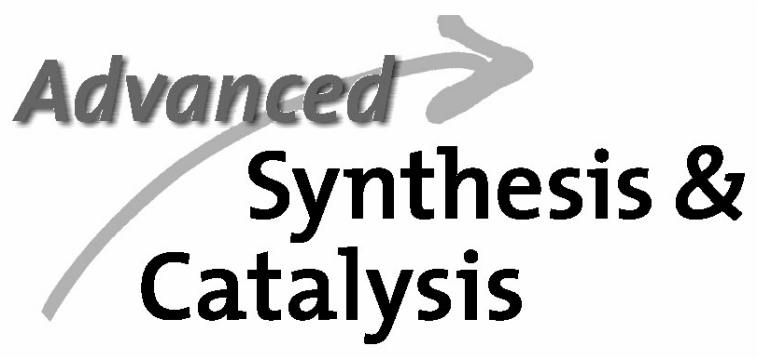


Supporting Information

Base-Base Bifunctional Catalysis: A Practical Strategy for Asymmetric Michael Addition of Malonates to α,β-Unsaturated Aldehydes

Yongcan Wang, Pengfei Li, Xinmiao Liang*, and Jinxing Ye*

Supporting Infomation

A: General Information and Starting Materials

General. The ^{1}H-NMR and ^{13}C-NMR were recorded on a Bruke DRX 400 (400 MHz) instrument. Chromatography was carried out with silica gel (350-400 mesh) using mixtures of petroleum ether and ethyl acetate as eluents. NMR data of known compounds are in agreement with literature values.

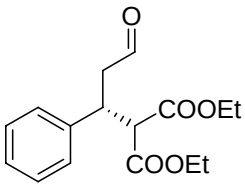
Materials. All solvent and inorganic reagents were of p.a. quality and used without purification. Malonates and a,β-Unsaturated aldehydes were obtained from commercial sources. Cinnamaldehyde and crotonaldehyde were purified by distillation before usage; other materials were used without purification. All acetate salts were obtained from commercial sources. Lithium benzoates and trifluoroacetate were prepared by the reaction of lithium hydroxide and corresponding acid. Catalyst **C1-1** was prepared as described in the literature.[1]

B: General Procedure for the Michael Addition

To a mixed solution of CH_2Cl_2:MeOH=9:1(v:v, 2.0 mL) was added a,β-unsaturated aldehyde **1** (1.0 mmol), malonate **2** (3.0 mmol), catalyst **C1-1** (3.3 mg, 0.01 mmol) and lithium 4-fluorobenzonate (7.3 mg, 0.05 mmol). The reaction mixture was stirred at room temperature for the time indicated in Table 6-7 and then water (5.0 mL) was added. The organic materials were extracted with CH_2Cl_2 three times. The combined organic phases were dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum. The residue was purified by column chromatography on silica gel (350-400 mesh) to yield the desired addition product.

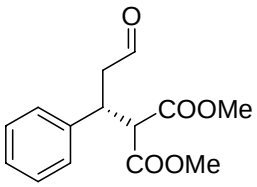
C: Characterization Data of Addition Products

Diethyl 2-(2-formyl-1-phenylethyl)malonate



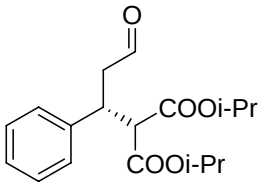
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.56 (t, *J*=1.6 Hz, 1H), 7.27 -7.16 (m, 5H), 4.20-4.14 (q, *J*=7.2 Hz, 2H), 4.00-3.96 (m, 1H), 3.93-3.88 (q, *J*=7.2 Hz, 2H), 3.70-3.67 (d, *J*=10.0 Hz, 1H), 2.89-2.85 (m, 2H), 1.24-1.21 (t, *J*=7.2 Hz, 3H), 0.98-0.94 (t, *J*=7.2 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 200.2, 168.1, 167.5, 139.9, 128.8, 128.6, 128.4, 128.3, 127.6, 61.9, 61.5, 57.6, 47.6, 39.6, 14.1, 13.8.

