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Syntheses of 1,2-Amino Alcohols and Their Applications for Oxazaborolidine Catalyzed Enantioselective Reduction of Aromatic Ketones

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Six new chiral 1,2-amino alcohol derivatives have been synthesized starting from (1*R*,2*R*)-2-amino-1-phenylpropane-1,3-diol. Asymmetric reduction of aryl ketones with in-situ generated oxazaborolidine from these amino alcohol derivatives and $BH_3 \cdot Me_2S$ afforded secondary alcohols with good yield and moderate to high enantiomeric excess.

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Introduction

The design of an asymmetric transformation reaction is a great challenge in organic chemistry, in particular, the development of enantioselective homogeneous catalysts in which a small amount of an optically active ligand can induce asymmetry for a given reaction. Enantioselective oxazaborolidine-catalyzed borane reduction of prochiral ketones to chiral secondary alcohols provides convenient access to a wide variety of optically active secondary alcohols, which are valuable chiral building blocks for the synthesis of natural products and bioactive compounds.[1–3] Oxazaborolidines prepared from chiral amino alcohols[4] give excellent enantiomeric excess (*ee*) values and often have wide substrate scope. Itsuno and coworkers[5] have carried out pioneering work on the asymmetric reduction of alkyl aryl ketones with the reagent prepared from (*S*)-(−)-2-amino-3-methyl-1,1-diphenylbutan-1-ol and borane. The secondary alcohols were obtained in 94–100% *ee* and in 100% chemical yields. The catalytic behaviour of the more sterically hindered oxazaborolidine based on (*S*)-(−)-2-diphenylhydroxymethylpyrrolidine was introduced[6] in the borane reduction of ketones by Corey et al. Optically active amino alcohols[7,8] have been documented recently as catalysts for the enantioselective reduction of various ketones. In 1987 Mandal et al.[9] carried out the asymmetric reduction of alkyl aryl ketones with borane–methyl sulfide and the reagent prepared from (1*S*,2*S*)-(+)-2-amino-3-methoxy-1-phenylpropan-1-ol, which is the antipode of **1** with the primary alcohol at C3 protected as its methyl ether. They obtained the corresponding secondary alcohols in 30–60% *ee*. Mandal's work prompted our inquisitiveness to protect the primary alcohol at C3 with a bulkier group and to determine the *ee* of the derived secondary alcohols. Very recently, Chen et al.[10] have carried out enantioselective reduction of a *meso*-cyclic imide to its cyclic *n*-acyl aminol in excellent *ee*. This is mediated by a chiral oxazaborolidine catalyst derived from (1*S*,2*S*)-(+)-*threo*-2-amino-1-(4-nitrophenyl)propane-1,3-diol. The catalyst has the primary alcohol at C3, which is protected as its *O*-triphenylmethyl ether, and there is a *p*-nitrophenyl moiety at C1. Chen's observation gave us the impetus to synthesize similar types of chiral catalysts in which the primary alcohol at C3 is protected as its *O-tert*-butyldiphenylsilyl (TBDPS) ether **2**, or its *O-tert*-butyldimethylsilyl (TBDMS) ether **3**, and to use these bulky ethers for the enantioselective reduction of prochiral ketones (Fig. 1). Again, for good optical yield, a tertiary hydroxy[1–3] functionality is essential and we resorted to synthesize C1 tertiary alcohols **4** and **5** and utilize these optically active amino alcohols for the asymmetric reduction of ketones. Sibi et al. used[11] borane and 10 mol% of an oxazaborolidine, derived from *cis*-2-aminoindanol ligand. The primary amino group of the parent amino indanol was modified to a secondary amino group with 2-pyridylmethyl, 2-pyridylcarbonyl, and 2-pyridylsulfonyl moieties. These bifunctional ligands have been evaluated in the reduction of prochiral ketones with high chemical efficiency and fair to high enantioselectivity. Again, Martens and coworkers[8] have developed acyclic and cyclic secondary amino alcohols for the enantiocontrolled catalytic reduction of alkyl aryl ketones in good *ee*. The work of Sibi et al.,[11] Martens and coworkers,[8] and others[1] led us to transform the C2 primary amine to its secondary amino compound **6** and to observe the enantioselectivity for the reduction of ketones.

It would also be highly interesting and thought provoking to build the oxazaborolidine with the primary alcohol at C3 and the amino group at C2. For this the secondary C1 hydroxy group was protected as its TBDMS ether to afford compound **7** and this amino alcohol was applied for the asymmetric borane reduction of alkyl aryl ketones. Oxazaborolidine generated from this type of acyclic amino diol in which the secondary alcohol is protected has not been previously reported. We report here the syntheses of six new chiral amino alcohols **2–7**, their use for the enantioselective reduction of aryl ketones, and the optical yields of the derived secondary alcohols.

Results and Discussion

Commercially available[12] and inexpensive chiral amino alcohol (1*R*,2*R*)-2-amino-1-phenylpropane-1,3-diol **1**, a precursor for the preparation of chloramphenicol, has been used by us for the synthesis of all six new chiral auxiliaries. The amino alcohols

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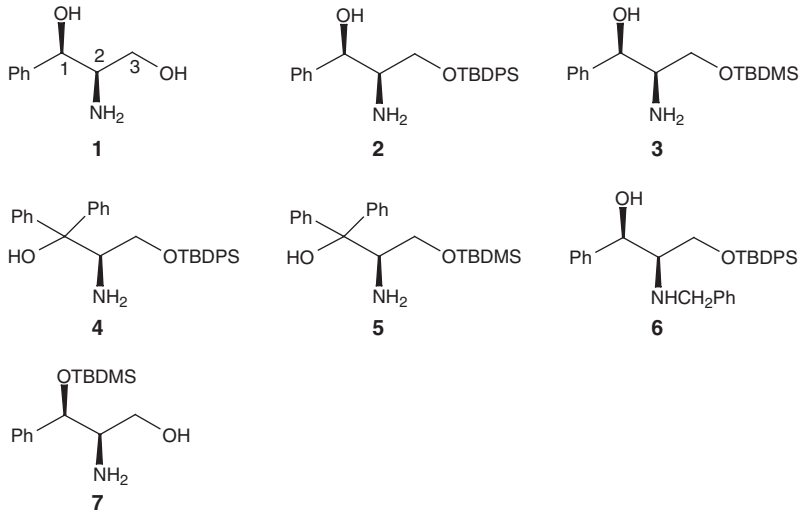
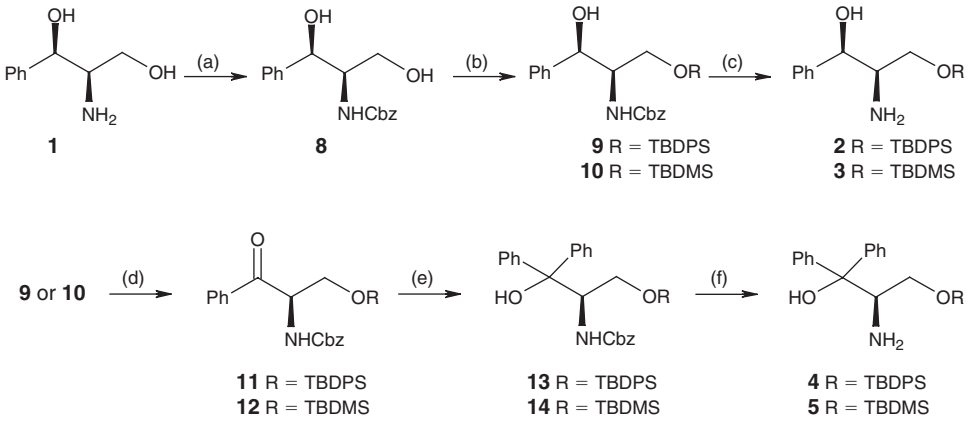


Fig. 1. Amino alcohols **2**–**7** synthesized from **1**.



