Supporting information for

Kinetic resolution displaying zeroth order dependence on substrate consumption: Copper-catalyzed asymmetric alcoholysis of azlactones.

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General

^{1}H NMR (400 MHz, 600 MHz) and ^{13}C NMR (100 MHz, 150 MHz) spectra were recorded on Bruker ARX 400 or JEOL JMN-ECX400 and JMN-ECX600 instruments. Optical rotations were measured with a HORIBA SEPA-300 polarimeter. Column chromatography was performed on silica-gel (Kanto Chemicals, Sillica Gel 60N (spherical, neutral), 40-100 μm). Recycling preparative HPLC was performed with Japan Analytical Industry LC-918 equipped with GPC columns JAIGEL-1H and 2H. Elemental analysis was performed at the Center for Instrumental Analysis of Hokkaido University. GC analysis was carried out using Agilent GC 6850 equipped with Agilent HP-1 Column (length 30 m, 0.32 mm I.D.). The enantiomeric excess (ee) was determined by GC using Chiraldex G-TA (ASTEC) and HPLC using CHIRALPAK AD-H (DAICEL), CHIRALCEL OD (DAICEL).

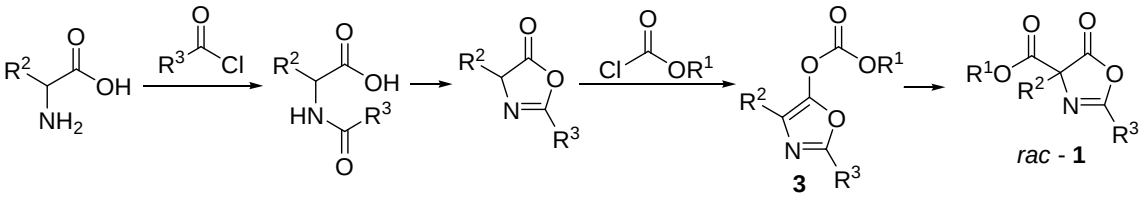
Materials

$CDCl_3$ (Cambridge Isotope Laboratories, Inc.) and DMSO-d_6 (ACROS) were used as solvent for obtaining NMR spectra. Benzene (Wako Chemicals), THF (Kanto Chemicals), $CHCl_3$ (Wako Chemicals), EtOH (Wako Chemicals) were used spectrochemical analysis grade for measurement of optical rotation. Toluene was dried by distillation with CaH_2 before use. 2-Methoxyethanol (Wako Chemicals) was dried by molecular sieves 4A before use. (*S*)-DTBM-SEGPHOS and

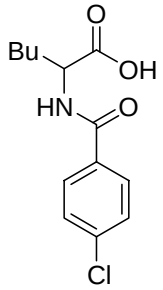
(*R*)-DTBM-SEGPHOS were provided from Takasago International Corporation. All other chemical reagents were used in commercial grade.

Synthesis of Substrates

2-Phenyl-4-methyl-5-oxazalone[1], 2-Phenyl-4-ethyl-5-oxazalone[1], 2-Phenyl-4-propyl-5-oxazalone[1] 2-Phenyl-4-butyl-5-oxazalone[1] and 5-ethoxycarbonyloxy-4-methyl-2-(4-methoxyphenyl)oxazole[2] were synthesized by literature methods. Synthesis of the substrates was summarized by the following scheme.



Synthesis of *N*-(4-chlorobenzoyl)norleucine



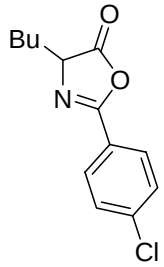
A mixture of DL-norleucine (5.45 g, 40.0 mmol) and KOH (6.07 g, 92.0 mmol) in H_2O (67 mL) were stirred at 0 °C. To this was added 4-chlorobenzoyl chloride (5.21 mL, 40.0 mmol) and the mixture was stirred at room temperature for 21 h. The reaction was quenched by the dropwised addition of conc. HCl until pH ~ 1, which resulted in the formation of a white precipitate. The solid was isolated by filtration and then recrystallized from H_2O/EtOH to give *N*-(4-chlorobenzoyl)norleucine (10.0 g, 93%) as colorless solid.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 0.85 (t, 3H, *J* = 6.9 Hz), 1.24-1.40 (m, 4H), 1.72-1.85 (m, 2H), 4.31-4.35 (m, 1H), 7.54 (d, 2H, *J* = 8.4 Hz), 7.90 (d, 2H, *J* = 8.4 Hz), 8.66 (d, 1H, *J* = 7.2 Hz), 12.58 (brs).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.0, 21.9, 28.2, 30.5, 52.9, 128.5 (2C), 129.6 (2C), 132.9, 136.4, 165.7, 174.0.

Elemental analysis calcd (%) for $C_{13}H_{16}NO_3Cl$: C 57.89, H 5.98, N 5.19; found: C 57.74, H 5.91, N 5.02.

