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Mn(III) salen complexes-catalyzed enantioselective addition of trimethyl silylcyanide to *N*-benzylimines in the presence of 4-phenyl pyridine-N-oxide as an additive

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ABSTRACT

Chiral monomeric and dimeric Mn(III) salen complexes viz., [(*S*,*S*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminato manganese(III) chloride and 5,5-methylene di-[(*S*,*S*)-{*N*-(3-*tert*-butyl salicylidine)-*N*′-(3′,5′-di-*tert*-butyl salicylidene)}-1,2-cyclohexanediaminato manganese(III) chloride were used as catalysts for the highly enantioselective Strecker reaction of various imines (derived by the condensation of aldehydes and amine) with TMSCN as a source of cyanide in toluene. Excellent yield (95%) of α-amino nitrile with ee >99% was achieved when *N*-(2-methoxybenzylidine)-1-phenylmethanamine was used as a substrate and 4-phenyl pyridine-N-oxide (4-PPNO) as an additive at −55 °C in 28 h. The dimeric catalyst was found to be more reactive and enantioselective than the monomeric catalyst. The chiral dimeric catalyst used in the present study was recoverable and recyclable several times with retention of its performance.

1. Introduction

The classical Strecker reaction is one of the simplest and most economical methods for the production of racemic α-amino acids and pharmacologically useful compounds.[1–3] The enantioselective versions of this process are of great interest, due to the application of (*R*)- and/or (*S*)-α-amino acids[4–7] in the synthesis of valuable nitrogen-containing heterocycles such as imidazoles, thiodiazoles, and others.[8–11] To prepare α-amino nitrile (precursor to α-amino acids) generally an imine is reacted with a cyanide source, notable among them are HCN,[12] KCN,[13] $(EtO)_2P(O)CN$, Et_2AlCN, Bu_3SnCN, and TMSCN.[14–20] Among these cyanide sources, TMSCN is relatively easy to handle and highly soluble in organic solvents. In order to route the Strecker reaction through an enantioselective pathway, usually a chiral catalyst is required. In recent years, considerable efforts have been made toward the development of chiral catalytic systems for the Strecker reaction[5] using organocatalysts,[13,21–25] Jacobsen′s Schiff base complexes,[26–29] bifunctional catalyst,[30] and various metal complexes of salen ligands.[31–39] Among these, Jacobsen salen complexes have emerged as efficient catalysts for the asymmetric Strecker reaction.[31,40] Although, Jacobsen salen complexes are highly efficient, their recyclability is an important issue from an economical and an environmental point of view. In view of our ongoing interest in the development of asymmetric Strecker reaction[41] and recyclable catalysts, earlier we have reported the applications of chiral Mn(III) salen complexes in various organic transformations viz., asymmetric cyantion of ketones,[42] epoxidation of non-functionalized alkenes,[43–46] and oxidative kinetic resolution of secondary alcohols.[47,48] Herein, we have explored the use of chiral monomeric and dimeric Mn(III) salen complexes as efficient catalysts for the asymmetric Strecker reaction of imines using TMSCN as cyanide source. Excellent yields (up to 95%) of α-amino nitriles were achieved in high ees (99%) when chiral dimeric complex **2** was used as a catalyst in the presence of 4-phenyl pyridine-N-oxide as an additive. The complex **2** was recycled efficiently for several times.

2. Results and discussion

Chiral monomeric and dimeric Mn(III) salen complexes **1** and **2** were synthesized by the reaction of (*1S,2S*)-*N,N′-bis*[3,5-di-*tert*-butylsalicylidene] cyclohexane-1, 2-diamine/5,5-methylenedi-[(1*S,2S*)-{*N*-(3-*tert*-butylsalicylidine)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)]-1,2-cyclohexanediamine] with manganese acetate followed by the addition of LiCl under auto-oxidation condition (Fig. 1).[46]

To assess the viability of chiral monomeric Mn(III) salen complex **1** as a catalyst (15 mol %) in the asymmetric Strecker reaction, we have initiated our systematic study by taking 4-methoxy imine **7** as a model substrate with TMSCN in toluene at −20 °C. Moderate isolated yield (65%) and enantioselectivity (ee, 52%) for the product α-amino nitrile were achieved in 18 h (Table 1, entry 1). It has been reported in the literature that the use of an additive affords a

