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Resolution of 1-arylalkylamines with 3-*O*-hydrogen phthalate glucofuranose derivatives: role of steric bulk in a family of resolving agents

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Abstract—The development of three new acidic resolving agents which are hydrogen phthalates of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **1**, 1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranose **2** and 1,2-*O*-cyclohexylidene-5,6-*O*-diphenylmethylidene-α-D-glucofuranose **3** is shown for the resolution of 1-arylalkylamines **7a–k**. The salts between **1**, **2** and (*RS*)-1-arylalkylamines **7a–k** selectively crystallize **1**·(*S*) **7a–j** and **2**·(*S*) **7a–h** salts, allowing us to recover the corresponding bases (*S*) **7a–j** and (*S*) **7a–h**, respectively, in good yield and enantiomeric excess (73–95% ee). Whereas, the salts between **3** and (*RS*)-1-arylalkylamines **7a–c**,**g–i**,**k** selectively crystallize **3**·(*S*)-**7a–c**,**g–i** salts to recover the corresponding bases (*S*)-**7a–c**,**g–i** in poor enantiomeric excess (4–35% ee). The difference between the resolving ability of **1** and **2** for 1-arylalkylamines **7a–h** is very slight, but there is considerable difference compared to *ortho*-substituted 1-arylalkylamines **7i** and **7j**. The role of substituents on a family of resolving agents **1**, **2** and **3** is also discussed to interpret their resolving ability.

1. Introduction

The global demand for single enantiomer pharmaceutical and agrochemical products continues to show growth.[1] Such products are invariably manufactured by the resolution of racemates via the formation of diastereomeric salts with a resolving agent.[2] Unfortunately, the selection of a resolving agent suitable for a given target racemate is difficult as tt requires understanding of the relationship between the physical properties of the pairs of diastereomeric salts and their molecular and/or crystal structure. Accordingly, unravelling the intricacies of a chiral recognition mechanism by diastereomeric salt formation method remains a major scientific challenge.[3]

Empirical guidelines useful for selecting a resolving agent, based on rational design and practical experience, have been developed. Among the methods developed over the recent decade, the habit modification[4] of diastereomeric salt with an optically active additive in a classical crystallization process and nucleation inhibition by a stereochemically homogenous additive by the Dutch resolution[5] method have added finesse to the resolution technology. In spite of these recent techniques, failures continue to occur while single isomer new chemical entities are being developed from discovery research. The natural products such as quinine, brucine, cinchonine and their derivatives continue to be one of the primary sources of resolving agents; yet the huge arsenal of carbohydrates[6] available has not been fully exploited for this purpose. We initiated investigations on the development of new acidic resolving agents from carbohydrate families due to their easy availability in various chiral forms, conformations and because of our strength in carbohydrate chemistry.[7] We targeted the resolution of 1-arylalkylamines and, while designing the resolving agents, we chose glucofuranose as the key template and incorporated a hydrogen phthalate ester to provide stabilizing CH$\cdots\pi$ interactions and hydrogen bonding.[7,8] This family of resolving agents differed only in the nature of the substituent on the 1,3-dioxalane. The steric bulk of the substituent of the resolving agent was considered for studying the resolution efficiency, as it would offer conformational rigidity due to

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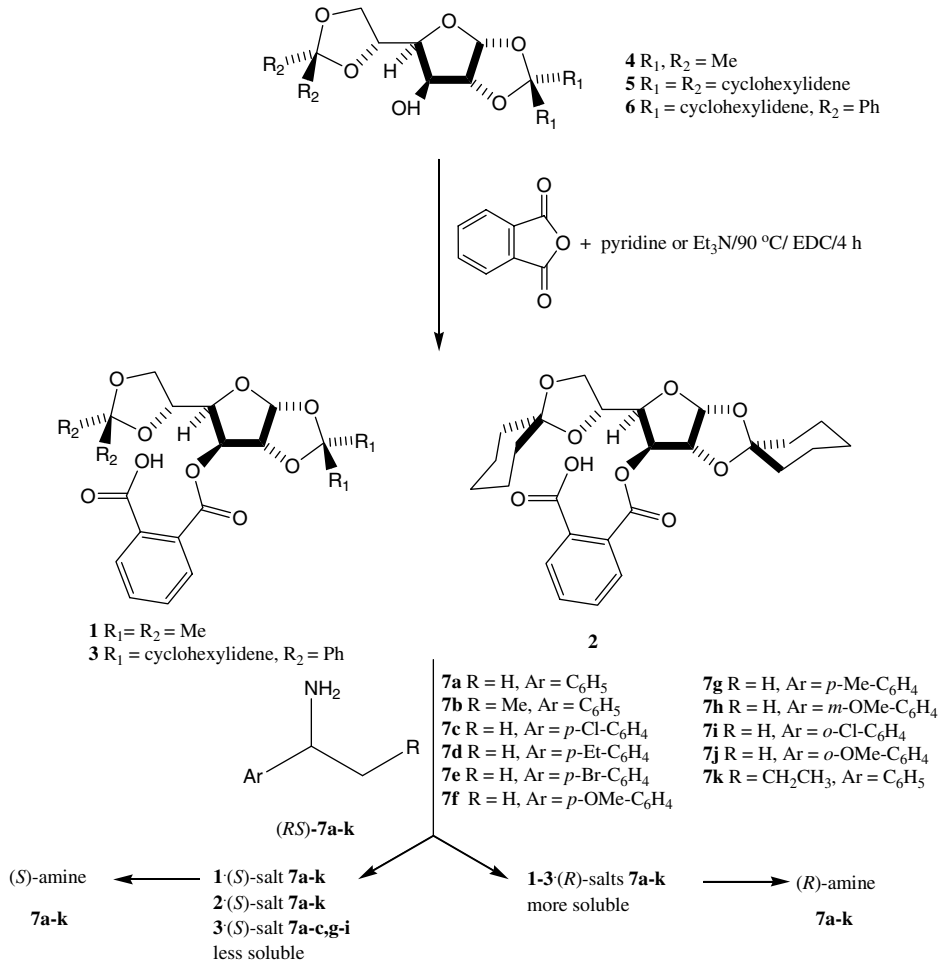
restricted rotation, and thereby provide a suitable recognition site.