Synthesis of 2-(4-chlorophenyl)-4-butyl-5-oxazalone



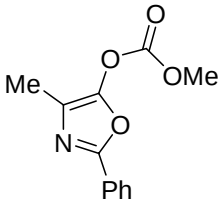
To a stirred suspension of *N*-(4-chlorobenzoyl)norleucine (10.0 g, 37.1 mmol) in CH_2Cl_2 (93 mL) at 0 °C and under Ar was added *N*,*N*'-dicyclohexylcarbodiimide (8.05 g, 37.1 mmol) in small portion. The reaction mixture was stirred at 0 °C for 30 min and at room temperature for 24 h then filtered. The filtrate was concentrated to give a crude product (9.34 g, quant) as white solid that was used next step without further purification. For characterization of this compound, the crude product was recrystallized from hexane to give colorless crystal.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, 3H, *J* = 7.0 Hz), 1.34-1.50 (m, 4H), 1.80-1.90 (m, 1H), 1.97-2.06 (m, 1H), 4.39 (dd, 1H, *J* = 6.6, 6.6 Hz), 7.46 (d, 2H, *J* = 8.6 Hz), 7.93 (d, 2H, *J* = 8.6 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.8, 22.3, 27.3, 31.2, 65.4, 124.4, 129.2 (4C), 139.0, 160.7, 178.2.

Elemental analysis calcd (%) for $C_{13}H_{14}NO_2Cl$: C 62.03, H 5.61, N 5.56; found: C 61.99, H 5.57, N 5.51.

Synthesis of 5-methoxycarbonyloxy-4-methyl-2-phenyloxazole (3a)



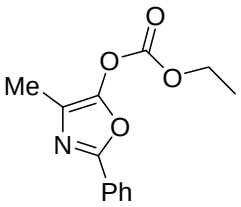
A mixture of 2-phenyl-4-methyl-5-oxazalone (1.75 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added methyl chloroformate (0.866 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give the product (1.64 g, 71%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 3H), 3.92 (s, 3H), 7.37-7.40 (m, 3H), 7.88-7.94 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.3, 56.6, 120.5, 125.9 (2C), 127.2, 128.8 (2C), 130.3, 146.1, 152.3, 154.8.

Elemental analysis calcd (%) for $C_{12}H_{11}NO_4$: C 61.80, H 4.75, N 6.01; found: C 61.82, H 4.74, N 5.99.

5-Ethoxycarbonyloxy-4-methyl-2-phenyloxazole (3b)



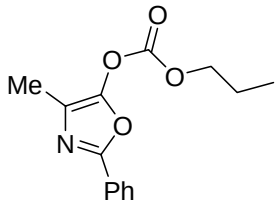
A mixture of 2-phenyl-4-methyl-5-oxazalone (6.13 g, 35.0 mmol) and NEt_3 (3.68 mL, 38.5 mmol) in THF (300 mL) were stirred at 0 °C. To this was added ethyl chloroformate (3.68 mL, 38.5 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (6.67 g, 77%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, 3H, *J* = 7.2 Hz), 2.17 (s, 3H), 4.40 (q, 2H, *J* = 7.2 Hz), 7.43-7.45 (m, 3H) 7.96-7.98 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.3, 14.0, 66.4, 120.4, 125.8 (2C), 127.1, 128.7 (2C), 130.2, 146.0, 151.5, 154.7.

Elemental analysis calcd (%) for $C_{13}H_{13}NO_4$: C 63.15, H 5.30, N 5.67; found: C 63.06, H 5.50, N 5.69.

5-Propoxycarbonyloxy-4-methyl-2-phenyloxazole (3c)



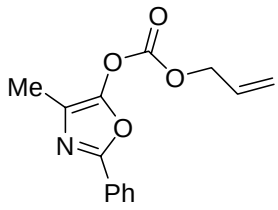
A mixture of 2-phenyl-4-methyl-5-oxazalone (1.75 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added propyl chloroformate (1.30 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (1.44 g, 55%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, 3H, *J* = 7.6 Hz), 1.80 (tq, 2H, *J* = 6.5, 7.6 Hz), 2.14 (s, 3H), 4.28 (t, 2H, *J* = 6.5 Hz), 7.40-7.43 (m, 3H) 7.92-7.95 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.2, 10.4, 21.9, 71.9, 120.4, 125.9 (2C), 127.2, 128.8 (2C), 130.3, 146.2, 151.7, 154.8.

Elemental analysis calcd (%) for $C_{14}H_{15}NO_4$: C 64.36, H 5.79, N 5.36; found: C 64.19, H 5.99, N 5.38.

5-Allyloxycarbonyloxy-4-methyl-2-phenyloxazole (3d)



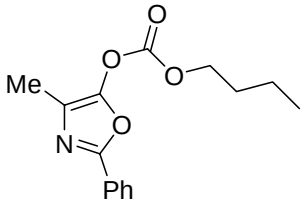
A mixture of 2-phenyl-4-methyl-5-oxazalone (1.75 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added allyl chloroformate (1.19 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (1.87 g, 72%) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.14 (s, 3H), 4.79 (d, 2H, *J* = 6.0 Hz), 5.38 (dd, 1H, *J* = 1.0, 10.8 Hz), 5.46 (dd, 1H, *J* = 1.0, 16.0 Hz), 5.96-6.03 (m, 1H), 7.40-7.43 (m, 3H) 7.92-7.95 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.4, 70.6, 120.5 (2C), 125.9 (2C), 127.2, 128.8 (2C), 130.3, 130.4, 146.1, 151.5, 154.9.