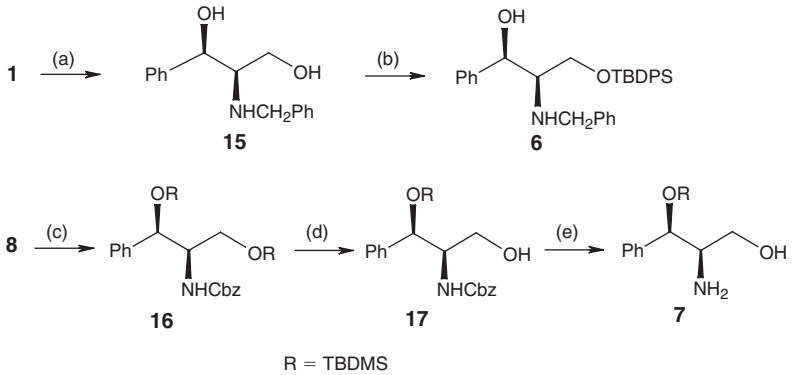
Scheme 1. *Reagents and conditions:* (a) $PhCH_2OCOCl$, Na_2CO_3, water–dioxan, 30°C, 2 h, 99%; (b) compound **9**: TBDPSCl, imidazole, DMF, 30°C, 10 min, 92%; compound **10**: TBDMSCl, imidazole, DMF, 25°C, 0.5 h, 90%; (c) H_2/Pd–C, MeOH, 30°C, 10 h, 75 psi, 98% for **2** and 99% for **3**; (d) IBX, EtOAc, reflux, 5 h, 98% for **11** and 97% for **12**; (e) bromobenzene, Mg, THF, 25°C, 1 h, 84% for **13** and 87% for **14**; (f) H_2/Pd–C, MeOH, 30°C, 10 h, 75 psi, 99% for **4** and **5**.

2 and **3** were prepared from (1*R*,2*R*)-2-amino-1-phenylpropane-1,3-diol **1** (Scheme 1). The amino group in compound **1** was protected as its carbamate **8** and primary alcohol at C3 was then converted into a TBDPS ether **9** or TBDMS ether **10**. Deprotection of the carbamate by hydrogenation gave the required amino alcohol derivatives **2** and **3** in excellent yield. Compounds **4** and **5** with *tert*-alcohol functionality were synthesized from the primary amino and primary hydroxy protected alcohols **9** and **10**. The secondary hydroxy group in compounds **9** and **10** were subjected to oxidation with *o*-iodoxybenzoic acid (IBX)[13] in ethyl acetate to afford ketones **11** and **12**. The tertiary alcohols **13** and **14** were obtained on exposure of ketones **11** and **12** to an excess of Grignard reagent prepared from bromobenzene in tetrahydrofuran (THF). Lastly, deprotection of the carbamate by hydrogenation gave the required amino alcohols **4** and **5**. Both compounds **4** and **5** were synthesized from **1** in five steps with an overall yield of 74%.

The secondary amino alcohol **6** has been synthesized from amino diol **1** (Scheme 2). Compound **1** was converted into an imine with benzaldehyde, which was reduced with sodium borohydride to give *N*-benzylated compound **15** with an overall yield of 76% in two steps. The primary hydroxy group in compound **15** was selectively converted into its *tert*-butyldiphenylsilyl ether **6** in good yield.

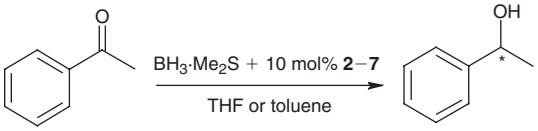
Protection of the secondary hydroxy group at C1 in compound **7** was carried out successfully as shown in Scheme 2. Initially, both the primary and secondary hydroxy groups in compound **8** were protected with TBDMSCl (2.4 mol) and imidazole in *N*,*N*-dimethylformamide (DMF) to furnish compound **16**. Selective deprotection of the primary *O*-TBDMS group with camphorsulfonic acid (CSA)[14] in methanol afforded alcohol **17**. Deprotection of the carbamate group by catalytic hydrogenation gave amino alcohol **7** in four steps with an overall yield of 92%.

It is well known[1–3] that the temperature and amount of catalyst have important effects on the enantioselectivity of the reduction. The application of catalysts **2**–**7** to the reduction of acetophenone was investigated with respect to temperature and catalyst concentration; the results are summarized in Tables 1 and 2.[15]



Scheme 2. *Reagents and conditions:* (a) (i) PhCHO, anhydrous $MgSO_4$, CH_2Cl_2/MeOH (3:1), reflux, 2 h; (ii) $NaBH_4$, MeOH, 0–25°C, 3 h, 76% in two steps; (b) TBDPSCl, imidazole, DMF, 25°C, 0.5 h, 83%; (c) TBDMSCl, imidazole, DMF, 30°C, 13 h, 99%; (d) CSA, MeOH, 10 min, 20°C, 96%; (e) H_2/Pd–C, MeOH, 30°C, 10 h, 75 psi, 98%.

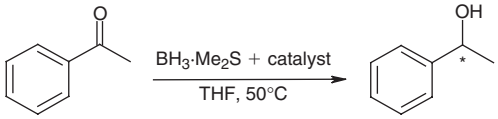
Table 1. Effect of temperature on the enantioselectivity of reduction



Entry	Catalyst	Temp. [°C]	Time [min]	*ee*[C] [%]	Isolated yield [%]	Configuration
1	**2**	0	65[B]	11	78	*S*
2	**2**	25	30	46	88	*S*
3	**2**	50	5	81	89	*S*
4	**2**	65	4	79	89	*S*
5	**2**	25[A]	55	8	88	*S*
6	**2**	50[A]	10	14	89	*S*
7	**2**	75[A]	5	11	88	*S*
8	**2**	100[A]	3	9	85	*S*
9	**3**	0	67[B]	7	83	*S*
10	**3**	25	30	49	90	*S*
11	**3**	50	5	62	89	*S*
12	**3**	65	4	60	90	*S*
13	**4**	0	15[B]	63	81	*S*
14	**4**	25	35	80	90	*S*
15	**4**	50	5	88	89	*S*
16	**4**	65	4	87	87	*S*
17	**4**	25[A]	50	40	89	*S*
18	**4**	50[A]	10	67	89	*S*
19	**4**	75[A]	5	60	88	*S*
20	**4**	100[A]	2	51	86	*S*
21	**5**	0	28[B]	30	84	*S*
22	**5**	25	30	80	89	*S*
23	**5**	50	5	88	90	*S*
24	**5**	65	4	86	89	*S*
25	**6**	0	25[B]	4	81	*S*
26	**6**	25	30	7	87	*S*
27	**6**	50	5	7	86	*S*
28	**6**	65	4	2	87	*S*
29	**7**	0	17[B]	42	85	*R*
30	**7**	25	30	63	92	*R*
31	**7**	50	5	53	91	*R*