2. Results and discussion

For the intended study, we decided to synthesize three hydrogen phthalate esters of 1,2:5,6-di-*O*-alkyl-/arylidene glucofuranose. The substituents were varied with the aim of obtaining conformational rigidity and π-stacking to promote chiral recognition. Accordingly, the resolving agents namely 3-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl)-hydrogen phthalate **1**, 3-(1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranosyl)-hydrogen phthalate **2** and 3-(1,2-*O*-cyclohexylidene-5,6-*O*-diphenylmethylidene-α-D-glucofuranosyl)-hydrogen phthalate **3** were synthesized by modification of the published reactions (Scheme 1).[8a] The reaction of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **4**[9] with phthalic anhydride (1 mol equivalent) and pyridine (1.1 mol equivalent) at 90 °C for 4 h gave **1** in low yield due to contamination with phthalic acid and was difficult to purify. Several reaction conditions including variation of the base (Et_3N, pyridine), temperature and solvent were examined to improve the yield and purity of **1**–**3**. Thus, among the reaction conditions established, the reaction of sugar alcohol **4** (1 mol) with phthalic anhydride (2 mol equiv), pyridine (3.7 mol equiv) in ethylene chloride and at 90 °C for 4 h after careful workup and purification gave 3-hydrogen phthalate derivative **1** in 69% yield as a crystalline solid (mp 155–157 °C). A similar reaction of sugar alcohol **5** with phthalic anhydride gave 3-hydrogen phthalate derivative **2** in 82% yield (mp 60–62 °C). Surprisingly, the reaction of sugar alcohol **6** with phthalic anhydride under similar reaction conditions failed to give **3** and starting material was recovered. When Et_3N (1.1 mol equiv) was used as a base instead of pyridine, the reaction of **3** proceeded with phthalic anhydride in ethylene chloride at 90 °C for 3 h to give compound **3** in 91% yield (mp 89–90 °C). 1,2-Di-*O*-cyclohexylidene-5,6-*O*-phenylmethylidene-α-D-glucofuranose **6** was prepared in 80% yield (mp 177–179 °C) from 1,2-*O*-cyclohexylidene-α-D-glucofuranose by reaction with 1,1-dichlorodiphenylmethane in Et_3N/CH_2Cl_2 at reflux temperature for 6 h and then fully characterized.

Resolving agents **1**, **2** and **3** were characterized by ^1H NMR spectra from the appearance of H-1′ at δ 5.80–5.90 ($J_{1,2} = 5.7$ Hz) and H-3′ at δ 5.32–5.45 (d, $J_{3,4} = 2.7$ Hz). In order to test their resolving ability, **1** and **2** were treated with a wide range of (*RS*)-1-aryl-



Scheme 1.

alkylamines **7a**–**k** by briefly boiling in methanol (2 mL/g) [or 2-propanol (5 mL/g) when resolution efficiency was low] and allowed to cool gradually to −10 °C for 6–36 h. The precipitates formed were then filtered and washed with chilled methanol (or 2-propanol) in order to obtain the corresponding less soluble diastereomeric salts **1**·(*S*)-**7a**–**k** and **2**·(*S*)-**7a**–**k**, respectively. The salts **1**·(*S*)-**7a**–**k** were decomposed to isolate the corresponding (*S*)-1-arylalkylamines **7a**–**j** in 73–90% ee and **7k** in 11% ee (Table 1). Likewise, diastereomeric salts **2**·(*S*)-**7a**–**k** were decomposed to obtain the corresponding (*S*)-1-arylalkylamines (*S*)-**7a**–**h** in 76–95% ee and (*S*)-**7i**–**k** in 7–21% ee (Table 2).

Table 1. Resolution of (*RS*)-1-arylalkylamines **7a**–**k** by **1**

Entry	(*RS*)-Amine	Yield (%) diastereomeric salt	(*S*)-Amine[a] $[\alpha]_D$[b]	ee (%)[c]	Resolution efficiency[d]	Ref.
1	**7a**	76.8	−29.9	90	0.69	8a
2	**7b**	81.2	−18.0	90	0.73	8b
3	**7c**	76.2	−18.9	90	0.68	8b
4	**7d**	74.0	−29.5	88	0.65	—
5	**7e**	86.0	−21.5	87	0.74	8a
6	**7f**	81.8	−30.4	86	0.70	8a
7	**7g**	74.0	−27.1	89	0.65	8b
8	**7h**	84.0	−18.8	82	0.69	8c
9	**7i**	79.0	−30.1	80	0.63	8c
10	**7j**	84.0	−62.6	73	0.61	8f
11	**7k**	20.0	−2.3	11	0.02	5b,8e

[a] *c* 1.0, EtOH.
[b] At 25 °C.
[c] % Enantiomeric excess (ee) of the liberated amines determined by HPLC analysis [Daicel Crownpak CR(+)].
[d] Product of the yield of the diastereomeric salt and ee of the amine.

Resolving agents **1** and **2** efficiently resolved 1-phenylethylamine **7a** (entry 1) and its one carbon higher homolog 1-phenylpropylamine **7b** (entry 2); whereas, the two carbon higher homolog 1-phenylbutylamine **7k** (entry 11) was resolved with low efficiency (Tables 1 and 2).[5b,8e] The resolving agent **1** exhibited selectivity for the resolution of 1-phenylethylamines having *O*-chloro-**7i** (entry 9) and *O*-methoxy **7j** (entry 10) substituents (Table 1), whereas **2** was not selective (Table 2, entries 9 and 10) probably because of its inability to form ammonium cations due to the steric bulk of the cyclohexylidene substituents on the resolving agent also the *ortho*-substituent of 1-arylalkylamines. A close relationship between the bulk of substituents of the acidic resolving agents **1**, **2** and amines **7** seems to exist for obtaining optimum resolution efficiency.

Table 2. Resolution of (*RS*)-1-arylalkylamines **7a**–**k** by **2**

Entry	(*RS*)-Amine	Yield (%) diastereomeric salt	(*S*)-Amine[a] $[\alpha]_D$[b]	ee (%)[c]	Resolution efficiency[d]	Ref.
1	**7a**	80.0	−31.2	95	0.76	8a
2	**7b**	83.0	−18.9	94	0.78	8b
3	**7c**	76.0	−19.8	94	0.71	8b
4	**7d**	76.5	−29.7	91	0.69	—
5	**7e**	84.0	−21.8	90	0.75	8a
6	**7f**	85.0	−31.7	90	0.76	8a
7	**7g**	84.8	−28.1	90	0.76	8b
8	**7h**	82.0	−17.4	76	0.63	8c
9	**7i**	52.0	−8.1	21	0.09	8c
10	**7j**	42.6	−6.4	7	0.03	8f
11	**7k**	20.0	−2.8	10	0.02	8e

[a] *c* 1.0, EtOH.
[b] At 25 °C.
[c] % Enantiomeric excess (ee) of the liberated amines determined by HPLC analysis [Daicel Crownpak CR(+)].
[d] Product of the yield of the diastereomeric salt and ee of the amine.