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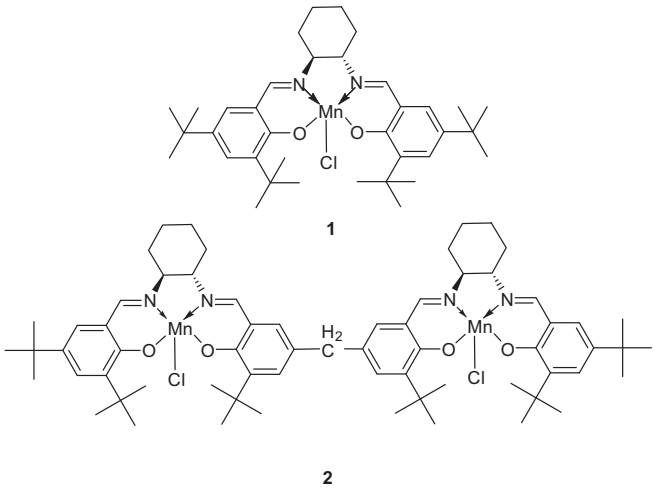
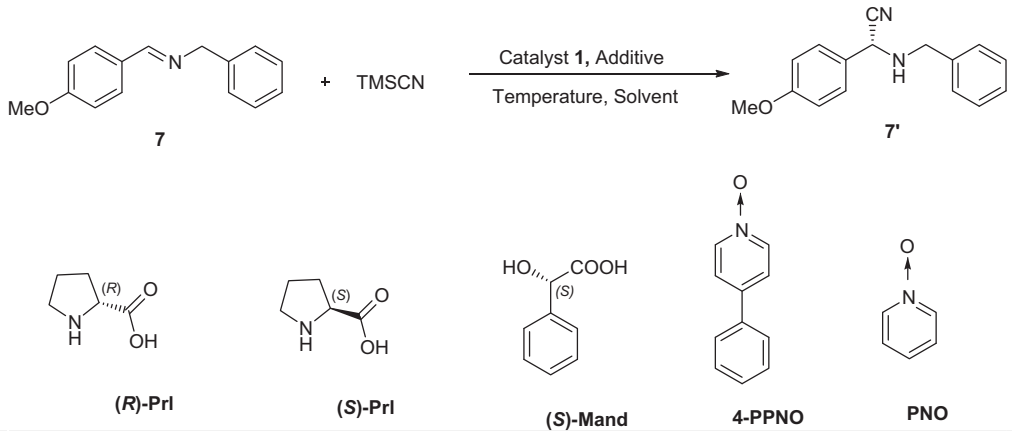


Figure 1. Structure of the catalysts **1** and **2**.

beneficial effect on the reaction rate and enantioselectivity.[42] Thus we have examined the role of different additives viz., (*R*)-proline **(*R*)-Prl**, (*S*)-proline **(*S*)-Prl**, (*S*)-mandelic acid **(*S*)-Mand**, 4-phenyl pyridine N-oxide **4-PPNO**, and pyridine N-oxide **PNO** for this reaction (Table 1, entries 2–6). Noticeably, the chirality of the additive as in the case of **(*R*)-Prl** and **(*S*)-Prl** played no role in the enantioselectivity of the reaction (entries 2 and 3). Among the various additives used, **4-PPNO** was found to be the most efficient to give the desired product in high isolated yield (80%) and ee (71%) (entry 5). Having established that 4-phenyl pyridine N-oxide **4-PPNO** as an additive is the most suitable, we next varied the loadings of additive (**4-PPNO**) and catalyst **1** for this reaction. Accordingly, we first increased the additive loading from 15 mol % to 20 mol % at a catalyst loading of 15 mol % by keeping the other reaction conditions constant. However, this change was inconsequential as there was only a marginal increase in isolated yield with no change in enantioselectivity (entry 7). However, on decreasing the additive loading (10 mol %) there was a decrease in the yield and enantioselectivity (yield, 71%; ee, 62%) (entry 8). Further, when the catalyst loading was increased from 15 mol % to 20 mol % keeping the optimum additive loading (15 mol %) there was only a slight increase in the isolated yield of the product with no significant change in the enantioselectivity of the product (entry 9). A decrease in the catalyst loading to 10 mol % caused a decrease in the yield and enantioselectivity (entry 10; yield, 73%; ee, 64%). Thus, the use of 4-phenyl pyridine N-oxide **4-PPNO** (15 mol %) as an additive and catalyst **1** (15 mol %) is optimum to catalyze the enantioselective Strecker reaction of 4-methoxy imine **7** with TMSCN at −20 °C (entry 5). Temperature also plays a crucial role in achieving high chiral induction in asymmetric catalysis. Therefore, we varied the reaction temperature in a stepwise manner. Consequently, an increase