[A]Toluene used as solvent.
[B]Time in hours.
[C]Determined by comparison with standard specific rotation for (*S*)-1-phenylethanol, $[\alpha]_D^{20}$ −45.50 (*c* 2.0 in MeOH).[15]

Table 2. Effect of catalyst concentration on the enantioselectivity of reduction

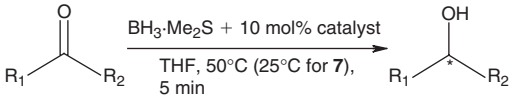


Entry	Catalyst	Catalyst [mol%]	*ee*[A] [%]	Isolated yield [%]	Configuration
1	**2**	2	67	88	*S*
2	**2**	5	75	90	*S*
3	**2**	7.5	79	90	*S*
4	**2**	10	81	89	*S*
5	**2**	20	81	88	*S*
6	**4**	2	45	90	*S*
7	**4**	5	72	92	*S*
8	**4**	7.5	80	91	*S*
9	**4**	10	88	89	*S*
10	**4**	20	88	88	*S*
11	**7**	2	48	91	*R*
12	**7**	5	58	89	*R*
13	**7**	7.5	61	90	*R*
14	**7**	10	63	92	*R*
15	**7**	20	63	90	*R*

[A]Determined by comparison with standard specific rotation value.

For the study of temperature effect, the catalyst concentration was fixed (10 mol%) for all reactions. As shown in Table 1, catalyst **2** at 50°C in THF (entry 3) resulted in 81% *ee*. Neither higher (65°C, reflux temperature of THF), nor lower temperature (25 or 0°C) was beneficial to the catalytic activities. The reduction using catalyst **3** at 50°C lead to low *ee* (62%, Table 1, entry 11) as compared to catalyst **2** and this may be as a result of the decrease in the bulk of the primary alcohol protecting group. The best results (88% *ee*) were obtained for the reduction of acetophenone with catalyst **4** and **5** at 50°C (Table 1, entries 15 and 23). We have also used toluene as solvent for the enantioselective reduction of acetophenone with catalysts **2** and **4** (Table 1, entries 5–8 and 17–20). The *ee* obtained for the secondary alcohol at temperatures of 25, 50, 75, and 100°C in toluene is less in comparison to THF. This may be caused by the polarity difference

Table 3. Asymmetric reduction of prochiral ketones catalyzed by 2–7



Entry	Ketone	Catalyst	*ee*[A] [%]	Isolated yield [%]	Configuration
1	PhCOMe	**2**	81	88	*S*
2	PhCOMe	**3**	62	89	*S*
3	PhCOMe	**4**	88	89	*S*
4	PhCOMe	**5**	88	90	*S*
5	PhCOMe	**6**	7	86	*S*
6	PhCOMe	**7**	63	92	*R*
7	4-MePhCOMe	**2**	72	91	*S*
8	4-MePhCOMe	**3**	63	87	*S*
9	4-MePhCOMe	**4**	75	90	*S*
10	4-MePhCOMe	**5**	83	92	*S*
11	4-MePhCOMe	**6**	2	89	*S*
12	4-MePhCOMe	**7**	62	92	*R*
13	PhCOEt	**2**	71	89	*S*
14	PhCOEt	**3**	69	91	*S*
15	PhCOEt	**4**	86	91	*S*
16	PhCOEt	**5**	88	89	*S*
17	PhCOEt	**6**	4	90	*S*
18	PhCOEt	**7**	69	92	*R*
19	1,2,3,4-Tetrahydronaphthalen-1-one	**2**	71	88	*S*
20	1,2,3,4-Tetrahydronaphthalen-1-one	**3**	51	90	*S*
21	1,2,3,4-Tetrahydronaphthalen-1-one	**4**	59	90	*S*
22	1,2,3,4-Tetrahydronaphthalen-1-one	**5**	87	91	*S*
23	1,2,3,4-Tetrahydronaphthalen-1-one	**6**	5	89	*S*
24	1,2,3,4-Tetrahydronaphthalen-1-one	**7**	57	90	*R*
25	PhCOPr^i	**2**	46	87	*R*
26	PhCOPr^i	**3**	54	90	*R*
27	PhCOPr^i	**4**	43	86	*R*
28	PhCOPr^i	**5**	46	86	*R*
29	PhCOPr^i	**6**	2	89	*R*
30	PhCOPr^i	**7**	57	88	*S*
31	2-Acetylnaphthalene	**2**	36	90	*S*
32	2-Acetylnaphthalene	**3**	70	93	*S*
33	2-Acetylnaphthalene	**4**	92	93	*S*
34	2-Acetylnaphthalene	**5**	94	92	*S*
35	2-Acetylnaphthalene	**6**	1	91	*S*
36	2-Acetylnaphthalene	**7**	74	92	*R*

[A]Determined by comparison with standard specific rotations, for (*S*)-1-(4-methylphenyl)ethanol $[\alpha]_D^{25}$ −57.3 (*c* 0.190 in $CHCl_3$),[16] for (*S*)-1-phenylpropanol $[\alpha]_D^{25}$ −45.45 (*c* 5.15 in $CHCl_3$),[17] for (*S*)-1,2,3,4-tetrahydronaphth-1-ol $[\alpha]_D^{25}$ +32.65 (*c* 2.5 in $CHCl_3$),[18] for (*R*)-2-methyl-1-phenylpropanol $[\alpha]_D^{25}$ +47.7 (*c* 6.8 in diethyl ether),[19] and for (*R*)-1-(naphthalen-2-yl)ethan-1-ol $[\alpha]_D^{25}$ +55.8 (*c* 4.8 in $CHCl_3$).[20]

between THF and toluene.* It should be noted that negligible asymmetric induction was observed with catalyst **6**. This may be a result of the steric repulsion of the *N*-benzyl of the oxazaborolidine, which prevents approach of the ketone towards borane and favours direct reduction by BH_3 (good isolated yield). In the case of catalyst **7**, maximum enantioselectivity (63% *ee*) was obtained at 25°C.

Having studied the optimum temperature, attention was turned towards the optimum concentration of the catalyst. All the reactions were carried out at the optimized temperature of 50°C (25°C for catalyst **7**) to study the effect of catalyst concentration on enantioselectivity. As shown in Table 2, increasing the amount of catalyst from 2 to 10 mol% improves the enantioselectivity of the reactions. However, no obvious change in enantioselectivity was observed on increasing the catalyst concentration to 20 mol%. Therefore, the best experimental conditions found for the asymmetric reduction of acetophenone required the use of 10 mol% of catalyst at 50°C (25°C in case of catalyst **7**). It is worth mentioning here that with loadings of 7.5 and 10% of catalysts **2** and **7**, there is no significant change of optical and chemical yields (1–2% change), hence a lower catalyst loading of 7.5 mol% can also be used.

The reduction of a variety of prochiral ketones was then examined using the catalysts derived from chiral amino alcohols **2**–**7** under optimized temperature and catalyst concentration. The results are summarized in Table 3.

