Syntheses of optically active α-amino nitriles by asymmetric transformation of the second kind using a principle of O. Dimroth

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A mixture of solids $\mathbf{A}_s$ and $\mathbf{B}_s$ in equilibrium with the dissolved compounds $\mathbf{A}_1$ and $\mathbf{B}_1$ is transformed completely into one pure solid, say $\mathbf{B}_s$, if the dissolved compounds $\mathbf{A}_1 \rightleftharpoons \mathbf{B}_1$ are equilibrating in solution. This is applied to transform 1 : 1 mixtures of solid diastereomeric amygdalates (2-hydroxy-2-phenylacetates; mandelates) (*R*,*R*)-**3** + (*S*,*R*)-**3** prepared from racemic α-amino nitriles (*R*,*S*)-**1** with (*R*)-mandelic acid **2** into stereochemically pure single diastereomers (*R*,*R*)-**3**, or (*S*,*R*)-**3** (de > 97%) ('asymmetric transformation of the second kind by application of Dimroth's principle'). Decomposition of the amygdalates (*R*,*R*)-**3**, or (*S*,*R*)-**3**, with aqueous base affords the enantiomerically pure α-amino nitriles (*R*)-**1**, or (*S*)-**1** (ten examples). The chiral auxiliary (*R*)-mandelic acid is recovered almost quantitatively. The optically active α-amino nitriles are hydrolyzed to amides **6**, and further to α-*N*-alkylamino acids **7**. *N*-Benzylamino acids **7** are hydrogenated to α-amino acids **8**. Some of the optically active α-amino nitriles **1** are reduced to optically active 1,2-diamines **9**. In most cases, absolute configurations could be assigned by comparison of the specific rotations observed with those of authentic compounds.

Introduction

According to Kuhn equilibration $\mathbf{A}_1 \rightleftharpoons \mathbf{B}_1$ of two optically active stereoisomers $\mathbf{A}_1$ and $\mathbf{B}_1$ in solution is called an 'asymmetric transformation of the first kind' (*asymmetrische Umlagerung erster Art*). If a single stereoisomer crystallizes preferentially from a solution of two (or more) equilibrating chiral stereoisomers, the process is termed an 'asymmetric transformation of the second kind' (*asymmetrische Umlagerung zweiter Art*).[1–5] The special case of an asymmetric transformation of the second kind, in which a mixture of two solid chiral stereoisomers $\mathbf{A}_s$ and $\mathbf{B}_s$ (solubility products $L_A = [\mathbf{A}]$, $L_B = [\mathbf{B}]$) being in equilibrium with a solution of the equilibrating stereoisomers $\mathbf{A}_1 \rightleftharpoons \mathbf{B}_1$, (equilibrium constant K), is completely transformed into a single solid stereoisomer, say $\mathbf{B}_s$, was denoted by Kuhn as 'asymmetric transformation by application of a principle of Otto Dimroth'.[6,7] This principle of Dimroth is not restricted to chiral compounds but applies generally to coupled equilibria $\mathbf{A}_s \rightleftharpoons \mathbf{A}_1 \rightleftharpoons \mathbf{B}_1 \rightleftharpoons \mathbf{B}_s$ (*cf.* Fig.1).[7]

If **A** and **B** are solid diastereomers of type $\mathbf{A}_s = (\mathbf{a}\cdot\mathbf{b})_s$ and $\mathbf{B}_s = (\mathbf{a}^*\cdot\mathbf{b})_s$, where **a** and **a*** are enantiomers with respect to each other and **b** is a chiral auxiliary chemically bound to **a** and **a***, *e.g.* by salt formation, and if epimerization $\mathbf{a}_1 \rightleftharpoons \mathbf{a}^*_1$ (equilibrium constant K) occurs in solution, then, according to Dimroth's principle, for $L_A \cdot K > L_B$ a mixture of A_s and B_s should be transformed into stereochemically pure $\mathbf{B}_s$. Chemical cleavage of $\mathbf{B}_s = (\mathbf{a}^*\cdot\mathbf{b})_s$ furnishes the optically pure enantiomer **a*** together with the chiral auxiliary **b**, which may be recovered. If the amount of solvent is small, the amount of dissolved $\mathbf{A}_1 \rightleftharpoons \mathbf{B}_1$ can be neglected, that is, $\mathbf{A}_s$ is transformed into $\mathbf{B}_s$ more or less quantitatively. For $L_A \cdot K < L_B$ one ends up with pure $\mathbf{A}_s$, while for $L_A \cdot K = L_B$ neither transformation of $\mathbf{A}_s$ into $\mathbf{B}_s$ nor *vice versa* is possible. Thus, in contradiction to the opinion occasionally found in the literature (*e.g.*[8–11]), it is not necessarily the less soluble diastereomer, which crystallizes. It is the product $L_A \cdot K \neq L_B$, which determines whether $\mathbf{A}_s$ or $\mathbf{B}_s$ is formed.

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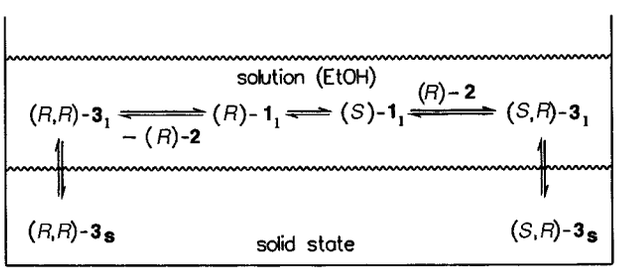


Fig. 1 Transformation of the diastereomeric amygdalates **3** by application of Dimroth's principle.

Difficulties in application of Dimroth's transformation are likely to arise if $\mathbf{A}_s$ and $\mathbf{B}_s$ form mixed crystals or solid solutions. For instance, if $\mathbf{A}_s$ and $\mathbf{B}_s$ form a mixed crystal $n_1\mathbf{A}_s \cdot n_2\mathbf{B}_s$ composed of n_1 parts of $\mathbf{A}_s$ and n_2 parts of $\mathbf{B}_s$ three different solids are involved in the equilibria described above. Application of Dimroth's principle may well result in the disappearance of both $\mathbf{A}_s$ and $\mathbf{B}_s$, in favour of the mixed crystal $n_1\mathbf{A}_s \cdot n_2\mathbf{B}_s$.

Most examples of successful asymmetric transformations of the second kind reported in the literature are of type $\mathbf{A}_1 \rightleftharpoons \mathbf{B}_1 \rightleftharpoons \mathbf{B}_s$ ('crystallization-induced asymmetric transformation'[2]). For instance, Schiff bases formed from α-amino acids and carbonyl compounds racemize under mild conditions.[12] Thus, when L-histidine was heated with one equivalent of D-tartaric acid in the presence of 0.1 equivalents of salicylaldehyde in acetic acid, the salt of D-tartaric acid and D-histidine crystallized, from which D-histidine was obtained in 95% yield with 100% optical purity.[10,11,13–16] In two patents crystallization-induced asymmetric transformations of racemic amino acid amides in the presence of aldehydes with mandelic acid as chiral auxiliary were reported.[17,18] Belokon and his group have used fast epimerization in solutions of diastereomeric transition metal complexes of amino acids for syntheses of optically enriched amino acids.[19,20] If enantiomers are quickly racemizing in an oversaturated solution, seeding with crystals of one enantiomer may induce crystallization of this optically pure enantiomer even though $L_A \cdot K = 1$.[21,22] Related to asym-

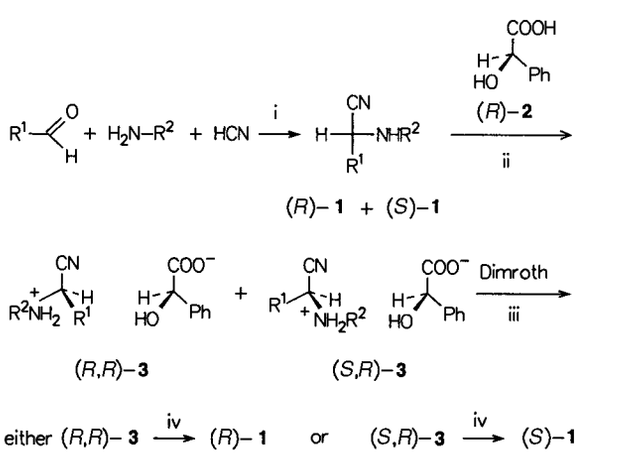
metric transformations of the second kind are 'dynamic kinetic resolutions', in which rapidly interconverting diastereomers undergo chemical reactions at different rates.[2,23]

First preparations of enantiomerically pure α-amino nitriles by application of Dimroth's principle to mixtures of diastereomers obtained by Strecker reaction of monosaccharides with amines and hydrocyanic acid were published by Kuhn *et al.*[6,24] Later, Weinges and co-workers obtained stereochemically pure diastereomeric α-amino nitriles by Strecker reaction of achiral carbonyl compounds with an optically active amine and hydrocyanic acid.[8,25,26] The high stereoselectivities observed by Kunz *et al.*, who used glycosylamines as chiral amines in Strecker syntheses, may well be caused by asymmetric transformation of the second kind although other explanations were given by the authors.[27] A patent reports asymmetric transformation of a tartrate of 2-amino-2-phenylacetonitrile,[28] and another patent describes similar transformations of 2-amino-2-phenylacetonitriles in the presence of tartaric acid and carbonyl compounds.[29]

Here we describe asymmetric transformation of the second kind by application of Dimroth's principle to amygdalates **3** of 2-amino nitriles **1**.

Results and discussion

The racemic 2-amino nitriles **1a**–**o** were prepared by Strecker synthesis from aldehydes, primary amines, and hydrocyanic acid or from azomethines and trimethylsilyl cyanide, following literature procedures.[30–41] With (*R*)-mandelic acid the amino nitriles **1a**–**k** formed crystalline 1 : 1 mixtures of the diastereomeric amygdalates (*R*,*R*)-**3** and (*S*,*R*)-**3** (Scheme 1). Stirring the



	R^1	R^2		R^1	R^2
a	Ph	$PhCH_2$	**i**	$PhCH_2$	$PhCH_2$
b	4-MeC_6H_4	$PhCH_2$	**j**	Et_2CH	Pr^i
c	4-$MeOC_6H_4$	$PhCH_2$	**k**	Bu^i	Pr^i
d	4-FC_6H_4	$PhCH_2$	**l**	Ph	Ph_2CH
e	4-ClC_6H_4	$PhCH_2$	**m**	Bu^t	$PhCH_2$
f	Pr^i	$PhCH_2$	**n**	PhMeCH	$PhCH_2$
g	Bu^i	$PhCH_2$	**o**	Bu^s	$PhCH_2$
h	Et_2CH	$PhCH_2$			

Scheme 1 *Reagents and conditions*: i, either: KCN, AcOH–MeOH, 23–51 °C, 18 h, 80–97%, or CH_2Cl_2, Al_2O_3, −20 to 23 °C, 75 min; then Me_3SiCN, 23 °C, 8 h, no solvent, 74–82%; ii, EtOH; iii, 23 °C, 12 h to 15 d, 81–95%; iv, $NaHCO_3$–H_2O–Et_2O, 79–94%.

suspension of such a diastereomeric mixture at 23 °C in a small amount of ethanol for times between twelve hours and fifteen days resulted—with the exception of **3e**—in complete transformation of the solid bottom products into one crystalline diastereomer, either (*R*,*R*)-**3** or (*S*,*R*)-**3**. Isolation by filtration and decomposition of the stereochemically pure amygdalate with aqueous sodium hydrogen carbonate afforded the enantiomerically pure (ee > 97%) amino nitrile (*R*)-**1** or (*S*)-**1**.

The method is suitable for multigram preparations of optically pure α-amino nitriles **1**. For example, on addition of one mole equivalent of (*R*)-mandelic acid to a solution of 250 mmol (55.58 g) of racemic 2-benzylamino-2-phenylacetonitrile (*R*,*S*)-**1a** in 50 ml of ethanol a 1 : 1 mixture of the crystalline diastereomeric amygdalates **3a** precipitated {$[a]_D^{23}$ −60 (*c* 1; ethanol)}. The suspension was stirred at 23 °C for twelve hours, after which the solid consisted of the stereochemically pure diastereomer (*S*,*R*)-**3a** {$[a]_D^{23}$ −99 (*c* 1; ethanol)}, which was isolated in 90% yield. Decomposition of the salt with cold aqueous sodium hydrogen carbonate afforded the optically active amino nitrile (*S*)-**1a** (45.01 g, 90%) with $[a]_D^{23}$ −75 (*c* 1; CCl_4) {lit.,[42] (*S*)-**1a** $[a]_D^{23}$ −71 (*c* 1; $CHCl_3$)}. The chiral auxiliary (*R*)-mandelic acid was recovered optically pure in 97% yield. At essentially no higher cost the enantiomer (*R*)-**1a** can be prepared using commercially available (*S*)-mandelic acid as chiral auxiliary.

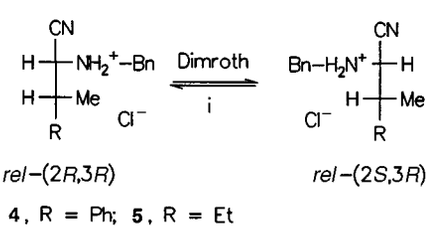
The corresponding homochiral amino nitriles **1b**–**d**, **f**–**k** were prepared (Table 1). For the amino nitriles with R^1 = alkyl the time required for complete transformation of the diastereomeric mixture of amygdalates into one diastereomer had to be extended to many days (*e.g.* **3f** required fifteen days at 23 °C).

