SUPPORTING INFORMATION

FOR

**Dual Lewis Acid-Lewis Base Activation in Enantioselective
Cyanation of Aldehydes using Acetyl Cyanide and Cyanoformate
as Cyanides Sources**

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General Methods: CH₂Cl₂, NEt₃ and DIEA were distilled over CaH₂. Aldehydes, ethyl cyanoformate and acetyl cyanide were purchased from Aldrich, stored under N₂, and used without further purifications. The Ti-salen catalyst (**7**) was prepared following the published procedure: Belokon, Y. N.; Carta, P.; Gutnov, A. V.; Maleev, V.; Moskalenko, M. A.; Yashkina, L. V.; Ikonnikov N. S.; Voskoboev, N. V.; Khrustalev, V. N.; North, M. *Helv. Chim. Acta* **2002**, 85, 3301-3312 and references therein. All catalytic reactions were performed under N₂. Conversions were determined by GC/MS and the enantiomeric excesses by GC analysis using a chiral column (Chiraldex, G-TA (gamma cyclodextrin trifluoroacetyl), 30 m x 0.25 mm). Absolute configurations were determined by comparison of the sign of optical rotation with literature data.

General procedure for enantioselective addition of ethyl cyanoformate to aldehydes

Aldehyde (1 equiv) was added to a solution of **7** (132 mg, 5 mol%) and base (10 mol%) in dichloromethane (10 mL). The solution was cooled to -40 °C before ethyl cyanoformate (1.2 equiv) was added in one portion. The reaction was monitored with GC/MS. After dilution with Et₂O, the reaction mixture was filtrated through silica and the solvent was evaporated under vacuum. The residue was distilled to give the pure product.

O-Ethoxycarbonyl-(*S*)-2-hydroxy-2-phenylacetonitrile (**5a**):

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 120 °C; detection temp. 225 °C; retention time (t_R) of 22.5 min (minor), 23.5 min (major). Spectral data are in accordance with those previously published: Yamagiwa, N.; Tian, J.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, 127, 3413-3422 (¹H NMR and ¹³C NMR), Belokon, Y. N.; Blacker, A. J.; Clutterbuck, L. A.; North, M. *Org. Lett.* **2003**, 5, 4505-4507 (optical rotation).

O-Ethoxycarbonyl-(*S*)-2-hydroxy-2-(4-methylphenyl)acetonitrile (**5b**):

Chiral GC, pressure 25 psi; injection temp. 225 °C; column temp. 120 °C; detection temp. 225 °C; retention time (t_R) of 35.3 min (minor), 37.4 min (major). Spectral data are in accordance with those previously published: Belokon, Y. N.; Blacker, A. J.; Carta, C.; Clutterbuck, L. A.; North, M. *Tetrahedron* **2004**, 60, 10433-10447 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Ethoxycarbonyl-(*S*)-2-hydroxy-2-(4-methoxyphenyl)acetonitrile (5c):**

Chiral GC, pressure 25 psi; injection temp. 225 °C; column temp. 120 °C; detection temp. 225 °C; retention time (t_R) of 103.7 min (minor), 109.9 min (major). Spectral data are in accordance with those previously published: Belokon, Y. N.; Blacker, A. J.; Carta, C.; Clutterbuck, L. A.; North, M. *Tetrahedron* **2004**, 60, 10433-10447 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Ethoxycarbonyl-(*S*)-2-hydroxy-2-(4-chlorophenyl)acetonitrile (5d):**

Chiral GC, pressure 25 psi; injection temp. 225 °C; column temp. 120 °C; detection temp. 225 °C; retention time (t_R) of 56.2 min (minor), 61.6 min (major). Spectral data are in accordance with those previously published: Belokon, Y. N.; Blacker, A. J.; Carta, C.; Clutterbuck, L. A.; North, M. *Tetrahedron* **2004**, 60, 10433-10447. (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Ethoxycarbonyl-(*S*)-2-hydroxy-4-phenylbut-3-enonitrile (5e):**

Chiral GC, pressure 25 psi; injection temp. 225 °C; column temp. 120 °C; detection temp. 225 °C; retention time (t_R) of 111.4 min (minor), 120.2 min (major). Spectral data are in accordance with those previously published: Tian, J.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 3636-3638 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Ethoxycarbonyl-(*S*)-2-hydroxy-3,3-dimethylbutanonitrile (5f):**

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 106 °C; detection temp. 225 °C; retention time (t_R) of 4.8 min (minor), 5.3 min (major). Spectral data are in accordance with those previously published: Tian, J.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 3636-3638 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Ethoxycarbonyl-(*S*)-2-hydroxyheptanonitrile (5g):**

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 106 °C; detection temp. 225 °C; retention time (t_R) of 17.5 min (major), 18.9 min (minor). Spectral data are in accordance with those previously published: Tian, J.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 3636-3638 (^1H NMR, ^{13}C NMR and optical rotation).