* THF and toluene are expected to give different enantiomeric excesses under a similar range of temperatures. This is because of the very different polarity between THF and toluene. We thank a referee for this point.

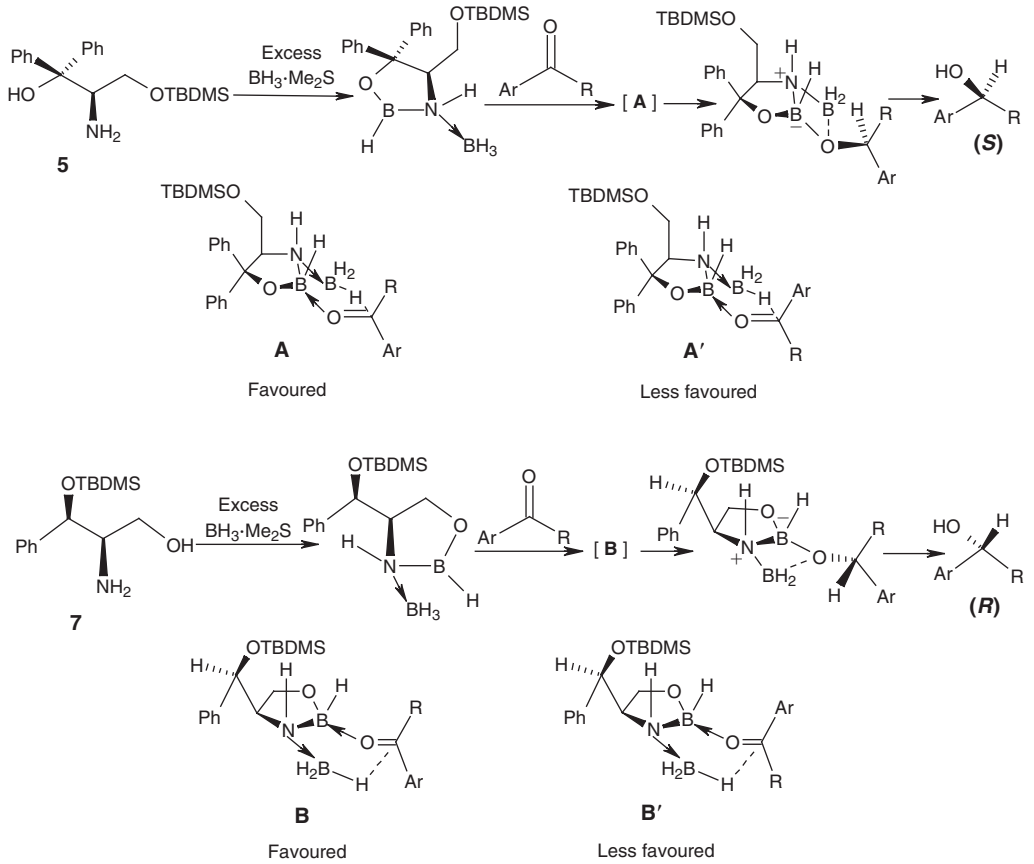


Fig. 2. Proposed models for oxazaborolidine reduction.

The level of asymmetric induction was found to be influenced by the nature of the substrate and catalyst. As seen from Table 3, asymmetric reduction of aromatic ketones with chiral amino alcohols gave fair to excellent *ee* (36–94%), except for amino alcohol **6**. Amino alcohol **6** gave very poor *ee* in all cases. As expected, reduction with the bulky primary hydroxy protected ether at C3 and 2-amino-1-diphenyl alcohols **4** and **5** proceeds with very good to excellent optical yields (86–94%; Table 3, entries 3, 4, 15, 16, 22, 33, 34). Reduction of ketones with the oxazaborolidine formed with the C1 hydroxy-protected amino diol **7** yielded the secondary alcohols in moderate *ee* (57–74%) with an opposite configuration with respect to all other catalysts.

Steric bulk around the prochiral carbonyl group plays an important role in the enantiomeric discrimination, as revealed by the low *ee* observed in the reduction of isopropylphenyl ketone with all six catalysts (Table 3, entries 25–30).

From the proposed model (Fig. 2) the configuration of the obtained chiral alcohol can be deduced. However, catalyst **7** and isopropylphenyl ketone gave the (*S*)-configuration, and all other catalysts **2**–**6** with isopropyl phenyl ketone gave the (*R*)-configuration. These results are of some concern to us. This may be caused by the isopropyl group in isopropylphenyl ketone predominating over the phenyl, which changes the favoured transition state to the less favoured transition state.

Conclusions

Six new chiral amino alcohols **2**–**7** have been synthesized from readily available (1*R*,2*R*)-2-amino-1-phenylpropane-1,3-diol **1** in excellent yields. The structures of these amino alcohols **2**–**7** have been fully characterized and used for the enantioselective reduction of aromatic ketones. The secondary alcohols were obtained in fair to excellent enantiomeric excesses (up to 94%) for the reduction of all the aromatic ketones studied. The *tert*-alcohol at C1 with a bulky *O*-protected group at C3 (**4** and **5**) gave uniformly encouraging results in all cases. Moderate *ee* was observed with the C3 primary alcohol **7**. As the reactions are rapid and high yielding, these chiral amino alcohols may be used as an alternative to the existing amino alcohols.

Experimental

General

Commercially available reagents were used without further purification. Air- and moisture-sensitive liquids and solutions were transferred by syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 45°C at ~20 mmHg. All non-aqueous reactions were carried out under anhydrous conditions using flame-dried glassware under an argon atmosphere in dry, freshly distilled solvents, unless otherwise noted. All melting points were determined on a Yanco Micro melting point apparatus. Optical rotations were obtained on a Bellingham and Stanly ADP-220 polarimeter. Reactions were monitored by thin-layer chromatography (TLC) using silica gel 60-F_{254} precoated TLC aluminium sheets, Merck, Germany, and the spots were located using UV light as the visualizing agent or by spraying with ethanolic phosphomolybdic acid (PMA) or ninhydrin solution followed by heating. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 (200 MHz) at 200.13 and 50.32 MHz, or on a Bruker MSL-300 at 300.13

and 75.47 MHz, or on a Bruker DRX-500 spectrophotometer at 500.13 and 125.78 MHz, respectively. Chemical shifts are given in δ values relative to tetramethylsilane as internal standard, and J values are given in Hz. IR spectra were recorded on a Schimadzu 8400 series FTIR instrument and values are reported in cm^{-1}. Mass spectra were recorded by a LC-TOF-MS (API QSTAR PULSAR) spectrometer, with samples introduced by the infusion method using the electrospray ionization technique and matrix-assisted laser desorption–ionization time-of-flight mass spectrometry (MALDI-TOF-MS, Voyager DE STR Biospectrometry). Elemental analyses were performed with a CHNS-O EA 1108-Elemental analyzer, Carloerba Instrument (Italy) or Elementor Vario EL (Germany).

