Supporting Information for: z 14595

A Catalytic Asymmetric Strecker-type Reaction: Interesting Reactivity Difference between TMSCN and HCN

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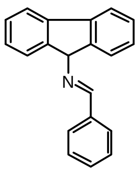
General: NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, opening at 500 MHz for ^{1}H NMR, 125.65 MHz for ^{13}C NMR, 470.4 MHz for ^{19}F NMR, and 202 MHz for ^{31}P NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (= 0) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CHCl_3$ (77.00 ppm for ^{13}C NMR) as an internal reference. ^{19}F NMR were taken with trifluoroacetic acid in $CDCl_3$ as an external standard. ^{31}P NMR were carried out with phosphinic acid (85%) as an external standard. Optical rotations were measured on a JASCO P-1010 polarimeter. Column chromatography were performed with silica gel Merck 60 (230-400 mesh ASTM). The enantiomeric excess (ee) was determined by HPLC analysis. HPLC analysis was performed on JASCO HPLC systems consisting of the following: pump, 880-PU or PU-980; detector, 875-UV or UV-970, measured at 254 nm; column, DAICEL CHIRALPAK AS, AD, or DAICEL CHIRALCEL OJ, OD; mobile phase, hexane-2-propanol ; flow rate, 0.7-1.0mL/min. In general, reactions were carried out in dry solvents under an argon atmosphere, unless noted otherwise. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Diethylaluminum chloride in hexane (1 M) was purchased from KANTO CHEMICAL. CO., INC., 2-8, Nihonbashi, Honcho 3-chome, Chuo-ku, Tokyo, 103-0023, Japan (fax: +813-3667-6892). Other reagents were purified by usual methods.

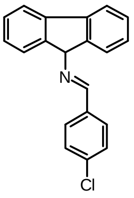
General procedure for the preparation of imines (GP 1):

The starting material 9-fluorenylamine was prepared by washing CH_2Cl_2 solution of 9-aminofluorene hydrogen chloride with sat. aq $NaHCO_3$ before use. Into a mixture of 9-fluorenylamine and MS 4A in toluene was added the starting material aldehyde (1.1 eq) at ambient temperature (In the case of aliphatic and α,β-unsaturated imines, the reaction was carried out at 0 °C). After stirring for 1 h, MS 4A was filtered off and the resulting solution was evaporated at 25 °C to give the desired imines quantitatively. When the product was solid, further purification was carried out by recrystallization from hexane. However, in the case of unstable imines such as aliphatic and α,β-unsaturated ones, the resulting imine was directly used as a CH_2Cl_2 solution.



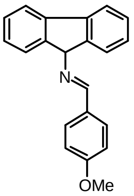
Benzaldehyde 9-fluorenyl imine (3a):

^{1}H NMR ($CDCl_3$) δ 8.77 (s, 1H), 7.88-7.78 (m, 2H), 7.75 (d, J = 7.3 Hz, 2H), 7.47-7.34 (m, 7H), 7.33-7.25 (m, 2H), 5.41 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 163.4, 144.8, 141.1, 136.0, 131.0, 128.6, 128.5, 128.4, 127.4, 125.3, 120.1, 74.7.



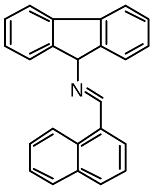
***p*-Chlorobenzaldehyde 9-fluorenyl imine (3b):**

^{1}H NMR ($CDCl_3$) δ 8.71 (s, 1H), 7.78-7.71 (m, 4H), 7.44-7.34 (m, 6H), 7.29 (dt, J = 7.4, 1.0 Hz, 2H), 5.41 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 161.9, 144.5, 141.0, 137.0, 134.5, 129.7, 128.9, 128.5, 127.5, 125.2, 120.2, 74.5.



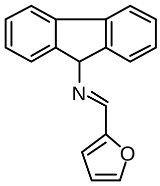
***p*-Methoxybenzaldehyde 9-fluorenyl imine (3c):**

^{1}H NMR ($CDCl_3$) δ 8.70 (s, 1H), 7.77-7.71 (m, 4H), 7.42-7.35 (m, 4H), 7.28 (dt, J = 7.7, 1.2 Hz, 2H), 6.94-6.88 (m, 2H), 5.37 (s, 1H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.8, 161.9, 145.0, 141.0, 130.1, 129.0, 128.4, 127.4, 125.2, 120.1, 114.0, 74.7, 55.4.



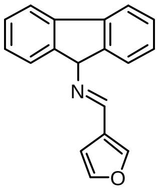
1-Naphthaldehyde 9-fluorenyl imine (3d):

^{1}H NMR ($CDCl_3$) δ 9.43 (s, 1H), 8.89 (d, J = 8.6 Hz, 1H), 7.98 (d, J = 7.4 Hz, 1H), 7.91 (d, J = 8.3 Hz, 1H), 7.87 (d, J = 7.4 Hz, 1H), 7.78 (d, J = 7.6 Hz, 2H), 7.57-7.38 (m, 7H), 7.31 (t, J = 7.3, 2H), 5.51 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 162.9, 145.0, 141.1, 133.8, 131.5, 131.4, 129.1, 128.6, 128.4, 127.5, 127.3, 126.1, 125.3, 125.2, 124.3, 120.1, 75.6.



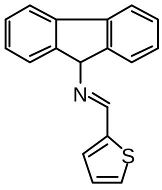
2-Furaldehyde 9-fluorenyl imine (3e):

^{1}H NMR ($CDCl_3$) δ 8.51 (s, 1H), 7.72 (d, J = 7.7 Hz, 2H), 7.50 (d, J = 1.3 Hz, 1H), 7.45-7.33 (m, 4H), 7.28 (dt, J = 7.3, 0.6, 2H), 6.83 (d, J = 3.4 Hz, 1H), 6.47 (dd, J = 3.4, 1.9, 1H), 5.42 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 151.5, 151.4, 145.0, 144.5, 141.1, 128.5, 127.4, 125.4, 120.0, 114.5, 111.8, 74.2.



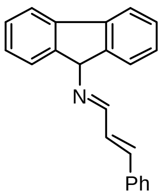
3-Furaldehyde 9-fluorenyl imine (3f):

^{1}H NMR ($CDCl_3$) δ 8.69 (s, 1H), 7.80 (s, 1H), 7.74 (d, J = 7.6 Hz, 2H), 7.45-7.35 (m, 5H), 7.34-7.26 (m, 2H), 6.84 (d, J = 1.5 Hz, 1H), 5.34 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 155.0, 145.6, 144.7, 144.1, 141.0, 128.4, 127.4, 125.5, 125.2, 120.1, 108.2, 74.8.