In order to further verify the hypothesis, hydrogen phthalate derivative **3**, bearing bulky diphenyl substituents, was treated with selected racemic amines **7a**–**c**,**g**–**i**,**k** by boiling in 2-propanol and allowed the solution to cool gradually to −10 °C for 12–48 h to obtain the corresponding less soluble diastereomeric salts **3**·(*S*)-**7a**–**c**,**g**–**i**, respectively, in low yields. Resolving agent **3** did not form any precipitate with **7k**. Salts **3**·(*S*)-**7a**–**c**,**g**–**i** were decomposed to isolate the corresponding (*S*)-1-arylalkylamines **7a**–**c**,**g**–**i** in 4–35% ee and poor yields (Table 3). Thus, compared to resolving agents **1** and **2**, the resolving agent **3** with its bulky diphenyl substituents exhibited a very low resolving efficiency [0.03–0.17 for (*S*)-amines] (Table 3) indicating the decisive role of the bulk of substituents of the resolving agents.

Overall, it was observed that the resolving ability of **1** and **2** for 1-arylalkylamines **7a**–**h** is very slight, but there is a considerable difference against *ortho* substituted 1-arylalkylamines **7i** and **7j** (Tables 1 and 2), whereas, the corresponding glucofuranose derivative **3** with diphenyl substituents was much less efficient [0.03–0.17 for (*S*)-amines] (Table 3).

Table 3. Resolution of (*RS*)-1-arylalkylamines **7a**–**c**,**g**–**i**,**k** by **3**

Entry	(*RS*)-amine	Yield (%) diastereomeric salt	(*S*)-amine[a] $[\alpha]_D$[b]	ee (%)[c]	Resolution efficiency[d]	Ref.
1	**7a**	75.0	−3.6	11	0.08	8a
2	**7b**	49.0	−7.0	35	0.17	8b
3	**7c**	66.0	−2.7	13	0.09	8b
4	**7g**	58.0	−1.8	6	0.03	8b
5	**7h**	61.0	−1.8	8	0.05	8c
6	**7i**	68.0	−1.5	4	0.03	8c
7	**7k**	—	—	—	—	

[a] *c* 1.0, EtOH.
[b] At 25 °C.
[c] % Enantiomeric excess (ee) of the liberated amines determined by an HPLC analysis [Daicel Crownpak CR(+)].
[d] Product of the yield of the diastereomeric salt and ee of the amine.

The resolving efficiency of **1** and **2** was superior to 5-(1,2-*O*-isopropylidene-3,6-anhydro-α-D-glucofuranosyl)-hydrogen phthalate and 6-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyrano-syl)-hydrogen phthalate developed earlier by us.[7] The resolving efficiency of **1** and **2** could be interpreted on the basis of conformational rigidity, leading to a 'chiral cavity'. In the case of **1** the hydrogen phthalate aligns over the 2,2′-dimethyl-1,3-dioxolane of C_5–C_6 of the glucofuranose creating a

chiral cavity for recognition of the (*S*)-base.[10] In the case of compound **2**, cyclohexylidene groups provide a much more rigid structure favouring a rigid chiral cavity thereby exhibiting a slightly higher resolving efficiency than **1**. However, the bulky cyclohexylidene group hinders the approach of *ortho*-substituted base (Table 2, entries 9 and 10). Attempts to obtain crystalline diastereomeric salts suitable, for single crystal X-ray crystallography to justify the hypothesis, were unsuccessful. The low resolving efficiency of **3** was in agreement with the finding. The conformational rigidity combined with the optimum steric bulk, is responsible for achieving good resolution efficiency. The establishment of these factors plays a critical role in designing a chiral resolving agent.

3. Conclusion

In conclusion, we have found that the hydrogen phthalates of glucofuranose derivatives **1** and **2** were suitable resolving agents for 1-arylalkylamines. The optimum bulk of substituents played a major role in recognition phenomena. Increasing the bulk of the substituents from isopropylidene to cyclohexylidene did not affect the efficiency in resolving less hindered *para*- and *meta*-substituted 1-arylalkylamines, whereas, the corresponding *ortho*-substituted 1-alkylarylamines were affected. Resolving agent **3** which bore bulky diphenyl substituents was not an efficient resolving agent. These results suggest that increasing the bulk of substituents contributes to undoing the otherwise positive implications of chiral recognition, it impedes the acidic and basic functional groups to be proximal to react and to render themselves asymmetric. The precise reason for chiral recognition needs to be evaluated further.

4. Experimental

4.1. Materials and methods

^{1}H NMR spectra were recorded on a BRUKER Avance (300 MHz) instrument. Chemical shift values are expressed in ppm values on the δ scale. IR spectra were scanned on Perkin–Elmer 683 or 1310 spectrometer with sodium chloride optics. Optical rotations were determined on a JASCO DIP 370 digital polarimeter. Thin layer chromatography was carried out using E. Merck 0.25 mm silica gel plates. Spots were visualized by UV light or by treatment with 2% phosphomolybdic acid in 15% aq H_2SO_4 solution and heating on a hot plate. Melting point was recorded on Buchi 535 melting apparatus and is uncorrected. All solvents used were freshly distilled. Mass spectra were recorded on a VG Micromass 7070H and Finnigan Mat 1020B Mass spectrometers operating at 70 eV using a direct inlet probe. HPLC analytical method: Ee was determined by reverse-phase chiral HPLC analysis on a Crownpak CR (+) column from Daicel at λ 254 nm wavelength and a flow rate of 0.8 mL/min (elutant: aq $HClO_4$ and 10% methanol at pH 1.3).

4.2. 3-(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl)-hydrogen phthalate 1

A solution of diacetone glucose (25.0 g, 0.096 mol), phthalic anhydride (28.46 g, 0.19 mol) and pyridine (31.1 mL, 0.36 mol) in ethylene chloride (125 mL) was heated to 90 °C for 4 h. After completion of the reaction, the reaction mixture was diluted with ethylene chloride (500 mL), transferred to a separatory funnel and washed with 2 M H_2SO_4 (245 mL). The organic phase was separated, washed with water (3×200 mL) and extracted into saturated aq $NaHCO_3$ (375 mL). The aqueous sodium bicarbonate layer was separated, washed with ethylene chloride (2×50 mL), neutralized with 2% HCl (200 mL) and extracted into ethylene chloride (2×150 mL). The organic phase was separated, dried (anhydrous Na_2SO_4) and concentrated to obtain the title compound in 69% yield (27.24 g); mp 155–157 °C; $[\alpha]_D^{25} = -9.5$ (*c* 1.0, EtOH); ν_{max} (KBr) 3150, 3100, 2995, 2900, 1750, 1720, 1670, 1660, 1590, 1580, 1370 and 1250 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.90–7.50 (m, 4H, Ar-H), 5.84 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.35 (d, 1H, $J_{3,4}$ 2.7 Hz, H-3), 4.73 (d, 1H, H-2), 4.30–4.00 (m, 4H, H-4,5,6,6′), 1.53, 1.47, 1.33, 1.29 (4s, 12H, $2 \times CMe_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.9, 166.7, 132.7, 132.1, 131.0, 130.1, 129.7, 128.7, 112.9, 110.0, 104.8, 81.6, 79.9, 76.6, 72.1, 67.0, 25.5, 24.8, 23.9, 23.1; FABMS *m*/*z* 408 (M^+). Anal. Calcd for $C_{20}H_{24}O_9$ (408.14): C, 58.82; H, 5.92. Found: C, 58.61; H, 5.94.

