1. Synthesis of cyanohydrin carbonates derived from achiral cyanoformates

1.1 General experimental procedure for the synthesis of cyanohydrin carbonates using potassium cyanide:
To a stirred solution of aldehyde (9.4 mmol) and catalyst 1 (229 mg, 0.2 mmol) in dichloromethane (25 ml) was added KCN (61 mg, 0.9 mmol). The mixture was cooled to -40 °C, then the cyanoformate (11.3 mmol) was added and the reaction stirred vigorously at -40 °C for 24 hours. The reaction was warmed to room temperature and passed through a plug of silica gel, eluting with dichloromethane. The solvent was removed \textit{in vacuo} to give the product. Enantiomeric excesses were determined by chiral gas chromatography using the conditions reported earlier (Belokon, Y.N.; Blacker, J.; Carta, P.; Clutterbuck, L.A.; North, M. Tetrahedron, 2004, 60, 10433.) or given below for compounds not previously studied.

1.2 General experimental procedure for the synthesis of cyanohydrin ethyl carbonates using potassium cyanide/18-crown-6 complex:
KCN/18-crown-6 complex (6.6 mg, 0.02 mmol) and catalyst 1 (36 mg, 0.03 mmol) were dissolved in dichloromethane (5 ml). The solution was cooled to -40 °C, then aldehyde (2.0 mmol) and ethyl cyanoformate (0.24 ml, 2.4 mmol) were added. The resulting solution was allowed to stir for 24 hours at -40 °C. The reaction was warmed to room temperature and passed through a plug of silica gel, eluting with dichloromethane. The solvent was removed \textit{in vacuo} to give the product. Enantiomeric excesses were determined by chiral gas chromatography using the conditions reported
1.3 Characterizing data for cyanohydrin carbonates

1.3.1 (S)-2-Hydroxy-2-phenylethanonitrile tert-butyl carbonate.

\[ \alpha \]_D^{20} -14.2 (c, 1.25 CHCl₃)

Other data as previously reported for the racemate (Thomas, H.G.; Greyn, H.D. Synthesis 1990, 129-130).

1.3.2 (S)-2-Hydroxy-3,3-dimethylbutanonitrile methyl carbonate.

\[ \alpha \]_D^{20} -74.1 (c, 1.2 CHCl₃)

GC conditions: γ-CD butyryl, fused silica capillary column (30m x 0.25 mm): carrier gas H₂, flow rate 1 ml per minute; 70 °C for 2 minutes, then ramp rate of 0.1 °C per minute to a final temperature of 75 °C. Retention times: 35.4 and 36.7 minutes; ee 69%.

Other data as previously reported for the racemate (Scholl, M.; Lim, C.-K.; Fu, G.C. J. Org. Chem. 1995, 60, 6229-6231).

1.3.3 (S)-2-Hydroxy-3,3-dimethylbutanonitrile benzyl carbonate.
1.3.4 (S)-2-Hydroxy-3,3-dimethylbutanonitrile tert-butyl carbonate.

\[
\alpha_D^{20} - 40.9 \text{ (c, 1.1 CHCl}_3) 
\]

GC conditions: $\gamma$-CD butyryl, fused silica capillary column (30m x 0.25 mm): carrier gas H$_2$, flow rate 1 ml per minute; 70 °C for 2 minutes, then ramp rate of 0.1 °C per minute to a final temperature of 80 °C. Retention times: 73.4 and 74.9 minutes; ee 69%.

1.3.5 (S)-2-Hydroxy-2-(2-chlorophenyl)ethanonitrile ethyl carbonate.

\[
\alpha_D^{20} - 55.3 \text{ (c, 1.1 CHCl}_3) 
\]

GC conditions: $\gamma$-CD butyryl, fused silica capillary column (30m x 0.25 mm): carrier gas H$_2$, flow rate 1.6 ml per minute; 100 °C for 2 minutes, then ramp rate of 2 °C per minute to a final temperature of 200 °C. Retention times: 41.0 and 42.0 minutes; ee 93%.