Elemental analysis calcd (%) for $C_{14}H_{13}NO_4$: C 64.86, H 5.05, N 5.40; found: C 64.56, H 5.28, N 5.48.

5-Butoxycarbonyloxy-4-methyl-2-phenyloxazole (3e)



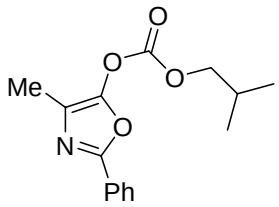
A mixture of 2-phenyl-4-methyl-5-oxazalone (526 mg, 3.00 mmol) and NEt_3 (0.460 mL, 3.30 mmol) in THF (30 mL) were stirred at 0 °C. To this was added butyl chloroformate (0.428 mL, 3.30 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (20 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 5/1) to give (578 mg, 70%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, 3H, *J* = 7.3 Hz), 1.43 (tq, 2H, *J* = 7.4, 7.3 Hz), 1.73 (tt, 2H, *J* = 7.4, 6.6 Hz), 2.13 (s, 3H), 4.30 (t, 2H, *J* = 6.6 Hz), 7.39-7.41 (m, 3H) 7.91-7.94 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.4, 13.7, 18.9, 30.5, 70.3, 120.4, 125.9 (2C), 127.2, 128.8 (2C), 130.3, 146.2, 151.7, 154.8.

Elemental analysis calcd (%) for $C_{15}H_{17}NO_4$: C 65.44, H 6.22, N 5.09; found: C 65.26, H 6.39, N 5.10.

5-(2-Methylpropyl)carbonyloxy-4-methyl-2-phenyloxazole (3f)



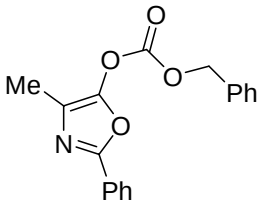
A mixture of 2-phenyl-4-methyl-5-oxazalone (1.75 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added 2-methylpropyl chloroformate (1.47 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and t the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (1.93 g, 70%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ =1.01 (d, 6H, *J* = 6.8 Hz), 2.04-2.11 (m, 1H), 2.14 (s, 3H), 4.10 (d, 2H, *J* = 6.4 Hz), 7.40-7.43 (m, 3H), 7.92-7.96 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.4, 18.8 (2C), 27.8, 76.3, 120.4, 125.9 (2C), 127.2, 128.8 (2C), 130.3, 146.2, 151.7, 154.8.

Elemental analysis calcd (%) for $C_{15}H_{17}NO_4$: C 65.44, H 6.22, N 5.09; found: C 65.25, H 6.37, N 5.25.

5-Benzyloxycarbonyloxy-4-methyl-2-phenyloxazole (3g)



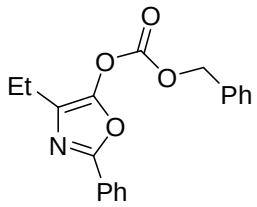
A mixture of 2-phenyl-4-methyl-5-oxazalone (3.50 g, 20.0 mmol) and NEt_3 (3.11 mL, 22.0 mmol) in THF (200 mL) were stirred at 0 °C. To this was added benzyl chloroformate (3.31 mL, 22.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (5.40 g, 87%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (s, 3H), 5.32 (s, 2H), 7.39-7.47 (m, 8H), 7.91-7.94 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.4, 71.9, 120.5, 126.0 (2C), 127.2, 128.77 (2C), 128.82 (2C), 128.9 (2C), 129.3, 130.4, 133.9, 146.1, 151.6, 154.9.

Elemental analysis calcd (%) for $C_{18}H_{15}NO_4$: C 69.89, H 4.89, N 4.53; found: C 69.98, H 4.95, N 4.57.

5-Benzyloxycarbonyloxy-4-ethyl-2-phenyloxazole (3h)



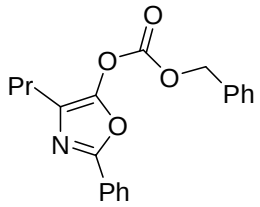
A mixture of 2-phenyl-4-ethyl-5-oxazalone (1.89 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added benzyl chloroformate (1.65 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica gel column chromatography (Hexane/Et_2O = 3/1) to give (2.31 g, 71%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, 3H, *J* = 7.7 Hz), 2.53 (q, 2H, *J* = 7.7 Hz), 5.32 (s, 2H), 7.39-7.49 (m, 8H), 7.93-7.98 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.5, 18.5, 71.8, 125.9, 126.0 (2C), 127.3, 128.76 (2C), 128.8 (2C), 128.9 (2C), 129.3, 130.3, 134.0, 145.5, 151.9, 155.0.

Elemental analysis calcd (%) for $C_{19}H_{17}NO_4$: C 70.58, H 5.30, N 4.33; found: C 70.50, H 5.26, N 4.39.