Table 1
Data for the optimization of reaction conditions for asymmetric addition of TMSCN to 4-MeO benzylimine **7** as a representative substrate in the presence of Mn(III) salen complex **1**[a]



Entry	Catalyst (mol %)	Additive (mol %)	Solvent	Time (h)	Temp (°C)	Yield[b] (%)	ee[c] (%)
1	15	—	Toluene	18	−20	65	52
2	15	**(*R*)-Prl** (15)	Toluene	12	−20	65	56
3	15	**(*S*)-Prl** (15)	Toluene	12	−20	68	58
4	15	**(*S*)-Mand** (15)	Toluene	15	−20	62	58
5	15	**4-PPNO** (15)	Toluene	10	−20	80	71
6	15	**PNO** (15)	Toluene	8	−20	79	60
7	15	**4-PPNO** (20)	Toluene	10	−20	83	71
8	15	**4-PPNO** (10)	Toluene	10	−20	71	62
9	20	**4-PPNO** (15)	Toluene	8	−20	87	71
10	10	**4-PPNO** (15)	Toluene	12	−20	73	64
11	15	**4-PPNO** (15)	Toluene	3	rt	92	30
12	15	**4-PPNO** (15)	Toluene	6	0	85	44
13	15	**4-PPNO** (15)	Toluene	12	−30	88	72
14	15	**4-PPNO** (15)	Toluene	16	−40	90	77
15	15	**4-PPNO** (15)	Toluene	36	−55	91	83
16	15	**4-PPNO** (15)	CH_2Cl_2	28	−55	80	24
17	15	**4-PPNO** (15)	$CHCl_3$	28	−55	78	10
18	15	**4-PPNO** (15)	THF	28	−55	60	Racemic

[a] Strecker reaction of 4-methoxy imine **7** was carried out with 1.5 equiv of TMSCN by using catalyst **1** in the presence of various additives.
[b] Isolated yield.
[c] Ee were determined by using chiral OD column.

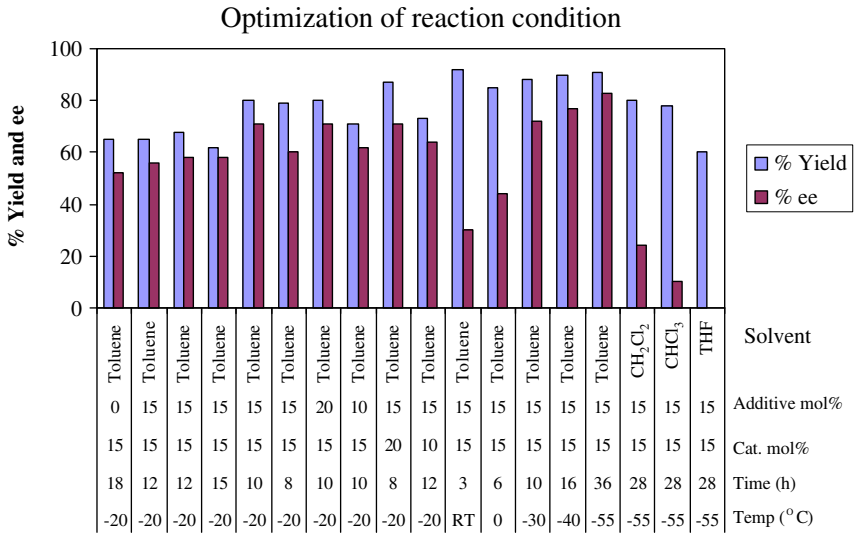
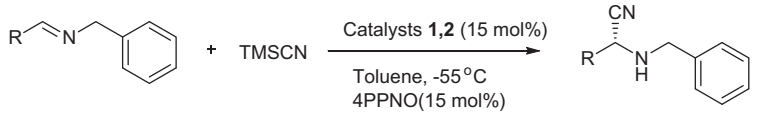