General procedure for enantioselective addition of acetyl cyanide to aldehydes

Aldehyde (1 equiv) was added to a solution of **7** (132 mg, 5 mol%) and base (10 mol%) in dichloromethane (10 mL). The solution was cooled to -40 °C before acetyl cyanide (2 equiv) was added in one portion. The reaction was monitored with GC/MS. After dilution with Et₂O, the reaction mixture was filtrated through silica and the solvent was evaporated under vacuum. The residue was distilled to give the pure product.

***O*-Acetyl-(*S*)-2-hydroxy-2-phenylacetonitrile (6a):**

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 115 °C; detection temp. 225 °C; retention time (t_R) of 12.7 min (minor), 20.1 min (major). Spectral data are in accordance with those previously published: Inagaki, M.; Hiratake, J.; Nishioka, T.; Oda, J. *J. Org. Chem.* **1992**, 57, 5643-5649 (^1H NMR and ^{13}C NMR), Bevinakatti, H. S.; Banerji, A. A.; Newadkar, R. V. *J. Org. Chem.* **1989**, 54, 2453-2455 (optical rotation).

***O*-Acetyl-(*S*)-2-hydroxy-2-(4-methylphenyl)acetonitrile (6b):**

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 115 °C; detection temp. 225 °C; retention time (t_R) of 9.5 min (minor), 20.9 min (major). Spectral data are in accordance with those previously published: Inagaki, M.; Hiratake, J.; Nishioka, T.; Oda, J. *J. Org. Chem.* **1992**, 57, 5643-5649 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Acetyl-(*S*)-2-hydroxy-2-(4-methoxyphenyl)acetonitrile (6c):**

Chiral GC, pressure 25 psi; injection temp. 225 °C; column temp. 115 °C; detection temp. 225 °C; retention time (t_R) of 61.9 min (minor), 103.8 min (major). Spectral data are in accordance with those previously published: Schmidt, M.; Hervé, S.; Klempier, N.; Griengl, H. *Tetrahedron* **1996**, 52, 7833-7840 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Acetyl-(*S*)-2-hydroxy-2-(4-chlorophenyl)acetonitrile (6d):**

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 115 °C; detection temp. 225 °C; retention time (t_R) of 9.6 min (minor), 21.1 min (major). Spectral data are in accordance with those previously published: Veum, L.; Kuster, M.; Telalovic, S.; Hanefeld, U.; Maschmeyer, T. *Eur. J. Org. Chem.* **2002**, 1516-1522 (^1H NMR and ^{13}C NMR), Inagaki, M.; Hiratake, J.; Nishioka, T.; Oda, J. *J. Org. Chem.* **1992**, 57, 5643-5649 (optical rotation).

***O*-Acetyl-(*S*)-2-hydroxy-4-phenyl-but-3-enonitrile (6e):**

Chiral GC, pressure 25 psi; injection temp. 225 °C; column temp. 115 °C; detection temp. 225 °C; retention time (t_R) of 62.9 min (minor), 112.2 min (major). Spectral data are in accordance with those previously published: Hamashima, Y.; Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, 121, 2641–2642 (^1H NMR, ^{13}C NMR and optical rotation).

***O*-Acetyl-(*S*)-2-hydroxy-3,3-dimethylbutanonitrile (6f):**

Chiral GC, pressure 20 psi; injection temp. 225 °C; column temp. 106 °C; detection temp. 225 °C; retention time (t_R) of 4.4 min (minor), 8.7 min (major). Spectral data are in accordance with those previously published: Ooi, T.; Miura, T.; Takaya, K.; Ichikawa, H.; Maruoka, K. *Tetrahedron* **2001**, 57, 867-873 (^1H NMR and ^{13}C NMR), www.sigma-aldrich.com (optical rotation)

***O*-Acetyl-(*S*)-2-hydroxy-heptanonitrile (6g):**

Chiral GC, pressure 22 psi; injection temp. 225 °C; column temp. 106 °C; detection temp. 225 °C; retention time (t_R) of 9.3 min (minor), 18.2 min (major). Spectral data are in accordance with those previously published: Inagaki, M.; Hiratake, J.; Nishioka, T.; Oda, J. *J. Org. Chem.* **1992**, 57, 5643-5649 (^1H NMR, ^{13}C NMR and optical rotation).