5-Benzyloxycarbonyloxy-4-propyl-2-phenyloxazole (3i)



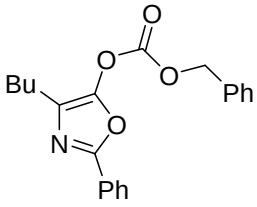
A mixture of 2-phenyl-4-propyl-5-oxazalone (2.03 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added benzyl chloroformate (1.65 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (2.85 g, 85%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, 3H, *J* = 7.3 Hz), 1.68 (tq, 2H, *J* = 7.5, 7.3 Hz), 2.45 (t, 2H, *J* = 7.5 Hz), 5.32 (s, 2H), 7.38-7.48 (m, 8H), 7.93-7.97 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 21.2, 26.8, 71.7, 124.4, 125.8 (2C), 127.2, 128.6 (4C), 128.7 (2C), 129.1, 130.1, 133.8, 145.8, 151.7, 154.8.

Elemental analysis calcd (%) for $C_{20}H_{19}NO_4$: C 71.20, H 5.68, N 4.15; found: C 71.00, H 5.63, N 4.30.

5-Benzyloxycarbonyloxy-4-butyl-2-phenyloxazole (3j)



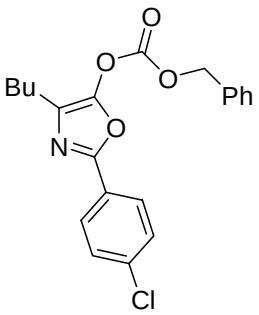
A mixture of 2-phenyl-4-butyl-5-oxazalone (2.61 g, 10.0 mmol) and NEt_3 (1.55 mL, 11.0 mmol) in THF (100 mL) were stirred at 0 °C. To this was added benzyl chloroformate (1.65 mL, 11.0 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 3/1) to give (3.21 g, 76%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.6 Hz), 1.35 (tq, 2H, *J* = 7.5, 7.6 Hz), 1.62 (tt, 2H, *J* = 7.7, 7.8 Hz), 2.46 (t, 2H, *J* = 7.8 Hz), 5.32 (s, 2H), 7.38-7.46 (m, 8H), 7.93-7.95 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.4, 24.7, 30.1, 71.8, 124.8, 126.0 (2C), 127.3, 128.8 (4C), 128.9 (2C), 129.2, 130.3, 134.0, 145.8, 151.8, 155.0.

Elemental analysis calcd (%) for $C_{21}H_{21}NO_4$: C 71.78, H 6.02, N 3.99; found: C 71.72, H 6.14, N 3.94.

5-Benzyloxycarbonyloxy-4-butyl-2-(4-chlorophenyl)oxazole (3k)



A mixture of 2-(4-chlorophenyl)-4-butyl-5-oxazalone (3.02 g, 12.0 mmol) and NEt_3 (1.86 mL, 13.2 mmol) in THF (100 mL) were stirred at 0 °C. To this was added benzyl chloroformate (1.98 mL, 13.2 mmol) and the mixture was stirred at room temperature for 20 h. H_2O (100 mL) was added, and the mixture was extracted with Et_2O (50 mL x 3). The organic layer was dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 10/1) to give (3.35 g, 72%) as colorless oil.

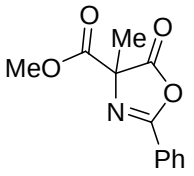
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.4 Hz), 1.35 (tq, 2H, *J* = 7.6, 7.4 Hz), 1.62 (tt, 2H, *J* = 7.6, 7.6 Hz), 2.46 (t, 2H, *J* = 7.6 Hz), 5.33 (s, 2H), 7.39-7.43 (m, 7H), 7.88 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 22.2, 24.5, 29.9, 71.8, 124.9, 125.7, 127.2 (2C), 128.7 (2C), 128.8 (2C), 129.0 (2C), 129.2, 133.8, 136.2, 145.8, 151.6, 153.9.

Elemental analysis calcd (%) for $C_{21}H_{20}NO_4Cl$: C 65.37, H 5.22, N 3.63; found: C 65.35, H 5.24, N 3.59.

Synthesis of substrate *rac*-azlactones 1

Typical procedure: synthesis of 4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid methyl ester (1a)



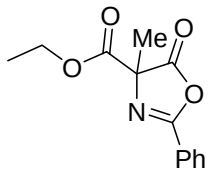
To a solution of **3a** (1.64 g, 7.03 mmol) in CH_2Cl_2 (14 mL) was added 4-pyrrolidinoprydine (0.104 g, 0.703 mmol). This mixture was stirred at room temperature for 14 h. The mixture was passed through a plug of silica. The silica was washed with Hexane/Et_2O = 1/1 to elute the product. The volatiles were removed by rotary evaporation, then the residue was purified by silica-gel column chromatography to give **1a** (1.20 g, 73%) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.78(s, 3H), 3.79 (s, 3H), 7.50 (dd, 2H, *J* = 7.3, 8.2 Hz), 7.61 (t, 1H, *J* = 7.3 Hz), 8.03 (d, 2H, *J* = 8.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7, 53.8, 72.8, 125.3, 128.4 (2C), 129.0 (2C), 133.5, 163.3, 166.5, 175.1.

Elemental analysis calcd (%) for $C_{12}H_{11}NO_4$: C 61.80, H 4.75, N 6.01; found: C 61.80, H 4.90, N 5.94.