The synthetic utility of the method is curtailed by several limitations. For example, while the *p*-fluorophenyl amygdalate (*S*,*R*)-**3d** was obtained optically pure after stirring at 23 °C for twenty four hours, the 1 : 1 mixture of the diastereomeric *p*-chlorophenyl amygdalates **3e** remained unchanged even after stirring in ethanol for many days. Possibly, the diastereomers (*R*,*R*)-**3e** and (*S*,*R*)-**3e** form a mixed crystal or a solid solution, while the diastereomers (*R*,*R*)-**3d** and (*S*,*R*)-**3d** crystallize in separate lattices (*cf.* above).

Of course, the applicability of Dimroth's principle requires crystalline amygdalates. The amygdalate **3m** was obtained as an oil, which could not be crystallized. According to the NMR spectra the amino nitrile **11** was not protonated by mandelic acid.

Another problem was encountered with diastereomeric salts formed from racemic amino nitriles **1** and (1*S*)-camphor-10-sulfonic acid. Although highly crystalline salts were obtained, attempts to transform them into one diastereomer by application of Dimroth's principle failed in all cases. A rationale could be that only the unprotonated amino nitriles **1** racemize in solution. With a weak acid such as mandelic acid **2** dissociation of the amygdalate in solution provides a sufficient concentration of the unprotonated amino nitrile **1** (Fig. 1). However, with the strong acid camphorsulfonic acid the corresponding equilibrium lies too far on the side of the protonated amino nitrile, which is sterically stable under the reaction conditions.

Still another problem arose with amino nitriles **1n**,**o** with two centers of asymmetry. The amino nitriles were obtained as 1 : 1 mixtures of the diastereomers, from which the crystalline hydrochlorides **4**,**5** were prepared (Scheme 2). When suspen-



Scheme 2 *Reagents and conditions*: i, EtOH, 60 °C, 14 d; **4**, 1 : 1 mixture of *rel*-(2*R*,3*R*)-**4** and *rel*-(2*S*,3*R*)-**4** ⟶ one pure diastereomer, 94%; **5**, 1 : 1 mixture of *rel*-(2*R*,3*R*)-**5** and *rel*-(2*S*,3*R*)-**5** ⟶ 4 : 1 mixture of the diastereomers, 89%.

sions of these hydrochlorides in ethanol were stirred at 60 °C for fourteen days the bottom solids changed their compositions. The 1 : 1 mixture of the diastereomeric hydrochlorides **4** was

Table 1 Specific rotations $[\alpha]_D^{23}$ and configurations of the optically active compounds prepared

	1[a]	**3**[b]	**6**[c]	**7**	**8**	**9**[d]	Config.[e]
a	−75[f]	−99	+71	+90[g] [+92.4[43]]	+150[h] [−156.3[28], (*R*)-**8a**]	+62	(*S*)
b	−57	−89	+80	+94[i]	+151[h] [+152.3[44]]	+67	(*S*)
c	−42	−76		+84[i]	+142[h] [+142.2[45]]	+73	(*S*)
d	−85	−91	+69	+66[i]	+95[h] [+105.5[45]]		(*S*)
e	—	−52[j]	—	—	—	—	—
f	+150	+8	+31	−11[k] [+14.1[46], (*S*)-**7f**]	−21[l] [+28.1[47], (*S*)-**8f**]	−20	(*R*)
g	+128	+4	+31	−13[l] [+13.0[48], (*S*)-**7g**]	−11[m] [−15.2[49]]	−15	(*R*)
h	+118	+8	+33	−45[l]	−34[n] [+37[50], (*S*)-**8h**]	−34	(*R*)
i	+98	−6		−24[o] [+26.9[48], (*S*)-**7i**]	+30[p] [−35.2[51], (*S*)-**8i**]		(*R*)
j	+58	−52	+37		—	—	(*R*) (?)
k	+81	−47		−34[i]	—	—	(*R*) (?)

[a] ee > 97%; *c* 1; CCl_4. [b] (*R*)-Amygdalate; ee > 97%; *c* 1; EtOH. [c] *c* 1; $CDCl_3$. [d] *c* 1; CCl_4. [e] Absolute configuration. [f] Ref. 42 $[\alpha]_D^{23}$ −71 (*c* 1; $CHCl_3$). [g] *c* 1; AcOH. [h] *c* 1; 1 M HCl. [i] *c* 1; AcOH. [j] 1:1 Mixture of the diastereomers (*S*,*R*)-**3e** and (*R*,*R*)-**3e**. [k] *c* 1; 2 M HCl. [l] *c* 2; 6 M HCl. [m] *c* 1; 5 M HCl. [n] *c* 0.5; 5 M HCl. [o] *c* 0.5; 6 M HCl–AcOH = 1:1. [p] *c* 1; H_2O.

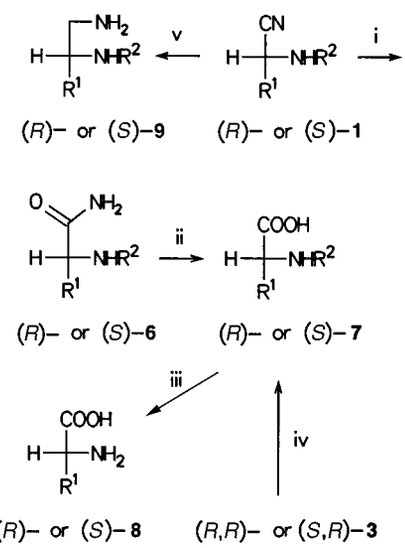
transformed into a single diastereomer (88%) of unknown configuration. However, instead of giving one stereochemically pure diastereomer, the originally 1:1 mixture of the diastereomeric hydrochlorides **5** only changed to a 4:1 mixture (89%). Further stirring at 60 °C had no influence on the composition of this mixture. An explanation could again be formation of a mixed crystal of the diastereomers or a non-ideal behaviour of the solution of **5**. For instance, the solubility products L_A,L_B of the diastereomers could be concentration dependent.

The enantiomeric purities of the optically active amino nitriles **1** were determined by NMR spectroscopy. At 250 MHz only in a few cases were the ^{1}H chemical shift differences for the diastereomeric amygdalates (*R*,*R*)-**3** and (*S*,*R*)-**3** large enough to make possible a determination of the diastereomeric composition by integration. In the ^{13}C NMR spectrum at 62.9 MHz of the 1:1 mixture of diastereomers (*R*,*R*)-**3j** and (*S*,*R*)-**3j** two resonances of equal intensity were observed for C≡N (117.9, 118.0 ppm in $CDCl_3$) as well as for the carbon atoms α to the nitrile group (48.6, 48.7 ppm). After asymmetric transformation the spectra showed only a single ^{13}C resonance for CN (118.4 ppm) as well as for the α-carbon atom (48.3 ppm). Large shift differences were observed in the NMR spectra of the diastereomeric hydrochlorides **4** and **5** (see Experimental).

The enantiomeric purities of the optically active amino nitriles **1** were determined by ^{1}H NMR spectroscopy from solutions in $CDCl_3$ after addition of (1*R*)- or (1*S*)-camphor-10-sulfonic acid. For instance, after addition of a non-stoichiometric amount of (1*R*)-camphor-10-sulfonic acid to the solution of the racemic amino nitrile **1a** in $CDCl_3$ the 250 MHz ^{1}H NMR spectrum revealed two signals of equal intensities for H–C–CN at 5.25 and 5.41 ppm. For the amino nitrile (*S*)-**1a** prepared from the amygdalate (*S*,*R*)-**3a** only a single resonance was observed at 5.40 ppm indicating that within the accuracy of the NMR method the amino nitrile (*S*)-**1a** was stereochemically pure (ee > 97%). The shift differences proved to be markedly dependent on the amount of added (1*R*)-camphor-10-sulfonic acid. It turned out that *all* α-amino nitriles **1a**–**d**, **f**–**k** set free from their amygdalates after asymmetric transformation were optically pure (ee > 97%).

No, or at best minor, shift differences could be resolved for solutions of racemic amino nitriles **1** in $CDCl_3$ in the presence of L-tartaric acid or chiral europium shift reagents.

Only a specific rotation of $[\alpha]_D^{23}$ −71 (*c* 1; $CHCl_3$) for α-amino nitrile (*S*)-**1a** has been reported in the literature.[42] Our optically active α-amino nitrile **1a** showed $[\alpha]_D^{23}$ −75 (*c* 1; $CHCl_3$) and thus has the (*S*)-configuration. In a different assault on the problem of assigning absolute configurations to the optically active amino nitriles **1** obtained, we transformed them into derivatives of known configuration (Scheme 3, Table 1). Thus, hydrolysis of the optically active amino nitriles **1** with concentrated sulfuric acid afforded the *N*-alkyl amides **6**, which were further hydrolysed in boiling 3 M hydrochloric acid to *N*-alkylated amino



Scheme 3 *Reagents and conditions*: i, conc. H_2SO_4, 0–23 °C, 12 h, 77–99%; ii, (1) 3 M HCl, reflux, 4 h, (2) NaOH, 71–96%; iii, R^2 = Bn:H_2–Pd, AcOH, 72–99%; iv, (1) conc. HCl–AcOH, reflux, 6 h, (2) NaOH, 50–94%; i, $LiAlH_4$–Et_2O, 0–23 °C, 73–93%.

acids **7**. Alternatively, the amino acids **7** were prepared by acid hydrolysis directly from the amygdalates **3**. Hydrogenation of the *N*-benzylamino acids **7a**–**d**, **f**–**i** afforded the amino acids **8a**–**d**, **f**–**i**, the specific rotations of which could be compared with values from the literature. The data of Table 1 seem to indicate that hydrolysis of the amino nitriles **1** or the amygdalates **3**, was accompanied by some racemization. Only for the *N*-isopropylamino nitriles **1j**,**k** did lack of reference data prevent unequivocal assignment of absolute configurations. Comparison of the specific rotations determined for **1j**,**k** with those found for the other α-amino nitriles **1** suggests an (*R*)-configuration in both cases.

From Table 1 it can be seen that with (*R*)-mandelic acid as chiral auxiliary, α-amino nitriles **1** with (*S*)-configuration were obtained for R^1 = aryl, and with (*R*)-configuration for R^1 = alkyl. More data are certainly required before this observation can be generalized. Also, it has to be kept in mind that, in contrast to other asymmetric syntheses, the outcome of asymmetric transformations by application of Dimroth's principle depends on the properties of the crystal lattices of the solid diastereomers, *e.g.* the amygdalates **3**, and not on properties such as steric encumbrance within dissolved molecules.

Experimental

Reactions were carried out in solvents dried by standard methods. IR spectra: Perkin-Elmer FTIR 1600. ^{1}H and ^{13}C

NMR spectra: Bruker AC-250 and WM-250 spectrometers; internal reference $SiMe_4$; δ scale; J values are given in Hz. Optical rotations: Perkin-Elmer 241 polarimeter; $[a]_\lambda$ values are in units of 10^{-1} deg cm^2 g^{-1}.

Preparation of racemic 2-aminonitriles: general procedures

Method A.[33,35,36] A solution of the amine (100 mmol) in AcOH (25 ml) was added to a stirred suspension of KCN (13.02 g, 200 mmol) and the aldehyde (100 mmol) in dry MeOH (150 ml). The mixture was subjected to ultrasonic irradiation for 18 h.[35] During this time the temperature of the ultrasonic bath rose from 23 to 51 °C. The solvent was evaporated at 23 °C and the residue was dissolved in Et_2O (80 ml). The solution was extracted with H_2O (80 ml), the ether layer was separated and the aqueous layer was extracted with Et_2O (2 × 40 ml). The combined ether extracts were neutralized with saturated aqueous $NaHCO_3$ and finally washed with H_2O (30 ml). Drying over Na_2SO_4 and evaporation of the solvent afforded the amino nitrile **1**.

Method B.[30–32,34,37,41] A solution of freshly distilled aldehyde (100 mmol) in CH_2Cl_2 (40 ml) was added to a cold (−20 °C) mixture of the amine (100 mmol) and chromatographic alumina (Merck 60) (30.60 g, 300 mmol). After stirring at −20 °C for 15 min, then at 0 °C for 1 h and finally at 23 °C for 1 h, filtration from the alumina and evaporation of the solvent afforded the Schiff base, to which at 0 °C Me_3SiCN (9.92 g, 100 mmol) was added. The mixture was stirred at 23 °C for 8 h. After dilution with Et_2O (50 ml) and addition of ice (100 g) the phases were separated and the organic phase was washed with H_2O (2 × 50 ml) and dried over Na_2SO_4. Evaporation of the solvent afforded the amino nitrile **1**.

Asymmetric transformation of the second kind of (*R*)-amygdalates 3 of racemic amino nitriles 1: general procedure

A solution of racemic **1** (50 mmol) in EtOH (10 ml) was added to a cold (0 °C) solution of (*R*)-**2** (7.61 g, 50 mmol) in EtOH (10 ml). After sonication with ultrasound for a few minutes a clear solution was obtained, from which the amygdalate (2-hydroxy-2-phenylacetate) soon started to crystallize. The mixture was kept (with stirring as long as possible) at 23 °C for the time specified. Collection by filtration and washing of the residue with cold EtOH (2 × 5 ml) followed by Et_2O (2 × 10 ml), and drying afforded crystalline powders.

Preparation of optically active amino nitriles 1 from their amygdalates 3 and recovery of the chiral auxiliary (*R*)-2: general procedure

A suspension of the diastereochemically pure amygdalate **3** (50 mmol) and $NaHCO_3$ (4.62 g, 55 mmol) in H_2O (100 ml) and Et_2O (100 ml) was shaken vigorously until a clear solution was obtained. The organic layer was separated, washed with H_2O (4 × 15 ml) and dried over Na_2SO_4. Evaporation of the solvent afforded the optically active amino nitrile, either (*R*)-**1** or (*S*)-**1**, with spectra undiscernible from those of the racemic amino nitrile (*R*,*S*)-**1**.

