li-

gands, and reduced representatives of this group (salan ligands)[7] are usually prepared by a two-step condensation/reduction route. We decided to elaborate a new one-step protocol for the synthesis of these compounds directly from cyclohexane-1,2-diamine salts.

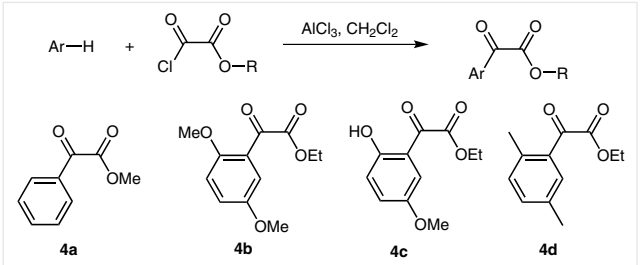
We were pleased to find that diamines **3** could be obtained in one step from diamine salts **1** and the appropriate aldehydes by reductive amination without an external hydrogen source, a method that we have recently developed.[8,9] Although reductive amination can lead to mixtures of polyalkylated diamines and Schiff bases, we found that the desired diamines **3** were the main products of the reaction, which proceeded in 24–87% yield.[10] An alternate classical two-step approach led to a series of Schiff bases **2a–k**, which were subsequently reduced with sodium borohydride to give diamines **3a–k**.[11] The two-step approach gave overall yields of 16–85% (Table 1).[12]

Table 1 Synthesis of Chiral Catalysts



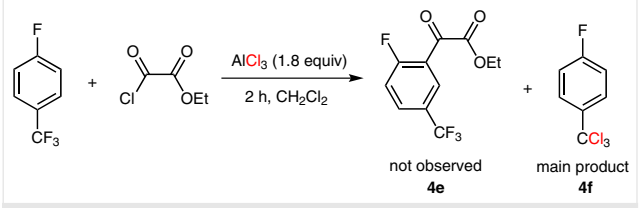
Entry	Product	R	One-step yield (%)	Two-step yield (%)
1	**3a**	2-ClC_6H_4	61	76
2	**3b**	4-$MeOC_6H_4$	81	79
3	**3c**	3-$MeOC_6H_4$	85	82
4	**3d**	1-naphthyl	64	75
5	**3e**	4-ClC_6H_4	62	41
6	**3f**	2-pyridyl	50	30
7	**3g**	3-pyridyl	48	85
8	**3h**	4-$Me_2NC_6H_4$	43	16
9	**3i**	2-HOC_6H_4	24	45
10	**3j**	Ph	77	38
11	**3k**	3,4,5-$(MeO)_3C_6H_2$	87	55

For the synthesis of α-hydroxy γ-keto esters, we chose the Friedel–Crafts acylation of arenes by methyl or ethyl chlorooxoacetate as a first step (see Scheme 1). The reaction proceeded smoothly with benzene or *p*-xylene to give keto esters **4a** and **4d**, respectively. However, in the case of the more active substrate *p*-dimethoxybenzene, the monodemethylation product **4c** was obtained, together with the expected dimethoxy derivative **4b**.



Scheme 1 Synthesis of α-keto esters from arenes

Interestingly, when 1-fluoro-4-(trifluoromethyl)benzene was used as a substrate, the expected product **4e** was not obtained (Scheme 2). ^1H, ^{13}C, and ^{19}F NMR spectroscopy and mass spectrometry revealed that 1-fluoro-4-(trichloromethyl)benzene (**4f**) was formed as the main product (isolated in 80% yield). Apparently, $AlCl_3$ induces substitution of all three fluorine atoms in the trifluoromethyl group of 1-fluoro-4-(trifluoromethyl)benzene, even at 0 °C (similar reactions have been previously reported).[13]

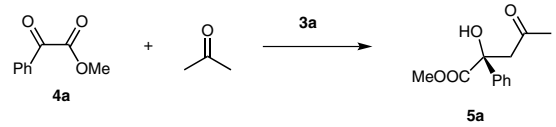


Scheme 2 Friedel–Crafts acylation of 1-fluoro-4-(trifluoromethyl)benzene versus substitution of the trifluoromethyl group by $AlCl_3$