Dimethyl 2-(2-formyl-1-phenylethyl)malonate



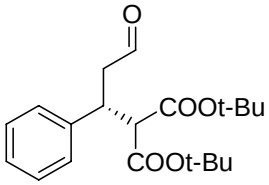
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.59 (t, *J*=1.6 Hz, 1H), 7.31- 7.21 (m, 5H), 4.03-4.01 (m, 1H), 3.76 (s, 1H), 3.73 (s, 3H), 3.49 (s, 3H), 2.93-2.90 (m, 2H). ^{13}C-NMR ($CDCl_3$): δ 200.2, 168.6, 168.0, 139.9, 128.9, 128.7, 128.2, 127.7, 57.4, 52.9, 52.6, 47.4, 39.7.

Diisopropyl 2-(2-formyl-1-phenylethyl)malonate



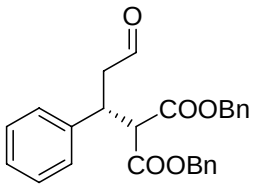
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.60-9.59 (q, *J*=1.2 Hz, 1H), 7.30-7.20 (m, 5H), 5.09-5.03 (m, 1H), 4.81-4.75 (m, 1H), 4.03- 3.97 (m, 1H), 3.67-6.65 (d, *J*=10.4 Hz, 1H), 2.92-2.86 (m, 2H), 1.27-1.23 (m, 6H), 1.05-1.04 (d, *J*=6.0 Hz, 3H), 0.96-0.94 (d, *J*=6.4 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 200.4, 167.7, 167.1, 140.1, 128.8, 128.4, 127.6, 69.6, 69.1, 57.9, 47.9, 39.6, 21.8, 21.7, 21.5, 21.4.

Di-tert-butyl 2-(2-formyl-1-phenylethyl)malonate



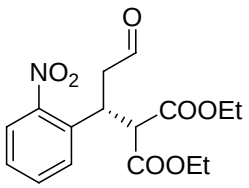
White Solid. ^{1}H-NMR ($CDCl_3$): δ 9.60 (s, 1H), 7.30-7.19 (m, 5H), 3.94-3.87 (m, 1H), 3.54-3.52 (d, *J*=10.4 Hz, 1H), 2.95-2.90 (m, 1H), 2.83-2.77 (m, 1H), 1.46 (s, 9H), 1.19 (s, 9H). ^{13}C-NMR ($CDCl_3$): δ 167.7, 166.9, 140.4, 128.8, 128.6, 127.5, 82.5, 81.9, 59.4, 48.3, 39.7, 28.1, 27.7.

Dibenzyl 2-(2-formyl-1-phenylethyl)malonate



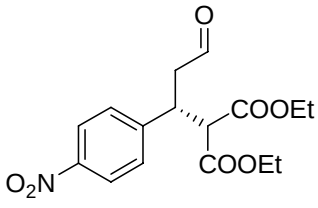
White Solid. ^{1}H-NMR ($CDCl_3$): δ 9.54-9.53 (t, *J*=1.6 Hz, 1H), 7.34-7.05 (m, 15H), 5.14 (d, *J*=1.2 Hz, 2H), 4.89-4.88 (d, *J*=3.6 Hz, 2H), 4.03 (m, 1H),3.84-3.82 (d, *J*=10.0 Hz, 1H), 2.88-2.85 (m, 2H). ^{13}C-NMR ($CDCl_3$): δ 200.1, 167.9, 167.4, 139.8, 135.3, 135.2, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 127.8, 67.7, 67.4, 57.7, 47.4, 39.7.

Diethyl 2-(2-formyl-1-(2-nitrophenyl)ethyl)malonate



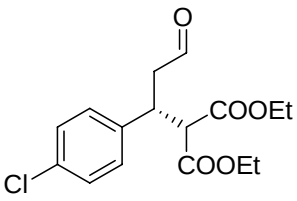
Light yellow oil. ^{1}H-NMR ($CDCl_3$): δ 9.69-9.68 (t, *J*=1.6 Hz, 1H), 7.83-7.81 (m, 1H), 7.58-7.54 (m ,1H), 7.47-7.45 (m, 1H), 7.42-7.38 (m, 1H), 4.59-4.57 (m ,1H), 4.23-4.17 (m, 2H), 4.04- 3.98 (m, 2H), 3.95-3.93 (d, *J*=9.2 Hz, 1H), 3.09-3.02 (m, 2H), 1.28-1.24 (t, *J*=7.1 Hz, 3H), 1.09-1.05 (t, *J*=7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 199.7, 167.8, 167.3, 150.4, 135.0, 133.1, 129.4, 128.5, 125.0, 62.2, 62.1, 56.5, 47.0, 33.9, 14.2, 13.9.