4.3. 3-(1,2:5,6-Di-*O*-cyclohexylidine-α-D-glucofuranosyl)-hydrogen phthalate 2

A solution of 1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranose (20.0 g, 0.06 mol) and phthalic anhydride (17.8 g, 0.12 mol), pyridine (19 mL, 0.22 mol) in ethylene chloride (76 mL) was heated to 90 °C for 4 h. After completion of the reaction, it was diluted with ethylene chloride (150 mL) and washed with 2 M H_2SO_4 (170 mL). The organic phase was separated and washed with aq sodium bicarbonate (150 mL) and water (200 mL). The organic phase was separated and passed over a bed of active carbon and concentrated to obtain the title compound in 82% yield (23.49 g) as a solid; mp 60–62 °C; $[\alpha]_D^{25} = -7.2$ (*c* 1.0, EtOH); ν_{max} (KBr): 3130, 3050, 2930, 2850, 1750, 1720, 1600, 1570, 1280 and 1260 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.90–7.50 (m, 4H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.9 Hz, H-1), 5.32 (d, 1H, $J_{3,4}$ 2.9 Hz, H-3), 4.72 (d, 1H, H-2), 4.25–3.80 (m, 4H, H-4,5,6,6′), 1.80–1.20 (m, 20H, $2 \times C_6H_{10}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.5, 166.0, 132.1, 131.2, 130.1, 129.1, 128.7, 128.0, 112.5, 109.0, 104.2, 81.2, 78.7, 76.4, 71.7, 66.8, 36.5, 36.2, 35.2, 34.0, 24.3, 23.9, 22.4, 22.1; FABMS *m*/*z* 488 (M^+). Anal. Calcd for $C_{26}H_{32}O_9$ (488.20): C, 63.92; H, 6.60. Found: C, 63.74; H, 6.62.

4.4. 3-(1,2-*O*-Cyclohexylidene-5,6-*O*-diphenylmethylidene-α-D-glucofuranosyl)-hydrogen phthalate 3

A suspension of 1,2-*O*-cyclohexylidine-5,6-*O*-diphenylmethylidene-α-D-glucofuranose (60 g, 0.14 mol), phtha-

lic anhydride (42.4 g, 0.28 mol) and Et_3N (148 mL, 1.10 mol) was refluxed for 3 h. The reaction mixture was diluted with CH_2Cl_2 (300 mL), washed with 10% aq HCl (2 × 120 mL), water and filtered through a bed of active carbon (12 g). The filtrate was concentrated to obtain the title compound **3** (73.7 g, 91%) as a colourless solid; mp 89–90 °C; $[\alpha]_D^{25} = -43.2$ (*c* 1.0, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.90–7.10 (m, 14H, Ar-H), 5.83 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 5.50 (d, 1H, $J_{3,4}$ 2.8 Hz, H-3), 4.73 (d, 1H, H-2), 4.40–4.00 (m, 4H, H-4,5,6,6′) 1.70–1.30 (m, 10H, C_6H_{10}); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 171.7, 166.6, 141.9, 132.4, 131.1, 129.8, 128.7, 128.1, 125.9, 113.1, 109.8, 104.8, 82.1, 79.7, 77.5, 72.8, 68.3, 36.2, 35.6, 24.8, 23.7, 23.4; FABMS *m*/*z* 572 (M^+). Anal. Calcd for $C_{33}H_{32}O_9$ (572.20): C, 69.22; H, 5.63. Found: C, 68.96; H, 5.67.

4.5. 1,2-*O*-Cyclohexylidine-5,6-*O*-diphenylmethylidene-α-D-glucofuranose 6

To a solution of 1,2-*O*-cyclohexylidine-α-D-glucofuranose (50 g, 0.19 mol) in CH_2Cl_2 (250 mL), Et_3N (76 mL, 0.56 mol) was added 1,1-dichlorodiphenylmethane (45.0 g, 0.19 mol) and refluxed for 6 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with 10% aq HCl (40 mL) and water (50 mL). The organic phase was separated, dried over Na_2SO_4, concentrated to a residue and triturated with hexane to obtain the title compound (65.6 g, 80%); Mp 177–179 °C; $[\alpha]_D^{25} = +30.8$ (*c* 1.0, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.50–7.25 (m, 10H, Ar-H), 5.89 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 4.48 (d, 1H, H-2), 4.45–4.30 (m, 2H, H-3,4), 4.20–4.00 (m, 3H, H-5,6,6′), 2.18 (d, 1H, OH), 1.70–1.35 (m, 10H, C_6H_{10}); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 141.6, 132.3, 130.0, 128.3, 126.3, 112.5, 110.1, 104.8, 84.7, 81.2, 75.1, 73.7, 68.3, 36.4, 35.7, 24.8, 23.8, 23.5; FABMS *m*/*z* 424 (M^+). Anal. Calcd for $C_{25}H_{28}O_6$ (424.19): C, 70.74; H, 6.65. Found: C, 70.84; H, 6.71.

4.6. (*S*)-1-Phenylethylamine (*S*)-7a by resolution with 1

The resolving agent **1** (6.65 g, 16.3 mmol) and amine **7a** (1.97 g, 16.3 mmol) were combined in methanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly to about 5 °C for 8 h to yield a white precipitate of **1**·(*S*)-**7a** salt (3.31 g, 76.8% of theoretical amount); mp 159–160 °C; $[\alpha]_D^{25} = -42.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.80–7.20 (m, 9H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.39 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.83 (d, 1H, H-2), 4.35–3.90 (m, 5H, H-4,5,6,6′, C*H*Me), 1.63 (d, 3H, CH*Me*), 1.52, 1.39, 1.31, 1.28 (4s, 12H, 2 × CMe_2). Salt **1**·(***S***)-**7a** was decomposed by treatment with 10% aq HCl and CH_2Cl_2. The aqueous phase was separated, made alkaline with 1 N NaOH, extracted into chloroform, dried over Na_2SO_4 and concentrated to give (*S*)-**7a** (0.76 g, 76.8% of theoretical amount) as an oil; $[\alpha]_D^{25} = -29.9$ (*c* 1.0, EtOH); ee of (*S*)-**7a** 90% (by HPLC method described in Section 4.1).