2-Thiophenecarboxaldehyde 9-fluorenyl imine (3g):

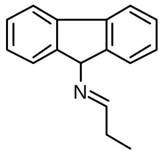
^{1}H NMR ($CDCl_3$) δ 8.79 (s, 1H), 7.73 (d, J = 7.7 Hz, 2H), 7.45-7.35 (m, 6H), 7.29 (dt, J = 7.7, 1.3 Hz, 2H), 7.07 (dd, J = 4.9, 3.7 Hz, 1H), 5.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 156.2, 144.6, 142.3, 141.0, 130.9, 129.5, 128.4, 127.4, 127.3, 125.3, 120.1, 74.0.



Cinnamaldehyde 9-fluorenyl imine (3h):

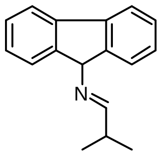
^{1}H NMR (C_6D_6) δ 8.12 (d, J = 9.0 Hz, 1H), 7.57 (d, J = 7.4 Hz, 2H), 7.38 (d, J = 7.4 Hz, 2H), 7.23 (t, J = 7.7 Hz, 2H), 7.0-7.1 (m, 4H), 6.64 (d, J = 16.1 Hz, 1H), 5.31 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 164.7, 144.8, 142.2, 141.0, 135.6, 129.3, 128.8, 128.4, 128.2, 127.5, 127.3, 125.2, 120.0, 74.4.

Propionaldehyde 9-fluorenyl imine (3k):



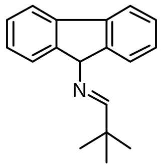
^{1}H NMR ($CDCl_3$) δ 8.18 (t, *J* = 4.9, 1H), 7.71 (d, *J* = 7.7 Hz, 2H), 7.43-7.25 (m, 6H), 5.15 (s, 1H), 2.41 (m, 2H), 1.18 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.9, 144.8, 141.0, 128.3, 127.3, 125.0, 120.0, 74.3, 29.4, 10.6.

Isobutyraldehyde 9-fluorenyl imine (3l):



^{1}H NMR ($CDCl_3$) δ 8.05 (dd, *J* = 5.2, 0.6 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.45-7.26 (m, 6H), 5.12 (s, 1H), 2.60 (m, 1H), 1.17 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 173.1, 144.9, 141.0, 128.3, 127.3, 124.9, 120.0, 74.3, 34.4, 19.6.

Pivalaldehyde 9-fluorenyl imine (3m):



^{1}H NMR ($CDCl_3$) δ 8.06 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.45-7.25 (m, 6H), 5.10 (s, 1H), 1.16 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 175.6, 145.1, 140.9, 128.2, 127.3, 124.8, 120.0, 74.5, 36.5, 27.2.

General procedure for the preparation of the catalyst (GP 2):

The chiral ligand (13 mg, 18 *m*mol) was placed in the flame dried flask and dissolved in 0.5 mL of CH_2Cl_2. To this solution was added Et_2AlCl (17 *m*L, 16 μmol, 0.96 M in hexane) under argon. The resulting mixture was stirred at room temperature for 1 h to give the clear solution. This solution was directly used as a catalyst in the catalytic asymmetric Strecker-type reaction.

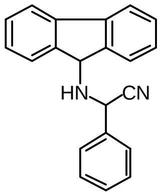
General procedure for the catalytic asymmetric Strecker-type reaction (System 1):

To a stirred solution of the above mentioned catalyst (0.5 mL, 16 *m*mol) was added the solution of the imine (0.17 mmol) in CH_2Cl_2 (0.6 mL) at -40 °C, followed by the addition of TMSCN (45 *m*L, 0.34 mmol). After 30 min, the solution of phenol (3 *m*L, 34 *m*mol) in CH_2Cl_2 (0.2 mL) was slowly added over 17 h. The reaction mixture was allowed to stir for the time shown in Table 1. Sat. aq $NaHCO_3$ was added for quenching and the mixture was diluted with ether. The organic layer was separated, and the water layer was extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. The further purification was performed by flash column chromatography on SiO_2 to afford the desired aminonitrile.

General procedure for the catalytic asymmetric Strecker-type reaction (System 2):

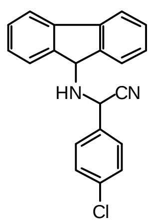
To the CH_2Cl_2 solution (1.0 mL) of the catalyst (33 *m*mol) prepared as above, was added the solution of the imine (0.352 mmol) in CH_2Cl_2 (1.0 mL) and TMSCN (70 *m*mol) at -40 °C. To this mixture, the solution of HCN (0.422 mmol) in CH_2Cl_2 (0.26 mL) was slowly added over 24 h. After 12 h (total 36 h), the reaction was worked up as described above.

***N*-(9-Fluorenylamino)-phenylacetonitrile (4a):**



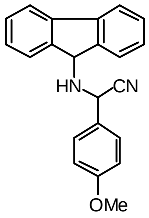
^{1}H NMR ($CDCl_3$) δ 7.78–7.68 (m, 3H), 7.53–7.26 (m, 10H), 5.14 (s, 1H), 4.57 (s, 1H), 2.34 (bs, 1H); ^{13}C NMR ($CDCl_3$) 143.6, 143.5, 141.1, 140.7, 135.8, 129.01, 128.98, 128.9, 128.8, 127.6, 127.4, 125.7, 125.0, 120.2, 120.1, 119.6, 62.2, 50.3; $[\alpha]^{24}_{D}$ –14.0° (c = 1.0, $CHCl_3$) (95% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 90/10, 1.0 mL/min) t_R 13.3 min and 25.0 min.

***N*-(9-Fluorenylamino)-*p*-chlorophenylacetonitrile (4b):**



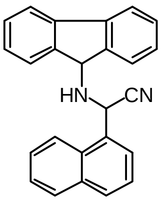
^{1}H NMR ($CDCl_3$) δ 7.75–7.68 (m, 3H), 7.50–7.26 (m, 9H), 5.12 (s, 1H), 4.47 (s, 1H), 2.39 (bs, 1H); ^{13}C NMR ($CDCl_3$) 143.3, 143.2, 141.1, 140.8, 135.0, 134.4, 129.1, 129.0, 128.9, 128.8, 127.6, 125.7, 125.0, 120.3, 120.2, 119.3, 62.2, 49.4; $[\alpha]^{24}_{D}$ –50.8° (c = 1.0, $CHCl_3$) (95% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 90/10, 1.0 mL/min) t_R 12.4 min and 15.2 min.