Diethyl 2-(2-formyl-1-(4-nitrophenyl)ethyl)malonate



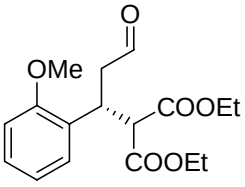
Light yellow oil. ^{1}H-NMR ($CDCl_3$): δ 9.64 (s, 1H), 8.19-8.15 (m, 2H), 7.48-7.44 (m, 2H), 4.59-4.57 (m ,1H), 4.25-4.19 (m, 2H), 4.01- 3.98 (m, 2H), 3.76-3.74 (d, *J*=10.0 Hz, 1H), 3.06-3.00 (m, 2H), 1.30-1.24 (m, 3H), 1.08-1.02 (m, 3H). ^{13}C-NMR ($CDCl_3$): δ 199.7, 167.8, 167.3, 150.4, 135.0, 133.1, 129.4, 128.5, 125.0, 62.2, 62.1, 56.5, 47.0, 33.9, 14.2, 13.9.

Diethyl 2-(1-(4-chlorophenyl)-2-formylethyl)malonate



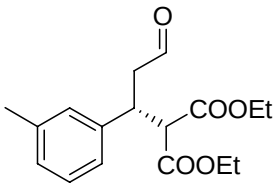
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.59 (s, 1H), 7.27- 7.19 (m, 4H), 4.23-4.17 (m, 2H), 4.01-3.94 (m, 3H), 3.70-3.67 (d, *J*=10.0 Hz, 1H), 2.91-2.88 (m, 2H), 1.28- 1.24 (m, 3H), 1.06-1.03 (m, 3H). ^{13}C-NMR ($CDCl_3$): δ 199.7, 168.0, 167.5, 138.7, 133.4, 129.8, 129.0, 128.8, 128.7, 62.1, 61.9, 57.4, 47.5, 38.9, 14.2, 14.0.

Diethyl 2-(2-formyl-1-(2-methoxyphenyl)ethyl)malonate



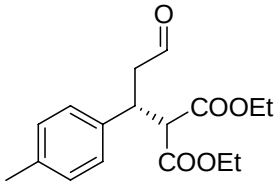
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.60 (t, *J*=1.2 Hz, 1H), 7.20- 7.16 (m, 2H), 6.86-6.83 (m, 2H), 4.22-4.19 (m, 3H), 4.08-4.05 (d, *J*=10.0 Hz, 1H), 3.94-3.90 (m, 2H), 3.85 (s, 3H), 3.02-2.96 (m, 1H), 2.88-2.82 (m, 1H), 1.27-1.24 (m, 3H), 1.01-0.97 (m, 3H). ^{13}C-NMR ($CDCl_3$): δ 201.4, 168.7, 168.1, 157.6, 130.4, 129.0, 128.8, 127.5, 120.8, 120.6, 111.1, 61.8, 61.4, 61.3, 55.5, 55.2, 54.8, 46.0, 36.6, 36.0, 14.2, 14.0.

Diethyl 2-(2-formyl-1-(3-methylphenyl)ethyl)malonate



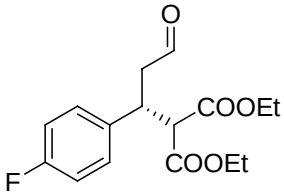
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.59 (t, *J*=1.5 Hz, 1H), 7.18-7.15 (m, 1H), 7.04-7.02 (m, 3H), 4.23-4.17 (m, 2H), 4.00-3.94 (m, 3H), 3.70-3.68 (d, *J*=8.0 Hz, 1H), 2.93-2.83 (m, 2H), 2.31 (s, 3H), 1.28-1.25 (t, *J*=5.7 Hz, 3H), 1.03-1.00 (t, *J*=5.7 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 200.1, 168.0, 167.4, 139.7, 138.1, 128.8, 128.5, 128.1, 125.0, 61.6, 61.3, 57.5, 47.3, 39.5, 21.3, 13.9, 13.6.