4.7. (*S*)-1-Phenylpropylamine (*S*)-7b by resolution with 1

Compounds **1** (8.98 g, 22.0 mmol) and **7b** (2.97 g, 22.0 mmol) were combined in methanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly to about 5 °C for 8 h to yield a white precipitate of **1**·(*S*)-**7b** salt (4.85 g, 81.2% of theoretical amount); mp 140–141 °C; $[\alpha]_D^{25} = -24.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.80–7.25 (m, 9H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.38 (d, 1H, $J_{3,4}$ 2.5 Hz, H-3), 4.85 (d, 1H, H-2), 4.80–3.80 (m, 5H, H-4,5,6,6′, PhC*H*), 2.20–1.65 (m, 2H, CH_2Me), 1.57, 1.41, 1.33, 1.29 (4s, 12H, 2 × CMe_2), 0.86 (t, 3H, *J* 6.0 Hz, CH_2*Me*). Salt **1**·(*S*)-**7b** was decomposed as described above to give (*S*)-**7b** (1.04 g, 70% of theoretical amount) as an oil; $[\alpha]_D^{25} = -18.0$ (*c* 1.0, EtOH); ee of (*S*)-**7b** 90% (by HPLC method described in Section 4.1).

4.8. (*S*)-1-(4-Chlorophenyl)ethylamine-(*S*)-7c by resolution with 1

Compounds **1** (7.3 g, 17.8 mmol) and **7c** (2.76 g, 17.8 mmol) were combined in 2-propanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 8 h to yield a white precipitate of **1**·(*S*)-**7c** salt (3.83 g, 76.2% of theoretical amount); mp 138–139 °C; $[\alpha]_D^{25} = -31.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.75–7.20 (m, 8H, Ar-H), 5.80 (d, 1H, $J_{1,2}$ 5.9 Hz, H-1), 5.40 (d, 1H, $J_{1,2}$ 2.5 Hz, H-3), 4.82 (d, 1H, H-2), 4.45–3.85 (m, 5H, H-4,5,6,6′, C*H*Me), 1.58, 1.41, 1.35, 1.27 (4s, 12H, 2 × CMe_2), 1.54 (d, 3H, *J* 6.2 Hz, CH*Me*). Salt **1**·(*S*)-**7c** was decomposed as described above to give (*S*)-**7c** (1.02 g, 72.9% of theoretical amount) as an oil; $[\alpha]_D^{25} = -18.9$ (*c* 1.0, EtOH); ee of (*S*)-**7c** 90% (by HPLC method described in Section 4.1).

4.9. (*S*)-1-(4-Ethylphenyl)ethylamine (*S*)-7d by resolution with 1

Compounds **1** (11.2 g, 27.4 mmol) and **7d** (4.1 g 27.4 mmol) were combined in 2-propanol (22 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 6 h to yield a white precipitate of **1**·(*S*)-**7d** salt (5.66 g, 74% of theoretical amount); mp 138–140 °C; $[\alpha]_D^{25} = -43.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.60–7.00 (m, 8H, Ar-H), 5.83 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.38 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.75 (d, 1H, H-2), 4.25–3.95 (m, 5H, H-4,5,6,6′, C*H*Me), 2.57 (q, 2H, *J* 6.6 Hz, CH_2Me), 1.46, 1.44, 1.37, 1.24 (4s, 12H, 2 × CMe_2), 1.10 (t, 3H, CH_2*Me*), 1.07 (d, 3H, *J* 6.2 Hz, CH*Me*). Salt **1**·(*S*)-**7d** was decomposed as described above to give (*S*)-**7d** (1.43 g, 71.5% of theoretical amount) as an oil; $[\alpha]_D^{25} = -29.5$ (*c* 1.0, EtOH); ee of (*S*)-**7d** 88% (by HPLC method described in Section 4.1).

4.10. (*S*)-1-(4-Bromophenyl)ethylamine (*S*)-7e by resolution with 1

Compounds **1** (8.2 g, 20.0 mmol) and **7e** (4.0 g, 20.0 mmol) were combined in 2-propanol (20 mL) and

heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 8 h to yield a white precipitate of **1**·(*S*)-**7e** salt (5.24 g, 86% of theoretical amount); mp 126–127 °C; $[\alpha]_D^{25} = -35.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.80–7.20 (m, 8H, Ar-H), 5.85 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.40 (d, 1H, $J_{3,4}$ 2.5 Hz, H-3), 4.80 (d, 1H, H-2), 4.35–3.85 (m, 5H, H-4,5,6,6′, C*H*Me), 1.60, 1.57, 1.42, 1.22 (4s, 12H, $2 \times CMe_2$), 1.54 (d, 3H, CH*Me* merged). Salt **1**·(*S*)-**7e** was decomposed to give (*S*)-**7e** (1.53 g, 76.5% of theoretical amount) as an oil; $[\alpha]_D^{25} = -21.5$ (*c* 1.0, EtOH); ee of (*S*)-**7e** 87% (by HPLC method described in Section 4.1).

4.11. (*S*)-1-(4-Methoxyphenyl)ethylamine (*S*)-7f by resolution with 1

Compounds **1** (8.1 g, 19.8 mmol) and **7f** (3.0 g, 19.8 mmol) were combined in 2-propanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **1**·(*S*)-**7f** salt (4.53 g, 81.8% of theoretical amount); mp 156–157 °C; $[\alpha]_D^{25} = -43.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65–6.65 (m, 8H, Ar-H), 5.80 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.30 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.70 (d, 1H, H-2), 4.30–3.95 (m, 5H, H-4,5,6,6′, C*H*Me), 3.60 (s, 3H, OMe), 1.51, 1.38,1.30,1.15 (4s, 12H, $2 \times CMe_2$), 1.49 (d, 3H, CH*Me*, merged). Salt **1**·(*S*)-**7f** was decomposed to give (*S*)-**7f** (1.03 g, 71%) as an oil; $[\alpha]_D^{25} = -30.4$ (*c* 1.0, EtOH); ee of (*S*)-**7f** 86% (by HPLC method described in Section 4.1).

4.12. (*S*)-1-(4-Methylphenyl)ethylamine (*S*)-7g by resolution with 1

Compounds **1** (8.1 g, 19.8 mmol) and **7g** (2.67 g, 19.8 mmol) were combined in 2-propanol (18 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 8 h to yield a white precipitate of **1**·(*S*)-**7g** salt (4.0 g, 74% of theoretical amount); mp 134–136 °C; $[\alpha]_D^{25} = -34.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.85–7.05 (m, 8H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.8 Hz, H-1), 5.30 (d, 1H, $J_{3,4}$ 2.5 Hz, H-3), 4.90 (d, 1H, H-2), 4.40–3.80 (m, 5H, H-4,5,6,6′, C*H*Me), 2.38 (s, 3H, $ArCH_3$), 1.60 (d, 3H, $J_{1,2}$ 6.2 Hz, CH*Me*), 1.55, 1.18, 1.04, 1.00 (4s, 12H, $2 \times CMe_2$). Salt **1**·(*S*)-**7g** was decomposed to give (*S*)-**7g** (0.93 g, 70% of theoretical amount) as an oil; $[\alpha]_D^{25} = -27.1$ (*c* 1.0, EtOH); ee of (*S*)-**7g** 89% (by HPLC method described in Section 4.1).