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid ethyl ester (1b)



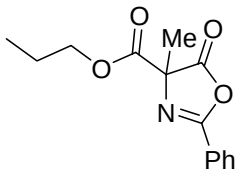
Colorless oil (66%).

^{1}H NMR (400 MHz, $CDCl_3$): δ =1.26 (t, 3H, *J* = 7.3 Hz) 1.77 (s, 3H), 4.20-4.30 (m, 2H), 7.50 (dd, 2H, *J* = 7.3, 8.2 Hz), 7.60 (t, 1H, *J* = 7.3 Hz), 8.03 (d, 2H, *J* = 8.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 20.4, 63.0, 72.9, 125.3, 128.2 (2C), 128.8 (2C), 133.3, 163.1, 165.9, 175.1.

Elemental analysis calcd (%) for $C_{13}H_{13}NO_4$: C 63.15, H 5.30, N 5.67; found: C 63.18, H 5.33, N 5.69.

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid propyl ester (1c)



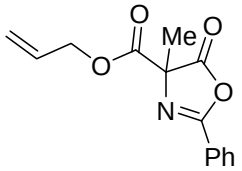
White solid (66%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3H, *J* = 7.3 Hz), 1.65 (qdd, 2H, *J* =7.3, 7.1, 7.1 Hz), 1.77 (s, 3H), 4.10-4.21 (m, 2H), 7.50 (dd, 2H, *J* = 7.6, 7.3 Hz), 7.60 (t, 1H, *J* = 7.6 Hz), 8.03 (d, 2H, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.1, 20.4, 21.8, 68.4, 73.0, 125.4, 128.3 (2C), 129.0 (2C), 133.4, 163.3, 166.1, 175.3.

Elemental analysis calcd (%) for $C_{14}H_{15}NO_4$: C 64.36, H 5.79, N 5.36; found: C 64.33, H 5.86, N 5.35.

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid allyl ester (1d)



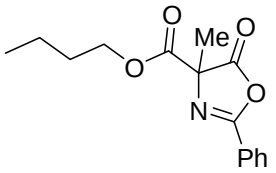
Colorless oil (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.79 (s, 3H), 4.64-4.73 (m, 2H), 5.24 (d, 1H, *J* = 10.5 Hz), 5.30 (dd, 1H, *J* = 17.5, 0.92 Hz), 5.82-5.89 (m, 1H), 7.50 (dd, 2H, *J* = 7.3, 8.0 Hz), 7.61 (t, 1H, *J* = 7.3 Hz), 8.03 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 67.2, 73.0, 119.2, 125.3, 128.4 (2C), 129.0 (2C), 130.8, 133.4, 163.3, 165.7, 175.1.

Elemental analysis calcd (%) for $C_{14}H_{13}NO_4$: C 64.86, H 5.05, N 5.40; found: C 64.80, H 5.03, N 5.42.

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid butyl ester (1e)



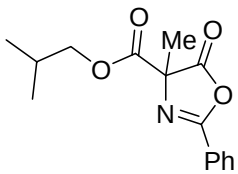
White solid (54%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, 3H, *J* = 7.3 Hz), 1.28-1.37 (m, 2H), 1.57-1.65 (m, 2H), 1.77 (s, 3H), 4.13-4.26 (m, 2H), 7.50 (dd, 2H, *J* = 7.3, 7.6 Hz), 7.61 (t, 1H, *J* = 7.3 Hz), 8.03 (d, 2H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 18.9, 20.4, 30.4, 66.9, 73.0, 125.4, 128.3 (2C), 129.0 (2C), 133.4, 163.2, 166.1, 175.3.

Elemental analysis calcd (%) for $C_{15}H_{17}NO_4$: C 65.44, H 6.22, N 5.09; found: C 65.27, H 6.20, N 5.07.

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid (2-methylpropyl) ester (1f)



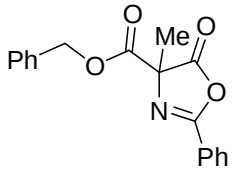
Colorless oil (54%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (d, 6H, *J* = 6.9 Hz), 1.77 (s, 3H), 1.90-1.97 (m, 1H), 3.90-4.00 (m, 2H), 7.49 (dd, 2H, *J* = 7.8, 8.3 Hz), 7.60 (t, 1H, *J* = 7.8 Hz), 8.02 (d, 2H, *J* = 8.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 (2C), 20.3, 27.7, 72.7, 73.1, 125.4, 128.3 (2C), 129.0 (2C), 133.4, 163.3, 166.0, 175.3.

Elemental analysis calcd (%) for $C_{15}H_{17}NO_4$: C 65.44, H 6.22, N 5.09; found: C 65.56, H 6.33, N 5.02.

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1g)



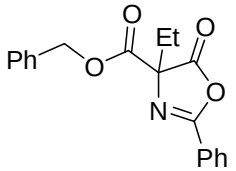
Colorless oil (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.80 (s, 3H), 5.20 (d, 1H, *J* = 12.4 Hz), 5.27 (d, 1H, *J* = 12.4 Hz), 7.27-7.35 (m, 5H), 7.51 (dd, 2H, *J* = 7.4, 8.0 Hz), 7.62 (t, 1H, *J* = 7.4 Hz), 8.02 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 68.3, 73.0, 125.3, 127.9 (2C), 128.4 (2C), 128.6, 128.7 (2C), 129.0 (2C), 133.4, 134.8, 163.4, 165.9, 175.1.