Other data as previously reported for the racemate (Buck, J.S. *J. Am. Chem. Soc.* 1933, 55, 2593-2597).

1.3.6 (S)-2-Hydroxy-(E)-pent-3-enonitrile ethyl carbonate.

\[
\alpha_D^{20} + 6.6 \text{ (c, 1.0 CHCl}_3) 
\]
GC conditions: γ-CD butyryl, fused silica capillary column (30m x 0.25 mm): carrier gas H₂, flow rate 1.6 ml per minute; 100 °C for 2 minutes, then ramp rate of 0.2 °C per minute to a final temperature of 110 °C. Retention times: 22.6 and 24.4 minutes; ee 93%.


1.3.7 (S)-2-Hydroxy-(E)-hex-3-enonitrile ethyl carbonate.

\[
\begin{align*}
\mathrm{C_9H_{13}NO_3Na} & \quad \text{(M+Na)}^+ \quad \text{requires} \quad 206.0787.
\end{align*}
\]

1.3.8 (S)-2-Hydroxy-3-methyl-(E)-pent-3-enonitrile ethyl carbonate.

\[
\begin{align*}
\mathrm{C_9H_{13}NO_3Na} & \quad \text{(M+Na)}^+ \quad \text{requires} \quad 206.0787.
\end{align*}
\]
2. Synthesis of chiral cyanoformates 2 and 3

2.1 Ethyl (S or R)-1-phenylethyl oxalate

A solution of (S or R)-1-phenylethanol (5.0 g, 40.9 mmol) and pyridine (3.3 g, 41.8 mmol) in dichloromethane (18 ml) was cooled in an ice-bath and ethyloxalyl chloride (5.7 g, 41.7 mmol) was added with stirring over 1 hour. The reaction was stirred in the ice-bath for a further 4 hours, then overnight at room temperature. The reaction was washed with water (2 x 5 ml), dried (MgSO₄), and evaporated in vacuo to leave the title compounds (9.0 g, 97%) as colourless liquids.

\[ \alpha_D^{20} -60.0 \text{ (c, 1.1 CHCl}_3) \text{ (S)-enantiomer} \]

\[ \alpha_D^{20} +60.0 \text{ (c, 1.25 CHCl}_3) \text{ (R)-enantiomer} \]

2.2 (S or R)-1-Phenylethyl oxamide

To a solution of ethyl (S or R)-1-phenylethyl oxalate (9.0 g, 40.7 mmol) in ethanol (4.2 ml) was added 0.88 ammonia (2.8 ml) in 4-5 portions with stirring over 3-5 minutes. The resulting solution was allowed to stand at room temperature for 12 hours, then diluted with dichloromethane (80 ml). The organic layer was separated and the aqueous layer extracted with dichloromethane (25 ml). The combined organic phases were washed with water (2 x 25 ml), dried (MgSO₄) and evaporated in vacuo to leave an oil which solidified on cooling. The solid was recrystallized by suspension in toluene (24 ml), filtration, and addition of 60-90 petroleum ether (24 ml) to the toluene solution. The title compounds precipitated (2.9-3.5 g, 37-45%) as white solids.
2.3 (S or R)-1-Phenylethyl cyanoformate 2 or 3

![Chemical structure](attachment:structure.png)

To a stirred mixture of (S or R)-1-Phenylethyl oxamide (2.9 g, 15.0 mmol) and pyridine (4.6 g, 57.8 mmol) in dichloromethane (27 ml), in an ice-bath, trifluoroacetic anhydride (3.8 g, 17.9 mmol) was added dropwise over 10 minutes. The ice-bath was removed and the thick reaction mixture was allowed to stir at room temperature for 2 hours. Water (58 ml) was added, the organic layer was separated, washed with water (43 ml), and the aqueous layer extracted with dichloromethane (2 x 30 ml). The combined dichloromethane layers were again washed with water (50 ml), dried (MgSO₄) and evaporated in vacuo. The residue was purified by bulb to bulb distillation (120-170 °C at 150 mmHg) to give compounds 2 or 3 (1.9-2.0 g, 71-75%) as colourless oils.