4.13. (*S*)-1-(3-Methoxyphenyl)ethylamine (*S*)-7h by resolution with 1

Compounds **1** (7.2 g, 17.6 mmol) and **7h** (2.66 g, 17.6 mmol) were combined in 2-propanol (18 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **1**·(*S*)-**7h** salt (4.14 g, 84% of theoretical amount); mp 148–149 °C; $[\alpha]_D^{25} = -33.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.60–6.65 (m, 8H, Ar-H), 5.85 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 5.35 (d, 1H, $J_{3,4}$ 2.4 Hz, H-3), 4.70 (d, 1H, H-2), 4.30–3.95 (m, 5H, H-4,5,6,6′, C*H*Me), 3.60 (s, 3H, OMe), 1.51 (d, 3H, *J* 6.2 Hz, CH*Me*), 1.47, 1.38, 1.32, 1.11 (4s, 12H, $2 \times CMe_2$,). Salt **1**·(*S*)-**7h** was decomposed to give (*S*)-**7i** (0.97 g, 71.8% of theoretical amount) as an oil; $[\alpha]_D^{25} = -18.8$ (*c* 1.0, EtOH); ee of (*S*)-**7h** 82% (by HPLC method described in Section 4.1).

4.14. (*S*)-1-(2-Chlorophenyl)ethylamine (*S*)-7i by resolution with 1

Compounds **1** (7.3 g, 17.8 mmol) and **7i** (2.8 g, 17.8 mmol) were combined in methanol (18 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **1**·(*S*)-**7i** salt (4.0 g, 79% of theoretical amount); mp 137–139 °C; $[\alpha]_D^{25} = -45.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.70–7.10 (m, 8 H, Ar-H), 5.85 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 5.39 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.78 (q, 1H, *J* 6.2 Hz, C*H*Me), 4.65 (d, 1H, H-2), 4.35–3.90 (m, 4H, H-4,5,6,6′), 1.56 (d, 3H, CH*Me*), 1.50, 1.38, 1.31, 1.15 (4s, 12H, $2 \times CMe_2$). Salt **1**·(*S*)-**7i** was decomposed to give (*S*)-**7i** (0.99 g, 70.7% of theoretical amount) as an oil; $[\alpha]_D^{25} = -30.1$ (*c* 1.0, EtOH); ee of (*S*)-**7i** 80% (by HPLC method described in Section 4.1).

4.15. (*S*)-1-(2-Methoxyphenyl)ethylamine (*S*)-7j by resolution with 1

Compounds **1** (7.7 g, 18.8 mmol) and **7j** (2.8 g, 18.8 mmol) were combined in 2-propanol (22 mL) and heated to boiling temperature for 15 min. The resulting solution was allowed to cool and maintained at 5 °C for 26 h to yield a white precipitate of **1**·(*S*)-**7j** salt (4.4 g, 84% of theoretical amount); mp 159–161 °C; $[\alpha]_D^{25} = -92.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65–6.60 (m, 8H, Ar-H), 5.80 (d, 1H, $J_{1,2}$ 5.5 Hz, H-1), 5.37 (d, 1H, $J_{3,4}$ 2.5 Hz, H-3), 4.70 (d, 1H, H-2), 4.30–3.95 (m, 5H, H-4,5,6,6′, C*H*Me), 3.64 (s, 3H, OMe), 1.54 (d, 3H *J* 6.2 Hz, CH*Me*), 1.48, 1.37, 1.33, 1.14 (4s, 12H, $2 \times CMe_2$,). Salt **1**·(*S*)-**7j** was decomposed to give (*S*)-**7j** (0.99 g 71% of theoretical amount) as an oil; $[\alpha]_D^{25} = -62.6$ (*c* 1.0, EtOH); ee of (*S*)-**7j** 73% (by HPLC method described in Section 4.1).

4.16. (*S*)-1-Phenylbutylamine (*S*)-7k by resolution with 1

Compounds **1** (7.2 g, 17.6 mmol) and **7k** (2.62 g, 17.6 mmol) were combined in 2-propanol (18 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h after which it failed to form a precipitate. However, prolonged cooling at −10 °C gave salt **1**·(*S*)-**7k** that was filtered and decomposed to give (*S*)-**7k** (0.25 g, 20% of theoretical amount) as an oil; $[\alpha]_D^{25} = -2.3$ (*c* 1.0, EtOH); ee of (*S*)-**7k** 11%.

4.17. (*S*)-1-Phenylethylamine (*S*)-7a by resolution with 2

Compounds **2** (8.4 g, 17.2 mmol) and **7a** (2.10 g, 17.2 mmol) were combined in methanol (18 mL) and

heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **2**·(*S*)-**7a** salt (4.2 g, 80% of theoretical amount); mp 170–171 °C; $[\alpha]_D^{25} = -40.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.90–7.20 (m, 9H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.9 Hz, H-1), 5.32 (d, 1H, $J_{3,4}$ 2.9 Hz, H-3), 4.92 (d, 1H, H-2), 4.38 (q, 1H, *J* 6.2 Hz, C*H*Me), 4.20–3.85 (m, 4H, H-4,5,6,6′), 1.80–1.20 (m, 23H, $2 \times C_6H_{10}$, CH*Me*). Salt **2**·(*S*)-**7a** was decomposed to give (*S*)-**7a** (0.86 g, 82% of theoretical amount) as an oil; $[\alpha]_D^{25} = -31.2$ (*c* 1.0, EtOH); ee of (*S*)-**7a** 95% (by HPLC method described in Section 4.1).

4.18. (*S*)-1-Phenylpropylamine (*S*)-7b by resolution with 2

Compounds **2** (9.2 g, 18.8 mmol) and **7b** (2.54 g, 18.8 mmol) were combined in methanol (23 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **2**·(*S*)-**7b** salt (4.87 g, 83% of theoretical amount); mp 148–149 °C; $[\alpha]_D^{25} = -27.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65–7.20 (m, 9H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 5.40 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.70 (d, 1H, H-2), 4.37 (t, 1H, *J* 5.8 Hz, PhC*H*), 4.20–3.90 (m, 4H, H-4,5,6,6′), 2.05–1.20 (m, 22H, $2 \times C_6H_{10}$, CH_2Me), 0.80 (t, 3H, *J* 6.3 Hz, CH_2Me). Salt **2**·(*S*)-**7b** was decomposed to give (*S*)-**7b** (0.97 g, 77.6% of theoretical amount) as an oil; $[\alpha]_D^{25} = -18.9$ (*c* 1.0, EtOH); ee of (*S*)-**7b** 94% (by HPLC method described in Section 4.1).