Eelemental analysis calcd (%) for $C_{18}H_{15}NO_4$: C 69.89, H 4.89, N 4.53; found: C 69.65, H 4.88, N 4.40.

4-Ethyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1h)



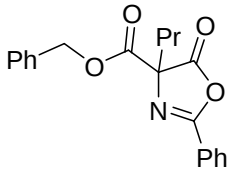
Colorless oil (54%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.6 Hz), 2.21-2.39 (m, 2H), 5.20 (d, 1H, *J* = 12.4 Hz), 5.25 (d, 1H, *J* = 12.4 Hz), 7.27-7.35 (m, 5H), 7.49 (dd, 2H, *J* = 7.5, 8.0 Hz), 7.60 (t, 1H, *J* = 7.5 Hz), 8.03 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 27.9, 68.1, 77.3, 125.1, 127.9 (2C), 128.3 (2C), 128.4, 128.6 (2C), 128.8 (2C), 133.3, 134.8, 163.2, 165.6, 174.2.

Elemental analysis calcd (%) for $C_{19}H_{17}NO_4$: C 70.58, H 5.30, N 4.33; found: C 70.47, H 5.39, N 4.35.

4-Propyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1i)



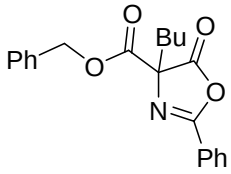
Colorless oil (63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, 3H, *J* = 7.3 Hz), 1.19-1.41 (m, 2H), 2.30 (ddd, 1H, *J* = 14.1, 11.4, 5.0 Hz), 2.18 (ddd, 1H, *J* = 14.1, 12.2, 4.8 Hz), 5.20 (d, 1H, *J* = 12.8 Hz), 5.26 (d, 1H, *J* = 12.8 Hz), 7.27-7.36 (m, 5H), 7.50 (dd, 2H, *J* = 7.8 Hz), 7.60 (t, 1H, *J* = 7.1 Hz), 8.03 (d, 2H, *J* = 8.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 16.9, 36.5, 68.2, 76.9, 125.3, 128.0 (2C), 128.4 (2C), 128.6, 128.7 (2C), 129.0 (2C), 133.4, 134.9, 163.2, 165.7, 174.4.

Elemental analysis calcd (%) for $C_{20}H_{19}NO_4$: C 71.20, H 5.68, N 4.15; found: C 71.16, H 5.80, N 4.23.

4-Butyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1j)



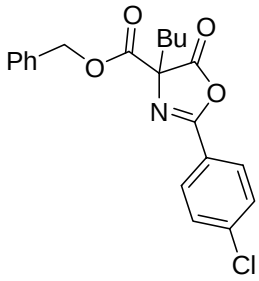
White solid (76%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, 3H, *J* = 7.1 Hz), 1.11-1.38 (m, 4H), 2.31 (ddd, 1H, *J* = 13.7, 11.4, 5.0 Hz), 2.20 (ddd, 1H, *J* = 13.8, 12.1, 4.6 Hz), 5.20 (d, 1H, *J* = 12.8 Hz), 5.26 (d, 1H, *J* = 12.8 Hz), 7.27-7.35 (m, 5H), 7.50 (dd, 2H, *J* = 7.6, 6.9 Hz), 7.60 (t, 1H, *J* = 7.6 Hz), 8.03 (d, 2H, *J* = 6.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 22.3, 25.3, 34.1, 68.1, 76.8, 125.1, 127.9 (2C), 128.3 (2C), 128.4, 128.6 (2C), 128.8 (2C), 133.2, 134.7, 163.0, 165.6, 174.3.

Elemental analysis calcd (%) for $C_{21}H_{21}NO_4$: C 71.78, H 6.02, N 3.99; found: C 71.66, H 6.03, N 3.98.

4-Butyl-5-oxo-2-(4-chlorophenyl)-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1k)



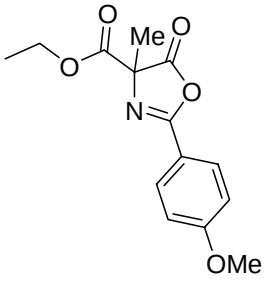
Colorless oil (26%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, 3H, *J* = 7.3 Hz), 1.11-1.42 (m, 4H), 2.19 (ddd, 1H, *J* = 14.0, 11.6, 4.8 Hz), 2.31 (ddd, 1H, *J* = 14.0, 13.6, 4.8 Hz), 5.21 (d, 1H, *J* = 12.3 Hz), 5.26 (d, 1H, *J* = 12.3 Hz) 7.25-7.40 (m, 5H), 7.48 (d, 2H, *J* = 8.3 Hz), 7.97 (d, 2H, *J* = 8.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 22.3, 25.4, 34.2, 68.2, 76.8, 123.6, 127.9 (2C), 128.5, 128.6 (2C), 129.3 (2C), 129.6 (2C), 134.7, 139.7, 162.2, 165.5, 173.9.