The combined aqueous extracts were adjusted to pH 5–6 with conc. HCl. Extraction with Et_2O (3 × 100 ml) and work-up of the combined organic extracts afforded (*R*)-**2** as a powder (*ca.* 7.38 g, 97%); $[a]_D^{23}$ −153 (*c* 1; H_2O) [(*R*)-**2** purchased from Fluka: $[a]_D^{23}$ −153 (*c* 1; H_2O)].

(*R*,*S*)-2-Benzylamino-2-phenylacetonitrile (*R*,*S*)-1a[38,39]

From benzaldehyde (10.61 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1a** was obtained as a yellow oil (20.01 g, 90%) (lit.,[38] mp 30–32 °C); $C_{15}H_{14}N_2$ (M = 222.3); ν_{max} (CCl_4)/cm^{-1} 2240, 3346; δ_H(250 MHz; $CDCl_3$) 1.86 (br, NH), 3.95 (AB-q, *J* 13.0, CH_2), 4.69 (s, CH), 7.27–7.52 (several m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 51.2, 53.4 (CH_2, CH), 118.7 (CN), 127.3, 127.6, 128.4, 128.6, 128.9, 129.0, 134.7, 138.1 (phenyl).

(*S*)-2-Benzylamino-2-phenylacetonitrile (*S*)-1a[42]

From the (*S*,*R*)-amygdalate (*S*,*R*)-**3a** (18.72 g, 50 mmol). *Title compound* (*S*)-**1a** was obtained as a powder (10.05 g, 90%); mp 49–51 °C (decomp.); $[a]_D^{23}$ −75; $[a]_{546}^{23}$ −89 (*c* 1; CCl_4) [lit.,[42] $[a]_D^{23}$ −71 (*c* 1; $CHCl_3$)].

(*R*,*S*)-2-Benzylamino-2-(4-methylphenyl)acetonitrile (*R*,*S*)-1b[39,40]

From 4-methylbenzaldehyde (12.02 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1b** was obtained as a yellow oil (21.27 g, 90%); $C_{16}H_{16}N_2$ (M = 236.3); ν_{max}(CCl_4)/cm^{-1} 2230, 3338; δ_H(250 MHz; $CDCl_3$) 1.80 (br, NH), 2.34 (CH_3), 3.96 (AB-q, *J* 13.1, CH_2), 4.67 (s, CH), 7.16–7.40 (several m, aryl); δ_C(62.9 MHz; $CDCl_3$) 21.1 (CH_3), 51.2, 53.2 (CH_2, CH), 118.9 (CN), 127.2, 127.6, 128.4, 128.6, 129.6, 131.8, 138.2, 138.9 (aryl).

(*S*)-2-Benzylamino-2-(4-methylphenyl)acetonitrile (*S*)-1b

From the (*S*,*R*)-amygdalate (*S*,*R*)-**3b** (19.43 g, 50 mmol). *Title compound* (*S*)-**1b** was obtained as a powder (9.65 g, 82%); mp 31–33 °C (decomp.); $[a]_D^{23}$ −57; $[a]_{546}^{23}$ −68 (*c* 1; CCl_4).

(*R*,*S*)-2-Benzylamino-2-(4-methoxyphenyl)acetonitrile (*R*,*S*)-1c[40]

From 4-methoxybenzaldehyde (13.62 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1c** was obtained as a yellow oil (22.46 g, 89%) (Found: C, 75.95; H, 6.38; N, 11.40. $C_{16}H_{16}N_2O$ (M = 252.3) requires C, 76.16; H, 6.39; N, 11.10%); ν_{max}(CCl_4)/cm^{-1} 2240, 3340; δ_H(250 MHz; $CDCl_3$) 1.86 (br, NH), 3.70 (CH_3), 3.87 (AB-q, *J* 13.1, CH_2), 4.58 (s, CH), 6.82–7.38 (several m, aryl); δ_C(62.9 MHz; $CDCl_3$) 51.0, 52.8, 55.2 (CH_3, CH_2, CH), 119.0 (CN), 114.2, 126.9, 127.5, 128.3, 128.5 (2 C), 138.3, 159.9 (aryl).

(*S*)-2-Benzylamino-2-(4-methoxyphenyl)acetonitrile (*S*)-1c

From the (*S*,*R*)-amygdalate (*S*,*R*)-**3c** (20.23 g, 50 mmol). *Title compound* (*S*)-**1c** was obtained as a yellow oil 10.50 g, 83%); $[a]_D^{23}$ −42; $[a]_{546}^{23}$ −49 (*c* 1; CCl_4).

(*R*,*S*)-2-Benzylamino)-2-(4-fluorophenyl)acetonitrile (*R*,*S*)-1d[39]

From 4-fluorobenzaldehyde (12.41 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1d** was obtained as a yellow oil (22.22 g, 90%) (Found: C, 74.86; H, 5.47; N, 11.35. $C_{15}H_{13}FN_2$ (M = 240.3) requires C, 74.98; H, 5.45; N, 11.66%); ν_{max}(CCl_4)/cm^{-1} 2205, 3325; δ_H(250 MHz; $CDCl_3$) 1.94 (br, NH), 3.93 (AB-q, *J* 13.0, CH_2), 4.67 (s, CH), 7.01–7.51 (several m, aryl); δ_C(62.9 MHz; $CDCl_3$) 51.1, 52.7 (CH_2, CH), 118.6 (CN), 127.7, 128.4, 128.7, 138.1 (phenyl), 115.9 (d, *J* 23, FC-*C*), 129.2 (d, *J* 8, FCC-*C*), 130.7 (d, *J* 3, FCCC-*C*), 163.0 (d, *J* 248, F-C) (aryl).

(*S*)-2-Benzylamino-2-(4-fluorophenyl)acetonitrile (*S*)-1d

From the (*S*,*R*)-amygdalate (*S*,*R*)-**3d** (19.62 g, 50 mmol). *Title compound* (*S*)-**1d** was obtained as a colourless oil (11.35 g, 94%); $[a]_D^{23}$ −85; $[a]_{546}^{23}$ −98 (*c* 1; CCl_4).

(*R*,*S*)-2-Benzylamino-2-(4-chlorophenyl)acetonitrile(*R*,*S*)-1e[39]

From 4-chlorobenzaldehyde (14.06 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1e** was obtained as a yellow oil (23.40 g, 91%) (Found: C, 69.81; H, 5.11; N, 11.18. $C_{15}H_{13}ClN_2$ (M = 256.7) requires C, 70.17; H, 5.10; N, 10.91%); ν_{max}(CCl_4)/cm^{-1} 2231,

3332; δ_H(250 MHz; $CDCl_3$) 1.96 (br, NH), 3.89 (AB-q, *J* 13.1, CH_2), 4.63 (s, CH), 7.23–7.42 (several m, aryl); δ_C(62.9 MHz; $CDCl_3$) 51.1, 52.7 (CH_2, CH), 118.3 (CN), 127.7, 128.3, 128.6, 128.7, 129.0, 133.3, 134.9, 138.0 (aryl).

(*R*,*S*)-2-Benzylamino-3-methylbutanenitrile (*R*,*S*)-1f

From 2-methylpropanal (7.21 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1f** was obtained as a yellow oil (15.25 g, 81%) (Found: C, 76.40; H, 8.77; N, 15.00. $C_{12}H_{16}N_2$ (M = 188.3) requires C, 76.55; H, 8.57; N, 14.88%); $\nu_{max}(CCl_4)/cm^{-1}$ 2240, 3350; δ_H(250 MHz; $CDCl_3$) 0.98 (d, *J* 6.8), 1.00 (d, *J* 6.7) (CH_3), 1.59 (br, NH), 1.87 (m), 3.15 (d, *J* 6.2) (CH), 3.71 (d, *J* 13.2), 3.96 (d, *J* 13.2) (CH_2), 7.16–7.32 (several m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 18.3, 19.1 (CH_3), 31.4, 51.6, 56.2 (CH_2, CH), 119.4 (CN), 127.3, 128.2, 128.4, 138.7 (phenyl).

(*R*)-2-Benzylamino-3-methylbutanenitrile (*R*)-1f

From the (*R*,*R*)-amygdalate (*R*,*R*)-**3f** (17.02 g, 50 mmol). *Title compound* (*R*)-**1f** was obtained as a colourless oil (7.44 g, 79%); $[\alpha]_D^{23}$ +150; $[\alpha]_{546}^{23}$ +180 (*c* 1; CCl_4).

(*R*,*S*)-2-Benzylamino-4-methylpentanenitrile (*R*,*S*)-1g

From 3-methylbutanal (8.61 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1g** was obtained as a yellow oil (16.39 g, 81%) (Found: C, 77.18; H, 8.87; N, 14.00. $C_{13}H_{18}N_2$ (M = 202.3) requires C, 77.18; H, 8.97; N, 13.85%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3338; δ_H(250 MHz; $CDCl_3$) 0.90 (d, *J* 6.6), 0.92 (d, *J* 6.6) (CH_3), 1.45 (br, NH), 1.64 (t, *J* 7.4, CH_2), 1.93 (m, CH), 3.52 (br m, CH), 3.82 (d, *J* 12.9), 4.05 (d, *J* 12.9) (CH_2), 7.24–7.37 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 22.1, 22.3 (CH_3), 24.9, 42.4, 48.2, 51.6 (CH_2, CH), 120.4 (CN), 127.5, 128.3, 128.6, 138.5 (phenyl).

(*R*)-2-Benzylamino-4-methylpentanenitrile (*R*)-1g

From the (*R*,*R*)-amygdalate (*R*,*R*)-**3g** (17.73 g, 50 mmol). *Title compound* (*R*)-**1g** was obtained as a yellow oil (9.50 g, 94%); $[\alpha]_D^{23}$ +128; $[\alpha]_{546}^{23}$ +152 (*c* 1; CCl_4).

(*R*,*S*)-2-Benzylamino-3-ethylpentanenitrile (*R*,*S*)-1h

From 2-ethylbutanal (10.02 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1h** was obtained as a yellow oil (18.60 g, 86%) (Found: C, 77.70; H, 9.25; N, 13.02. $C_{14}H_{20}N_2$ (M = 216.3) requires C, 77.73; H, 9.32; N, 12.95%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3346; δ_H(250 MHz; $CDCl_3$) 0.88 (t, *J* 7.2), 0.89 (t, *J* 7.2) (CH_3), 1.53 (m, 6 H, NH, 2 CH_2, CH), 3.48 (br d, *J* = 3.9, CH), 3.80 (d, *J* 13.0), 4.07 (d, *J* 13.0) (CH_2), 7.23–7.38 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 11.1, 11.2 (CH_3), 22.4 (2 C), 44.2, 51.9, 52.6 (CH_2, CH), 120.0 (CN), 127.5, 128.4, 128.5, 138.5 (phenyl).

(*R*)-2-Benzylamino-3-ethylpentanenitrile (*R*)-1h

From the (*R*,*R*)-amygdalate (*R*,*R*)-**3h** (18.43 g, 50 mmol). *Title compound* (*R*)-**1g** was obtained as a colourless oil (9.75 g, 90%); $[\alpha]_D^{23}$ +118; $[\alpha]_{546}^{23}$ +139 (*c* 1; CCl_4).

(*R*,*S*)-2-Benzylamino-3-phenylpropanenitrile (*R*,*S*)-1i

From freshly distilled phenylethanal (12.01 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according either to method A or B. *Title compound* (*R*,*S*)-**1i** was obtained as a yellow oil (method A: 18.91 g, 80%; method B: 19.34 g 82%) (Found: C, 81.34; H, 6.85; N, 12.10. $C_{16}H_{16}N_2$ (M = 236.3) requires C, 81.32; H, 6.82; N, 11.85%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3342; δ_H(250 MHz; $CDCl_3$) 1.56 (br, NH), 2.98 (m, CH_2), 3.66 (br m, CH), 3.75 (d, *J* 13.1), 3.98 (d, *J* 13.1) (CH_2), 7.23–7.31 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 39.3, 50.8, 51.4 (CH_2, CH), 119.5 (CN), 127.5, 128.2, 128.5, 128.7, 129.5, 135.2, 138.2 (phenyl).

(*R*)-2-Benzylamino-3-phenylpropanenitrile (*R*)-1i

From the (*R*,*R*)-amygdalate (*R*,*R*)-**3i** (19.43 g, 50 mmol). *Title compound* (*R*)-**1i** was obtained as a yellow oil (10.05 g, 85%); $[\alpha]_D^{23}$ +98; $[\alpha]_{546}^{23}$ +106 (*c* 1; CCl_4).

(*R*,*S*)-3-Ethyl-2-(isopropylamino)pentanenitrile (*R*,*S*)-1j

From 2-ethylbutanal (10.02 g, 100 mmol) and isopropylamine (7.01 g, 120 mmol) according to method B. *Title compound* (*R*,*S*)-**1j** was obtained as a yellow oil (12.50 g, 74%) (Found: C, 71.22; H, 11.47; N, 16.50. $C_{10}H_{20}N_2$ (M = 168.3) requires C, 71.37; H, 11.98; N, 16.65%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3350; δ_H(250 MHz; $CDCl_3$) 0.94 (t, *J* 7.1), 0.95 (t, *J* 7.3), 1.03 (d, *J* 6.1), 1.13 (d, *J* 6.3) (CH_3), 1.18 (br, NH), 1.51 (m, 5 H, CH_2, CH), 3.07 (septet, *J* 6.2), 3.60 (d, *J* 4.2) (CH); δ_C(62.9 MHz; $CDCl_3$) 11.2, 11.3, 21.3, 22.3, 22.5, 23.8, 44.6, 47.0, 50.8 (CH_3, CH_2, CH), 120.4 (CN).