***N*-(9-Fluorenylamino)-*p*-methoxyphenylacetonitrile (4c):**



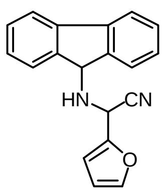
^{1}H NMR ($CDCl_3$) δ 7.77-7.64 (m, 3H), 7.52-7.22 (m, 7H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.08 (s, 1H), 4.52 (s, 1H), 3.76 (s, 3H), 2.29 (bs, 1H); ^{13}C NMR ($CDCl_3$) 160.0, 143.8, 143.7, 141.0, 140.7, 128.8, 128.7, 127.9, 127.5, 125.7, 125.0, 120.2, 120.1, 119.9, 114.3, 62.1, 55.3, 49.9; $[\alpha]^{26}_{D}$ –26.7° (c = 1.0, $CHCl_3$) (93% ee). HPLC (DAICEL CHIRALPAK AD, hexane/2-propanol 70/30, 1.0 mL/min) t_R 10.4 min and 14.3 min.

***N*-(9-Fluorenylamino)-1−naphthylacetonitrile (4d):**



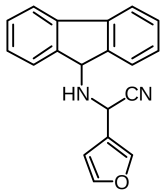
^{1}H NMR ($CDCl_3$) δ 8.50-7.97 (m, 1H), 7.88–7.81 (m, 3H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 7.0 Hz, 1H), 7.55-7.28 (m, 7H), 7.20 (dt, *J* = 7.4, 1.0 Hz, 1H), 5.31 (s, 1H), 5.15 (s, 1H), 2.40 (bs, 1H); ^{13}C NMR ($CDCl_3$) 143.7, 141.0, 140.9, 134.1, 131.1, 130.2, 130.1, 129.0, 128.9, 128.8, 127.6, 127.4, 126.9, 126.5, 126.3, 125.7, 125.2, 125.1, 123.3, 120.3, 120.1, 119.8, 62.1, 49.1; $[\alpha]^{24}_{D}$ +65.5° (c = 1.0, $CHCl_3$) (88% ee). HPLC (DAICEL CHIRALPAK AD, hexane/2-propanol 90/10, 1.0 mL/min) t_R 20.3 min and 25.4 min.

***N*-(9-Fluorenylamino)-2-furylacetonitrile (4e):**



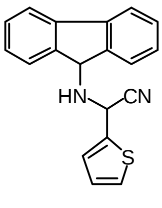
^{1}H NMR ($CDCl_3$) δ 7.74-7.65 (m, 3H), 7.45–7.32 (m, 5H), 7.26 (dt, *J* = 7.6, 1.0 Hz, 1H), 6.30-6.26 (m, 2H), 5.09 (s, 1H), 4.59 (s, 1H), 2.64 (bs, 1H); ^{13}C NMR ($CDCl_3$) 147.8, 143.45, 143.40, 143.2, 140.85, 140.77, 128.9, 128.7, 127.64, 127.58, 125.6, 124.8, 120.2, 120.1, 117.8, 110.7, 109.0, 61.9, 44.1; $[\alpha]^{24}_{D}$ –22.4° (c = 1.0, $CHCl_3$) (79% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 90/10, 1.0 mL/min) t_R 14.4 min and 22.1 min.

***N*-(9-Fluorenylamino)-3-furylacetonitrile (4f):**



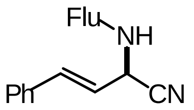
^1H NMR ($CDCl_3$) δ 7.73-7.65 (m, 3H), 7.51 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.45 (m, 1H), 7.43-7.31 (m, 4H), 7.28 (dt, *J* = 7.6, 1.2 Hz, 1H), 5.40 (m, 1H), 5.06 (s, 1H), 4.40 (s, 1H), 2.40 (bs, 1H); ^{13}C NMR ($CDCl_3$) 144.0, 143.5, 143.4, 141.0, 140.7, 128.86, 128.84, 127.57, 127.55, 125.7, 124.9, 121.9, 120.2, 120.1, 119.4, 109.3, 62.0, 42.2; $[\alpha]^{24}_{D}$ +16.2° (c = 1.0, $CHCl_3$) (90% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 70/30, 1.0 mL/min) t_R 8.1 min and 14.6 min.

_N_-(9-Fluorenylamino)-2-thiopheneacetonitrile (4g):



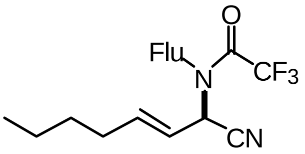
^1H NMR ($CDCl_3$) δ 7.77–7.68 (m, 3H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.47-7.26 (m, 5H), 7.11 (m, 1H), 6.93 (dd, *J* = 4.9, 3.4 Hz, 1H), 5.16 (s, 1H), 4.63 (s, 1H), 2.72 (bs, 1H); ^{13}C NMR ($CDCl_3$) 143.1, 143.0, 141.1, 140.7, 139.7, 129.0, 127.7, 127.6, 126.9, 126.8, 126.1, 125.8, 125.1, 120.24, 120.15, 119.0, 62.2, 45.5; $[\alpha]^{26}_{D}$ –36.3° (c = 1.0, $CHCl_3$) (89% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 70/30, 1.0 mL/min) t_R 7.7 min and 13.8 min.

_N_-(9-Fluorenylamino)-(_E_)-phenylbutenenitrile (4h):



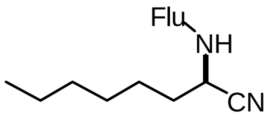
^1H NMR ($CDCl_3$) δ 7.56 (m, 1H), 7.50 (dd, *J* = 2.0, 6.0 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.22 (m, 2H), 7.16 (m, 1H), 7.0-7.1 (m, 6H), 6.51 (dd, *J* = 1.2, 15.5 Hz, 1H), 5.67 (dd, *J* = 5.5, 15.5 Hz, 1H), 4.67 (s, 1H), 3.72 (d, *J* = 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) 145.0, 144.3, 141.2, 141.0, 135.9, 133.4, 128.9, 128.8, 128.7, 128.5, 128.3, 127.7, 127.6, 127.1 (overlapped), 126.1 125.4, 124.3, 120.3, 120.2, 119.2, 62.3, 48.4; $[\alpha]^{24}_{D}$ –89.7° (c = 0.465, $CHCl_3$) (96% ee). HPLC (DAICEL CHIRALPAK AD, hexane/2-propanol 90/10, 0.8 mL/min) t_R 20.2 min and 22.6 min.