Diethyl 2-(2-formyl-1-(4-methylphenyl)ethyl)malonate



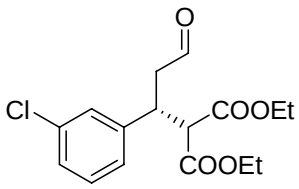
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.58 (t, *J*=1.5 Hz, 1H), 7.13-7.07 (m, 4H), 4.22-4.18 (m, 2H), 4.00-3.94 (m, 3H), 3.69-3.67 (d, *J*=8.0 Hz, 1H), 2.92-2.81 (m, 2H), 2.29 (s, 3H), 1.27-1.24 (t, *J*=5.7 Hz, 3H), 1.04-1.01 (t, *J*=5.7 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 200.2, 168.0, 167.5, 137.1, 136.8, 129.3, 128.0, 61.7, 61.4, 57.6, 47.5, 39.2, 20.1, 14.0, 13.7.

Diethyl 2-(1-(4-fluorophenyl)-2-formylethyl)malonate



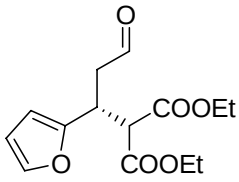
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.60 (m, 1H), 7.28-7.22 (m, 2H), 7.00-6.95 (m, 2H), 4.23-4.17 (m, 2H), 4.04-3.94 (m, 3H), 3.69-3.67 (d, *J*=8.0 Hz, 1H), 2.97-2.84 (m, 2H), 1.27-1.24 (t, *J*=5.7 Hz, 3H), 1.05-1.02 (t, *J*=5.7Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 199.7, 167.8, 167.3, 160.9, 135.7, 129.8, 115.3, 61.8, 61.4, 57.4, 47.5, 38.7, 13.9, 13.7.

Diethyl 2-(1-(3-chlorophenyl)-2-formylethyl)malonate



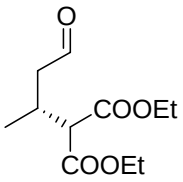
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.61 (t, *J*=1.1 Hz, 1H), 7.27-7.14 (m, 4H), 4.23-4.18 (m, 2H), 4.02-3.97 (m, 3H), 3.70-3.68 (d, *J*=7.8 Hz, 1H), 2.98-2.94 (m, 1H), 2.92-2.86 (m, 1H), 1.28-1.25 (t, *J*=5.7 Hz, 3H), 1.07-1.03 (t, *J*=6.7 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 199.3, 167.7, 167.2, 142.2, 134.3, 129.9, 128.3, 127.6, 126.5, 61.8, 61.5, 57.1, 53.4, 47.2, 39.0, 13.9, 13.7.

Diethyl 2-(2-formyl-1-(furan-2-yl)ethyl)malonate



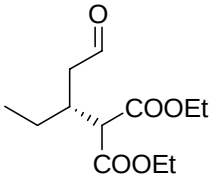
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.68 (s, 1H), 7.32-7.21 (m, 1H)，6.27-6.26 (m, 1H), 6.14-6.13 (m, 1H), 4.22-4.14 (m, 5H), 3.81-3.79 (m, 1H), 2.95- 2.91 (m, 2H), 1.28-1.23 (m, 3H), 1.19-1.15 (m, 3H). ^{13}C-NMR ($CDCl_3$): δ 199.9, 167.7, 152.7, 142.2, 110.4, 107.5, 61.7, 55.2, 44.8, 33.1, 14.2.

Diethyl 2-(1-formylpropan-2-yl)malonate



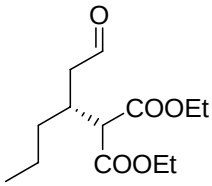
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.75-9.74 (m, 1H), 7.32-7.21 (m, 1H)，4.23-4.18 (m, 4H), 3.37-3.35 (d, *J*=7.2 Hz, 1H), 2.84 (m, 1H), 2.73-2.68 (m, 1H), 2.47-2.40 (m, 1H), 1.29-1.26 (m, 6H), 1.09-1.07 (d, *J*=6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 201.1, 168.5, 61.6, 56.6, 48.3, 28.0, 18.2, 14.3.

Diethyl 2-(1-formylbutan-2-yl)malonate



Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.76 (s, 1H), 4.24-4.17 (m, 4H), 3.54-3.52 (d, *J*=6.4 Hz, 1H), 2.74-2.68 (m, 2H), 2.55-2.50 (m, 1H), 1.50-1.44 (m, 2H), 1.29-1.26 (m, 6H), 0.95-.091 (t, *J*=7.6 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 201.4, 168.8, 168.6, 61.6, 61.5, 54.3, 45.7, 34.1, 25.4, 14.3, 11.4.