*(1*R*,2*R*)-(−)-2-Amino-(*N*-benzyloxycarbonyl)-1-phenylpropane-1,3-diol* ***8***

To the solution of **1** (1.002 g, 6 mmol) in water–dioxan (20 mL, 1:1) was added sodium carbonate (0.320 g, 3 mmol). The reaction mixture was stirred for 10 min at 30°C. To this mixture benzyl chloroformate (0.95 mL, 6.6 mmol) was added and the reaction mixture was stirred at 30°C for 2 h. Dioxan was removed under reduced pressure, 5 mL of water was added, and the reaction mixture was extracted with ethyl acetate (3 × 50 mL). The ethyl acetate extract was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to afford compound **8** as a white solid. The crude product was chromatographed on silica gel (methanol/dichloromethane, 5:95) to give pure product **8** (1.780 g, 99%). mp 105–106°C (ethyl acetate/petroleum spirits). $[\alpha]_D$ −68.12 (*c* 0.69 in $CHCl_3$). Found: C 67.4, H 6.3, N 4.8. $C_{17}H_{19}O_4N$ requires C 67.8, H 6.4, N 4.7%. δ_H (300 MHz, $CDCl_3$) 7.29 (10H, m, ArH), 5.55 (1H, d, J 6, NH, exchangeable with D_2O), 4.96 (3H, m, $PhCH_2OCO$, PhCHOH), 3.85 (1H, m, CHNHCbz), 3.72 (2H, m, CH_2O). δ_C (125 MHz, $CDCl_3$) 156.92, 141.03, 136.27, 128.44, 128.29, 128.02, 127.86, 127.77, 125.98, 73.67, 66.85, 63.49, 57.63. ν_{max} (Nujol)/cm^{-1} 3429 (–OH), 1667, 1512, 1454, 1377, 1255. *m*/*z* (LCMS) 319.05 (M + H_2O), 302.05 (M + 1).

*(1*R*,2*R*)-(−)-2-Amino-(*N*-benzyloxycarbonyl)-3-*O*-(*tert*-butyldiphenylsilyl)-1-phenylpropane-1,3-diol* ***9***

Compound **8** (3.01 g, 10 mmol) and imidazole (1.7 g, 25 mmol) were dissolved in dry DMF (8 mL). To this solution *tert*-butyldiphenylsilyl chloride (2.86 mL, 11 mmol) was added and the reaction mixture was stirred at 30°C for 10 min. Ice pieces were added and the reaction mixture was extracted with diethyl ether (3 × 60 mL). The organic phase was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel using ethyl acetate/petroleum spirits (12:88) as eluent to obtain compound **9** as a gummy material (4.964 g, 92%). $[\alpha]_D$ −32.38 (*c* 1.05 in $CHCl_3$). Found: C 73.1, H 6.9, N 2.8. $C_{33}H_{37}NO_4Si$ requires C 73.4, H 6.9, N 2.6%. δ_H (200 MHz, $CDCl_3$) 7.58–7.21 (20H, m, ArH), 5.33 (1H, d, J 9.39, CHNHCbz, exchangeable with D_2O), 5.02 (1H, m, PhCHOH), 4.93 (2H, s, $PhCH_2OCO$), 3.84 (1H, m, CHNHCbz), 3.73 (2H, m, CH_2OSi), 3.17 (1H, s, OH), 1.02 (9H, s, $C(CH_3)_3$). δ_C (50 MHz, $CDCl_3$) 156.40, 141.03, 136.33, 135.44, 132.54, 129.86, 128.31, 128.20, 127.76, 127.51, 125.96, 66.56, 64.65, 57.33, 26.79, 19.07. ν_{max} ($CHCl_3$)/cm^{-1} 3436 (–OH), 1718 (C=O), 1500, 1404, 1215. *m*/*z* (MALDI–TOF) 562.37 (M + Na).

*(1*R*,2*R*)-(−)-2-Amino-(*N*-benzyloxycarbonyl)-3-*O*-(tert-butyldimethylsilyl)-1-phenylpropane-1,3-diol* ***10***

Compound **8** (1.505 g, 5 mmol) and imidazole (0.85 g, 12.5 mmol) were dissolved in dry DMF (3.5 mL). To this solution *tert*-butyldimethylsilyl chloride (0.9 g, 6 mmol) was added and the reaction mixture was stirred at 25°C for 0.5 h. Ice pieces were added and the reaction mixture was extracted with diethyl ether (3 × 50 mL). The organic phase was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel using ethyl acetate/petroleum spirits (8:92) as eluent to give compound **10** as a white solid (1.877 g, 90%). mp 60–61°C (ethyl acetate/petroleum spirits). $[\alpha]_D$ −60.16 (*c* 0.96 in $CHCl_3$). Found: C 66.5, H 8.4, N 3.3. $C_{23}H_{33}NO_4Si$ requires C 66.5, H 8.0, N 3.4%. δ_H (500 MHz, $CDCl_3$) 7.37–7.26 (10H, m, ArH), 5.42 (1H, d, J 6.88, NHCbz), 5.05–4.99 (3H, m, PhCHOH, $PhCH_2OCO$), 4.71 (1H, br s, OH), 3.87 (2H, m, CH_2OSi), 3.80 (1H, m, CHNHCbz), 0.92 (9H, s, $C(CH_3)_3$), 0.06 (3H, s, $SiCH_3$). δ_C (125 MHz, $CDCl_3$) 156.58, 141.12, 136.51, 128.49, 128.35, 128.04, 127.95, 127.66, 126.03, 74.36, 66.76, 64.82, 57.07, 25.86, 18.19, −5.59. ν_{max} (Nujol)/cm^{-1} 3425 (–OH), 1701 (C=O), 1512, 1454, 1251. *m*/*z* (LCMS) 416.05 (M + 1).

*(1*R*,2*R*)-(−)-2-Amino-3-*O*-(tert-butyldiphenylsilyl)-1-phenylpropane-1,3-diol* ***2***

To a solution of **9** (1.5 g, 12.8 mmol) in methanol (25 mL) was added Pd–C catalyst (0.150 g, 10%) and hydrogenation was carried out using a Parr apparatus at 75 psi pressure, at 30°C for 10 h. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure to obtain (1*R*,2*R*)-2-amino-1-phenyl-3-*O*-*tert*-butyldiphenylsilylpropane-1,3-diol **2** (1.109 g, 98%) as a gummy material. $[\alpha]_D$ −11.23 (*c* 1.25 in $CHCl_3$). Found: C 74.3, H 7.9, N 3.2. $C_{25}H_{31}NO_2Si$ requires C 74.0, H 7.7, N 3.5%. δ_H (200 MHz, $CDCl_3$) 7.61 (5H, m, ArH), 7.37 (10H, m, PhSiPh), 4.60 (1H, d, J 5.48, OCHPh), 3.61 (2H, m, CH_2OSi), 2.92 (1H, m, $CHNH_2$), 1.05 (9H, s, $C(CH_3)_3$). δ_C (50 MHz, $CDCl_3$) 142.25, 135.41, 132.98, 132.91, 129.64, 128.09, 127.62, 127.21, 126.18, 73.43, 65.49, 58.47, 26.79, 19.11. ν_{max} ($CHCl_3$)/cm^{-1} 3396, 1471, 1427, 1215. *m*/*z* (MALDI–TOF) 406.38 (M + 1).