Having prepared the catalysts and substrates, we next focused on the optimization of the conditions for the asymmetric aldol reaction of methyl phenylglyoxylate (**4a**; Table 2). First, we checked the effect of solvents. In the presence of catalyst **3a**, the reaction in acetone (serving also as a reagent) gave hydroxy keto ester **5a** with 81.5:18.5 e.r. (Table 2, entry 1). Chlorinated solvents were less favorable. The reactions in dichloromethane and chloroform gave **5a** with 75:25 e.r. and 65:35 e.r., respectively (entries 2 and 3). Alcohols showed inconsistent results; the reaction proceeded with 65:35 e.r. in methanol (entry 5) and 75.5:24.5 e.r. in ethanol (entry 4). The reaction in ethyl acetate gave product **5a** with 74:36 e.r. (entry 6). The best enantiomeric ratio (87.5:12.5 e.r.) was achieved by using THF as a solvent; however, only traces of the product were obtained in this case (entry 7). Notably, in contrast to some reports in the literature,[14] no increase in enantioselectivity was observed in the presence of a Brønsted acid (entries 8 and 9).

As a next step, we investigated the effects of the substituents in catalysts **3a–k**. The *o*-chlorobenzyl derivative **3a** gave an enantioselectivity similar to that obtained with catalyst **3b**, which has an electron-donating *para*-methoxy substituent (Table 3, entries 1 and 2). The *meta*-methoxy

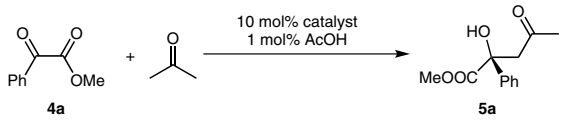
Table 2 Screening of Conditions for the Organocatalytic Asymmetric Cross-Aldol Reaction of Acetone and Methyl Benzoylformate[a]



Entry	**3a** (mol%)	Solvent	Additive	Yield (%)	e.r.[b]
1	10	acetone	–	75	81.5:18.5
2	10	$CHCl_3$	–	76	65:35
3	10	CH_2Cl_2	–	39	75:25
4	10	EtOH	–	64	75.5:24.5
5	10	MeOH	–	32	65:35
6	10	EtOAc	–	73	74:36
7[c]	10	THF	–	trace	87.5:12.5
8[d]	5	acetone	AcOH (5 mol%)	45–60	84:16
9[d]	10	acetone	AcOH (1 mol%)	57–75	81.5:18.5
10	5	acetone	–	48	81:19

[a] Reaction conditions: keto ester (0.15 mmol, 100 mol%), solvent (0.4 mL), acetone (0.1 mL), 25 °C, 14–28 d.
[b] Determined by chiral HPLC.
[c] 70 days.
[d] Combined results of three experiments.

Table 3 Screening of Various Diamines as Organocatalysts for the Asymmetric Cross-Aldol Reaction of Acetone with Methyl Benzoylformate[a]



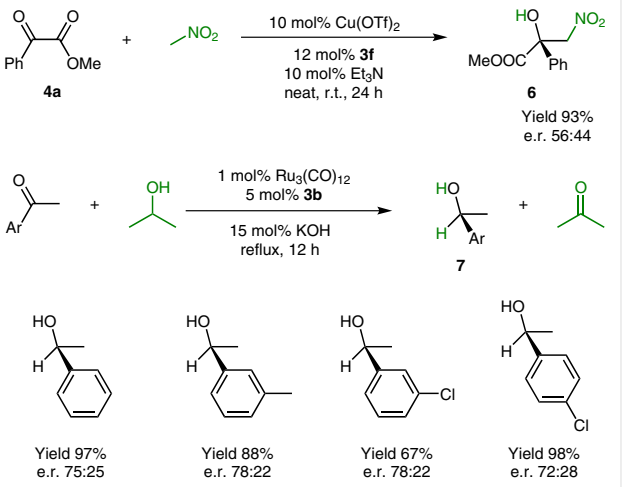
Entry	Catalyst	Yield (%)	e.r.[b]
1[c]	**3a**	57–75	81.5:18.5
2	**3b**	39	81.5:18.5
3	**3c**	96	81:19
4	**3d**	30	82.5:17.5
5[c]	**3e**	18–23	81:19
6	**3f**	36	84:16
7[c]	**3g**	93–96	84:16
8	**3h**	55	79:21
9[c]	**3i**	43–46	82:18
10[c]	**3j**	75–85	81:19
11[c]	**3k**	75–85	81:19
12[d]	**3g**	85	87.5:12.5