4.19. (*S*)-1-(4-Chlorophenyl)ethylamine (*S*)-7c by resolution with 2

Compounds **2** (8.2 g, 16.8 mmol) and **7c** (2.61 g, 16.8 mmol) were combined in 2-propanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 28 h to yield a white precipitate of **2**·(*S*)-**7c** salt (4.1 g, 76% of theoretical amount); mp 121–122 °C; $[\alpha]_D^{25} = -35.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.70–7.00 (m, 8H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 5.40 (d, 1H, $J_{3,4}$ 2.9 Hz, H-3), 4.65 (d, 1H, H-2), 4.40–3.90 (m, 5H, H-4,5,6,6′, C*H*Me), 1.80–1.10 (m, 23H, $2 \times C_6H_{10}$, CH*Me*). Salt **2**·(*S*)-**7c** was decomposed to give (*S*)-**7c** (0.89 g, 68% of theoretical amount) as an oil; $[\alpha]_D^{25} = -19.8$ (*c* 1.0, EtOH); ee of (*S*)-**7c** 94% (by HPLC method described in Section 4.1).

4.20. (*S*)-1-(4-Ethylphenyl)ethylamine (*S*)-7d by resolution with 2

Compounds **2** (6.2 g, 12.7 mmol) and **7d** (1.9 g, 12.7 mmol) were combined in 2-propanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **2**·(*S*)-**7d** salt (3.1 g 76.5% of theoretical amount); mp 155–157 °C; $[\alpha]_D^{25} = -29.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.60–7.00 (m, 8H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 5.45 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.70 (d, 1H, H-2), 4.45–4.00 (m, 5H, H-4,5,6,6′, C*H*Me), 2.58 (q, 2H, *J* 6.6 Hz, CH_2Me), 1.80–1.25 (m, 20H, $2 \times C_6H_{10}$, CH*Me*), 1.19 (t, 3H, CH_2Me). Salt **2**·(*S*)-**7d** was decomposed to give (*S*)-**7d** (0.66 g, 69% of theoretical amount) as an oil; $[\alpha]_D^{25} = -29.7$ (*c* 1.0, EtOH); ee of (*S*)-**7d** 91% (by HPLC method described in Section 4.1).

4.21. (*S*)-1-(4-Bromophenyl)ethylamine (*S*)-7e by resolution with 2

Compounds **2** (7.3 g, 14.9 mmol) and **7e** (3.0 g, 14.9 mmol) were combined in 2-propanol (22 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 36 h to yield a white precipitate of **2**·(*S*)-**7e** salt (4.32 g, 84% of theoretical amount); mp 116–118 °C; $[\alpha]_D^{25} = -35.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65–7.20 (m, 8H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 5.45 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.65 (d, 1H, H-2), 4.40–4.00 (m, 5H, H-4,5,6,6′, C*H*Me), 1.80–1.20 (m, 23H, $2 \times C_6H_{10}$, CH*Me*). Salt **2**·(*S*)-**7e** was decomposed to give (*S*)-**7e** (1.13 g 78% of theoretical amount) as an oil; $[\alpha]_D^{25} = -21.8$ (*c* 1.0, EtOH); ee of (*S*)-**7e** 90% (by HPLC method described in Section 4.1).

4.22. (*S*)-1-(4-Methoxyphenyl)ethylamine (*S*)-7f by resolution with 2

Compounds **2** (9.2 g, 18.8 mmol) and **7f** (2.83 g, 18.8 mmol) were combined in 2-propanol (22 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 36 h to yield a white precipitate of **2**·(*S*)-**7f** salt (5.1 g, 85% of theoretical amount); mp 143–144 °C; $[\alpha]_D^{25} = -38.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.60–6.60 (m, 8H, Ar-H), 5.85 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 5.40 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.65 (d, 1H, H-2), 4.35–3.90 (m, 5H, H-4,5,6,6′, C*H*Me), 3.70 (s, 3H, OMe), 1.75–1.15 (m, 23H, $2 \times C_6H_{10}$, CH*Me*). Salt **2**·(*S*)-**7f** was decomposed to give (*S*)-**7f** (1.13 g 80.7% of theoretical amount) as an oil; $[\alpha]_D^{25} = -31.7$ (*c* 1.0, EtOH); ee of (*S*)-**7f** 90% (by HPLC method described in Section 4.1).

4.23. (*S*)-1-(4-Methylphenyl)ethylamine (*S*)-7g by resolution with 2

Compounds **2** (7.1 g, 14.5 mmol) and **7g** (1.95 g, 14.5 mmol) were combined in 2-propanol (22 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 36 h to yield a white precipitate of **2**·(*S*)-**7g** salt (3.84 g 84.8% of theoretical amount); mp 148–149 °C; $[\alpha]_D^{25} = -40.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.80–7.10 (m, 8H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 5.32 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.64 (d, 1H, H-2), 4.40–3.80 (m, 5H, H-4,5,6,6′, C*H*Me), 2.40 (s, 3H, Ar-Me), 1.80–1.20 (m, 23H, $2 \times C_6H_{10}$, CHMe). Salt **2**·(*S*)-**7g** was decomposed to give (*S*)-**7g** (0.75 g, 77% of theoretical amount) as an oil; $[\alpha]_D^{25} - 28.1$ (*c* 1.0, EtOH); ee of (*S*)-**7g** 90% (by HPLC method described in Section 4.1).

4.24. (*S*)-1-(3-Methoxyphenyl)ethylamine (*S*)-7h by resolution with 2

Compounds **2** (6.2 g, 12.7 mmol) and **7h** (1.9 g, 12.7 mmol) were combined in 2-propanol (22 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 36 h to yield a white precipitate of **2**·(*S*)-**7h** salt (3.33 g, 82% of theoretical amount); mp 165–168 °C; $[\alpha]_D^{25} = -33.0$ (*c* 1.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.60–6.75 (m, 8H, Ar-H), 5.90 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 5.45 (d, 1H, $J_{3,4}$ 2.6 Hz, H-3), 4.70 (d, 1H, H-2), 4.35–4.00 (m, 5H, H-4,5,6,6′, C*H*Me), 3.65 (s, 3H, OMe), 1.80–1.20 (m, 23H, $2 \times C_6H_{10}$, CH*Me*). Salt **2**·(*S*)-**7h** was decomposed to give (*S*)-**7h** (0.64 g, 67% of theoretical amount) as an oil; $[\alpha]_D^{25} = -17.4$ (*c* 1.0, EtOH); ee of (*S*)-**7h** 76% (by HPLC method described in Section 4.1).