*(1*R*,2*R*)-(−)-2-Amino-3-*O*-(tert-butyldimethylsilyl)-1-phenylpropane-1,3-diol* ***3***

Compound **3** was synthesized following the experimental procedure described for compound **2** and was obtained as a gummy material (99% yield). $[\alpha]_D$ −20.63 (*c* 2 in $CHCl_3$). Found: C 64.1, H 9.6, N 5.1. $C_{15}H_{27}NO_2Si$ requires C 64.0, H 9. 7, N 5.0%. δ_H (300 MHz, $CDCl_3$) 7.26–7.17 (5H, m, ArH), 4.66 (1H, d, J 4.40, PhCHOH), 3.64 (1H, dd, J 9.53, 3.66, CH_2OSi), 3.57 (1H, dd, J 9.53, 3.66, CH_2OSi), 2.96–2.93 (1H, m, $CHNH_2$), 2.29 (3H, br s, OH + NH_2), 0.91 (9H, s, $C(CH_3)_3$), 0.06 (6H, s, $SiCH_3$). δ_C (75 MHz, $CDCl_3$) 142.13, 128.15, 127.39, 126.32, 73.55, 64.24, 58.41, 25.73, 18.04, −5.68. ν_{max} ($CHCl_3$)/cm^{-1} 3371 (–OH, –NH_2), 1577, 1492, 1463, 1255, 1215. *m*/*z* (MALDI–TOF) 282.51 (M + 1).

*(2*R*)-2-Amino-(*N*-benzyloxycarbonyl)-3-*O*-(tert-butyldiphenylsilyl)-1-oxo-1-phenylpropan-3-ol* ***11***

To the solution of carbamate alcohol **9** (10 g, 18.53 mmol) in ethyl acetate (60 mL) was added *o*-iodoxybenzoic acid (15.56 g, 55.58 mmol). The reaction mixture was refluxed for 5 h and

then it was filtered. The filtrate was concentrated under reduced pressure. The crude material was chromatographed on silica gel (ethyl acetate/petroleum spirits, 5:95) to obtain pure compound **11** (9.803 g, 98%) as a thick oil. $[\alpha]_D$ −42.05 (*c* 1.28 in $CHCl_3$). Found: C 73.6, H 6.9, N 2.7. $C_{33}H_{35}NO_4Si$ requires C 73.7, H 6.6, N 2.6%. δ_H (200 MHz, $CDCl_3$) 7.92 (2H, d, *J* 8.33, ArH), 7.65–7.15 (18H, m, ArH), 6.05 (1H, d, *J* 8, NHCbz), 5.45–5.38 (1H, m, CHNHCbz), 5.13 (2H, s, $PhCH_2OCO$), 3.99 (2H, d, *J* 3.67, CH_2OSi), 0.90 (9H, s, $-C(CH_3)_3$). δ_C (100 MHz, $CDCl_3$) 196.12, 155.73, 136.33, 135.35, 134.87, 133.42, 132.53, 132.43, 129.68, 129.55, 128.64, 128.46, 128.40, 127.97, 127.87, 127.64, 127.52, 66.73, 64.87, 57.44, 26.44, 18.99. ν_{max} ($CHCl_3$)/cm^{-1} 3423 (–NH), 1685 (NH–COO), 1718 (PhCO–). *m*/*z* (LCMS) 538.73 (M + 1).

*(2R)-2-Amino-(*N*-benzyloxycarbonyl)-3-*O*-(*tert*-butyldimethylsilyl)-1-oxo-1-phenylpropan-3-ol* ***12***

Compound **12** was synthesized following the experimental procedure described for compound **11**. Colourless oil, 97% yield. $[\alpha]_D$ −36.43 (*c* 2.64 in $CHCl_3$). Found: C 67.3, H 7.3, N 3.5. $C_{23}H_{31}NO_4Si$ requires C 66.8, H 7.6, N 3.4%. δ_H (200 MHz, $CDCl_3$) 7.94 (2H, d, *J* 6, ArH), 7.57–7.37 (8H, m, ArH), 5.98 (1H, d, *J* 7.71, NHCbz), 5.44–5.36 (1H, m, CHNHCbz), 5.15 (2H, s, $PhCH_2OCO$), 4.02–3.90 (2H, m, CH_2OSi), 0.75 (9H, s, $-C(CH_3)_3$), −0.13 (3H, s, $SiCH_3$), −0.17 (3H, s, $SiCH_3$). δ_C (50 MHz, $CDCl_3$) 197.00, 155.74, 136.28, 135.07, 133.37, 128.53, 128.45, 128.37, 127.97, 127.92, 66.75, 66.12, 64.12, 57.61, 25.47, 17.93, −5.91, −6.00. ν_{max} ($CHCl_3$)/cm^{-1} 3427 (–NH), 1689 (NH–COO), 1716 (PhC=O). *m*/*z* (LCMS) 414.44 (M + 1), 436.35 (M + Na).

*(2R)-2-Amino-(*N*-benzyloxycarbonyl)-3-*O*-(*tert*-butyldiphenylsilyl)-1,1-diphenylpropane-1,3-diol* ***13***

Magnesium turnings (2.5 g, 103 mmol) were placed in a flame-dried two-necked round bottom flask fitted with a reflux condenser. The flask was cooled to room temperature by flushing with argon gas. Dry THF (50 mL) was added by syringe under an argon atmosphere. Freshly distilled bromobenzene (5.41 mL, 51.45 mmol) was added at such a rate that a mild reflux of THF resulted. The reaction between bromobenzene and magnesium is exothermic and dropwise addition of bromobenzene took 15 min. The contents were further stirred for 15 min. The *N*-carbamate ketone **11** (9.258 g, 17.15 mmol) in dry THF (30 mL) was added dropwise by syringe over 20 min at 25°C. The whole reaction mixture was further stirred at 25°C for 1 h. The reaction was quenched with saturated ammonium chloride. THF was removed completely and the residue was extracted with ethyl acetate (3 × 100 mL). The combined extract was washed wither water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude material was purified on flash silica gel with a mixture of ethyl acetate/petroleum spirits (4:96) to obtain a white solid **13** (8.9 g) in 84% yield, mp 58°C (dichloromethane/petroleum spirits). $[\alpha]_D$ 9 (*c* 1.26 in $CHCl_3$). Found: C 75.9, H 7.0, N 2.5. $C_{39}H_{41}NO_4Si$ requires C 76.1, H 6.7, N 2.3%. δ_H (200 MHz, $CDCl_3$) 7.61–7.20 (25H, m, ArH), 5.90 (1H, d, *J* 8.59, NHCbz), 5.05 (2H, s, $PhCH_2OCO$), 4.77–4.73 (1H, m, CHNHCbz), 3.85 (2H, d, *J* 26, CH_2OSi), 1.01 (9H, s, $C(CH_3)_3$). δ_C (50 MHz, $CDCl_3$) 155.93, 145.47, 144.23, 136.53, 135.35, 135.14, 131.46, 131.25, 130.02, 129.81, 128.50, 128.42, 128.21, 127.87, 127.72, 127.57, 126.91, 126.76, 125.07, 81.16, 66.50, 65.64, 55.46, 26.59, 18.90. ν_{max} ($CHCl_3$)/cm^{-1} 3438 (–OH), 1712 (C=O). *m*/*z* (LCMS) 638.50 (M + Na).