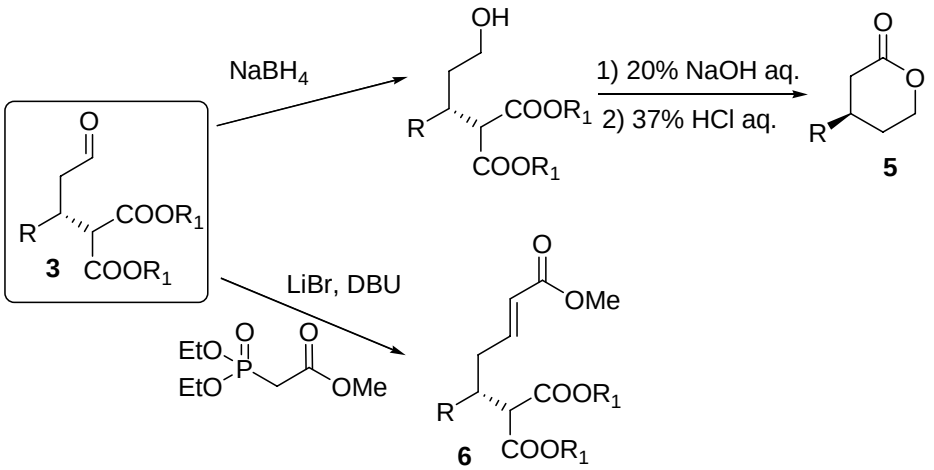
Diethyl 2-(1-formylpentan-2-yl)malonate



Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 9.76 (s, 1H), 4.22-4.17 (m, 4H), 3.52-3.51 (d, *J*=6.0 Hz, 1H), 2.75-2.70 (m, 2H), 2.53-2.52 (m, 1H), 1.40-1.32 (m, 4H), 1.29-1.25 (m, 6H), 0.92-0.89 (m, 3H). ^{13}C-NMR ($CDCl_3$): δ 201.5, 169.0, 168.7, 61.7, 61.6, 54.7, 46.2, 34.9, 32.6, 20.3, 14.3, 14.2.

D: Derivation of Addition Products for Chiral Analysis

Two derivation methods attempted to detect the enantiomeric excess of addition product **3** were established as shown in Scheme 1.



Scheme 1. Synthetic Transformations of Addition Product **3**

Addition product **3** can be converted to corresponding lactone **5** via a reduction and one-pot hydrolization, lactonation and decarboxylation sequences. [2] The enantiomeric excess of some lactone **5** can be detected on CSP-GC. This method was suitable to the chiral analysis of the addition products of cinnamylaldehyde and its derivates, but unsuitable for other kind of enals.

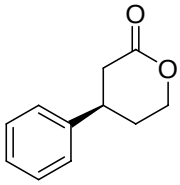
Another derivation method is converted the addition product **3** by Wittig reaction with methyl 2-(diethoxyphosphoryl)acetate to corresponding product **6**. [3] The enantiomeric excess of product **6** can be detected on CSP-HPLC. This method was suitable to the chiral analysis of the addition products of alkyl enals and 3-(2-furanyl)acrolein.

E: General Procedure for the Preparation of Lactones

A solution of addition product **3** (0.8 mmol) in methanol (3.0 mL) was cooled to 0 ^{o}C and $NaBH_4$ (45 mg, 1.2 mmol) was added in portion. The mixture was then stirred at room temperature for 30 minutes and quenched with water. The organic materials were extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum. The residue was added DMF (2.0 mL) and 20% sodium hydroxide aqueous (2.0 mL). The mixture was heated to reflux for 4 hours and then cooled to room temperature. Concentrated hydrochloric acid was added until acidic condition was afforded. The acidic mixture was heated to reflux for 16 hours and then cooled to room temperature. Brine (10 mL) was added and the organic materials were extracted with ethyl acetate three times. The combined organic phases were dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum. The residue was purified by column chromatography on silica gel (350-400 mesh) to yield the desired lactones.