(*R*)-3-Ethyl-2-(isopropylamino)pentanenitrile (*R*)-1j

From the (*R*,*R*)-amygdalate (*R*,*R*)-**3j** (16.02 g, 50 mmol). *Title compound* (*R*)-**1j** was obtained as a yellow oil (6.90 g, 82%); $[\alpha]_D^{23}$ +58; $[\alpha]_{546}^{23}$ +71 (*c* 1; CCl_4).

(*R*,*S*)-2-Isopropylamino-4-methylpentanenitrile (*R*,*S*)-1k

From 3-methylbutanal (8.61 g, 100 mmol) and isopropylamine (7.01 g, 120 mmol) according to method B. *Title compound* (*R*,*S*)-**1k** was obtained as a yellow oil (10.62 g, 74%) (Found: C, 70.15; H, 11.59; N, 18.02. $C_9H_{18}N_2$ (M = 154.3) requires C, 70.08; H, 11.76; N, 18.16%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3326; δ_H(250 MHz; $CDCl_3$) 0.95 (t, *J* 6.7), 0.96 (d, *J* 6.5), 1.04 (d, *J* 6.1), 1.12 (d, *J* 6.3) (CH_3), 1.08 (br, NH), 1.64 (m, CH_2), 1.92 (m, CH), 3.12 (septet, *J* 6.2), 3.60 (t, *J* 7.7) (CH); δ_C(62.9 MHz; $CDCl_3$) 21.3, 22.1, 22.4, 23.9, 25.0 (CH_3, CH_2), 43.0, 46.6, 47.0 (CH), 120.8 (CN).

(*R*)-2-Isopropylamino-4-methylpentanenitrile (*R*)-1k

From the (*R*,*R*)-amygdalate (*R*,*R*)-**3k** (15.32 g, 50 mmol). *Title compound* (*R*)-**1k** was obtained as a yellow oil (7.00 g, 91%); $[\alpha]_D^{23}$ +81; $[\alpha]_{546}^{23}$ +94 (*c* 1; CCl_4).

(*R*,*S*)-2-Diphenylmethylamino-2-phenylacetonitrile (*R*,*S*)-1l

From benzaldehyde (10.61 g, 100 mmol) and (diphenylmethyl)-amine (18.32 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1l** was obtained as a powder (28.99 g, 97%), which was recrystallized from EtOH; mp 98–100 °C (Found: C, 84.60; H, 6.07; N, 9.10. $C_{21}H_{18}N_2$ (M = 298.4) requires C, 84.53; H, 6.08; N, 9.39%); $\nu_{max}(CCl_4)/cm^{-1}$ 2234, 3334; δ_H(250 MHz; $CDCl_3$) 2.12 (br, d, *J* 12.3, NH), 4.56 (d, *J* 12.3), 5.23 (s) (CH), 7.19–7.57 (several m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 52.3, 65.6 (CH), 118.7 (CN), 127.1, 127.2, 127.4, 127.7, 127.9, 128.7, 128.9, 129.0, 134.9, 141.1, 142.7 (phenyl).

(*R*,*S*)-2-Benzylamino-3,3-dimethylbutanenitrile (*R*,*S*)-1m

From 2,2-dimethylpropanal (8.61 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* (*R*,*S*)-**1m** was obtained as a yellow oil (16.09 g, 80%) (Found: C, 77.06; H, 8.92; N, 13.98. $C_{13}H_{18}N_2$ (M = 202.3) requires C, 77.18; H, 8.97; N, 13.85%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3342; δ_H(250 MHz; $CDCl_3$) 1.06 (CH_3), 1.51 (br, NH), 3.08 (CH), 3.80 (d, *J* 13.2), 4.11 (d, *J* 13.2) (CH_2), 7.28–7.39 (phenyl); δ_C(62.9 MHz; $CDCl_3$) 26.2 (CH_3), 34.3, 52.2, 60.3 (CH_2, CH, C), 119.6 (CN), 127.5, 128.3, 128.5, 138.6 (phenyl).

2-Benzylamino-3-phenylbutanenitrile *rel*-[(2*R*,3*R*) and (2*R*,3*S*)]-1n

From 2-phenylpropanal (13.42 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* **1n** was obtained as a pale yellow oil (22.81 g, 91%) consisting of a 1:1 mixture of the racemic diastereomers (Found: C, 81.58; H, 7.37; N, 10.99. $C_{17}H_{18}N_2$ (M = 250.4) requires C, 81.56; H, 7.25; N, 11.19%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3338; δ_H(250 MHz; $CDCl_3$) 1.47 (d, *J* 7.1, CH_3), 3.14 (m), 3.60 (dd, *J* 6.5 and 12.0) (CH), 3.79 (dd, *J* 3.5 and 13.3), 4.00 (dd, *J* 3.8 and 13.3) (CH_2), 7.19–7.39 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$; 1:1 mixture of the diastereomers) 17.4, 18.0 (CH_3), 42.4, 42.6, 51.5, 51.6, 55.8, 55.9 (CH_2, CH), 118.9, 119.4 (CN), 127.5, 127.7, 127.8, 128.1, 128.3, 128.5, 128.7, 128.8, 138.2, 138.3, 140.2, 140.7 (phenyl).

2-Benzylamino-3-phenylbutanenitrile *rel*-[(2*R*,3*R*) or *rel*-(2*R*,3*S*)]-1n

From the hydrochloride **4** (2.86 g, 10 mmol) according to the general procedure for the preparation of optically active amino nitriles **1** from their amygdalates **3**. A single diastereomer, either *rel*-(2*R*,3*R*)-**1n** or *rel*-(2*S*,3*R*)-**1n**, was obtained as a colourless oil (2.20 g, 88%); δ_H(250 MHz; $CDCl_3$) 1.40 (br, NH), 1.47 (d, *J* 7.1, CH_3), 3.13 (m), 3.63 (d, *J* 5.8, CH), 3.79 (d, *J* 13.2), 4.00 (d, *J* 13.2) (CH_2), 7.23–7.36 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 18.0 (CH_3), 42.3, 51.5, 55.9 (CH_2, CH), 118.9 (CN), 127.5, 127.8, 128.1, 128.3, 128.6, 128.8, 138.3, 140.2 (phenyl).

2-Benzylamino-3-methylpentanenitrile *rel*-[(2*R*,3*R*) and (2*R*,3*S*)]-1o

(a) From 2-methylbutanal (8.61 g, 100 mmol) and benzylamine (10.72 g, 100 mmol) according to method A. *Title compound* **1o** was obtained as a yellow oil (18.99 g, 94%) consisting of a 1:1 mixture of racemic diastereomers (Found: C, 77.00; H, 8.98; N, 14.00. $C_{13}H_{18}N_2$ (M = 202.3) requires C, 77.18; H, 8.97; N, 13.85%); $\nu_{max}(CCl_4)/cm^{-1}$ 2227, 3346; δ_H(250 MHz; $CDCl_3$) 0.89 (t, *J* 7.3), 0.90 (t, *J* 7.4), 1.05 (d, *J* 6.7) (CH_3), 1.25–1.80 (several m, CH_2, CH, NH), 3.35 (d, *J* 5.6), 3.40 (d, *J* 5.6, CH), 3.79 (d, *J* 13.1), 3.81 (d, *J* 13.0), 4.06 (d, *J* 13.0) (CH_2), 7.23–7.37 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 11.2, 11.3, 15.2, 15.6 (CH_3), 25.4, 26.1, 37.9, 51.8, 51.9, 54.7, 55.0 (CH_2, CH), 119.4, 119.9 (CN), 127.5, 128.4, 128.5, 138.4, 138.5 (phenyl).

(b) From the hydrochloride 5 (2.29 g, 10 mmol) according to the general procedure for the preparation of optically active amino nitriles 1 from their amygdalates 3. A 4:1 mixture of the diastereomers **5** was obtained as a colourless oil (1.62 g, 80%); δ_H(250 MHz; $CDCl_3$; major component) 0.90 (t, *J* 7.4), 1.05 (d, *J* 6.7) (CH_3), 1.25–1.80 (m, CH_2, CH, NH), 3.40 (d, *J* 5.6, CH), 3.81 (d, *J* 13.0), 4.06 (d, *J* 13.0) (CH_2); δ_C(62.9 MHz; $CDCl_3$; major component) 11.2, 15.2, 26.1, 38.0, 51.9, 55.0 (CH_3, CH_2, CH), 119.4 (CN), 127.5, 128.4, 128.6, 138.5 (phenyl).

(*R*,*S*)-Benzyl[cyano(phenyl)methyl]ammonium (*R*)-amygdalate (*R*,*R*) and (*S*,*R*)-3a

A solution of racemic amino nitrile (*R*,*S*)-**1a** (2.22 g, 10 mmol) in EtOH (2 ml) was added to a stirred cold (−10 °C) solution of (*R*)-mandelic acid (*R*)-**2** (1.52 g, 10 mmol) in EtOH (2 ml). After keeping at −15 °C for 12 h a crystalline powder was collected by filtration, washed with cold EtOH (2 × 2 ml), and dried to afford 2.95 g (79%) of a 1:1 mixture of diastereomers (*R*,*R*) and (*S*,*R*)-**3a**; mp 93–95 °C (decomp.); $[\alpha]_D^{23}$ −60 (*c* 1.0; EtOH) (Found: C, 73.75; H, 5.95; N, 7.47. $C_{23}H_{22}N_2O_3$ (M = 374.4) requires C, 73.78; H, 5.92; N, 7.48%); ν_{max}(KBr)/cm^{-1} 1632, 1571; δ_H(250 MHz; $CDCl_3$:CD_3SOCD_3 4:1) 3.91 (AB-q, *J* 13.2, CH_2), 4.77, 5.08 (s, CH), 7.25–7.76 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$:CD_3SOCD_3 4:1) 50.6 (CH_2), 53.0 (CH), 72.6 (CH, mandelic acid), 118.9 (CN), 126.6, 127.2, 127.7, 128.1, 128.2, 128.3, 128.6, 128.7, 135.0, 138.4, 139.8 (phenyl), 174.6 (CO).

(*S*)-Benzyl[cyano(phenyl)methyl]ammonium (*R*)-amygdalate (*S*,*R*)-3a

Racemic amino nitrile (*R*,*S*)-**1a** (55.58 g, 250 mmol) was added in portions to a stirred solution of (*R*)-mandelic acid (*R*)-**2** (38.04 g, 250 mmol) in EtOH (50 ml). Stirring was continued at 23 °C for 12 h. Filtration and washing of the residue with cold EtOH (4 × 3 ml) followed by Et_2O (3 × 4 ml), and drying afforded *title compound* (*S*,*R*)-**3a** as a crystalline powder (83.94 g, 90%); mp 98–100° (decomp.); $[\alpha]_D^{23}$ −99; $[\alpha]_{546}^{23}$ −116 (*c* 1; EtOH). The NMR spectra were undiscernible from those of the 1:1 mixture of diastereomers (*S*,*R* and *R*,*R*)-**3a**.

(*S*)-Benzyl[cyano(4-methylphenyl)methyl]ammonium (*R*)-amygdalate (*S*,*R*)-3b

From amino nitrile (*R*,*S*)-**1b** (2.36 g, 10 mmol) following the general procedure. After 12 h at 23 °C *title compound* (*S*,*R*)-**3b** was isolated as a crystalline powder (3.46 g, 89%); mp 93–97 °C (decomp.); $[\alpha]_D^{23}$ −89; $[\alpha]_{546}^{23}$ −105 (*c* 1; EtOH) (Found: C, 73.84; H, 6.27; N, 6.92. $C_{24}H_{24}N_2O_3$ (M = 388.5) requires C, 74.21; H, 6.23; N, 7.21%); ν_{max}(KBr)/cm^{-1} 1633, 1572; δ_H(250 MHz; CD_3SOCD_3) 2.31 (CH_3), 3.79 (AB-q, *J* 13.5, CH_2), 4.94, 5.01 (CH), 7.22–7.45 (m, aryl); δ_C(62.9 MHz; CD_3SOCD_3) 20.6 (CH_3), 50.2, 52.5, 72.4 (CH_2, CH), 119.6 (CN), 126.6, 126.9, 127.2, 127.5, 127.9, 128.0, 128.2, 129.2, 132.8, 137.8, 139.2, 140.3 (aryl), 174.1 (CO).

(*S*)-Benzyl[cyano(4-methoxyphenyl)methyl]ammonium (*R*)-amygdalate (*S*,*R*)-3c

From amino nitrile (*R*,*S*)-**1c** (2.52 g, 10 mmol). After 12 h at 23 °C *title compound* (*S*,*R*)-**3c** was isolated as a crystalline powder (3.67 g, 91%); mp 75–77 °C (decomp.); $[\alpha]_D^{23}$ −76; $[\alpha]_{546}^{23}$ −91 (*c* 1; EtOH) (Found: C, 71.21; H, 5.94; N, 6.77. $C_{24}H_{24}N_2O_4$ (M = 404.5) requires C, 71.27; H, 5.98; N, 6.93%); ν_{max}(KBr)/cm^{-1} 3465, 1636, 1609, 1578; δ_H(250 MHz; CD_3SOCD_3) 3.76 (OCH_3), 3.81 (AB-q, *J* 13.5, CH_2), 4.92, 5.03 (CH), 6.97–7.47 (several m, aryl); δ_C(62.9 MHz; CD_3SOCD_3) 50.2, 52.1, 55.1, 72.4 (CH_3, CH_2, CH), 119.8 (CN), 114.0, 126.6, 126.9, 127.5, 127.7, 127.9, 128.0, 128.2, 128.6, 139.2, 140.3, 159.3 (aryl), 174.1 (CO).