[α]$_D$°$^{20}$ -95.6 (c, 1.35 CHCl₃) (S)-enantiomer: 2

[α]$_D$°$^{20}$ +95.6 (c, 1.65 CHCl₃) (R)-enantiomer: 3

3. Synthesis of diastereomeric cyanohydrin carbonates derived from cyanoformates 2 and 3

3.1 General procedure for the synthesis of diastereomeric cyanohydrin carbonates derived from cyanoformates 2 and 3

To a stirred solution of aldehyde (2.4 mmol) and catalyst 1 (57.8 mg, 0.05 mmol) in dichloromethane (6 ml) was added KCN (7.7 mg, 0.1 mmol). The mixture was cooled to -40 °C, then (S or R)-1-phenylethyl cyanoformate 2 or 3 (0.5 g, 2.9 mmol) was added and the reaction stirred vigorously at -40 °C for 24 hours. The reaction was warmed to room temperature and passed
through a plug of silica gel, eluting with dichloromethane. The solvent was removed in vacuo to give the product.

3.2 Characterizing data for the diastereomeric cyanohydrins derived from benzaldehyde and cyanoformate 2

\[
\begin{align*}
\text{major} & : & \text{minor} \\
\delta^1H (\text{CDCl}_3, \text{major diastereomer}) & : & 1.52 (3H, d J 6.5Hz, CH}_3CH), 5.70 (1H, q J 6.5Hz, OCHMe), 6.10 (1H, s, OCHCN), 7.2-7.8 (10H, m, ArCH); (visible resonance for minor diastereomer) 6.15 (1H, s, OCHCN). Ratio of major : minor diastereomer = 18:1 which corresponds to 89% de.
\end{align*}
\]

3.3 Characterizing data for the diastereomeric cyanohydrins derived from benzaldehyde and cyanoformate 3

\[
\begin{align*}
\text{major} & : & \text{minor} \\
\delta^1H (\text{CDCl}_3, \text{major diastereomer}) & : & 1.51 (3H, d J 6.8Hz, CH}_3CH), 5.68 (1H, q J 6.8Hz, OCHMe), 6.15 (1H, s, OCHCN), 7.2-7.8 (10H, m, ArCH); (visible resonance for minor diastereomer) 6.10 (1H, s, OCHCN). Ratio of major : minor diastereomer = 28:1 which corresponds to 93% de.
\end{align*}
\]

3.4 Characterizing data for the diastereomeric cyanohydrins derived from pivaldehyde and cyanoformate 2

\[
\begin{align*}
\text{major} & : & \text{minor} \\
\delta^1H (\text{CDCl}_3, \text{major diastereomer}) & : & \text{Me}_3C (3H, d J 6.5Hz, CH}_3CH), 5.70 (1H, q J 6.5Hz, OCHMe), 6.10 (1H, s, OCHCN). Ratio of major : minor diastereomer = 18:1 which corresponds to 89% de.
\end{align*}
\]
δ_H (CDCl₃, major diastereomer) 1.10 (9H, s, (CH₃)₃), 1.65 (3H, d J 6.6Hz, CH₂CH), 4.89 (1H, s, OCHCN), 5.79 (1H, q J 6.6Hz, OCHMe), 7.3-7.5 (5H, m, ArCH); (visible resonance for minor diastereomer) 1.13 (9H, s, (CH₃)₃), 4.95 (1H, s, OCHCN). Ratio of major : minor diastereomer = 3.6:1 which corresponds to 57% de.

3.5 Characterizing data for the diastereomeric cyanohydrins derived from pivaldehyde and cyanoformate 3

δ_H (CDCl₃, major diastereomer) 1.13 (9H, s, (CH₃)₃), 1.66 (3H, d J 6.6Hz, CH₂CH), 4.95 (1H, s, OCHCN), 5.79 (1H, q J 6.6Hz, OCHMe), 7.3-7.5 (5H, m, ArCH); (visible resonances for minor diastereomer) 1.10 (9H, s, (CH₃)₃), 4.89 (1H, s, OCHCN). Ratio of major : minor diastereomer = 5.3:1 which corresponds to 68% de.