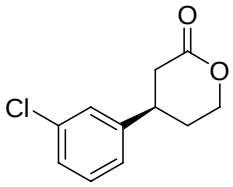
F: Characterization Data of Lactones

Tetrahydro-4-phenylpyran-2-one



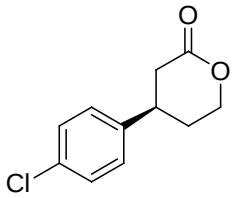
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 7.38-7.20 (m, 5H), 4.52-4.48 (m, 1H), 4.42-4.38 (m, 1H), 3.25-3.22 (m, 1H), 2.95-2.88 (m, 1H), 2.64-2.60 (m, 1H), 2.16-2.15 (m, 1H), 2.06-2.02 (m. 1H), ^{13}C-NMR ($CDCl_3$): δ 171.0, 143.0, 129.0, 127.5, 126.6, 68.9, 37.7, 37.6, 30.5. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 10°C/min from 70 °C to 180°C then hold for 15 min.]: 24.3 min (minor), 24.6 min (major).

4-(3-Chlorophenyl)-tetrahydropyran-2-one



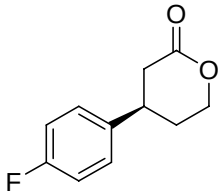
Colorless Oil. ^{1}H-NMR ($CDCl_3$): δ 7.31-7.09 (m, 4H), 4.53-4.49 (m, 1H), 4.40-4.36 (m, 1H), 3.25-3.20 (m, 1H), 2.94-2.89 (m, 1H), 2.69-2.67 (m, 1H), 2.20-2.13 (m. 1H), 2.06-1.98 (m, 1H). ^{13}C-NMR ($CDCl_3$): δ 170.4, 144.8, 134.8, 132.9, 130.1, 127.5, 126.8, 124.7, 68.5, 53.5, 37.2, 30.1. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 200°C isothermal.]: 15.9 min (minor), 15.9 min (major).

4-(4-Chlorophenyl)-tetrahydropyran-2-one



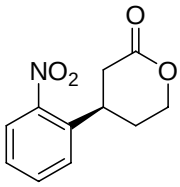
White Solid. ^{1}H-NMR ($CDCl_3$): δ 7.34-7.32 (m, 2H), 7.16-7.14 (m, 2H), 4.52-4.48 (m, 1H), 4.42-4.38 (m, 1H), 3.24-3.21 (m, 1H), 2.94-2.88 (m, 1H), 2.62-2.55 (m, 1H), 2.16-2.15 (m. 1H), 2.03-1.99 (m, 1H). ^{13}C-NMR ($CDCl_3$): δ 170.5, 141.4, 133.2, 129.4, 128.0, 68.7, 37.6, 37.1, 30.4. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 180°C isothermal.]: 42.2 min (minor), 42.4 min (major).

4-(4-Fluorophenyl)-tetrahydropyran-2-one



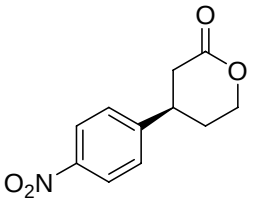
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 7.19-7.15 (m, 2H), 7.06-6.98 (m, 2H), 4.52-4.48 (m, 1H), 4.41-4.36 (m, 1H), 3.27-318 (m, 1H), 2.67-2.54 (m, 2H), 2.19-2.12 (m. 1H), 2.05-1.96 (m. 1H). ^{13}C-NMR ($CDCl_3$): δ 170.6, 160.9, 129.0, 128.0, 115.6, 68.6, 42.3, 37.9, 36.8. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 10°C/min from 70 °C to 150°C hold for 60 min then 10°C/min to 200°C and hold for 8 min.]: 72.3 min (minor), 72.5 min (major).

4-(2-Nitrophenyl)-tetrahydropyran-2-one



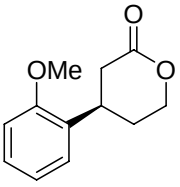
Yellow oil. ^{1}H-NMR ($CDCl_3$): δ 7.89-7.87 (m, 1H), 7.68-7.64 (m ,1H), 7.47-7.43 (m, 2H), 4.52-4.42 (m, 1H), 3.93-3.77 (m, 1H), 3.09-3.03 (m, 1H), 2.70-2.60 (m, 2H), 2.21-2.10 (m, 1H), 2.08-1.99 (m, 1H). ^{13}C-NMR ($CDCl_3$): δ 170.5, 141.4, 133.8, 129.1, 128.4, 124.9, 68.5, 38.4, 32.8, 29.9. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 190°C isothermal.]: 37.5 min (major).