_N_-(9-Fluorenyl)-_N_-trifluoroacetyl-2-amino-(_E_)-3-octenenitrile (4i);



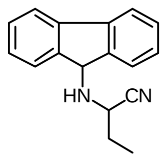
^1H NMR ($CDCl_3$) 7.71 (d, *J* = 2.5 Hz, 1H), 7.70 (d, *J* = 2.8 Hz, 1H), 7.54 (d, *J* = 7.3 Hz, 1H), 7.48-7.36 (m, 4H), 7.30 (d, *J* = 7.75 Hz, 1H), 7.26 (d, *J* = 7.3 Hz, 1H), 5.93(s, 1H), 5.37 (dd, *J* = 15.3, 7.3 Hz, 1H), 5.10 (ddd, *J* = 7.7, 7.3, 6.7 Hz, 1H), 3.52 (d, *J* = 7.0 Hz, 1H), 1.82-1.72 (m, 2H), 1.15-1.05 (m, 4H), 0.76 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) 156.8 (q, *J* = 37 Hz), 140.9, 140.7, 140.4, 138.7, 138.6, 130.4, 130.3, 128.9, 128.2, 126.0, 125.9, 120.8, 119.0, 115.1, 115.0, 62.8, 48.2, 31.5, 29.7, 22.0, 13.7; $[\alpha]^{21}_{D}$ –12.6 (c = 5.3, $CHCl_3$) (85% ee). HPLC (DAICEL CHIRALPAK AD, hexane/2-propanol 200/1, 0.7 mL/min) t_R 15.6 min and 26.5 min.

_N_-(9-Fluorenyl)-2-amino-_n_-octanenitrile (4j):



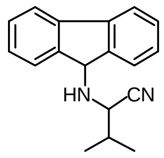
^1H NMR ($CDCl_3$) 7.63 (d, *J* = 6.7 Hz, 2H), 7.62 (d, *J* = 6.4 Hz, 2H), 7.5 (d, *J* = 7.3 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.34-7.23 (m, 4H), 5.0 (s, 1H), 3.29 (t, *J* = 7.1 Hz, 1H), 1.65-1.54 (m, 2H), 1.46-1.32 (m, 6H), 0.78 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) 143.9, 143.9, 140.6, 140.1, 128.7, 127.5, 127.4, 125.5, 124.9, 121.1, 120.1, 120.0, 62.2, 46.5, 34.9, 31.4, 28.6, 25.3, 22.43, 13.9; $[\alpha]^{24}_{D}$ +27.2 (c = 3.9, $CHCl_3$) (80% ee); HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 9/1, 1.0 mL/min) t_R 8 min and 11 min.

N-(9-Fluorenylamino)-ethylacetonitrile (4k):



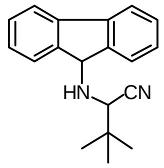
^{1}H NMR ($CDCl_3$) δ 7.72–7.64 (m, 2H), 7.62 (d, *J* = 7.3 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.42-7.25 (m, 4H), 4.99 (s, 1H), 3.28 (t, *J* = 6.8 Hz, 1H), 2.06 (bs, 1H), 1.67 (m, 2H), 1.00 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) 143.93, 143.87, 140.8, 140.6, 128.7, 127.5, 127.4, 125.6, 124.9, 120.9, 120.1, 120.0, 62.2, 47.8, 28.3, 10.0; $[\alpha]^{24}_D$ +66.6° (c = 1.0, $CHCl_3$) (70% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 95/5, 1.0 mL/min) t_R 10.8 min and 14.2 min.

N-(9-Fluorenylamino)-isopropylacetonitrile (4l):



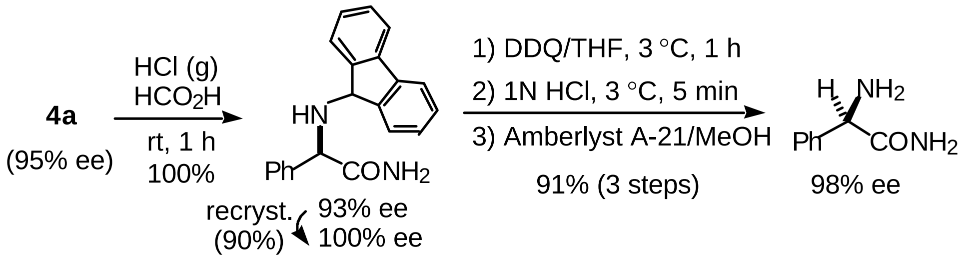
^{1}H NMR ($CDCl_3$) δ 7.74-7.67 (m, 2H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.44-7.28 (m, 4H), 5.04 (s, 1H), 3.15 (d, *J* = 5.2 Hz, 1H), 2.07 (bs, 1H), 1.85 (m, 1H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) 143.8, 140.9, 140.6, 128.72, 128.70, 127.5, 127.4, 125.7, 125.2, 120.2, 120.1, 120.0, 62.4, 52.7, 32.9, 18.9, 17.9; $[\alpha]^{24}_D$ +62.5° (c = 1.0, $CHCl_3$) (72% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 95/5, 1.0 mL/min) t_R 7.6 min and 11.0 min.

N-(9-Fluorenylamino)-*tert*-butylacetonitrile (4m):



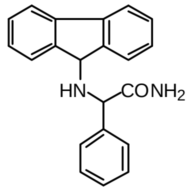
^{1}H NMR ($CDCl_3$) δ 7.74–7.67 (m, 2H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.63 (d, *J* = 7.3 Hz, 1H), 7.44-7.37 (m, 2H), 7.34 (dt, *J* = 7.3, 1.3 Hz, 1H), 7.31 (dt, *J* = 7.3, 1.0 Hz, 1H), 5.05 (s, 1H), 2.91 (s, 1H), 2.08 (bs, 1H), 1.01 (s, 9H); ^{13}C NMR ($CDCl_3$) 143.7, 143.5, 141.0, 140.6, 128.72, 128.67, 127.4, 127.3, 125.9, 125.7, 120.6, 120.1, 119.9, 62.8, 56.7, 35.1, 26.0; $[\alpha]^{26}_D$ +58.3° (c = 1.0, $CHCl_3$) (78% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 95/5, 1.0 mL/min) t_R 6.5 min and 12.7 min.