Elemental analysis calcd (%) for $C_{21}H_{20}NO_4Cl$: C 65.37, H 5.22, N 3.63; found: C 65.35, H 5.24, N 3.59.

4-Methyl-5-oxo-2-(4-methoxyphenyl)-4,5-dihydrooxazole-4-carboxylic acid ethyl ester (1l)



White solid (71%).

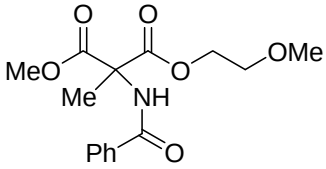
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, 3H, *J* = 7.1 Hz), 1.76 (s, 3H), 3.88 (s, 3H), 4.18-4.32 (m, 2H), 6.98 (d, 2H, *J* = 8.7 Hz), 7.97 (d, 2H, *J* = 8.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 20.6, 55.6, 63.0, 72.9, 114.4 (2C), 117.6, 130.3 (2C), 162.9, 163.7, 166.3, 175.5.

Elemental analysis calcd (%) for $C_{14}H_{15}NO_5$: C 60.64, H 5.45, N 5.05; found: C 60.54, H 5.55, N 5.03.

Synthesis of *rac*-products 2 as authentic samples

Typical procedure: synthesis of *rac*-2-Benzoylamino-2-methylmalonic acid methyl ester (2-methoxyethyl) ester (*rac*-2a)



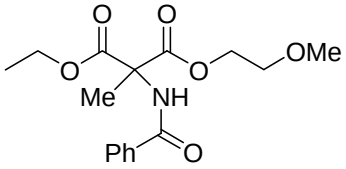
To a mixture of **1a** (23.3 mg, 0.100 mmol) and $Sc(OTf)_3$ (4.9 mg, 0.010 mmol) in toluene (0.50 mL) was added 2-methoxyethanol (80 μL, 1.0 mmol). The mixture was stirred at room temperature for 16 h. The product was isolated by silica-gel column chromatography (hexane/Et_2O = 1/2) to give ***rac*-2a** (24.7 mg, 80%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (s, 3H), 3.27 (s, 3H), 3.49-3.59 (m, 2H), 3.78 (s, 3H), 4.32 (t, 2H, *J* = 4.6 Hz), 7.40 (dd, 2H, *J* = 7.3, 7.3 Hz), 7.48 (t, 1H, *J* = 7.3 Hz), 7.54 (brs, 1H), 7.79 (d, 2H, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 53.6, 59.0, 63.2, 65.5, 70.1, 127.2 (2C), 128.7 (2C), 132.0, 133.4, 166.0, 168.8, 169.3.

Elemental analysis calcd (%) for $C_{15}H_{19}NO_6$: C 58.25, H 6.19, N 4.53; found: C 58.15, H 6.19, N 4.35.

***rac*-2-Benzoylamino-2-methylmalonic acid ethyl ester (2-methoxyethyl) ester (*rac*-2b)**



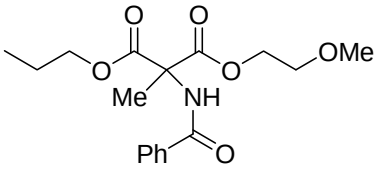
Colorless oil (85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, 3H, *J* = 7.3 Hz), 1.87 (s, 3H), 3.29 (s, 3H), 3.54-3.57 (m, 2H), 4.21-4.30 (m, 2H), 4.35 (t, 2H, *J* = 4.5 Hz), 7.43 (dd, 2H, *J* = 7.6, 7.8 Hz), 7.51 (t, 1H, *J* = 7.6 Hz), 7.55 (brs, 1H), 7.80 (d, 2H, *J* = 7.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 21.1, 59.0, 62.9, 63.2, 65.4, 70.1, 127.2 (2C), 128.7 (2C), 132.0, 133.5, 166.0, 168.8, 168.9.

Elemental analysis calcd (%) for $C_{16}H_{21}NO_6$: C 59.43, H 6.55, N 4.33; found: C 59.30, H 6.66, N 4.29.

***rac*-2-Benzoylamino-2-methylmalonic acid propyl ester (2-methoxyethyl) ester (*rac*-2c)**



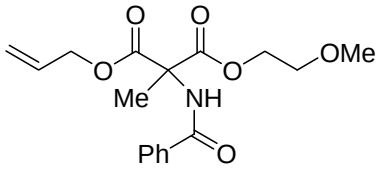
Colorless oil (95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3H, *J* = 7.5 Hz), 1.60-1.70 (m, 2H), 1.87 (s, 3H), 3.28 (s, 3H), 3.53-3.57 (m, 2H), 4.13-4.22 (m, 2H), 4.29-4.38 (m, 2H), 7.42 (dd, 2H, *J* = 7.2, 7.6 Hz), 7.50 (t, 1H, *J* = 7.2 Hz), 7.55 (brs, 1H), 7.79 (d, 2H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.3, 21.1, 21.9, 59.0, 63.2, 65.4, 68.3, 70.1, 127.2 (2C), 128.7 (2C), 132.0, 133.5, 166.0, 168.8, 169.0.