(*S*)-Benzyl[cyano(4-fluorophenyl)methyl]ammonium (*R*)-amygdalate (*S*,*R*)-3d

From amino nitrile (*R*,*S*)-**1d** (2.40 g, 10 mmol), but in 5 ml of EtOH. After 24 h at 23 °C *title compound* (*S*,*R*)-**3d** was isolated as a crystalline powder (3.49 g, 89%); mp 76–78 °C (decomp.); $[\alpha]_D^{23}$ −91; $[\alpha]_{546}^{23}$ −107 (*c* 1; EtOH) (Found: C, 70.64; H, 5.41; N, 7.32. $C_{23}H_{21}FN_2O_3$ (M = 392.4) requires C, 70.40; H, 5.39; N, 7.14%); ν_{max}(KBr)/cm^{-1} 3460, 1580, 1510; δ_H(250 MHz; CD_3SOCD_3) 3.82 (AB-q, *J* 13.5, CH_2), 5.02 (2 CH), 7.22–7.84 (several m, aryl); δ_C(62.9 MHz; CD_3SOCD_3) 50.3, 52.1, 72.5 (CH_2, CH), 119.5 (CN), 115.5 (d, *J* 22, FC-*C*), 129.4 (d, *J* 9, FCC-*C*), 132.1 (d, *J* 3, FCCC-*C*), 162.0 (d, *J* 244, F-*C*), 174.2 (CO).

(*R*,*S*)-Benzyl[cyano(4-chlorophenyl)methyl]ammonium (*R*)-amygdalate (*S*,*R*)- and (*R*,*R*)-3e

From amino nitrile (*R*,*S*)-**1e** (12.84 g, 50 mmol) in the manner described for (*S*,*R*)-**3d**. Even after prolonged stirring at 23 °C no change of the optical rotation of the mixture of the diastereomers was observed. *Title compound* (*S*,*R*) and (*R*,*R*)-**3e** was isolated as a crystalline powder (19.42 g, 95%); mp 68–71 °C (decomp.); $[\alpha]_D^{23}$ −52; $[\alpha]_{546}^{23}$ −62 (*c* 1; EtOH) (Found: C, 67.44; H, 5.17; N, 6.76. $C_{23}H_{21}ClN_2O_3$ (M = 408.9) requires C, 67.56; H, 5.18; N, 6.85%); ν_{max}(KBr)/cm^{-1} 3450, 1713; δ_H(250

MHz; CD_3SOCD_3) 3.82 (AB-q, *J* 13.4, CH_2), 5.02, 5.04 (CH), 7.22–7.59 (m, aryl); δ_C(62.9 MHz; CD_3SOCD_3) 49.5, 51.3, 71.7 (CH_2, CH), 118.4 (CN), 125.7, 126.1, 126.5, 127.1, 127.4, 127.8, 128.3, 132.3, 134.0, 138.2, 139.8 (aryl), 173.4 (CO).

(*R*)-Benzyl[1-cyano-2-methylpropyl]ammonium (*R*)-amygdalate (*R*,*R*)-3f

From amino nitrile (*R*,*S*)-**1f** (1.88 g, 10 mmol) in 0.5 ml of EtOH. After 15 d at 23 °C *title compound* (*R*,*R*)-**3f** was isolated as a crystalline powder (2.32 g, 81%); mp 59–61 °C (decomp.); $[\alpha]_D^{23}$ +8; $[\alpha]_{546}^{23}$ +9 (*c* 1; EtOH) (Found: C, 70.51; H, 7.22; N, 8.08. $C_{20}H_{24}N_2O_3$ (M = 340.4) requires C, 70.57; H, 7.11; N, 8.23%); ν_{max}(KBr)/cm^{-1} 3440, 2290 (CN), 1670; δ_H(250 MHz; CD_3SOCD_3) 0.98 (d, *J* 6.4), 1.00 (d, *J* 6.3) (CH_3), 1.94 (m), 3.36 (d, *J* 6.6) (CH), 3.69 (d, *J* 13.6), 3.92 (d, *J* 13.6) (CH_2), 5.02 (OCH), 7.22–7.44 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 18.3, 19.0 (CH_3), 30.6, 50.8, 55.9, 72.3 (CH_2, CH), 119.6 (CN), 126.4, 126.7, 127.4, 127.7, 127.8, 128.0, 139.3, 140.1 (phenyl), 173.8 (CO).

(*R*)-Benzyl[1-cyano-3-methylbutyl]ammonium (*R*)-amygdalate (*R*,*R*)-3g

From amino nitrile (*R*,*S*)-**1f** (10.12 g, 50 mmol) in 12.5 ml of EtOH. After 3 d at 23 °C *title compound* (*R*,*R*)-**3g** was isolated as a crystalline powder (15.07 g, 85%); mp 102–104 °C (decomp.); $[\alpha]_D^{23}$ +4; $[\alpha]_{546}^{23}$ +4 (*c* 1; EtOH) (Found: C, 71.10; H, 7.37; N, 7.77. $C_{21}H_{26}N_2O_3$ (M = 354.5) requires C, 71.16; H, 7.39; N, 7.90%); ν_{max}(KBr)/cm^{-1} 3186, 2257 (CN), 1655; δ_H(250 MHz; CD_3SOCD_3) 0.85 (d, *J* 6.5), 0.86 (d, *J* 6.6) (CH_3), 1.60 (m, CH_2), 1.84 (m, CH), 3.58 (t, *J* 7.7, CH), 3.72 (d, *J* 13.4), 3.93 (d, *J* 13.4) (CH_2), 5.06 (CH), 7.13–7.48 (several m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 22.0 (2 C), 24.2, 41.4, 47.8, 50.7, 72.5 (CH_3, CH_2, CH), 120.8 (CN), 126.6, 126.9, 127.5, 127.9, 128.0, 128.2, 139.3, 140.3 (phenyl), 174.2 (CO).

(*R*)-Benzyl[1-cyano-2-ethylbutyl]ammonium (*R*)-amygdalate (*R*,*R*)-3h

From amino nitrile (*R*,*S*)-**1h** (10.82 g, 50 mmol). A clear solution was obtained after sonication of the suspension of the amygdalate in EtOH (2.5 ml) at 40 °C for 5 min. After 11 d at 23 °C *title compound* (*R*,*R*)-**3h** was isolated as a crystalline powder (15.29 g, 83%); mp 74–76 °C (decomp.); $[\alpha]_D^{23}$ +8; $[\alpha]_{546}^{23}$ +12 (*c* 1; EtOH) (Found: C, 71.46; H, 7.52; N, 7.38. $C_{22}H_{28}N_2O_3$ (M = 368.5) requires C, 71.71; H, 7.66; N, 7.60%); ν_{max}(KBr)/cm^{-1} 3440, 2250 (CN), 1690; δ_H(250 MHz; CD_3SOCD_3) 0.80 (t, *J* 7.3), 0.82 (t, *J* 7.0) (CH_3), 1.28–1.60 (several m, 2 CH_2, CH), 3.48 (d, *J* 5.9, CH), 3.69 (d, *J* 13.6), 3.94 (d, *J* 13.6) (CH_2), 5.03 (CH), 7.24–7.44 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 10.6, 10.8 (CH_3), 21.7, 21.9 (CH_2), 43.0, 51.0, 52.2, 72.4 (CH_2, CH), 120.2 (CN), 126.6, 126.9, 127.5, 128.0 (2 C), 128.2, 139.4, 140.3 (phenyl), 174.1 (CO).

(*R*)-Benzyl[1-cyano-2-phenylethyl]ammonium (*R*)-amygdalate (*R*,*R*)-3i

From amino nitrile (*R*,*S*)-**1i** (11.82 g, 50 mmol) in the manner described for (*R*,*R*)-**3h**. *Title compound* (*R*,*R*)-**3i** was isolated as a crystalline powder (15.73 g, 81%); mp 124–126 °C (decomp.); $[\alpha]_D^{23}$ −6; $[\alpha]_{546}^{23}$ −8 (*c* 1; EtOH) (Found: C, 73.99; H, 6.23; N, 7.10. $C_{24}H_{24}N_2O_3$ (M = 388.5) requires C, 74.21; H, 6.23; N, 7.21%); ν_{max}(KBr)/cm^{-1} 3345, 2256 (CN), 1680; δ_H(250 MHz; CD_3SOCD_3) 3.03 (m, CH_2), 3.73 (d, *J* 13.5), 3.93 (d, *J* 13.5) (CH_2), 3.88 (t, *J* 6.9), 4.98 (CH), 7.21–7.44 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 42.1, 50.5, 51.2, 72.9 (CH_2, CH), 120.1 (CN), 126.4, 126.7, 126.8, 127.7, 127.8, 128.1, 128.2, 128.4, 129.3, 136.5, 139.2, 141.7 (phenyl), 174.7 (CO).

(*R*)-[1-Cyano-2-ethylbutyl]isopropylammonium (*R*)-amygdalate (*R*,*R*)-3j

From amino nitrile (*R*,*S*)-**1j** (8.42 g, 50 mmol) in the manner described for (*R*,*R*)-**3h**. *Title compound* (*R*,*R*)-**3j** was isolated as a crystalline powder (14.10 g, 88%); mp 57–59 °C (decomp.); $[\alpha]_D^{23}$ −52; $[\alpha]_{546}^{23}$ −63 (*c* 1; EtOH) (Found: C, 67.14; H, 8.68; N, 8.54. $C_{18}H_{28}N_2O_3$ (M = 320.4) requires C, 67.47; H, 8.81; N, 8.74%); ν_{max}(KBr)/cm^{-1} 3388, 2250 (CN), 1640; δ_H(250 MHz; $CDCl_3$) 0.84 (t, *J* 7), 0.85 (t, *J* 7), 1.05 (d, *J* 6.2), 1.11 (d, *J* 6.4) (CH_3), 1.16–1.62 (several m, 5 H, 2 CH_2, CH), 3.14 (septet, *J* 6.3), 3.72 (d, *J* 4.1), 4.99 (CH), 6.75 (br, NH_2, OH), 7.23–7.35 (several m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 11.0, 11.1, 20.2, 20.3 (CH_3), 22.2, 22.5 (CH_2), 43.5, 48.3, 50.5, 73.4 (CH), 118.4 (CN), 126.6, 128.0, 128.4, 139.4 (phenyl), 177.1 (CO).

(*R*)-[1-Cyano-3-methylbutyl]isopropylammonium (*R*)-amygdalate (*R*,*R*)-3k

From amino nitrile (*R*,*S*)-**1k** (7.72 g, 50 mmol) in 8 ml of EtOH. After 2 d at 23 °C *title compound* (*R*,*R*)-**3k** was isolated as a crystalline powder (13.94 g, 91%); mp 57–59 °C (decomp.); $[\alpha]_D^{23}$ −47; $[\alpha]_{546}^{23}$ −52 (*c* 1; EtOH) (Found: C, 66.55; H, 8.44; N, 8.98. $C_{17}H_{26}N_2O_3$ (M = 306.4) requires C, 66.64; H, 8.55; N, 9.14%); ν_{max}(KBr)/cm^{-1} 3400, 1528; δ_H(250 MHz; $CDCl_3$) 0.80 (d, *J* 6.5), 0.84 (d, *J* 6.4), 1.02 (d, *J* 6.3), 1.12 (d, *J* 6.3) (CH_3), 1.42–1.76 (several m, 3 H, CH_2, CH), 3.19 (septet, *J* 6.4), 3.81 (m), 4.96 (CH), 7.25–7.38 (several m, phenyl), 7.70 (br, NH_2, OH); δ_C(62.9 MHz; $CDCl_3$) 19.0, 21.1, 21.4, 22.7, 25.0 (CH_3, CH_2), 39.8, 45.6, 48.5, 73.6 (CH), 117.2 (CN), 126.5, 127.8, 128.3, 140.0 (phenyl), 177.5 (CO).

Hydrochloride of 2-benzylamino-3-phenylbutanenitrile *rel*-[(2*R*,3*R*)-4 or *rel*-(2*S*,3*R*)]-4

At 0 °C dry HCl gas was passed into a solution of 25.00 g (100 mmol) of the 1 : 1 mixture of diastereomers **1n** in Et_2O (120 ml). After 15 min the precipitate was collected by filtration and washed with Et_2O and pentane to afford a 1 : 1 mixture of the diastereomers **4** (26.95 g, 94%); mp 148–151 °C (decomp.) (Found: C, 71.15; H, 6.72; N, 9.75. $C_{17}H_{19}ClN_2$ (M = 286.8) requires C, 71.19; H, 6.68; N, 9.77%); ν_{max}(KBr)/cm^{-1} 1436, 1455; δ_H(250 MHz; CD_3SOCD_3) 1.43 (d, *J* 7.0), 1.51 (d, *J* 7.0) (CH_3), 3.79 (m), 3.92 (m) (CH), 4.19 (AB-q, *J* 13.1), 4.28 (AB-q, *J* 12.9) (CH_2), 4.83 (br, m), 4.92 (br, m) (CH), 7.31–7.67 (several m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 15.1, 18.4 (CH_3), 38.0, 50.3, 53.7, 54.6 (CH_2, CH), 114.4, 116.6 (CN), 127.6, 127.7, 127.8, 128.1, 128.4, 128.6, 128.7, 128.9, 130.2, 130.3, 131.6, 139.5 (phenyl). A suspension of this mixture of diastereomers (5.74 g, 20 mmol) in EtOH (3 ml) was stirred at 60 °C for 14 d. Filtration of the hot suspension, washing of the residue with EtOH (2 ml) and drying afforded one pure diastereomer **4** (5.05 g, 88%) of unknown configuration; mp 154–156 °C (decomp.); δ_H(250 MHz; CD_3SOCD_3) 1.43 (d, *J* 7.0, CH_3), 3.81 (m, CH), 4.20 (AB-q, *J* 13.1, CH_2), 4.95 (br, m, CH), 7.31–7.64 (several m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 18.4 (CH_3), 38.5, 50.2, 53.6 (CH_2, CH), 116.0 (CN), 127.8, 128.1, 128.4, 128.7, 128.8, 128.9, 130.3, 139.5 (phenyl).