Determination of the absolute configuration of 4a

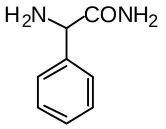


N-(9-fluorenyl)phenylglycinamide: To a solution of **4a** (100 mg, 0.34 mmol) in formic acid (10 mL), HCl gas was bubbled through until the solution was saturated. The mixture was allowed to stir at room temperature for 1 h and the solvent was removed *in vacuo*. The resulting residue was triturated in saturated $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (50 mL x 3). The organic layer was washed with water (50 mL x 2) and dried over $MgSO_4$. After the removal of the solvent the crude product (108 mg, 100%, 93% ee) was purified by recrystallization from THF / diethyl ether (96 mg, 90%, 100% ee).

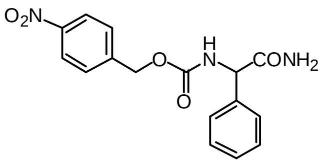
^{1}H NMR (CD_3OD) δ 7.77-7.68 (m, 3H), 7.46 (m, 1H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.30 (dt, *J* = 7.3, 1.2 Hz, 1H), 7.28-7.18 (m, 6H), 4.93 (s, 1H), 3.96 (s, 1H); ^{13}C NMR (DMSO-d_6) 174.2, 145.7, 145.6, 141.1, 140.1, 140.0, 127.9, 127.8, 127.2, 127.02, 126.97, 126.9, 125.3, 125.1, 119.79, 119.76, 62.3, 61.5; $[\alpha]^{24}_{D}$ –62.5° (c = 1.0, MeOH) (100% ee). HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 70/30, 1.0 mL/min) t_R 21.6 min and 27.0 min.



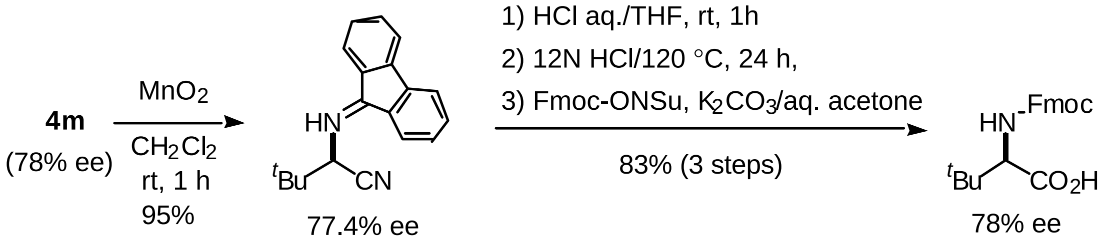
Phenylglycinamide: To a solution of DDQ (202 mg, 0.89 mmol) in THF (14 mL) was added 9-fluorenylaminophenylacetoamide (140 mg, 0.45 mmol) in THF (10 mL) at 3 °C. After stirring for 2 h at the same temperature, the reaction was quenched by addition of 1N HCl (0.89 mL) and allowed to warm up to room temperature. The solvents were removed *in vacuo* and the resulting residue was triturated in diethyl ether. The suspended residue was filtered and washed with diethyl ether (5 mL x 5) to afford phenylglycinamide HCl salt. (This conversion was found to be accomplished without any loss of enantiomeric purity.) A soluton of the HCl salt in MeOH (3 mL) was passed through a plug of Amberlyst A-21(OH form) with MeOH (20 mL) and concentrated *in vacuo* to afford a white powder of phenylglycinamide (61 mg, 91%).



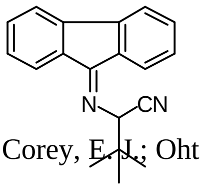
$[\alpha]^{24}_{D}$ -108° (c = 1.26, EtOH) (98% ee) [lit.[1] $[\alpha]^{22}_{D}$ -103° (c = 1.2, EtOH) for *R* enantiomer]. The enantiomeric excess was determined by HPLC after the conversion to *p*-nitro-Z derivative : ^{1}H NMR (acetone-d) δ 8.15-7.95 (m, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 7.3 Hz, 2H), 7.33-7.13 (m, 3H), 6.98 (bs, 1H), 6.86 (bs, 1H), 6.65-6.20 (m, 1H), 5.18 (d, *J* = 7.6 Hz, 1H), 5.15-5.04 (m, 2H); ^{13}C NMR (acetone-d) δ 172.3, 155.9, 148.4, 145.9, 140.0, 129.3, 128.9, 128.7, 128.2, 124.2, 65.5, 59.3; HPLC (DAICEL CHIRALCEL OJ, hexane/ 2-propanol 70/30, 1.0 mL/min) t_R 20.2 min and 25.6 min.; $[\alpha]^{21}_{D}$ –99.0° (c = 1.0, THF) (98% ee).



Determination of the absolute configuration of 4m



9-Fluorenylimino-*tert*-butylacetonitrile: To a solution of **4m** (150 mg, 0.54 mmol) in CH_2Cl_2 (10 mL) manganese oxide (555 mg, 5.43 mmol) was added at room temperature. After stirring



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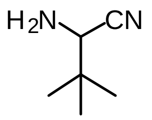
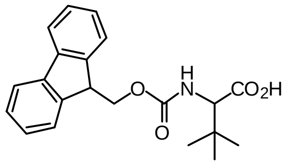
[1] Corey, E. J.; Ohtani, M. *Tetrahedron Lett.* **1989**, *30*, 5227-5230.

for 1h, manganese oxide was filtered off and washed with CH_2Cl_2 (5 mL x 4). Solvent was evaporated *in vacuo*, and the residue was purified by preparative TLC (hexane : acetone = 9 : 1) to give a yellowish solid (142 mg, 95%, 77.4% ee).

^{1}H NMR ($CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 7.3 Hz, 1H), 7.64 (d, *J* = 7.3 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.41 (dt, *J* = 7.3, 1.0 Hz, 1H), 7.36-7.25 (m, 2H), 4.80 (s, 1H), 1.24 (s, 9H); ^{13}C NMR ($CDCl_3$) 167.1, 144.3, 141.2, 138.1, 132.4, 131.8, 131.1, 128.6, 128.3, 127.9, 123.2, 120.8, 119.5, 117.5, 61.1, 36.2, 26.0; $[\alpha]^{18}_D$ +282.3° (c = 1.0, $CHCl_3$) (77.4% ee). HPLC (DAICEL CHIRALCEL OD, hexane/2-propanol 90/10, 1.0 mL/min) t_R 7.4 min and 14.1 min.