[a] Reaction conditions: **4a** (0.15 mmol), catalyst (0.015 mmol), acetone (0.5 mL), AcOH (0.0015 mmol), 25 °C, 7 d.
[b] Determined by chiral HPLC.
[c] Combined results of three experiments.
[d] With 1 mol% of the catalyst.

derivative **3c** also gave a similar result (entry 3). The 1-naphthyl-substituted catalyst **3d** gave an 82.5:17.5 e.r. (entry 4). Catalysts with *para*-substituents on the phenyl ring showed similar efficiencies (entries 5 and 8). When the phenyl groups were replaced with their pyridyl counterparts, a small increase in stereoselectivity was observed (entries 6 and 7). Furthermore, we found that the catalyst loading could be decreased to 1 mol% without loss of enantioselectivity (entry 12); however, a somewhat lower yield was obtained.

Under the optimized conditions (Table 3, entry 12), product **5a** was obtained in 85% yield and 87.5:12.5 e.r.[15] Simple recrystallization increased the enantiomeric ratio of the product to 96.5:3.5. The absolute configuration of methyl (*S*)-2-hydroxy-4-oxo-2-phenylpentanoate (**5a**) was established from anomalous scattering results in an analysis of the X-ray diffraction using CuKα radiation. Substrates **4** with increased steric hindrance could not be used: no reaction was observed for compounds **4b–d**.

Diamines **3** can also be used as chiral ligands. We decided to examine their performance in the copper-catalyzed Henry reaction of methyl oxo(phenyl)acetate with nitromethane (Scheme 3). Although the reaction rate was high, the enantiomeric ratio of the product **6** was very low (56:44). Better performance was observed in the case of the Meervein–Ponndorf–Verley reduction of acetophenone: when diamine ligand **3b** was used in combination with triruthenium dodecacarbonyl and potassium hydroxide, product **7** was obtained in 75:25 e.r. (Scheme 3). Substituted acetophenones (e.g., 3-methyl-, 3-chloro-, or 4-chloroacetophenones) showed similar results.



Scheme 3 Asymmetric Henry and Meervein–Ponndorf–Verley reactions

In summary, we have developed a one-step preparation of N,N′-dialkylated cyclohexane-1,2-diamines directly from cyclohexane-1,2-diamine salts. Although the yields from

the novel protocol were similar to those of the classical two-step route, the one-step procedure is operationally more convenient and less time-consuming. The resulting chiral amines were used as organocatalysts in two-step syntheses of α-hydroxy γ-keto esters from arenes; this permitted the preparation of methyl (*S*)-2-hydroxy-4-oxo-2-phenylpentanoate in 96.5:3.5 e.r. The absolute configuration of the product was determined by means of anomalous X-ray scattering. Some of the prepared diamines were also tested as chiral ligands for Henry and Meervein–Ponndorf–Verley reactions.

Acknowledgment

The work was supported financially by the Russian Science Foundation (Grant # 16-13-10393). We thank Dr. Dmitry Usanov for his feedback on this manuscript.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588382.