4-(4-Nitrophenyl)-tetrahydropyran-2-one



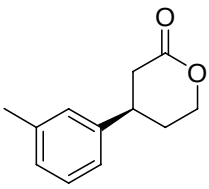
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 8.28-8.15 (m, 2H), 7.41- 7.39 (m, 2H), 4.54-4.43 (m, 1H), 4.13-3.91 (m, 1H), 3.41-3.38 (m, 1H), 2.96-2.94 (m, 1H), 2.77-2.61 (m, 1H), 2.13-1.99 (m. 2H), ^{13}C-NMR ($CDCl_3$): δ 175.3, 150.2, 147.4, 128.7, 127.7, 68.5, 37.7, 37.2, 30.2. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 190°C isothermal.]: 120.0 min (minor), 121.4 min (major).

4-(2-Methoxyphenyl)-tetrahydropyran-2-one



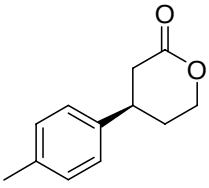
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 7.26-7.24 (m, 1H), 7.13-7.11 (m, 1H), 6.97-6.89 (m, 2H), 4.50-4.46 (m, 1H), 4.41-4.36 (m, 1H), 3.84 (s, 3H), 3.54 (m, 1H), 2.94-2.88 (m, 1H), 2.68-2.61 (m, 1H), 2.12-2.06 (m. 2H). ^{13}C-NMR ($CDCl_3$): δ 171.8, 157.1, 131.1, 128.4, 127.1, 121.0, 110.9, 68.9, 55.4, 36.2, 32.4, 28.7. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 150°C isothermal.]: 131.0 min (minor), 136.2 min (major).

4-(3-Methylphenyl)-tetrahydropyran-2-one



Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 7.26-7.23 (m, 1H), 7.09-7.07 (m, 1H), 7.01-6.99 (m, 2H), 4.52-4.48 (m, 1H), 4.40-4.35 (m, 1H), 3.22-3.16 (m, 1H), 2.92-2.87 (m, 1H), 2.66-2.60 (m, 1H), 2.35 (s, 3H), 2.19-2.13 (m. 1H), 2.06-1.99 (m, 1H). ^{13}C-NMR ($CDCl_3$): δ 170.8, 142.8, 138.7, 128.9, 128.0, 127.3, 123.5, 68.6, 37.5, 37.4, 30.4, 21.5. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 10°C/min from 70 °C to 180°C then hold for 20 min.]: 28.0 min (minor), 28.5 min (major).

4-(4-Methylphenyl)-tetrahydropyran-2-one



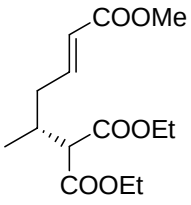
Colorless Oil. ^{1}H-NMR ($CDCl_3$): δ 7.11-7.05 (m, 4H), 4.51-4.47 (m, 1H), 4.40-4.35 (m, 1H), 3.26-3.16 (m, 1H), 2.92-2.87 (m, 1H), 2.67-2.57 (m, 1H), 2.34 (s, 3H), 2.31-2.27 (m, 1H), 2.05-1.97 (m. 1H). ^{13}C-NMR ($CDCl_3$): δ 172.0, 139.8, 136.8, 132.8, 126.3, 68.7, 53.4, 37.6, 30.4, 21.0. The enantiomeric excess was detected on GC. [Chirasil-Dex CB column, 10°C/min from 70 °C to 160°C then hold for 60 min.]: 59.2 min (minor), 59.6 min (major).

G: General Procedure for the Wittig Reaction

A solution of addition product **3** (0.5 mmol) in DMF (1.0 mL) was added lithium bromide (109 mg, 1.25 mmol), methyl 2-(diethoxyphosphoryl)acetate (262 mg, 1.25 mmol) and DBU (190 mg, 1.25 mmol). The reaction mixture was stirred at room temperature until the addition product **3** consumed (determined by TLC) and then purified by column chromatography on silica gel (350-400 mesh) to yield the desired product.