Figure 2. Optimization graph for the enantioselective addition of TMSCN to 4-MeO *N*-benzyl imines (**e**) using the catalyst **1**.

in reaction temperature (from −20 °C to 27 °C) caused an increase in the product yield (85–92%) in a shorter reaction time but there was a significant decrease in the enantioselectivity (44–30%) (entries 11 and 12). On the other hand, lowering of the reaction temperature (−30 to −55 °C) caused significant improvement in enantioselectivity (ee 83%) (entries 13–15), but the reaction took longer time (12–36 h) for completion. Hence, −55 °C was taken as the optimum reaction temperature for the present protocol for the synthesis of various α-amino nitriles. We next varied the reaction medium bearing in mind that the reactivity and enantioselectivity of the Strecker reaction are strongly dependent on the nature of the solvent used.[31,41] Therefore, the above optimized parameters (entry 15) were then used for the asymmetric Strecker reaction of 4-methoxy imine **7** in different solvents viz., toluene, dichloromethane, chloroform, and THF (Table 1; entries 15–19). Among all the solvents used the best results in terms of yield and ee of the product were achieved in the case of toluene as solvent (entry, 15) (Fig. 2).

To examine the general applicability of the above optimized reaction conditions, (Table 1, entry 15) we next carried out Strecker reaction of various *N*-benzyl imines **3**–**13** with catalyst **1** and the results are summarized in Table 2. Good to excellent isolated yield (60–88%) and ee (60–85%) of α-aminonitriles were achieved in most of the cases, which clearly show the usefulness of this protocol over a range of substrates synthesized from aromatic aldehyde and benzylamine (entries 1, 3, 5, 7, 9, 11, 13, 15, 17, 19). Surprisingly, electronic and steric factors for different substituents on *N*-benzyl imines did not have a noticeable effect on the yield and enantioselectivity of the products. In addition to this, *N*-benzylimine derived from aliphatic aldehydes and benzylamine gave the respective α-aminonitriles in moderate isolated yield and ee (Table 2, entry 21).

Table 2
Asymmetric addition of TMSCN to various *N*-benzyl imines **3**–**13** catalyzed by monomeric and dimeric Mn(III) salen complexes **1** and **2**[a]



R = C_6H_5 **3**
R = 4-Me-C_6H_4 **4**
R = 3-Me-C_6H_4 **5**
R = 2-Me-C_6H_4 **6**
R = 4-MeO-C_6H_4 **7**
R = 3-MeO-C_6H_4 **8**
R = 2-MeO-C_6H_4 **9**
R = 4-Cl-C_6H_4 **10**
R = 4-F-C_6H_4 **11**
R = $C_{10}H_7$ **12**
R = $(CH_3)_3CH$ **13**

3'-13'

S. No.	Imine	Time (h)	Yield[b] (%)	ee[c] (%)
1 (2)	$C_6H_5CH{=}NHCH_2C_6H_5$ **3**	36 (28)	72 (80)	64 (88)
3 (4)	4-$MeC_6H_4CH{=}NHCH_2C_6H_5$ **4**	36 (28)	75 (85)	72 (78)
5 (6)	3-$MeC_6H_4CH{=}NHCH_2C_6H_5$ **5**	36 (28)	70 (83)	63 (91)
7 (8)	2-$MeC_6H_4CH{=}NHCH_2C_6H_5$ **6**	36 (28)	72 (78)	60 (68)
9 (10)	4-$MeOC_6H_4CH{=}NHCH_2C_6H_5$ **7**	36 (28)	88 (88)	83 (85)
11 (12)	3-$MeOC_6H_4CH{=}NHCH_2C_6H_5$ **8**	36 (28)	71 (80)	64 (74)
13 (14)	2-$MeOC_6H_4CH{=}NHCH_2C_6H_5$ **9**	36 (28)	75 (95)	85 (>99)
15 (16)	4-$ClC_6H_4CH{=}NHCH_2C_6H_5$ **10**	36 (28)	64 (70)	65 (74)
17 (18)	4-$FC_6H_4CH{=}NHCH_2C_6H_5$ **11**	36 (28)	68 (75)	72 (80)
19 (20)	*N*-Benzyl-1-naphthylimine **12**	36 (28)	60 (70)	70 (75)
21 (22)	$(CH_3)_3CH{=}NHCH_2C_6H_5$ **13**	36 (28)	73 (76)	68 (73)