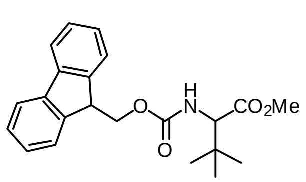


Amino-*tert*-butylacetonitrile HCl salt : To a solution of 9-fluorenylimino-*tert*-butylacetonitrile (200 mg, 0.73 mmol) in THF (15 mL) was added 1N-HCl (1.5 mL) and stirred at room temperature for 1h. After the solvents were removed *in vacuo*, the resulting residue was triturated in diethyl ether followed by filtrating and washing with diethyl ether (5 mL x 5) to give a white powder of amino-*tert*-butylacetonitrile HCl salt (90 mg, 83%). (This conversion was found to be accomplished without any loss of enantiomeric purity.) $[\alpha]^{18}_D$ +16.4° (c = 1.0, MeOH) (77.4% ee).



Fmoc-*tert*-leucine: A solution of amino-*tert*-butylacetonitrile HCl salt (80 mg, 0.54 mmol) in conc. HCl (2 mL) was heated to 120 °C in a sealed tube for 24 h. After cooling to ambient temperature the solvent was removed *in vacuo* to afford a 1:1 mixture of *tert*-leucine HCl salt and ammonium chloride. To a solution of the mixture in 50% aq acetone (4 mL) were added K_2CO_3 (140 mg, 1.0 mmol) and Fmoc-ONSu (370 mg, 1.1 mmol) and the whole was stirred at room temperature for 4h. After the removal of acetone *in vacuo*, the resulting precipitate was filtered off and washed with 5% K_2CO_3 (10 mL x 3). The combined aqueous layer was washed with diethyl ether (20 mL), acidified with 1N HCl and then extracted with diethyl ether (20 mL x 3). The combined organic layer was washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford Fmoc-*tert*-leucine (185 mg, 100%) as a colorless oil.

^{1}H NMR ($CDCl_3$) δ 7.78–7.68 (m, 2H), 7.62-7.50 (m, 2H), 7.38 (t, *J* = 7.1 Hz, 2H), 7.30 (t, *J* = 7.3, 2H), 6.12 (m, 0.1H), 5.38 (d, *J* = 9.8, 0.9H), 4.55-4.33 (m, 2H), 4.30-4.15 (m, 1.8H), 3.87 (m, 0.2H), 1.80-0.90 (m, 9H); ^{13}C NMR ($CDCl_3$) 176.4, 156.3, 143.8, 143.7, 141.3, 127.7, 127.1, 125.0, 120.0, 67.1, 62.1, 47.2, 34.6, 26.5; $[\alpha]^{21}_D$ +9.3° (c = 1.0, MeOH) (78% ee). [lit.[2] $[\alpha]^{20}_D$ -11.0° (c = 1, MeOH) for *S* enantiomer]. The enantiomeric excess was determined by HPLC after conversion to the methyl ester :



^{1}H NMR ($CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 7.0, 2H), 7.40 (t, *J* = 7.3, 2H), 7.31 (t, *J* = 7.3, 2H), 5.37 (d, *J* = 9.4, 0.9H), 5.05 (m, 0.1H), 4.50-4.32 (m, 2H), 4.26-4.16 (m, 2H), 3.74 (s, 3H), 1.10-0.80 (m, 9H); ^{13}C NMR ($CDCl_3$)

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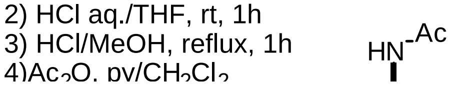
[2] Sasaki, Y.; Ambo, A.; Midorikawa, K.; Suzuki, K. Chem. Pharm. Bull. 1993, 41, 1391-1394.

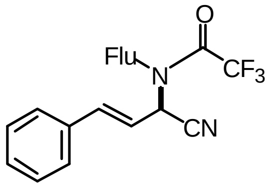


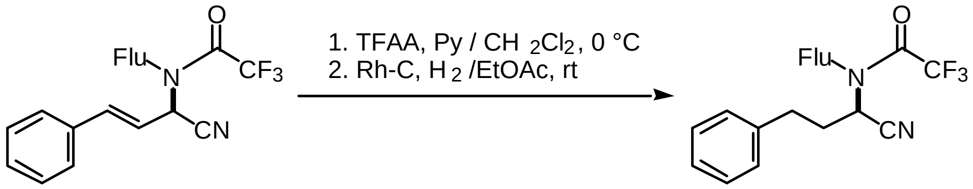
172.2, 156.1, 143.9, 143.8, 141.3, 127.7, 127.0, 125.06, 125.04, 119.97, 119.95, 67.0, 62.1, 51.8, 47.2, 34.7, 26.4; HPLC (DAICEL CHIRALCEL OD, hexane/2-propanol 70/30, 1.0 mL/min) t_R 7.7 min and 10.4 min.

Determination of the absolute configuration of 4k

4k (70% ee) was converted to the corresponding aminonitrile hydrochloride (47% yield, not optimized) in two steps (step 1 and 2) as described in the case of **4m**. To this aminonitrile (0.089 mmol) was added HCl in MeOH prepared by the reaction of $SOCl_2$ (0.2 mL) with dry MeOH (2 mL) (step 3). The whole was refluxed for 1 h and the solvent was evaporated under reduced pressure. The crude amino methyl ester hydrochloride was converted to the acetamide (Ac_2O, pyridine/CH_2Cl_2) (step 4). After purification by SiO_2 column chromatography, the absolute configuration was determined by the comparison of the optical rotation ($[\alpha]^{21}_{D}$ –20.1 (c = 0.12, $CHCl_3$), 80% optical yield) with the reported value.[3]

Procedure for hydrogenation of 3m to the saturated aminonitrile





Protection of a nitrogen atom of **4h** (84% ee) as trifluoroacetoamide was achieved by the usual method (TFAA, prydine / CH_2Cl_2,, 0 °C) without racemization. To a solution of protected **4h** (28 mg, 0.067 mmol, 84% ee) in ethyl acetate (1 mL) was added Rh-C (14 mg). The reaction mixture was allowed to stir vigorously at room temperature for 12 h under 1 atom pressure of hydrogen. Then, Rh-C was removed by filtration, and the filtrate was evaporated under reduced pressure.The resulting residue was purified on preparativeTLC (eluent; hexane : ehtyl acetate = 9 : 1) to give the saturated product (22 mg, y. 79%) as a colorless oil. This conversion was found to be accomplished without any loss of enantiomeric purity.