References and Notes

(1) List, B.; Lerner, R. A.; Barbas, C. F. III. *J. Am. Chem. Soc.* **2000**, *122*, 2395.
(2) Machajewski, T. D.; Wong, C.-H. *Angew. Chem. Int. Ed.* **2000**, *39*, 1352.
(3) Matsuo, J.-i.; Murakami, M. M. *Angew. Chem. Int. Ed.* **2013**, *52*, 9109.
(4) (a) List, B.; Pojarliev, P.; Castello, C. *Org. Lett.* **2001**, *3*, 573. (b) Pidathala, C.; Hoang, L.; Vignola, N.; List, B. *Angew. Chem. Int. Ed.* **2003**, *42*, 2785. (c) Mukherjee, S.; Yang, J. W.; Hoffman, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471. (d) Guellina, G.; Nájera, C.; Ramón, D. *Tetrahedron: Asymmetry* **2007**, *18*, 2249. (e) Trost, B. M.; Brindle, C. S. *Chem. Soc. Rev.* **2010**, *39*, 1600. (f) Ratjen, L.; García-García, P.; Lay, F.; Beck, M. E.; List, B. *Angew. Chem. Int. Ed.* **2011**, *50*, 754. (g) Bae, H. Y.; Sim, J. H.; Lee, J.-W.; List, B.; Song, C. E. *Angew. Chem. Int. Ed.* **2013**, *52*, 12143. (h) Zhang, Z.; List, B. *Asian J. Org. Chem.* **2013**, *2*, 957. (i) Martínez, A.; Zumbansen, K.; Döhring, A.; van Gemmeren, M.; List, B. *Synlett* **2014**, *25*, 932. (j) Kalesse, M.; Cordes, M.; Symkenberg, G.; Lu, H.-H. *Nat. Prod. Rep.* **2014**, *31*, 563. (k) Tap, A.; Blond, A.; Wakchaure, V. N.; List, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 8962.
(5) van Putten, P. L. *Antonie van Leeuwenhoek* **1979**, *45*, 622.
(6) (a) Tokuda, O.; Kano, T.; Gao, W.-L.; Ikemoto, T.; Maruoka, K. *Org. Lett.* **2005**, *7*, 5103. (b) Tang, Z.; Cun, L.-F.; Cui, X.; Mi, A.-Q.; Jiang, Y.-Z.; Gong, L.-Z. *Org. Lett.* **2006**, *8*, 1263. (c) Wang, F.; Xiong, Y.; Liu, X.; Feng, X. *Adv. Synth. Catal.* **2007**, *349*, 2665. (d) Xu, X.-Y.; Tang, Z.; Wang, Y.-Z.; Luo, S.-W.; Cun, L.-F.; Gong, L.-Z. *J. Org. Chem.* **2007**, *72*, 9905. (e) Liu, J.; Yang, Z.; Wang, Z.; Wang, F.; Chen, X.; Liu, X.; Feng, X.; Su, Z.; Hu, C. *J. Am. Chem. Soc.* **2008**, *130*, 5654. (f) Liu, Q.-Z.; Wang, X.-L.; Luo, S.-W.; Zheng, B.-L.; Qin, D.-B. *Tetrahedron Lett.* **2008**, *49*, 7434. (g) Raj, M.; Parashari, G. S.; Singh, V. K. *Adv. Synth. Catal.* **2009**, *351*, 1284. (h) Jiang, Z.; Lu, Y. *Tetrahedron Lett.* **2010**, *51*, 1884. (i) Clegg, W.; Harington, R. W.; North, M.; Pizzato, F.; Villuendas, P. *Tetrahedron: Asymmetry* **2010**, *21*, 1262. (j) Zhu, X.; Lin, A.; Fang, L.; Li, W.; Zhu, C.; Cheng, Y. *Chem. Eur. J.* **2011**, *17*, 8281. (k) Viózques, S.; Bañón-Caballero, A.; Guillena, G.; Nájera, C.; Gómez-Bengoa, E. *Org. Biomol. Chem.* **2012**, *10*, 4029. (l) Kang, G.; Jiang, J.; Liu, H.; Wu, H. *J. Braz. Chem. Soc.* **2012**, *23*, 5. (m) Mao, Z.; Zhu, X.; Lin, A.; Li, W.; Shi, Y.; Mao, H.; Zhu, C.; Cheng, Y. *Adv. Synth. Catal.* **2013**, *355*, 2029.
(7) (a) Kumar, S.; Chauhan, M. S.; Yadav, G. D.; Singh, S. *Synlett* **2016**, *27*, 267. (b) Egami, H.; Katsuki, T. *Synlett* **2008**, 1543. (c) Shimada, Y.; Kondo, S.; Ohata, Y.; Matsumoto, K.; Katsuki, T. *Synlett* **2007**, 2445. (d) Atwood, D. A. *Coord. Chem. Rev.* **1997**, *165*, 267.