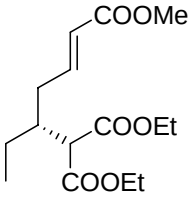
H: Characterization Data of Wittig Reaction Products

5,5-Diethyl 1-methyl 4-methylpent-1-ene-1,5,5-tricarboxylate



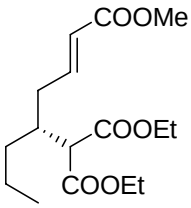
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 6.93-6.89 (m, 1H), 5.88-5.84 (d, *J*=15.6 Hz, 1H), 4.23-4.15 (m, 4H), 3.73 (s, 3H), 3.27-3.25 (d, *J*=7.2 Hz, 1H), 2.45-2.38 (m, 2H), 2.19 (m, 1H), 1.29-1.25 (m, 6H), 1.03-1.01 (m, 3H),. ^{13}C-NMR ($CDCl_3$): δ 168.7, 168.5, 166.9, 146.6, 123.4, 61.5, 56.9, 51.7, 37.2, 32.8, 17.3, 14.3. The enantiomeric excess was determined by HPLC. [OJ-H column, 215 nm, hexane: IPA = 60:1, 0.8 mL/min]: 18.4 min (major), 19.9 min (minor).

5,5-Diethyl 1-methyl 4-ethylpent-1-ene-1,5,5-tricarboxylate



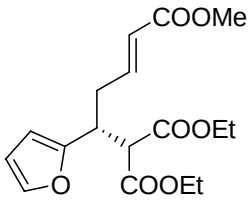
Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 6.97-6.90 (m, 1H), 5.91-5.87 (d, *J*=15.6 Hz, 1H), 4.30-4.20 (m, 4H), 3.76 (s, 3H), 3.45-3.43 (d, *J*=7.2 Hz, 1H), 2.41-2.30 (m, 3H), 1.32-1.27 (m, 8H), 0.97-0.94 (t, *J*=7.6 Hz, 3H),. ^{13}C-NMR ($CDCl_3$): δ 168.9, 168.8, 167.0, 146.9, 123.4, 61.6, 54.7, 51.7, 39.3, 33.6, 24.1, 14.3, 11.3. The enantiomeric excess was determined by HPLC. [AD-H column, 220 nm, hexane: IPA = 40:1, 0.8 mL/min]: 15.3 min (minor), 16.0 min (major).

5,5-Diethyl 1-methyl 4-propylpent-1-ene-1,5,5-tricarboxylate



Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 6.93-6.89 (m, 1H), 5.87-5.83 (d, *J*=15.6 Hz, 1H), 4.22-4.17 (m, 4H), 3.73 (s, 3H), 3.41-3.39 (d, *J*=6.8 Hz, 1H), 2.42-2.29 (m, 3H), 1.36-1.34 (m, 4H), 1.32-1.24 (m, 6H), 0.97-0.94 (m, 3H),. ^{13}C-NMR ($CDCl_3$): δ 168.9, 168.8, 167.0, 146.9, 123.4, 61.5, 54.9, 51.7, 37.6, 34.1, 33.6, 20.2, 14.3. The enantiomeric excess was determined by HPLC. [AD-H column, 220 nm, hexane: IPA = 40:1, 0.8 mL/min]: 14.8 min (minor), 15.8 min (major).

5,5-Diethyl 1-methyl 4-(furan-2-yl)pent-1-ene-1,5,5-tricarboxylate



Colorless oil. ^{1}H-NMR ($CDCl_3$): δ 7.32 (s, 1H), 6.81-6.77 (m, 1H), 6.26 (d, *J*=2.0, 1H), 6.11 (d, *J*=3.2, 1H), 5.80-5.76 (d, *J*=15.6 Hz, 1H), 4.24-4.19 (m, 2H), 4.08-4.02 (m, 2H), 3.71-3.66 (m, 5H), 2.67-2.63 (m, 2H), 1.29-1.25 (t, *J*=7.2, 3H), 1.15-1.11 (t, *J*=7.2, 3H),. ^{13}C-NMR ($CDCl_3$): δ 167.9, 167.7, 166.7, 153.0, 145.4, 142.1, 123.4, 110.3, 106.7, 61.9, 61.7, 55.9, 51.6, 38.2, 34.3, 14.2, 14.1. The enantiomeric excess was determined by HPLC. [OD-H column, 215 nm, hexane: IPA = 60:1, 0.8 mL/min]: 18.8 min (minor), 21.1 min (major).

I: References

1. Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2005**, *44*, 794.
2. Chen, J.; Fletcher, M. T.; Kitching, W. *Tetrahedron: Asymm.* **1995**, *6*, 967.
3. Zhao, G.-L.; Liao, W.-W.; Córdova, A. *Tetrahedron: Lett.* **2006**, *47*, 4929.