[a] Reaction was carried out at −55 °C in toluene using 15 mol % of catalysts **1** and **2** in the presence of 4-phenyl pyridine N-oxide **4**-**PPNO** (15 mol %) with *N*-benzyl imines **3**–**13** using 1.5 equiv of TMSCN.
[b] Isolated yield.
[c] Ee were determined using chiral OD and OD-H column.

Table 3
Catalyst **2** recycling data for enantioselective asymmetric Strecker reaction of 2-methoxy imine **9**[a]

Run	Time (h)	Yield[b] (%)	ee[c] (%)
1	28	95	>99
2	28	95	99
3	29	95	99
4	31	94	97
5	33	93	98

[a] Strecker reaction of 2-methoxy imine **9** was carried out at −55 °C in toluene using 15 mol % of catalyst **2** in the presence of 4-phenyl pyridine N-oxide **4-PPNO** (15 mol %) and 1.5 equiv of TMSCN.
[b] Isolated yield.
[c] Ee were determined using chiral OD-H column.

The Strecker reaction of substrates **3**–**13** was also conducted using the above optimized protocol with dimeric Mn(III) salen complex **2** as a catalyst, which gave the product α-amino nitrile in a shorter reaction time and in higher isolated yield (up to 95%) and enantioselectivity (ee, >99%) as compared to the products obtained with the use of catalyst **1** (Table 2, entry 14). This remarkable improvement in the performance of dimeric complex **2** over monomeric complex **1** suggests that the two catalytic centers are working in co-operation rather than in isolation.[42] Remarkably, the dimeric Mn(III) salen complex **2** as a catalyst was recoverable and recyclable while the monomeric complex **1** was difficult to recover due to more solubility of the catalyst in the reaction medium.

To the best of our knowledge, the chiral dimeric Mn(III) salen complex **2** is the most efficient recyclable catalyst reported so far for the asymmetric Strecker reaction of 2-methoxy imine **9** to give the corresponding chiral α-amino nitrile in quantitative yield with >99% ee (Table 2, entry 14). In all catalytic runs the (1*S*,2*S*) chiral monomeric and dimeric Mn(III) salen complexes gave the (*R*)-form of the corresponding α-amino nitrile.

In order to assess the recyclability of the dimeric complex **2**, the catalytic run for the asymmetric Strecker reaction of 2-methoxy imine **9** as a model substrate with TMCSN in toluene was carried out at −55 °C (Table 1, entry 15). Consequently, after the first catalytic run, an excess amount of hexane was added to the reaction mixture, and the resulting solid was collected by filtration. The recovered solid was thoroughly washed with hexane and vacuum dried before reuse. The recovered solid containing the catalyst **2** was used as such in the same manner as the fresh catalyst in Strecker reaction, and which showed similar activity and enantioselectivity in the recycle experiments (Table 3, runs 1–5), though there was some increase in the reaction time.

3. Conclusion

Chiral α-aminonitriles in high ees were obtained by the chiral monomeric and dimeric Mn(III) salen complex-catalyzed asymmetric Strecker reaction of various *N*-benzylimines using TMSCN as a source of cyanide at −55 °C in toluene. The dimeric catalyst **2** worked better than the catalyst **1** in terms of reactivity and enantioselectivity. High enantiomeric purity of α-aminonitrile (ee, >99%) was obtained from 2-MeO-imine **9** with catalyst **2** which was recycled several times without affecting its performance.