(8) Chusov, D.; List, B. *Angew. Chem. Int. Ed.* **2014**, *53*, 5199.
(9) Yagafarov, N. Z.; Usanov, D. L.; Moskovets, A. P.; Kagramanov, N. D.; Maleev, V. I.; Chusov, D. *ChemCatChem* **2015**, *7*, 2590.
(10) **Diamines 3a–k; One-Step General Procedure**
A glass vial in a 10-mL stainless-steel autoclave was charged with $Rh_2(OAc)_4$ (0.7 mg, 1.60 μmol, 1 mol%), (1*R*,2*R*)-cyclohexane-1,2-diamine dihydrochloride (30.0 mg, 0.160 mmol, 100 mol%), K_2CO_3 (26.6 mg, 0.192 mmol, 120 mol%), *i*-PrOH (0.1 mL), H_2O (0.1 mL), and the appropriate aldehyde (0.320 mmol, 200 mol%). The autoclave was then sealed, flushed three times with CO (5 atm), and pressurized with CO (50 atm). The reactor was placed in a preheated oil bath (140 °C). After 4 h, the reactor was cooled to r.t. and depressurized. The residue was collected by filtration and analyzed by ^{1}H NMR.
(11) **Schiff Bases 2a–k; General Procedure**
A mixture of (1*R*,2*R*)-cyclohexane-1,2-diaminium (*S*)-tartrate (1.0 equiv), K_2CO_3 (1.0 equiv), and H_2O (0.66 mL per mmol of K_2CO_3) was stirred until the solids were completely dissolved and then MeOH (5.2 mL/mmol of tartrate) was added. The mixture was heated to 65 °C and a solution of the appropriate aldehyde (2 equiv) in MeOH (2.2 mL/mmol of tartrate) was added over 30 min. The mixture was refluxed for an additional 4 h, then cooled to r.t. and concentrated in vacuo. The residue was dissolved in EtOAc (4 mL/mmol of tartrate) and the solution was washed with H_2O (2 × 1 mL/mmol of tartrate), dried (Na_2SO_4), and concentrated in vacuo to give a beige-colored crude product. The crude product containing some starting aldehyde was used in the next step without further purification.
(1*R*,2*R*)-2,2′-[Cyclohexane-1,2-diylbis(nitrilomethylylidene)]diphenol (2i)
Yellow oil; yield: 3.1 g (82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.32 (s, 2 H), 7.34–7.26 (m, 2 H), 7.21 (dd, *J* = 7.6, 1.5 Hz, 2 H), 6.95 (d, *J* = 8.2 Hz, 2 H), 6.89–6.82 (m, 2 H), 3.43–3.32 (m, 2 H), 2.06–1.88 (m, 4 H), 1.87–1.68 (m, 2 H), 1.62–1.46 (m, 2 H).
(12) **Diamines 3a–k; General Procedure from Schiff Bases 2a–k**
$NaBH_4$ (2.1 equiv) was added portionwise over 40 min to a solution of the appropriate Schiff base **2** (1.0 equiv) in MeOH (4 mL/mmol of Schiff base) at r.t. The mixture was refluxed with stirring for 1 h then cooled to r.t. H_2O (5 mL/mmol of Schiff base) was added, the mixture was extracted with CH_2Cl_2 (3 × 4 mL/mmol of Schiff base), and the organic layer was concentrated. If any aldehyde remained in the mixture, the residue was dissolved in 35% aq HCl (1 mL/mmol of Schiff base) and the solution was washed with CH_2Cl_2 (3 × 4 mL/mmol of Schiff base). Excess K_2CO_3 (4.5 equiv) was added to the aqueous phase, which was extracted with CH_2Cl_2 (3 × 3 mL/mmol of Schiff base). The organic layers were combined, dried, and concen-