*(2R)-2-Amino-(*N*-benzyloxycarbonyl)-3-*O*-(*tert*-butyldimethylsilyl)-1,1-diphenylpropane-1,3-diol* ***14***

Compound **14** was synthesized following the experimental procedure described for compound **13** to give a thick oil, 87% yield. $[\alpha]_D$ 34.64 (*c* 2.42 in $CHCl_3$). Found: C 71.1, H 7.2, N 3.0. $C_{29}H_{37}NO_4Si$ requires C 70.8, H 7.6, N 2.9%. δ_H (200 MHz, $CDCl_3$) 7.56–7.21 (15H, m, ArH), 5.78 (1H, d, *J* 8.71, NHCbz), 5.12 (2H, s, $PhCH_2OCO$), 4.78–4.72 (1H, m, CHNHCbz), 3.94 (1H, dd, *J* 10.61, 2.15, CH_2OSi), 3.75 (1H, dd, *J* 10.61, 2.15, CH_2OSi), 0.90 (9H, s, $C(CH_3)_3$), 0.00 (3H, s, $SiCH_3$), −0.07 (3H, s, $SiCH_3$). δ_C (50 MHz, $CDCl_3$) 156.02, 145.43, 144.28, 136.50, 128.34, 128.30, 128.15, 127.81, 127.51, 126.81, 126.69, 125.11, 124.88, 81.14, 66.44, 64.62, 55.13, 25.63, 17.91, −6.01, −6.11. ν_{max} ($CHCl_3$)/cm^{-1} 3434 (–OH), 1710 (C=O). *m*/*z* (LCMS) 514.63 (M + Na).

*(2R)-2-Amino-3-*O*-(*tert*-butyldiphenylsilyl)-1,1-diphenylpropane-1,3-diol* ***4***

Compound **4** was prepared using the same approach to **2** to give a gummy material, 99% yield. $[\alpha]_D$ 39.42 (*c* 1.37 in $CHCl_3$). Found: C 77.4, H 7.3, N 3.0. $C_{31}H_{35}NO_2Si$ requires C 77.3, H 7.3, N 2.9%. δ_H (200 MHz, $CDCl_3$) 7.62–7.14 (20H, m, ArH), 4.80 (1H, s, OH), 3.93 (1H, m, CHNHCbz), 3.73 (1H, dd, *J* 10.36, 6.57, CH_2OSi), 3.62 (1H, dd, *J* 10.35, 3.15, CH_2OSi), 1.64 (2H, s, NH_2), 1.04 (9H, s, $C(CH_3)_3$). δ_C (100 MHz, $CDCl_3$) 144.56, 146.66, 135.50, 135.32, 132.69, 132.66, 129.81, 129.67, 128.37, 128.07, 127.74, 127.66, 126.62, 126.40, 125.44, 125.01, 78.61, 65.25, 57.48, 26.80, 19.06. ν_{max} ($CHCl_3$)/cm^{-1} 3448 (–OH). *m*/*z* (LCMS) 482.87 (M + 1).

*(2R)-2-Amino-3-*O*-(*tert*-butyldimethylsilyl)-1,1-diphenylpropane-1,3-diol* ***5***

Compound **5** was synthesized following the experimental procedure described for compound **2** to give a gummy material, 99% yield. $[\alpha]_D$ 79.23 (*c* 2.6 in $CHCl_3$). Found: C 70.7, H 8.8, N 3.9. $C_{21}H_{31}NO_2Si$ requires C 70.5, H 8.7, N 3.9%. δ_H (200 MHz, $CDCl_3$) 7.60–7.16 (10H, m, ArH), 3.92 (1H, t, *J* 9.09, $CHNH_2$), 3.60 (2H, d, *J* 4.55, CH_2OSi), 0.86 (9H, s, $C(CH_3)_3$), −0.02 (3H, s, $SiCH_3$), −0.05 (3H, s, $SiCH_3$). δ_C (50 MHz, $CDCl_3$) 145.95, 144.99, 128.37, 128.07, 126.64, 126.46, 125.48, 125.03, 79.09, 64.45, 57.08, 25.73, 18.01, −5.67, −5.80. ν_{max} ($CHCl_3$)/cm^{-1} 3438 (–OH), 3400 (NH_2). *m*/*z* (LCMS) 359.14 (M + 2).

*(1R,2R)-(−)-2-Amino-(*N*-benzyl)-1-phenylpropane-1,3-diol* ***15***

Compound **1** (1.67 g, 10 mmol) was dissolved in dichloromethane/methanol (20 mL, 4/1), to which benzaldehyde (1.11 mL, 11 mmol) and anhydrous $MgSO_4$ (1.5 g) were added. The reaction mixture was refluxed for 2 h, filtered through Celite, and concentrated under reduced pressure to afford crude imine product (2.27 g). The solution of crude imine in methanol (15 mL) was cooled (0°C) and to it was added $NaBH_4$ (0.637 g, 20 mmol). The reaction mixture was then allowed to warm to 30°C and stirred for a further 3 h. The methanol was evaporated under reduced pressure, the product was dissolved in dichloromethane (20 mL), 2 N HCl (10 mL) was added, and the resulting mixture was stirred for 10 min. The reaction mixture was neutralized with aqueous Na_2CO_3 and extracted with dichloromethane (3 × 30 mL). The organic extract was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to yield crude product **15**. This was purified by column chromatography on silica

gel (methanol/dichloromethane, 5:95) to give a yellowish solid **15** (1.955 g, 76%). mp 75–76°C (ethyl acetate/petroleum spirits). $[\alpha]_D$ −87.48 (*c* 2 in $CHCl_3$). Found C 74.7, H 8.0, N 5.4. $C_{16}H_{19}NO_2$ requires C 74.7, H 7.4, N 5.4%. δ_H (200 MHz, $CDCl_3$) 7.34 (10H, m, ArH), 4.65 (1H, d, *J* 7.43, PhCHOH), 3.80 (1H, d, *J* 12.91, $NHCH_2Ph$), 3.66 (1H, d, *J* 12, $NHCH_2Ph$), 3.66 (1H, dd, *J* 11.34, 3.91, CH_2OH), 3.48 (1H, dd, *J* 10.96, 3.52, CH_2OH), 2.80 (1H, m, CHNH), 2.55 (3H, br s, OH + NH). δ_C (75 MHz, $CDCl_3$) 136.27, 141.21, 127.45, 127.02, 126.78, 126.13, 126.07, 125.43, 70.26, 63.18, 57.53, 49.63. ν_{max} ($CHCl_3$)/cm^{-1} 3380 (–OH), 1602, 1494, 1454, 1217. *m*/*z* (MALDI–TOF) 257.34 (M + 1).

*(1*R*,2*R*)-(−)-2-Amino-(*N*-benzyl)-3-(*tert*-butyldiphenylsilyl)-1-phenylpropane-1,3-diol* ***6***

To a solution of **15** (0.877 g, 3.4 mmol) and imidazole (0.578, 8.5 mmol) in dry DMF (5 mL) was added *tert*-butyldiphenylsilyl chloride (0.97 mL, 3.74 mmol) at 25°C, and the reaction mixture stirred for 0.5 h. The reaction was quenched with crushed ice and the mixture extracted with diethyl ether (3 × 40 mL). The organic layer was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified using a silica gel column with a mixture of ethyl acetate/petroleum spirits (2:98) as eluent to give compound **6** as colourless oil (1.452 g, 86%). $[\alpha]_D$ −46.17 (*c* 1 in $CHCl_3$). Found C 77.3, H 7.8, N 2.6. $C_{32}H_{37}NO_2Si$ requires C 77.5, H 7.5, N 2.8%. δ_H (200 MHz, $CDCl_3$) 7.62–7.24 (20H, m, ArH), 4.61 (1H, d, *J* 7.83, PhCHOH), 3.77–3.42 (4H, m, CH_2OSi, $NHCH_2Ph$), 2.66 (1H, m, CHNH), 1.08 (9H, s, $C(CH_3)_3$). δ_C (75 MHz, $CDCl_3$) 132.88, 132.79, 129.77, 128.46, 128.15, 127.72, 127.48, 127.42, 126.81, 71.93, 64.55, 60.86, 51.21, 26.92, 19.17. ν_{max} ($CHCl_3$)/cm^{-1} 3421 (–OH), 1469, 1454, 1427, 1217. *m*/*z* (MALDI–TOF) 496.05 (M + 1).