4. Experimental

4.1. Materials and characterization

NMR spectra were obtained with a Bruker F113V spectrometer (500 MHz) and are referenced internally with TMS. FTIR spectra were recorded on a Perkin Elmer Spectrum GX spectrophotometer in KBr window. High-resolution mass spectra were obtained with an LC–MS (Q-TOF) LC (Waters), MS (Micromass) instruments. Optical rotation was measured with a Digipol 781 Automatic Polarimeter Rudolph Instruments. Enantiomeric excess (ee) were determined by HPLC (Shimadzu SCL-10AVP) using Daicel Chiralpak OD-H and OD chiral columns with 2-propanol/hexane as the eluent. For the product purification flash chromatography was performed using silica gel 100–200 mesh, manganese acetate purchased from s.d. Fine-Chem Limited Mumbai (India). TMSCN, benzaldehyde, 2-methoxy benzaldehyde, 3-methoxy benzaldehyde, 4-methoxy benzaldehyde, 4-fluoro benzaldehyde, 4-chlorobenzaldehyde, trimethylacetaldehyde, 1-naphthaldehyde, (Aldrich Chemicals) 2-methyl benzaldehyde, 3-methyl benzaldehyde, 4-methyl benzaldehyde, and benzylamine (Merck Chemicals) were used as received. The monomeric and dimeric Mn(III) salen complexes **1** and **2** were synthesized by the interaction of [(*S,S*)-*N,N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine/5,5-methylene di-[(*S,S*)-{*N*-(3-*tert*-butylsalicylidine)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)]-1,2-cyclohexanediamine] with manganese acetate followed by the addition of LiCl under auto-oxidation process by our previously reported method.[46] All the solvents were distilled, dried by using standard procedures,[49] and stored under nitrogen.

4.2. Typical experimental procedure for addition of TMSCN to *N*-benzylimines

To a solution of chiral monomeric and dimeric Mn(III) salen complexes (10 mg, 0.009 mmol) in toluene (5 ml), 4-PPNO (0.009 mmol) was added and the resulting solution was cooled to −55 °C under N_2 atmosphere. To the cooled solution TMSCN (0.75 equiv) was added in a dropwise manner over 15 min with stirring. Subsequently *N*-benzylimine (0.06 mmol) was added to the above cooled solution and the stirring was continued for another 15 min. This was followed by the addition of additional quantity of TMSCN (0.75 equiv) over a period of 15 min. Consequently H_2O (15 μl) was added to the stirred solution and the progress of the reaction was monitored on TLC (silica plates) using hexane/ethyl acetate (90/10) as an eluent. After the reaction was over the solvent was removed on rotavapor and the product was purified by flash column chromatography on silica gel (eluted with hexane/ethyl acetate = 90:10). The purified products were characterized by ^{1}H NMR which was in agreement with the reported values.[31]

4.3. Characterization of the products

4.3.1. *N*-Benzyl (*R*)-2-amino-phenylacetonitrile 3′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.86 (br, s, 1H), 3.95 (d, J = 13.0 Hz, 1H), 4.06 (d, J = 13.0 Hz, 1H), 4.76 (s, 1H), 7.3–7.6 (m, 10H); $[\alpha]_D^{27} = +71$ (c 1, $CHCl_3$); HPLC analysis: CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 19.02 min, t_{r2} (major) = 20.42 min.

4.3.2. *N*-Benzyl (*R*)-2-amino-(4-methylphenyl) acetonitrile 4′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.83 (1H, br s), 2.36 (3H, s), 3.95 (d, J = 13.0 Hz, 1H), 4.06 (d, J = 13.0 Hz, 1H), 4.71 (s, 1H), 7.2–7.4 (m, 9H); $[\alpha]_D^{27} = +35$ (c 1, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 16.28 min, t_{r2} (major) = 17.61 min.