trated to give an oily product. If the product was not sufficiently pure, it was purified by column chromatography.

(1*R*,2*R*)-*N*,*N*′-Bis(4-chlorobenzyl)cyclohexane-1,2-diamine (3e)

Yellow oil; yield: 2.45 g (48%); $[\alpha]_D^{25}$ –64.7 (*c* 1.2, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.4 Hz, 4 H), 7.25 (d, *J* = 8.4 Hz, 4 H), 3.88 (d, *J* = 13.4 Hz, 2 H), 3.64 (d, *J* = 13.4 Hz, 2 H), 2.28–2.24 (m, 2 H), 2.17–2.12 (m, 2 H), 1.76–1.71 (m, 2 H), 1.27–1.18 (m, 2 H), 1.11–0.97 (m, 2 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.6, 132.5, 129.5, 128.6, 61.2, 50.5, 32.0, 25.5; MS (ESI): *m/z* = 363, 365, 367 $[M + H]^+$.

(13) (a) Riera, J.; Castañer, J.; Carilla, J.; Robert, A. *Tetrahedron Lett.* **1989**, *30*, 3825. (b) Terao, J.; Nakamura, M.; Kambe, N. *Chem. Commun.* **2009**, 6011. (c) Adonin, N. Yu.; Shabalin, A. Yu.; Bardin, V. V. *J. Fluor. Chem.* **2014**, *168*, 111.

(14) (a) Wang, C.; Jiang, Y.; Zhang, X.-x.; Huang, Y.; Li, B.-g.; Zhang, G.-l. *Tetrahedron Lett.* **2007**, *48*, 4281. (b) Guillena, G.; Nájera, C.; Viózquez, S. F. *Synlett* **2008**, 3031. (c) Zhang, S.-p.; Fu, X.-k.; Fu, S.-d. *Tetrahedron Lett.* **2010**, *50*, 1173. (d) Saha, S.; Moorthy, J. N. *Tetrahedron Lett.* **2010**, *51*, 912. (e) Mino, T.; Omura, A.; Uda, Y.; Wakui, K.; Haga, Y.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2011**, *22*, 2024. (f) Paladhi, S.; Das, J.; Mishra, P. K.; Dash, J. *Adv. Synth. Catal.* **2013**, *355*, 274. (g) Pedrosa, R.; Andrés, J. M.; Gamarra, A.; Manzano, R.; Pérez-López, C. *Tetrahedron* **2013**, *69*, 10811. (h) Deng, Y.-H.; Chen, J.-Q.; He, L.; Kang, T.-R.; Liu, Q.-Z.; Luo, S.-W.; Yuan, W.-C. *Chem. Eur. J.* **2013**, *19*, 7143. (i) Guo, W.; Wei, J.; Liu, Y.; Li, C. *Tetrahedron* **2014**, *70*, 6561. (j) Bayat, S.; Salleh, A. B.; Malek, E. A.; Yousefi, S.; Rahman, M. B. A. *Catal. Lett.* **2015**, *145*, 1750. (k) Kumar, T. P.; Shekhar, R. C.; Sander, K. S.; Vadaparthi, R. *Tetrahedron: Asymmetry* **2015**, *26*, 543. (l) Konda, S.; Guo, Q.-S.; Abe, M.; Huang, H.; Arman, H.; Zhao, J. C.-G. *J. Org. Chem.* **2015**, *80*, 806. (m) Kochetkov, S. V.; Kucherenko, A. S.; Zlotin, S. G. *Mendeleev Commun.* **2015**, *25*, 168. (n) Lisnyak, V. G.; Kucherenko, A. S.; Valeev, E. F.; Zlotin, S. G. *J. Org. Chem.* **2015**, *80*, 9570. (o) Zhang, Y.; Zhu, J.; Yu, N.; Yu, H. *Chin. J. Chem.* **2015**, *33*, 171. (p) Rojas Cabrera, H.; Huelgas, G.; Hernández Pèrez, J. M.; Walsh, P. J.; Somanathan, R.; Anaya de Parodi, C. *Tetrahedron: Asymmetry* **2015**, *26*, 163.

(15) **Methyl (2*S*)-2-Hydroxy-4-oxo-2-phenylpentanoate (5a)**

White crystals; yield: 31.5 mg (93%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.56 (dd, *J* = 8.1, 1.2 Hz, 2 H), 7.41–7.27 (m, 3 H), 4.50–4.40 (br s, 1 H), 3.75 (s, 3 H), 3.56 (d, *J* = 17.7 Hz, 1 H), 3.01 (d, *J* = 17.7 Hz, 1 H), 2.21 (s, 3 H).