***N*-(9-Fluorenyl)-*N*-trifluoroacetyl-2-amino-4-phenybutenenitrile :**

^{1}H NMR ($CDCl_3$) 7.82 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 7.4 Hz, 1H), 7.56-7.53 (m, 2H), 7.49-7.46 (m, 2H), 7.32 (dt, J = 0.6, 7.3 Hz, 2H), 7.29-7.24 (m, 2H), 7.13-7.10 (m, 2H), 6.07 (dd, J = 7.3, 15.9 Hz, 1H), 6.06 (s, 1H), 5.29 (d, J = 15.9 Hz, 1H), 3.82 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) 156.9 (q, J = 37 Hz), 141.0, 140.7, 138.7, 138.6, 138.1, 134.5, 130.6, 130.4, 129.0, 128.9, 128.6, 128.0, 127.0, 126.2, 125.5, 120.9, 120.9, 117.8, 114.6, 116.3 (q, J = 286 Hz), 62.8, 53.4, 48.3, 29.7; HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 9/1, 1.0 mL/min) t_R 9 min and 14 min.

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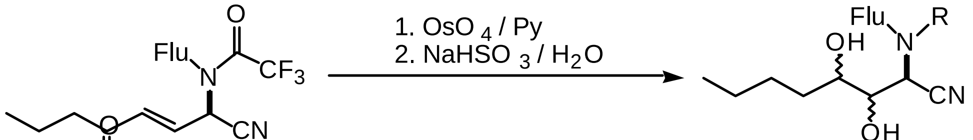
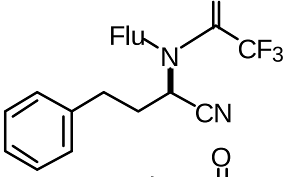
[3] Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125-10138.

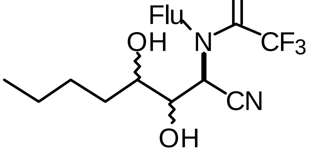
N-(9-Fluorenyl)-N-trifluoroacetyl-2-amino-4phenyl-butanenitrile :

^{1}H NMR (CDCl$_3$) 7.63-7.32 (m, 8H), 7.10-6.90 (m, 3H), 6.58 (d, *J* = 7.0 Hz, 2H), 5.87 (s, 1H), 2.81 (dd, *J* = 4.0, 11.0 Hz 1H), 2.73 (m, 1H), 2.58 (m, 1H), 2.2 (ddd, *J* = 4.3, 10.0, 14.3 Hz 1H), 1.47 (m, 1H); ^{13}C NMR (CDCl$_3$) 157.1 (q, *J* = 36 Hz), 140.8, 140.5, 138.3, 138.2, 137.8, 130.29, 130.24, 128.7, 128.5, 128.0, 127.5, 126.1, 125.0, 121.0, 120.6, 116.2 (q, *J* = 287 Hz), 115.3, 62.7, 45.8, 31.6, 31.3; HPLC (DAICEL CHIRALPAK AS, hexane/2-propanol 9/1, 1.0 mL/min) t$_R$ 5 min and 10 min.

Procedure for dihydroxylation of 4i







4i (30 mg, 0.075 mmol, 65% ee) was dissolved in pyridine (0.9 mL) and the resulting solution was cooled down to -40 °C. To this mixture was added a solution of osmium tetroxide in ^{t}BuOH (0.96 mL, 0.96 mmol, 0.1 M). After stirring for 3 h at the same temperature, 25 % aq NaHSO$_3$ (2 mL) was added for quenching , followed by dilution with ether (2 mL). The resulting mixture was allowed to stir at 0 °C for 10 h. The *N*-trifluoroacetyl group was deprotected in this reduction step. The organic layer was separated and the water layer was extracted with ethyl acetate (5 mL x 2). The combined organic layer was washed with sat. aq CuSO$_4$, water and brine. After drying this solution over Na$_2$SO$_4$, the solvent was evaporated under reduced pressure. Further purification was performed by flash column chromatography (eluent: hexane : acetone = 20 : 1 to 8 : 1) to afford the two diastereomer in a ratio of ca. 1 : 1 in ca. 70% total yield. In addition, this conversion was achieved without loss of enantiomeric purity, because two products had the same enantiomeric excess of 65% ee as that of the starting material. One of the diastereomers were characterized as the corresponding trifluoroacetamide.

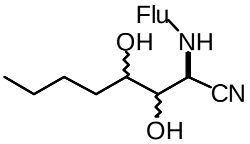
N-(9-Fluorenyl)-N-trifluoroacetyl-2-amino-3,4-dihydroxy-*n*-octanenitrile:

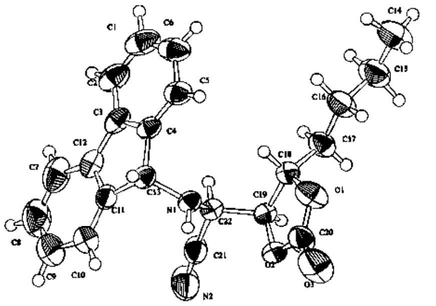
^{1}H NMR (CDCl$_3$) δ 7.8 (d, *J* = 7.7 Hz, 2H), 7.6 (d, *J* = 7.6 Hz, 1H), 7.59-7.44 (m, 4H), 7.37 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.05 (s, 1H), 3.57 (dd, *J* = 2.4, 2.4 Hz, 1H), 3.30 (d, *J* = 2.4 Hz, 1H), 2.6 (m, 1H), 1.2-1.0 (m, 6H), 0.83 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (CDCl$_3$) 140.6, 138.4, 130.9, 130.7, 129.1, 128.2, 125.8, 125.0, 121.3, 121.2, 120.3 (q), 74.4, 72.8, 63.2, 52.5, 32.4, 27.6, 22.3, 13.9; IR (neat) 3429, 1692, 1453 cm^{-1}; MS m/z 432 (M$^+$), 276, 165; HPLC (DAICEL CHIRALCEL OD, hexane/2-propanol 95/5, 0.7 mL /min) t$_R$ 33 min and 57 min.

^{1}H NMR (CDCL$_3$) for the corresponding NH product; ^{1}H NMR (CDCl$_3$) δ 7.73 (d, *J* = 3.95 Hz, 1H), 7.71 (d, *J* = 3.95 Hz, 1H), 7.65 (d, *J* = 7.35 Hz), 7.59 (d, *J* = 7.6 Hz, 1H), 7.45-7.38, (m, 4H), 5.10 (s, 1H), 3.92

(m, 1H), 3.48 (m, 2H), 1.55-1.10 (m, 6H), 0.89 (t, *J* = 8.3 Hz, 3H).