4.3.3. *N*-Benzyl (*R*)-2-amino-(3-methylphenyl)acetonitrile 5′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.53 (br s, 1H), 2.31 (s, 3H), 3.89 (d, J = 13.0 Hz, 1H), 4.01 (d, J = 13.0 Hz, 1H), 4.64 (s, 1H), 7.2–7.4 (m, 9H); $[\alpha]_D^{27} = +63.4$ (c 1, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 14.78 - min, t_{r2} (major) = 15.68 min.

4.3.4. *N*-Benzyl (*R*)-2-amino-(2-methylphenyl)acetonitrile 6′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.6 (br s, 1H), 2.22 (s, 3H), 3.89 (d, J = 13.0 Hz, 1H), 4.04 (d, J = 13.0 Hz, 1H), 4.69 (s, 1H), 7.1–7.5 (m, 9H); $[\alpha]_D^{27} = 74.6$ (c 1, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 16.52 min, t_{r2} (major) = 23.12 min.

4.3.5. *N*-Benzyl (*R*)-2-amino-(4-methoxyphenyl)acetonitrile 7′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.62 (br s, 1H), 3.81 (s, 3H), 3.95 (d, J = 13.0 Hz, 1H), 4.06 (d, J = 13.0 Hz, 1H), 4.69 (s, 1H), 6.92(d, J = 8.5 Hz, 2H), 7.3–7.5 (m, 7H); $[\alpha]_D^{27} = +25$ (c 0.5, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 23.75 min, t_{r2} (major) = 26.48 min.

4.3.6. *N*-Benzyl (*R*)-2-amino-(3-methoxyphenyl)acetonitrile 8′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.84 (br s, 1H), 3.82 (s, 3H), 3.95 (d, J = 13.0 Hz, 1H), 4.04 (d, J = 13.0 Hz, 1H), 4.72 (s, 1H), 7.3–7.5 (m, 9H); $[\alpha]_D^{27} = +29.1$ (c 1, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 26.66 -min, t_{r2} (major) = 29.40 min.

4.3.7. *N*-Benzyl (*R*)-2-amino-(2-methoxyphenyl)acetonitrile 9′

^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.0 (br s, 1H), 3.77 (s, 3H), 3.86 (d, J = 13.0 Hz, 1H), 3.99 (d, J = 13.0 Hz, 1H), 4.72 (s, 1H), 6.84(d, J = 8 Hz, 2H) 7.2–7.4 (m, 7H); CHIRALCEL OD-H column, hexane/2-propanol = 99:1, flow rate 0.8 ml/min, t_r (major) = 49.05 min.

4.3.8. *N*-Benzyl (*R*)-2-amino-(4-chlorophenyl)acetonitrile 10′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.6 (br s, 1H), 3.95 (d, J = 13.0 Hz, 1H), 4.05 (d, J = 13.0 Hz, 1H), 4.72 (s, 1H), 7.2–7.5 (m, 9H); $[\alpha]_D^{27} = +36$ (c 0.8, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 25.90 min, t_{r2} (major) =29.62 min.

4.3.9. *N*-Benzyl (*R*)-2-amino-(4-fluorophenyl)acetonitrile 11′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.78 (br s, 1H), 3.88 (d, J = 13.0 Hz, 1H), 3.98 (d, J = 13.0 Hz, 1H), 4.64 (s, 1H), 6.9–7.4 (m, 9H); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 20.71 min, t_{r2} (major) = 22.08 min.

4.3.10. *N*-Benzyl (*R*)-2-amino-(1-naphthyl)acetonitrile 12′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.815 (br s, 1H), 3.86 (d, J = 12.8 Hz, 1H), 3.99 (d, J = 13.0 Hz, 1H), 4.76 (s, 1H), 7.21–7.90 (m, 12H); $[\alpha]_D^{27} = +170.4$ (c 0.5, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 33.20 min, t_{r2} (major) = 35.32 min.

4.3.11. *N*-Benzyl (*R*)-2-amino-3,3-dimethyl butanonitrile 13′[31]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.18 (s, 9H), 3.03 (s, 1H), 3.88 (d, J = 13.0 Hz, 1H), 4.01 (s, 1H), 7.2–7.4 (m, 5H); $[\alpha]_D^{27} = +53$ (c 1, $CHCl_3$); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 17.54 min, t_{r2} (major) = 19.02 min.

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