Hydrochloride of 2-benzylamino-3-methylpentanenitrile *rel*-[(2*R*,3*R*) and (2*S*,3*R*)]-5

From the 1 : 1 mixture of diastereomers **1o** (10.12 g, 50 mmol) in the manner described for **4**. *Title compound* **5** was obtained as a 1 : 1 mixture of the diastereomers (9.67 g, 85%); mp 131–133 °C (Found: C, 65.57; H, 8.03; N, 11.77. $C_{13}H_{19}ClN_2$ (M = 228.8) requires C, 65.40; H, 8.02; N, 11.73%); ν_{max}(KBr)/cm^{-1} 1459, 1563. A suspension of this mixture of diastereomers (4.58 g, 20 mmol) in EtOH (2 ml) was stirred at 60 °C for 14 d. Filtration of the hot suspension, washing of the residue with EtOH (2 ml) and drying afforded a 4 : 1 mixture of the diastereomers **5** (4.06 g, 89%); mp 130–132 °C; δ_H(250 MHz; $CDCl_3$) major diastereomer; 0.86 (t, *J* 7.4), 1.35 (d, *J* 6.6) (CH_3), 1.47 (m, 2 H, CH_2), 2.35 (m), 3.73 (d, *J* 4.1) (CH), 4.19 (d, *J* 13.6), 4.51 (d, *J* 13.7) (CH_2), 7.34–7.74 (several m, phenyl), 10.94 (br, NH); minor

diastereomer: 0.95 (t, *J* 7.5), 1.15 (d, *J* 6.7) (CH_3), 2.09 (br, CH_2), 2.35 (m, CH), 3.64 (d, *J* 4.9, CH), 4.19 (d, *J* 13.6), 4.53 (d, *J* 13.7) (CH_2), 7.34–7.74 (several m, phenyl), 10.94 (br, NH); δ_C(62.9 MHz; $CDCl_3$) major diastereomer: 10.9, 15.3, 26.6, 35.3, 50.2, 51.6 (CH_3, CH_2, CH), 112.5 (CN), 128.3, 129.6, 130.3, 130.9 (phenyl); minor diastereomer: 11.0, 16.0, 24.9, 35.6, 50.2, 52.2 (CH_3, CH_2, CH), 112.9 (CN), 128.4, 129.6, 130.3, 130.9 (phenyl).

Hydrolysis of the amino nitriles 1 to amides 6: general procedure

Cold (0 °C) 97% H_2SO_4 (5 ml) was added dropwise to the amino nitrile **1** (10 mmol). After stirring at 0 °C for 30 min, then at 23 °C for 12 h the mixture was poured onto ice (30 g). The mixture was adjusted to pH 9–10 with 37% aq. NH_4OH. After stirring below 10 °C for 1 h, the amide **6** was isolated by filtration.

(*S*)-2-Benzylamino-2-phenylacetamide (*S*)-6a.[52,53] From (*S*)-**1a** (2.22 g, 10 mmol). *Title compound* (*S*)-**6a** was obtained as a powder (2.39 g, 99%), which was crystallized from EtOH; mp 132–134 °C; $[\alpha]_D^{23}$ +71; $[\alpha]_{546}^{23}$ +78 (*c* 1; $CHCl_3$) (Found: C, 74.84; H, 6.82; N, 11.58. $C_{15}H_{16}N_2O$ (M = 240.3) requires C, 74.97; H, 6.71; N, 11.66%); ν_{max}(KBr)/cm^{-1} 3290, 1685; δ_H(250 MHz; CD_3SOCD_3) 2.97 (br, NH, H_2O), 3.64 (AB-q, *J* 13.7, CH_2), 4.13 (CH), 7.12 (br), 7.52 (br) ($OCNH_2$), 7.18–7.44 (several m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 50.6 (CH_2), 64.9 (CH), 126.6, 127.1, 127.2, 127.9, 128.0, 128.1, 140.1, 140.2 (phenyl), 173.9 (CO).

(*S*)-2-Benzylamino-2-(4-methylphenyl)acetamide (*S*)-6b. From (*S*)-**1b** (2.36 g, 10 mmol). *Title compound* (*S*)-**6b** was obtained as a powder (2.00 g, 79%), which was crystallized from Pr^{i}OH; mp 103–105 °C; $[\alpha]_D^{23}$ +80; $[\alpha]_{546}^{23}$ +89 (*c* 1; $CHCl_3$) (Found: C, 75.28; H, 7.15; N, 10.77. $C_{16}H_{18}N_2O$ (M = 254.3) requires C, 75.56; H, 7.13; N, 11.01%); ν_{max}(KBr)/cm^{-1} 3280, 1675; δ_H(250 MHz; CD_3SOCD_3) 2.27 (CH_3), 3.62 (AB-q, *J* 13.7, CH_2), 4.08 (CH), 7.08 (br), 7.47 (br) ($OCNH_2$), 7.10–7.32 (several m, aryl); δ_C(62.9 MHz; CD_3SOCD_3) 20.6 (CH_3), 50.6 (CH_2), 64.6 (CH), 126.6, 127.1, 127.9, 128.1, 128.6, 136.2, 137.1, 140.3 (phenyl), 174.1 (CO).

(*S*)-2-Benzylamino-2-(4-fluorophenyl)acetamide (*S*)-6d. From (*S*)-**1d** (2.40 g, 10 mmol). *Title compound* (*S*)-**6d** was obtained as a powder (2.04 g, 79%), which was crystallized from AcOEt; mp 130–132 °C; $[\alpha]_D^{23}$ +69; $[\alpha]_{546}^{23}$ +79 (*c* 1; $CHCl_3$) (Found: C, 69.62; H, 6.00; N, 10.92. $C_{15}H_{15}FN_2O$ (M = 258.3) requires C, 69.75; H, 5.85; N, 10.85%); ν_{max}(KBr)/cm^{-1} 3280, 1700; δ_H(250 MHz; $CDCl_3$) 1.08 (br, NH), 3.77 (CH_2), 4.21 (CH), 6.07 (br), 6.92 (br) ($OCNH_2$), 6.98–7.38 (several m, aryl); δ_C(62.9 MHz; $CDCl_3$) 52.3 (CH_2), 66.0 (CH), 115.8 (d, *J* 22, FC-*C*), 129.1 (d, *J* 9, FCC-*C*), 134.8 (d, *J* 3, FCCC-*C*), 162.7 (d, *J* 247, F*C*), 127.5, 128.2, 128.7, 139.1 (aryl), 174.9 (CO).

(*R*)-*N*-Benzylvalinamide (*R*)-6f. From (*R*)-**1f** (1.88 g, 10 mmol). *Title compound* (*R*)-**6f** was obtained as a powder (1.75 g, 85%), which was recrystallized from EtOH; mp 67–69 °C; $[\alpha]_D^{23}$ +31; $[\alpha]_{546}^{23}$ +40 (*c* 1; $CHCl_3$) (Found: C, 70.05; H, 8.81; N, 13.54. $C_{12}H_{18}N_2O$ (M = 206.3) requires C, 69.87; H, 8.80; N, 13.58%); ν_{max}(Nujol)/cm^{-1} 3393, 1649, 1614; δ_H(250 MHz; $CDCl_3$) 0.94 (d, *J* 7.2), 0.97 (d, *J* 7.5) (CH_3), 1.92 (br, NH), 2.04 (m), 2.94 (d, *J* 4.9) (CH), 3.63 (d, *J* 13.1), 3.81 (d, *J* 13.1) (CH_2), 6.72 (br), 7.03 (br) ($OCNH_2$), 7.21–7.34 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 18.1, 19.5 (CH_3), 31.3, 53.2, 67.9 (CH_2, CH), 127.2, 128.1, 128.5, 139.7 (phenyl), 177.2 (CO).

(*R*)-*N*-Benzylleucinamide (*R*)-6g. From (*R*)-**1g** (2.02 g, 10 mmol). *Title compound* (*R*)-**6g** was obtained as a powder (1.90 g, 86%), which was crystallized from AcOEt; mp 120–122 °C; $[\alpha]_D^{23}$ +31; $[\alpha]_{546}^{23}$ +34 (*c* 1; $CHCl_3$) (Found: C, 70.97; H, 9.14; N, 12.72. $C_{13}H_{20}N_2O$ (M = 220.3) requires C, 70.87; H, 9.15; N, 12.72%); ν_{max}(KBr)/cm^{-1} 3690, 1680, 1610; δ_H(250 MHz; CD_3SOCD_3) 0.79 (d, *J* 6.6), 0.87 (d, *J* 6.6) (CH_3), 1.33 (m, CH_2), 1.76 (m), 2.96 (t, *J* 7.2) (CH), 3.49 (d, *J* 13.5), 3.72 (d, *J* 13.5) (CH_2), 6.96 (br), 7.36 (br) ($OCNH_2$), 7.18–7.34 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3) 22.1, 23.0, 24.3, 42.8, 51.1, 59.7 (CH_3, CH_2, CH), 126.5, 127.9, 128.0, 140.7 (phenyl), 176.9 (CO).

(*R*)-2-Benzylamino-3-ethylpentanamide (*R*)-6h. From (*R*)-**1h** (2.16 g, 10 mmol). *Title compound* (*R*)-**6h** was obtained as a powder (2.06 g, 88%), which was crystallized from benzene; mp 68–70 °C; $[\alpha]_D^{23}$ +33; $[\alpha]_{546}^{23}$ +43 (*c* 1; $CHCl_3$) (Found: C, 71.92; H, 9.42; N, 11.86. $C_{14}H_{22}N_2O$ (M = 234.3) requires C, 71.76; H, 9.46; N, 11.95%); ν_{max}(KBr)/cm^{-1} 3410, 1650; δ_H(250 MHz; $CDCl_3$) 0.85 (t, *J* 7.2), 0.87 (t, *J* 7.1) (CH_3), 1.22 (m, 2H), 1.46 (m, 2H) (CH_2), 1.66 (m), 3.17 (d, *J* 3.8) (CH), 3.64 (d, *J* 13.1), 3.82 (d, *J* 13.1) (CH_2), 6.48 (br), 7.19 (br) ($OCNH_2$), 7.30 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 11.9, 12.0 (CH_3), 22.2, 23.0 (CH_2), 44.7, 53.6, 63.9 (CH_2, CH), 127.3, 128.2, 128.6, 139.8 (phenyl), 177.7 (CO).

(*R*)-3-Ethyl-2-(isopropylamino)pentanamide (*R*)-6j. From (*R*)-**1j** (1.68 g, 10 mmol). *Title compound* (*R*)-**6j** was obtained as a powder (1.43 g, 77%), which was crystallized from EtOH; mp 120–122 °C; $[\alpha]_D^{23}$ +37; $[\alpha]_{546}^{23}$ +41 (*c* 1; $CHCl_3$) (Found: C, 64.49; H, 11.86; N, 15.09. $C_{10}H_{22}N_2O$ (M = 186.3) requires C, 64.47; H, 11.90; N, 15.04%); ν_{max}(CCl_4)/cm^{-1} 3513, 1686; δ_H(250 MHz; $CDCl_3$) 0.90 (t, *J* 7.3), 0.97 (t, *J* 7.5), 1.04 (d, *J* 6.4), 1.06 (d, *J* 6.4) (CH_3), 1.20 (m, 2H), 1.46 (m, 2H) (CH_2), 1.68 (m, CH), 2.74 (br, septet, *J* 6.2), 3.15 (d, *J* 3.5) (CH), 6.32 (br), 7.41 (br) ($OCNH_2$); δ_C(62.9 MHz; $CDCl_3$) 12.1, 12.3, 22.2, 23.0, 23.1, 23.6 (CH_3, CH_2), 45.0, 49.2, 62.4 (CH), 178.8 (CO).

Hydrolysis of the amygdalates 3 or the amides 6 to amino acids 7: general procedures

Method A. A solution of the amino nitrile **1** (10 mmol) or the amygdalate **3** (10 mmol), in 37% HCl (15 ml)–AcOH (15 ml) was boiled under reflux for 6 h. The mixture was cooled to 5 °C and adjusted to pH 6–7 with 15% aq. NaOH. After stirring at 5 °C for 1 h the product was isolated by filtration, washed with cold H_2O (2 × 3 ml), dried, and recrystallized from MeOH–H_2O or MeOH.

Method B. A solution of the amide **6** (10 mmol) in 3 M HCl (15 ml) was boiled under reflux for 4 h. Work-up was as described for method A.

(*S*)-*N*-(Benzyl)phenylglycine (*S*)-7a.[43,46] From amygdalate (*S*,*R*)-**3a** (3.74 g, 10 mmol). *Title compound* (*S*)-**7a** was obtained as a powder (2.13 g, 88%), which was recrystallized from MeOH–H_2O; mp 218–220 °C; $[\alpha]_D^{23}$ +90 (*c* 1; AcOH) [lit.,[43] $[\alpha]_D^{23}$ +92.4 (*c* 1; AcOH)]; $C_{15}H_{15}NO_2$ (M = 241.3); ν_{max}(KBr)/cm^{-1} 1570; δ_H[250 MHz; CD_3CN–CF_3CO_2D (4:1)] 4.21 (br s, CH_2), 5.09 (CH), 7.45–7.56 (several m, phenyl); δ_C[62.9 MHz; CD_3CN–CF_3CO_2D (4:1)] 52.6 (CH_2), 65.0 (CH), 129.9, 130.3, 130.4, 130.9, 131.4, 131.6, 131.9, 132.9 (phenyl), 171.3 (CO).