*(1*R*,2*R*)-(−)-2-Amino-(*N*-benzyloxycarbonyl)-1,3-*O*-(di-*tert*-butyldimethylsilyl)-1-phenylpropane-1,3-diol* ***16***

Compound **8** (5.117 g, 17 mmol) and imidazole (5.780 g, 85 mmol) were dissolved in dry DMF (18 mL). To this solution *tert*-butyldimethylsilyl chloride (6.120 g, 40.8 mmol) was added and the reaction mixture was stirred at 30°C for 13 h. Ice pieces were added and the reaction mixture was extracted with diethyl ether (3 × 70 mL). The organic phase was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was purified on silica gel by column chromatography using ethyl acetate/petroleum spirits (4:96) as eluent to give compound **16** as a colourless oil (8.9 g, 99%). $[\alpha]_D$ −45.57 (*c* 1.62 in $CHCl_3$). Found: C 65.7, H 8.7, N 3.0. $C_{29}H_{47}NO_4Si_2$ requires C 65.7, H 8.9, N 2.6%. δ_H (200 MHz, $CDCl_3$) 7.31–7.25 (10H, m, ArH), 5.13 (1H, d, *J* 8.84, NHCbz), 5.03 (1H, d, *J* 2.90, PhCH), 5.00 (2H, s, $PhCH_2OCO$), 3.76–3.67 (1H, m, CHNHCbz), 3.57 (2H, d, *J* 6.32, CH_2OSi), 0.93 (9H, s, $C(CH_3)_3$), 0.89 (9H, s, $C(CH_3)_3$), 0.09 (3H, s, $SiCH_3$), 0.07 (3H, s, $SiCH_3$), 0.04 (3H, s, $SiCH_3$), −0.15 (3H, s, $SiCH_3$). δ_C (125 MHz, $CDCl_3$) 155.99, 142.19, 136.60, 128.39, 127.95, 127.26, 126.16, 71.73, 66.45, 61.55, 58.97, 25.79, 18.13, 18.05, −5.47, −4.67, −5.28, −5.34. ν_{max} ($CHCl_3$)/cm^{-1} 3446 (–NH), 1726 (C=O). *m*/*z* (LCMS) 530.46 (M + 1), 552.45 (M + Na).

*(1*R*,2*R*)-(−)-2-Amino-(*N*-benzyloxycarbonyl)-1-*O*-(tert-butyldimethylsilyl)-1-phenylpropane-1,3-diol* ***17***

To a solution of **16** (10.255 g, 19.35 mmol) in methanol was added camphorsulfonic acid (4.495 g, 19.35 mmol) and the reaction mixture was stirred for 10 min at 20°C. Ice pieces were added and the methanol was evaporated on a rotary evaporator. The mixture was then extracted with ethyl acetate (3 × 60 mL). The combined extracts were washed with water and brine, dried over anhydrous sodium sulfate, and concentrated on the rotary evaporator. The crude product was chromatographed on silica gel using ethyl acetate/petroleum spirits (30:70) as eluent to furnish compound **17** as a colourless oil (7.716 g, 96%). $[\alpha]_D$ −46.65 (*c* 2.92 in $CHCl_3$). Found: C 66.2, H 7.9, N 3.6. $C_{23}H_{33}NO_4Si$ requires C 66.5, H 8.0, N 3.4%. δ_H (200 MHz, $CDCl_3$) 7.33–7.31 (10H, m, ArH), 5.20 (1H, d, *J* 8.09, NHCbz), 5.02 (2H, s, $PhCH_2OCO$), 4.97 (1H, d, *J* 3.41, PhCHO), 3.89–3.77 (1H, m, CHNHCbz), 3.70 (2H, d, *J* 5.81, CH_2OH), 0.91 (9H, s, $C(CH_3)_3$), 0.06 (3H, s, $SiCH_3$), −0.14 (3H, s, $SiCH_3$). δ_C (100 MHz, $CDCl_3$) 156.52, 141.54, 136.31, 128.33, 128.00, 127.87, 127.41, 126.15, 72.93, 66.62, 62.25, 59.09, 25.70, 18.00, −4.80, −5.36. ν_{max} ($CHCl_3$)/cm^{-1} 3434.98 (–OH), 1708 (C=O). *m*/*z* (LCMS) 416.26 (M + 1), 438.24 (M + Na).

*(1*R*,2*R*)-(−)-2-Amino-1-*O*-(tert-butyldimethylsilyl)-1-phenylpropane-1,3-diol* ***7***

Compound **7** was synthesized following the experimental procedure described for compound **2**. Yield 98%. mp 80°C (ethyl acetate/petroleum spirits). $[\alpha]_D$ −60.71 (*c* 1.12 in $CHCl_3$). Found: C 64.3, H 9.6, N 5.2. $C_{15}H_{27}NO_2Si$ requires C 64.0, H 9.7, N 5.0%. δ_H (200 MHz, $CDCl_3$) 7.32 (5H, s, ArH), 5.45 (br s, NH_2 and OH), 4.80 (1H, d, *J* 7.45, PhCH), 3.63 (1H, dd, *J* 11.87, 3.28, CH_2OH), 3.52 (1H, dd, *J* 11.88, 6.82, CH_2OH), 3.36–3.27 (1H, m, $CHNH_2$), 0.86 (9H, s, $C(CH_3)_3$), 0.09 (3H, s, $SiCH_3$), −0.23 (3H, s, $SiCH_3$). δ_C (125 MHz, $CDCl_3$) 140.02, 128.38, 128.24, 126.74, 73.41, 59.78, 59.71, 59.70, 25.70, 17.84, −4.73, −4.89. ν_{max} (Nujol)/cm^{-1} 3402. *m*/*z* (LCMS) 282.41 (M + 1).

General Procedure for the Asymmetric Reduction of Ketones

To a solution of amino alcohol **2**–**7** (0.2 mmol) in dry THF (3 mL) was added 10 M borane–dimethyl sulfide complex (0.23 mL, 2.3 mmol), and the reaction mixture was stirred under an argon atmosphere at 25°C for 10 min. The reaction temperature was increased to 50°C and a solution of ketone (2 mmol) in dry THF (3 mL) was added dropwise over 15 min. The reaction mixture was then stirred for a further 5 min. The reaction was quenched by adding 2 M HCl (5 mL), and the mixture extracted with diethyl ether (3 × 20 mL). The organic layer was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified on a silica gel column with ethyl acetate/petroleum spirits as eluent to give the chiral secondary alcohols.

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