4.25. (*S*)-1-(2-Chlorophenyl)ethylamine (S)-7i by resolution with 2

Compounds **2** (9.76 g, 20 mmol) and **7i** (3.15 g, 20 mmol) were combined in methanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 24 h to yield a white precipitate of **2**·(*S*)-**7i** salt (3.3 g, 52% of theoretical amount); mp 157–159 °C. Salt **2**·(*S*)-**7i** was decomposed to give (*S*)-**7i** (0.7 g, 45% of theoretical amount) as an oil; $[\alpha]_D^{25} = -8.1$ (*c* 1.0, EtOH); ee of (*S*)-**7i** 21%.

4.26. (*S*)-1-(2-Methoxyphenyl)ethylamine (*S*)-7j by resolution with 2

Compounds **2** (9.2 g, 18.8 mmol) and **7j** (2.84 g, 18.8 mmol) were combined in 2-propanol (25 mL) and heated to boiling temperature for 18 min. The resulting solution was allowed to cool slowly and maintained at 5 °C for 35 h to yield a white precipitate of **2**·(*S*)-**7j** salt (2.56 g, 42.6% of theoretical amount); mp 139–141 °C. Salt **2**·(*S*)-**7j** was decomposed to give (*S*)-**7j** (0.32 g 23.4% of theoretical amount) as an oil; $[\alpha]_D^{25} = -6.4$ (*c* 1.0, EtOH); ee of (*S*)-**7j** 7% (by HPLC method described in Section 4.1).

4.27. (*S*)-1-Phenylbutylamine (*S*)-7k by resolution with 2

Compounds **2** (9.76 g, 20 mmol) and **7k** (2.98 g, 20 mmol) were combined in 2-propanol (19 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly, maintained at 5 °C for 24 h and −10 °C for 12 h to form a precipitate (1.27 g, 20% of theoretical amount); mp 125–127 °C. Salt **1**·(*S*)-**7k** was filtered and decomposed to give (*S*)-**7k** (0.29 g, 20% of theoretical amount) as an oil; $[\alpha]_D^{25} = -2.8$ (*c* 1.0, EtOH); ee of (*S*)-**7k** 10% (by HPLC method described in Section 4.1).

4.28. (*S*)-1-Phenylethylamine (*S*)-7a by resolution with 3

Compounds **3** (6.2 g, 10.8 mmol) and **7a** (1.3 g, 10.8 mmol) were combined in 2-propanol (18 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool to about 5 °C for 48 h to yield a white precipitate **3**·(*S*)-**7a** (2.74 g, 75% of theoretical amount); mp 133–134 °C; $[\alpha]_D^{25} = -68.0$ (*c* 1.0, EtOH). Salt **3**·(*S*)-**7a** was decomposed as described above to give (*S*)-**7a** (0.33 g, 51% of theoretical amount) as an oil; $[\alpha]_D^{25} = -3.6$ (*c* 1.0, EtOH); ee of (*S*)-**7a** 11% (by HPLC method described in Section 4.1).

4.29. (*S*)-1-Phenylpropylamine (*S*)-7b by resolution with 3

Compounds **3** (12.4 g, 21.6 mmol) and **7b** (2.92 g, 21.6 mmol) were combined in methanol (45 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool and maintained at 0 °C for 48 h to yield a white precipitate of **3**·(*S*)-**7b** (3.75 g, 49%); mp 123–125 °C. Salt **3**·(*S*)-**7b** was decomposed to give (*S*)-**7b** (0.28 g, 15% of theoretical amount) as an oil; $[\alpha]_D^{25} = -7.0$ (*c* 1.0, EtOH); ee of (*S*)-**7b** 35% (by HPLC method described in Section 4.1).

4.30. (*S*)-1-(4-Chlorophenyl)ethylamine (*S*)-7c by resolution with 3

Compounds **3** (6.8 g, 11.8 mmol) and **7c** (1.83 g, 11.8 mmol) were combined in 2-propanol (17 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly to about 5 °C and kept at that temperature for 48 h to yield a white precipitate **3**·(*S*)-**7c** (2.84 g, 66% of theoretical amount); mp 132–133 °C; $[\alpha]_D^{25} = -5.3$ (*c* 1.0, EtOH). Salt **3**·(*S*)-**7c** was decomposed as described above to give (*S*)-**7c** (0.55 g, 59% of theoretical amount) as an oil; $[\alpha]_D^{25} = -2.7$ (*c* 1.0, EtOH); ee of (*S*)-**7c** 13% (by HPLC method described in Section 4.1).

4.31. (*S*)-1-(4-Methylphenyl)ethylamine (*S*)-7g by resolution with 3

Compounds **3** (6.2 g, 10.8 mmol) and **7g** (1.46 g, 10.8 mmol) were combined in 2-propanol (18 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at −10 °C for 12 h to yield a white precipitate of **3**·(*S*)-**7g** (2.2 g, 58%); mp 129–131 °C. The salt was decomposed to give (*S*)-**7g** (0.11 g, 16% of theoretical amount) as oil; $[\alpha]_D^{25} = -1.8$ (*c* 1.0, EtOH); ee of (*S*)-**7g** 6%.

4.32. (*S*)-1-(3-Methoxyphenyl)ethylamine (*S*)-7h by resolution with 3

Compounds **3** (7.55 g, 13.2 mmol) and **7h** (2 g, 13.2 mmol) were combined in 2-propanol (55 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at −10 °C for 36 h to yield a white precipitate of **3**·(*S*)-**7h** salt (2.9 g, 61%); mp 154–157 °C. The salt was decomposed to give (*S*)-**7h** (0.24 g, 24% of theoretical amount) as an oil; $[\alpha]_D^{25} = -1.8$ (*c* 1.0, EtOH); ee of (*S*)-**7h** 8%.

4.33. (*S*)-1-(2-Chlorophenyl)ethylamine (*S*)-7i by resolution with 3

Compounds **3** (7.5 g, 13.1 mmol) and **7i** (2.04 g, 13.1 mmol) were combined in 2-propanol (20 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly to 5 °C for 36 h to yield a white precipitate **3**·(*S*)-**7i** (3.24 g, 68% of theoretical amount); mp 121–122 °C, $[\alpha]_D^{25} = -4.4$ (*c* 1.0, EtOH). Salt **3**·(*S*)-**7i** was decomposed as described above to give (*S*)-**7i** (0.53 g, 54% of theoretical amount) as an oil; $[\alpha]_D^{25} = -1.5$ (*c* 1, EtOH); ee of (*S*)-7i 4% (by HPLC method described in Section 4.1).

4.34. (*S*)-1-Phenylbutylamine (*S*)-7k by resolution with 3

Compounds **3** (8.58 g, 15 mmol) and **7k** (2.23 g, 15 mmol) were combined in 2-propanol (65 mL) and heated to boiling temperature for 10 min. The resulting solution was allowed to cool slowly and maintained at −10 °C for 48 h. Formation of precipitate was not observed.

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