(*S*)-*N*-Benzyl(4-methylphenyl)glycine (*S*)-7b. From amygdalate (*S*,*R*)-**3b** (3.89 g, 10 mmol). *Title compound* (*S*)-**7b** was obtained as a powder (2.40 g, 94%), which was recrystallized from MeOH–H_2O; mp 217–219 °C; $[\alpha]_D^{23}$ +94 (*c* 1; AcOH) (Found: C, 75.14; H, 6.73; N, 5.49. $C_{16}H_{17}NO_2$ (M = 255.3) requires C, 75.27; H, 6.71; N, 5.49%); ν_{max}(KBr)/cm^{-1} 1610, 1570; δ_H[250 MHz; CD_3CN–CF_3CO_2D (4:1)] 2.39 (CH_3), 4.20 (br s, CH_2), 5.03 (CH), 7.36–7.45 (several m, aryl); δ_C[62.9 MHz; CD_3CN–CF_3CO_2D (4:1)] 21.4 (CH_3), 51.9 (CH_2), 64.2 (CH), 127.3, 130.2, 130.4, 130.9, 131.3, 131.5, 131.7, 142.9 (aryl), 169.3 (CO).

(*S*)-*N*-Benzyl(4-methoxyphenyl)glycine (*S*)-7c. From amygdalate (*S*,*R*)-**3c** (4.05 g, 10 mmol). *Title compound* (*S*)-**7c** was obtained as a powder (2.42 g, 89%), which was recrystallized from MeOH; mp 186–188 °C; $[\alpha]_D^{23}$ +84 (*c* 1; AcOH) (Found: C, 70.37; H, 6.35; N, 5.21. $C_{16}H_{17}NO_3$ (M = 271.3) requires C, 70.83; H, 6.32; N, 5.16%); ν_{max}(KBr)/cm^{-1} 1580; δ_H(250 MHz; CD_3SOCD_3; 353 K) 3.69 (br s, CH_2), 3.75 (CH_3), 4.20 (CH), 6.87–7.31 (several m, aryl); δ_C(62.9 MHz; CD_3SOCD_3; 353 K) 50.5, 55.2, 63.9 (CH_3, CH_2, CH), 113.8, 126.9, 128.1, 128.2, 128.8, 130.8, 139.2, 159.0 (aryl), 172.8 (CO).

(*S*)-*N*-Benzyl(4-fluorophenyl)glycine (*S*)-7d. From amygdalate (*S*,*R*)-**3d** (3.93 g, 10 mmol). *Title compound* (*S*)-**7d** was obtained as a powder (1.91 g, 74%), which was recrystallized from MeOH; mp 253–255 °C; $[\alpha]_D^{23}$ +66 (*c* 1; AcOH) (Found: C, 69.63; H, 5.72; N, 5.26. $C_{15}H_{14}FNO_2$ (M = 259.3) requires C, 69.49; H, 5.44; N, 5.40%); ν_{max}(KBr)/cm^{-1} 1610, 1570; δ_H(250 MHz; CF_3CO_2D) 4.40 (br s, CH_2), 5.31 (br s, CH), 7.24–7.61 (several m, aryl); δ_C(62.9 MHz; CF_3CO_2D) 53.6, 64.9 (CH_2, CH), 119.5 (d, *J* 23, FC-*C*), 125.4 (d, *J* 4, FCCC-*C*), 130.1–133.0 (6 lines, phenyl, FCC-*C*), 167.2 (d, *J* 252, FC), 173.7 (CO).

(*R*)-*N*-Benzylvaline (*R*)-7f.[46,48] From amide (*R*)-**6f** (2.06 g, 10 mmol). *Title compound* (*R*)-**7f** was obtained as a powder (1.99 g, 96%), which was recrystallized from MeOH–H_2O; mp 257–259 °C; $[\alpha]_D^{23}$ −11 (*c* 1; 2 M HCl) [lit.,[46] (*S*)-isomer $[\alpha]_D^{23}$ +14.1 (*c* 1; 2 M HCl)]; [lit.,[48] $[\alpha]_D^{23}$ +20.2 (*c* 1; 6 M HCl)] (Found: C, 69.44; H, 8.33; N, 6.78. $C_{12}H_{17}NO_2$ (M = 207.3) requires C, 69.54; H, 8.27; N, 6.76%); ν_{max}(KBr)/cm^{-1} 1607; δ_H(250 MHz; CD_3SOCD_3; 353 K) 0.91 (br d, *J* 6.8, CH_3), 1.90 (m), 2.89 (d, *J* 5.6) (CH), 3.61 (d, *J* 13.4), 3.82 (d, *J* 13.4) (CH_2), 7.20–7.34 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3; 353 K) 18.4, 19.1 (CH_3), 30.6, 51.7, 66.3 (CH_2, CH), 126.8, 128.1 (2 C), 139.9 (phenyl), 174.6 (CO).

(*R*)-*N*-Benzylleucine (*R*)-7g.[48] From amide (*R*)-**6g** (2.20 g, 10 mmol). *Title compound* (*R*)-**7g** was obtained as a powder (2.08 g, 94%), which was recrystallized from MeOH; mp 228–230 °C; $[\alpha]_D^{23}$ −38 (*c* 1; AcOH); $[\alpha]_D^{23}$ −13 (*c* 2; 6 M HCl) [lit.,[48] (*S*)-isomer $[\alpha]_D^{23}$ +13.0 (*c* 2; 6 M HCl)] (Found: C, 70.49; H, 8.57; N, 6.30. $C_{13}H_{19}NO_2$ (M = 221.3) requires C, 70.56; H, 8.65; N, 6.33%); ν_{max}(KBr)/cm^{-1} 1705, 1605; δ_H(250 MHz; CD_3SOCD_3; 363 K) 0.83 (d, *J* 6.6), 0.87 (d, *J* 6.6) (CH_3), 1.45 (m, CH_2), 1.79 (m), 3.13 (t, *J* 6.7) (CH), 3.65 (d, *J* 13.3), 3.81 (d, *J* 13.3) (CH_2), 7.18–7.34 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3; 363 K) 22.2, 22.7, 24.6 (CH_3, CH_2), 41.9, 51.1, 59.2 (CH_2, CH), 126.8, 128.1 (2 C), 139.8 (phenyl), 175.3 (CO).

(*R*)-2-Benzylamino-3-ethylpentanoic acid (*R*)-7h. From amide (*R*)-**6h** (2.34 g, 10 mmol). *Title compound* (*R*)-**7h** was obtained as a powder (1.66 g, 71%), which was recrystallized from MeOH; mp 225–228 °C; $[\alpha]_D^{23}$ −45 (*c* 1; AcOH) (Found: C, 71.31; H, 8.98; N, 6.09. $C_{14}H_{21}NO_2$ (M = 235.3) requires C, 71.46; H, 8.99; N, 5.95%); ν_{max}(KBr)/cm^{-1} 1608; δ_H(250 MHz; CD_3SOCD_3; 353 K) 0.79 (t, *J* 7), 0.81 (t, *J* 7) (CH_3), 1.21–1.51 (several m, 5 H, 2 CH_2, CH), 3.08 (d, *J* 4.4) (CH), 3.58 (d, *J* 13.4), 3.83 (d, *J* 13.4) (CH_2), 7.19–7.31 (m, phenyl); δ_C(62.9 MHz; CD_3SOCD_3; 353 K) 11.3, 11.4 (CH_3), 21.9, 22.6 (CH_2), 44.1, 51.9, 62.4 (CH_2, CH), 126.8, 128.0, 128.1, 140.0 (phenyl), 175.2 (CO).

(*R*)-*N*-(Benzyl)phenylalanine (*R*)-7i.[48] From amygdalate (*R*,*R*)-**3i** (3.89 g, 10 mmol). *Title compound* (*R*)-**7i** was obtained as a powder (2.15 g, 84%), which was recrystallized from MeOH; mp 238–241 °C (decomp.); $[\alpha]_D^{23}$ −40 (*c* 1; AcOH); $[\alpha]_D^{23}$ −24 (*c* 0.5; 6 M HCl–AcOH 1:1)] [lit.,[48] (*S*)-isomer $[\alpha]_D^{23}$ +26.9 (*c* 1; 6 M HCl–AcOH 1:1)] (Found: C, 75.02; H, 6.92; N, 5.35. $C_{16}H_{17}NO_2$ (M = 255.3) requires C, 75.27; H, 6.71; N, 5.49%); ν_{max}(KBr)/cm^{-1} 1580; δ_H(250 MHz; 1 M DCl–MeCN; shifts relative to MeCN: δ = 2.00 ppm) 3.26 (m), 4.22 (s) (CH_2), 4.19 (t, *J* 6.4, CH), 7.21–7.44 (several m, phenyl); δ_C(62.9 MHz; 1 M DCl–MeCN; shifts relative to MeCN: δ = 0.0 ppm) 34.0, 49.2, 59.1 (CH_2, CH), 127.1, 128.2, 128.3 (2 C), 128.7, 128.9, 129.2, 132.5 (phenyl), 169.3 (CO).

(*R*)-*N*-Isopropylleucine (*R*)-7k.[54] From amygdalate (*R*,*R*)-**3k** (3.06 g, 10 mmol). *Title compound* (*R*)-**7k** was obtained as a powder (0.86 g, 50%), after crystallization from MeOH; mp 289–292 °C; $[\alpha]_D^{23}$ −34 (*c* 1; AcOH) (Found: C, 62.53; H, 10.97; N, 7.96. $C_9H_{19}NO_2$ (M = 173.3) requires C, 62.39; H, 11.05; N, 8.08%); ν_{max}(KBr)/cm^{-1} 1575; δ_H(250 MHz; CF_3CO_2D) 1.09 (d, *J* 6), 1.10 (d, *J* 6), 1.53 (d, *J* 6.5), 1.54 (d, *J* 6.4) (CH_3), 1.94 (m, 3 H, CH_2, CH), 3.73 (septet, *J* 6.6), 4.25 (t, *J* 6.5) (CH); δ_C(62.9 MHz; CF_3CO_2D) 19.5, 20.1, 22.1, 22.8 (CH_3), 26.7 (CH_2), 41.1, 55.4, 59.2 (CH), 175.3 (CO).

Hydrogenation of *N*-benzylamino acids 7 to amino acids 8: general procedure

A solution of the *N*-benzylamino acid **7** (10 mmol) in AcOH (50 ml) was hydrogenated over Pd–C (10%, 0.5 g) for 24 h. Filtration and evaporation of the solvent afforded powders, which were crystallized from H_2O–MeOH.

(*S*)-Phenylglycine (*S*)-8a.[28,55] From (*S*)-**7a** (2.41 g, 10 mmol). *Title compound* (*S*)-**8a** was obtained as a powder (1.38 g, 91%), which was recrystallized from MeOH–H_2O; mp >290 °C; $[\alpha]_D^{23}$ +150 (*c* 1; 1 M HCl) [lit.,[28] (*R*)-isomer $[\alpha]_D^{23}$ −156.3 (*c* 1; 1 M HCl)]; $C_8H_9NO_2$ (M = 151.2); ν_{max}(KBr)/cm^{-1} 1610, 1510; δ_H[250 MHz; CD_3CN–CF_3CO_2D (3:1)] 5.13 (CH), 7.47–7.54 (m, phenyl); δ_C[62.9 MHz; CD_3CN–CF_3CO_2D (3:1)] 58.1 (CH), 129.8, 130.8, 131.8, 131.9 (phenyl), 169.6 (CO).

(*S*)-(4-Methylphenyl)glycine (*S*)-8b.[44] From (*S*)-**7b** (2.55 g, 10 mmol). *Title compound* (*S*)-**8b** was obtained as a powder (1.63 g, 99%), which was recrystallized from MeOH–H_2O; mp >212–214 °C; $[\alpha]_D^{23}$ +151 (*c* 1; 1 M HCl) [lit.,[44] $[\alpha]_D^{23}$ +152.3 (*c* 1; 1 M HCl)]; $C_9H_{11}NO_2$ (M = 165.2); ν_{max}(KBr)/cm^{-1} 1590, 1515; δ_H[250 MHz; 1 M DCl + 1 drop of MeCN, relative to δ(MeCN) = 2.00 ppm; 313 K] 2.28 (CH_3), 5.18 (CH), 7.26–7.38 (several m, aryl); δ_C[62.9 MHz; 1 M DCl + 1 drop of MeCN, relative to δ(CH_3CN) = 0.00 ppm; 313 K] 19.4 (CH_3), 55.3 (CH), 127.0, 127.2, 129.3, 140.0 (aryl), 169.7 (CO).

(*S*)-(4-Methoxyphenyl)glycine (*S*)-8c.[44,45,55] From (*S*)-**7c** (2.71 g, 10 mmol). *Title compound* (*S*)-**8c** was obtained as a powder (1.74 g, 96%), which was recrystallized from MeOH–H_2O; mp >246–248 °C; $[\alpha]_D^{23}$ +142 (*c* 1; 1 M HCl) [lit.,[45] $[\alpha]_D^{23}$ +142.2 (*c* 1; 1 M HCl)]; $C_9H_{11}NO_2$ (M = 181.2); ν_{max}(KBr)/cm^{-1} 1740; δ_H(250 MHz; CD_3SOCD_3) 3.77 (OCH_3), 4.95 (CH), 6.97–7.46 (several m, aryl); δ_C(62.9 MHz; CD_3SOCD_3) 55.0 (CH), 55.2 (OCH_3), 114.0, 125.3, 129.5, 159.7 (aryl), 169.8 (CO).