***N*-(9-Fluorenylamino)-3,4-dihydroxy-*n*-octanenitrile :**





^{1}H NMR ($CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 6.6 Hz, 1H), 7.46-7.33 (m, 4H), 5.1 (s, 1H), 3.61 (ddd, J = 1.2, 7.8, 8.3 Hz, 1H), 3.52 (dd, J = 1.2, 6.1 Hz, 1H), 3.33 (d, J = 6.1 Hz, 1H), 1.5-1.2 (m, 6H), 0.82 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) 142.5, 142.4, 141.3, 140.7, 129.2, 129.1, 127.8, 127.7, 125.7, 124.9, 120.3, 118.9, 76.7, 73.2, 71.2, 62.0, 48.8, 33.7, 27.7, 22.5, 13.9; MS m/z 336 (M^+), 291; HPLC (DAICEL CHIRALPAK AD, hexane/2-propanol 90/10, 0.7 mL/min) t_R 25 min and 34 min.

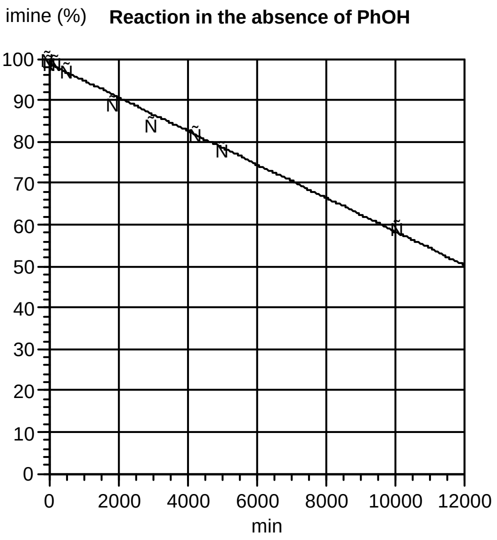
The relative configuration was determined by the X-ray crystallography of the corresponding cyclic carbocate.

Kinetic Studies with TMSCN

To a solution of the chiral ligand (7 mg, 9.8 *m*mol) in CD_2Cl_2 (0.3 mL) in a 5 mm NMR tube was added Et_2AlCl (9.2 *m*L, 8.8 *m*mol, 0.96 M in hexane) at room temperature and the mixture was stayed for 1 h. The resulting solution of **1** was cooled to –40 °C and a solution of the imine **3a** (0.093 mmol) in CD_2Cl_2 (0.4 mL) and TMSCN (25 *m*L, 0.186 mmol) was added. The reaction (the disappearance of **3a**) in the absence of PhOH was monitored from this point by NMR. After 10 min, PhOH (2 *m*L, 19 *m*mol, 20 mol % or 5 *m*L, 56*m*mol, 60 mol %) was added in one portion at –40 °C. The reactions (the disappearance of **3a**) in the presence of PhOH were monitored from this point by NMR. After **3a** disappeared completely, **4a** was isolated in > 84% yield.

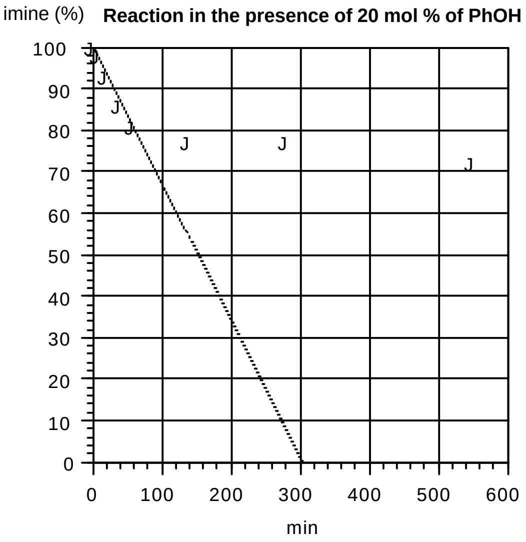
Kinetic Studies with HCN

To the solution of **1** (8.8 *m*mol) prepared as above was added the solution of the imine **3a** (0.093 mmol) in CD_2Cl_2 (0.3 mL) at -40 °C. After 30 min, HCN (0.1 mL, 0.186 mmol, 1.6 M in CH_2Cl_2) was added at -40 °C in one portion. The reaction (the disappearance of **3a**) was monitored from this point by NMR. The relative ratio of the initial reaction rates was determined by the ratio of the slopes of those graphs.


Reaction in the absence of PhOH

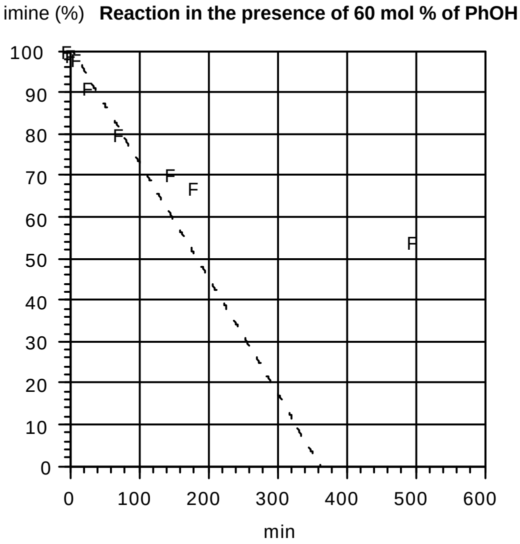
f(x) = -4.037000E-3*x + 9.874132E+1

R^2 = 9.886881E-1


Reaction in the presence of 20 mol % of PhOH

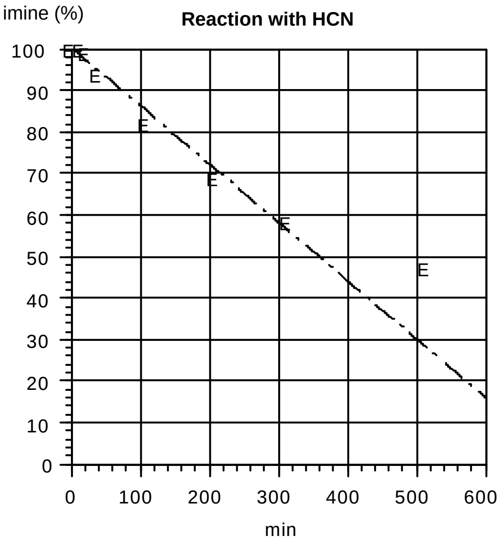
f(x) = -3.310345E-1*x + 1.002069E+2

R^2 = 9.884700E-1


Reaction in the presence of 60 mol % of PhOH

f(x) = -2.782380E-1*x + 1.006672E+2

R^2 = 9.837276E-1


Reaction with HCN

f(x) = -1.405729E-1*x + 1.002581E+2

R^2 = 9.876192E-1