(*S*)-(4-Fluorophenyl)glycine (*S*)-8d.[45] From (*S*)-**7d** (2.59 g, 10 mmol). *Title compound* (*S*)-**8d** was obtained as a powder (1.50 g, 89%), which was recrystallized from MeOH–H_2O; mp >252–256 °C; $[\alpha]_D^{23}$ +95 (*c* 1; 1 M HCl) [lit.,[45] $[\alpha]_D^{23}$ +105.5 (*c* 1; 1 M HCl)]; $C_8H_8FNO_2$ (M = 169.2); ν_{max}(KBr)/cm^{-1} 1590; δ_H(250 MHz; CF_3CO_2D) 5.45 (CH), 7.19–7.84 (m, aryl); δ_C(62.9 MHz; CD_3CO_2D) 59.3 (CH), 119.2 (d, *J* 23, FC-*C*), 126.6 (d, *J* 3, FCCC-*C*), 132.1 (d, *J* 9, FCC-*C*), 166.9 (d, *J* 253, FC) (aryl), 174.2 (CO).

(*R*)-Valine (*R*)-8f.[47] From (*R*)-**7f** (2.07 g, 10 mmol). After crystallization from H_2O–EtOH *title compound* (*R*)-**8f** was obtained as a powder (0.97 g, 83%); mp >300 °C; $[\alpha]_D^{23}$ −21 (*c* 0.5; 6 M HCl) [lit.,[47] (*S*)-isomer $[\alpha]_D^{17}$ +28.1 (*c* 2.2; 6 M HCl)]; $C_5H_{11}NO_2$ (M = 117.2); ν_{max}(KBr)/cm^{-1} 1586; δ_H[250 MHz; D_2O; relative to δ($Me_3Si(CH_2)_3SO_3Na$ = 0.00 ppm] 0.98 (d,

J 7.0), 1.03 (d, *J* 7.0) (CH_3), 2.26 (m), 3.59 (d, *J* 4.4) (CH); δ_C[62.9 MHz; D_2O; relative to $\delta(Me_3Si(CH_2)_3SO_3Na) = 0.0$ ppm] 19.3, 20.6, 31.7, 63.1 (CH_3, CH), 176.7 (CO).

(*R*)-Leucine (*R*)-8g.[49] From (*R*)-**7g** (2.21 g, 10 mmol). After crystallization from H_2O–EtOH *title compound* (*R*)-**8g** was obtained as a powder (1.28 g, 98%); mp >300 °C; $[\alpha]_D^{23}$ −11 (*c* 1; 5 M HCl) [lit.,[49] $[\alpha]_D^{25}$ −15.2 (*c* 4; 5 M HCl)]; $C_6H_{13}NO_2$ (M = 131.2); ν_{max}(KBr)/cm^{-1} 1710; δ_H[250 MHz; 3 M DCl + 1 drop of MeCN; relative to δ(MeCN) = 0.00 ppm] 0.89 (d, *J* 7), 0.91 (d, *J* 7) (CH_3), 1.74 (m, 3 H, CH, CH_2), 4.04 (br t, *J* 6.5, CH); δ_C[62.9 MHz; 3 M DCl + 1 drop of MeCN; relative to $\delta(MeCN) = 0.0$ ppm] 20.1, 20.6, 23.0, 37.8, 50.4 (CH_3, CH_2, CH), 171.4 (CO).

(*R*)-2-Amino-3-ethylpentanoic acid (*R*)-8h.[50] From (*R*)-**7h** (2.35 g, 10 mmol). After crystallization from H_2O–MeOH *title compound* (*R*)-**8h** was obtained as a powder (1.05 g, 72%); mp 258–260 °C; $[\alpha]_D^{23}$ −34 (*c* 0.5; 5 M HCl) [lit.,[50] (*S*)-isomer $[\alpha]_D^{23}$ +37 (*c* 0.33; 5 M HCl)] (Found: C, 57.81; H, 10.61; N, 9.52. $C_7H_{15}NO_2$ (M = 145.2) requires C, 57.90; H, 10.41; N, 9.65%); ν_{max}(Nujol)/cm^{-1} 1636, 1599, 1545, 1526; δ_H[250 MHz; CF_3-COOH–$CDCl_3$ (3:1)] 1.077, 1.081 (two t, *J* 7, 6 H, CH_3), 1.57 (m, 4 H, CH_2), 2.05 (m), 4.49 (m) (CH); δ_C[62.9 MHz; CF_3COOH–$CDCl_3$ (3:1)] 11.7, 11.9 (CH_3), 23.4, 23.5 (CH_2), 44.9, 57.9 (CH), 175.7 (br, CO).

(*R*)-Phenylalanine (*R*)-8i.[51] From (*R*)-**7g** (2.55 g, 10 mmol). After crystallization from H_2O–MeOH *title compound* (*R*)-**8i** was obtained as a powder (1.40 g, 85%); mp 269–271 °C; $[\alpha]_D^{23}$ +30 (*c* 1; H_2O) [lit.,[51] (*S*)-isomer $[\alpha]_D^{23}$ −35.2 (*c* 1.6; H_2O)]; $C_{19}H_{11}NO_2$ (M = 165.2); ν_{max}(KBr)/cm^{-1} 1625, 1561; δ_H(250 MHz; CF_3COOD), 3.36 (dd, *J* 8.8 and 15.0), 3.60 (dd, *J* 4.6 and 15.0) (CH_2), 4.65 (m, CH), 7.28–7.46 (phenyl); δ_C(62.9 MHz; CF_3COOD) 37.2, 57.2 (CH_2, CH), 130.8, 130.9, 131.6, 133.3 (phenyl), 174.6 (CO).

Reduction of *N*-benzylamino nitriles 1 to *N*-benzyldiamines 9: general procedure

A solution of amino nitrile **1** (10 mmol) in Et_2O (50 ml) was added dropwise under stirring to a cold (−20 °C) solution of $LiAlH_4$ (1.90 g, 50 mmol) in Et_2O (300 ml). The mixture was stirred at 0 °C for 30 min, then at 23 °C for 18 h and finally hydrolyzed at 0 °C with H_2O (25 ml). After addition of 15% aq. NaOH (4 ml) and stirring for 10 min, the mixture was filtered. The organic layer was separated and the aqueous layer was once more extracted with Et_2O (50 ml). The combined organic extracts were dried with Na_2SO_4. Evaporation of the solvent afforded the oily *title compound* **9**.

(*S*)-2-Amino-1-benzylamino-1-phenylethane (*S*)-9a.[56–58] From nitrile (*S*)-**1a** (2.22 g, 10 mmol). The oily product crystallized at −15 °C from CH_2Cl_2–pentane to furnish *title compound* (*S*)-**9a** as a powder (1.94 g, 86%), mp 53–54 °C; $[\alpha]_D^{23}$ +62; $[\alpha]_{546}^{23}$ +73 (*c* 1; CCl_4) (Found: C, 78.80; H, 7.99; N, 12.04. $C_{15}H_{18}N_2$ (M = 226.3) requires C, 79.60; H, 8.02; N, 12.38%); ν_{max}(CCl_4)/cm^{-1} 3029, 3068, 3322, 3396; δ_H(250 MHz; $CDCl_3$) 1.48 (br, NH), 2.81 (dd, *J* 7.3 and 12.5), 2.91 (dd, *J* 5.5 and 12.5) (CH_2), 3.58 (d, *J* 13.1), 3.71 (d, *J* 13.1) (CH_2), 3.63 (dd, *J* 5.5 and 7.3, CH), 7.23–7.40 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 48.9, 51.5, 64.9 (CH_2, CH), 126.9, 127.3, 127.4, 128.2, 128.4, 128.5, 140.6, 142.3 (phenyl).

(*S*)-2-Amino-1-benzylamino-1-(4-methylphenyl)ethane (*S*)-9b.[39,59] From nitrile (*S*)-**1b** (2.36 g, 10 mmol). The oily product crystallized at −15 °C from CH_2Cl_2–pentane to furnish *title compound* (*S*)-**9b** as a powder (1.93 g, 80%), mp 102–104 °C; $[\alpha]_D^{23}$ +67; $[\alpha]_{546}^{23}$ +80 (*c* 1; CCl_4) (Found: C, 79.62; H, 8.42; N, 11.01. $C_{16}H_{20}N_2$ (M = 240.4) requires C, 79.96; H, 8.39; N, 11.66%); ν_{max}(CCl_4)/cm^{-1} 3396, 3322; δ_H(250 MHz; $CDCl_3$) 1.45 (br, NH), 2.35 (CH_3), 2.80 (dd, *J* 7.3 and 12.7), 2.87 (dd, *J* 5.4 and 12.7) (CH_2), 3.56 (d, *J* 13.2), 3.71 (d, *J* 13.2) (CH_2), 3.59 (m, CH), 7.15–7.31 (m, aryl); δ_C(62.9 MHz; $CDCl_3$) 21.1 (CH_3), 48.9, 51.4, 64.6 (CH_2, CH), 126.8, 127.3, 128.2, 128.4, 129.3, 136.9, 139.3, 140.7 (aryl).

(*S*)-2-Amino-1-benzylamino-1-(4-methoxyphenyl)ethane (*S*)-9c.[59] From nitrile (*S*)-**1c** (2.52 g, 10 mmol). The oily product crystallized at −15 °C from CH_2Cl_2–pentane to furnish *title compound* (*S*)-**9c** as a yellow powder (2.11 g, 82%), mp 81–83 °C; $[\alpha]_D^{23}$ +73; $[\alpha]_{546}^{23}$ +84 (*c* 1; CCl_4) (Found: C, 74.06; H, 7.67; N, 10.33. $C_{16}H_{20}N_2O$ (M = 256.4) requires C, 74.96; H, 7.86; N, 10.93%); ν_{max}(CCl_4)/cm^{-1} 1609, 1517; δ_H(250 MHz; $CDCl_3$) 1.54 (br, NH), 2.80 (dd, *J* 7.2 and 12.7), 2.86 (dd, *J* 5.5 and 12.7) (CH_2), 3.56 (d, *J* 13.2), 3.70 (d, *J* 13.2) (CH_2), 3.56 (m, CH), 3.81 (OCH_3), 6.89–7.31 (several m, aryl); δ_C(62.9 MHz; $CDCl_3$) 48.9, 51.4, 55.3, 64.3 (CH_3, CH_2, CH), 114.0, 126.8, 128.2, 128.4, 128.5, 134.3, 140.7, 158.9 (aryl).

(*R*)-1-Amino-2-benzylamino-3-methylbutane (*R*)-9f. From nitrile (*R*)-**1f** (1.88 g, 10 mmol). *Title compound* (*R*)-**9f** was obtained as a colourless oil (1.40 g, 73%); $[\alpha]_D^{23}$ −20; $[\alpha]_{546}^{23}$ −23 (*c* 1; CCl_4) (Found: C, 74.66; H, 10.50; N, 14.50. $C_{12}H_{20}N_2$ (M = 192.3) requires C, 74.95; H, 10.48; N, 14.57%); ν_{max}-(CCl_4)/cm^{-1} 3319, 3396; δ_H(250 MHz; $CDCl_3$) 0.89 (d, *J* 6.9), 0.94 (d, *J* 6.9) (CH_3), 1.31 (br, NH), 1.87 (m), 2.28 (m) (CH), 2.54 (dd, *J* 7.4 and 12.7), 2.75 (dd, *J* 4.0 and 12.7) (CH_2), 3.77 (AB-q, *J* 13.1, CH_2), 7.18–7.37 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 18.3, 19.2 (CH_3), 28.8, 41.7, 51.9, 64.9 (CH_2, CH), 126.8, 128.1, 128.3, 141.2 (phenyl).

(*R*)-1-Amino-2-benzylamino-4-methylpentane (*R*)-9g. From nitrile (*R*)-**1g** (2.02 g, 10 mmol). *Title compound* (*R*)-**9g** was obtained as a pale yellow oil (1.92 g, 93%); $[\alpha]_D^{23}$ −15; $[\alpha]_{546}^{23}$ −16 (*c* 1; CCl_4) (Found: C, 75.58; H, 10.72; N, 13.50. $C_{13}H_{22}N_2$ (M = 206.3) requires C, 75.68; H, 10.75; N, 13.58%); ν_{max}(CCl_4)/cm^{-1} 3315, 3392; δ_H(250 MHz; $CDCl_3$) 0.87 (d, *J* 6.5), 0.90 (d, *J* 6.5) (CH_3), 1.11–1.44 (several m, 5 H, NH, CH_2), 1.65 (nonet, *J* 6.7, CH), 2.48–2.85 (several m, 3 H, CH_2, CH), 3.77 (br, CH_2), 7.18–7.36 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 23.0, 25.0, 42.1, 44.9, 51.3, 56.9 (CH_3, CH_2, CH), 126.8, 128.1, 128.3, 141.0 (phenyl).

(*R*)-1-Amino-2-benzylamino-3-ethylpentane (*R*)-9h. From nitrile (*R*)-**1h** (2.16 g, 10 mmol). *Title compound* (*R*)-**9h** was obtained as a pale yellow oil (1.69 g, 77%); $[\alpha]_D^{23}$ −34; $[\alpha]_{546}^{23}$ −40 (*c* 1; CCl_4) (Found: C, 76.28; H, 10.88; N, 12.50. $C_{14}H_{24}N_2$ (M = 220.4) requires C, 76.31; H, 10.98; N, 12.71%); ν_{max}(CCl_4)/cm^{-1} 3319, 3400; δ_H(250 MHz; $CDCl_3$) 0.88, 0.89 (two t, *J* 7, 6 H, CH_3), 1.11–1.49 (several m, 8 H, NH, CH_2, CH), 2.52 (m, CH_2), 2.74 (m, CH), 3.78 (AB-q, *J* 13.1, CH_2), 7.23–7.38 (m, phenyl); δ_C(62.9 MHz; $CDCl_3$) 12.2, 12.4 (CH_3), 22.0, 22.5 (CH_2), 42.0, 42.4, 52.0, 61.3 (CH_2, CH), 126.8, 128.2, 128.3, 141.3 (phenyl).

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