Elemental analysis calcd (%) for $C_{17}H_{23}NO_6$: C 60.52, H 6.87, N 4.15; found: C 60.50, H 6.87, N 3.92.

***rac*-2-Benzoylamino-2-methylmalonic acid allyl ester (2-methoxyethyl) ester (*rac*-2d)**



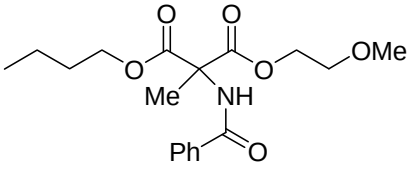
Colorless oil (89%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88 (s, 3H), 3.27 (s, 3H), 3.52-3.58 (m, 2H), 4.32-4.35 (m, 2H), 4.67-4.69 (m, 2H), 5.20-5.23 (m, 1H), 5.27-5.32 (m, 1H), 5.81-5.91 (m, 1H), 7.41 (dd, 2H, *J* = 7.6, 7.4 Hz), 7.49 (t, 1H, *J* = 7.4 Hz), 7.54 (brs, 1H), 7.79 (d, 2H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 59.0, 63.3, 65.5, 67.1, 70.1, 118.9, 127.2 (2C), 128.7 (2C), 131.2, 132.0, 133.4, 166.1, 168.5, 168.7.

Elemental analysis calcd (%) for $C_{17}H_{21}NO_6$: C 60.89, H 6.31, N 4.18; found: C 60.92, H 6.34, N 3.99.

***rac*-2-Benzoylamino-2-methylmalonic acid butyl ester (2-methoxyethyl) ester (*rac*-2e)**



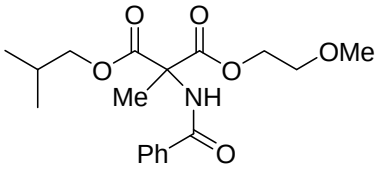
Colorless oil (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.6 Hz), 1.34 (qt, 2H, *J* = 7.6, 7.0 Hz), 1.63 (tt, 2H, *J* = 7.0, 7.0 Hz), 1.88 (s, 3H), 3.30 (s, 3H), 3.52-3.61 (m, 2H), 4.17-4.27 (m, 2H), 4.30-4.40 (m, 2H), 7.44 (dd, 2H, *J* = 7.3, 6.8 Hz), 7.52 (t, 1H, *J* = 7.3 Hz), 7.56 (brs, 1H), 7.81 (d, 2H, *J* = 6.8 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 19.0, 21.1, 30.4, 59.0, 63.2, 65.4, 66.6, 70.1, 127.2 (2C), 128.7 (2C), 132.0, 133.5, 166.0, 168.7, 169.0.

Elemental analysis calcd (%) for $C_{18}H_{25}NO_6$: C 61.52, H 7.17, N 3.99; found: C 61.31, H 7.16, N 3.91.

rac-2-Benzoylamino-2-methylmalonic acid (2-Methylpropyl) ester (2-methoxyethyl) ester (_rac_-2f)



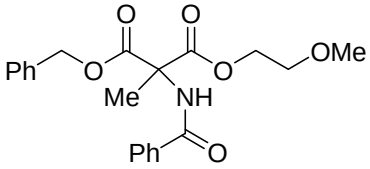
Colorless oil (87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, 6H, *J* = 6.9 Hz), 1.90 (s, 3H), 1.93-2.02 (m, 1H), 3.30 (s, 3H), 3.53-3.59 (m, 2H), 3.96-4.06 (m, 2H), 4.31-4.41 (m, 2H), 7.45 (dd, 2H, *J* = 7.6, 7.3 Hz), 7.53 (t, 1H, *J* = 7.3 Hz), 7.57 (brs, 1H), 7.82 (d, 2H, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.9 (2C), 21.1, 27.7, 59.0, 63.3, 65.4, 70.1, 72.7, 127.2 (2C), 128.7 (2C), 132.0, 133.5, 166.1, 168.7, 169.0.

Elemental analysis calcd (%) for $C_{18}H_{25}NO_6$: C 61.52, H 7.17, N 3.99; found: C 61.51, H 7.14, N 3.91.

rac-2-Benzoylamino-2-methylmalonic acid benzyl ester (2-methoxyethyl) ester (_rac_-2g)



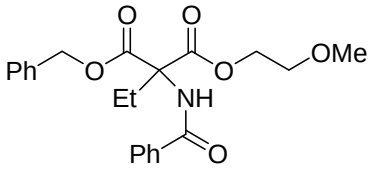
Colorless oil (85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.90 (s, 3H), 3.25 (s, 3H), 3.43-3.53 (m, 2H), 4.29 (t, 2H, *J* = 4.8 Hz), 5.25 (s, 2H), 7.29-7.36 (m, 5H), 7.44 (dd, 2H, *J* = 7.6, 7.3 Hz), 7.53 (t, 1H, *J* = 7.3 Hz), 7.56 (brs, 1H), 7.81 (d, 2H, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 59.0, 63.3, 65.5, 68.2, 69.9, 127.2 (2C), 128.2 (2C), 128.56, 128.64 (2C), 128.7 (2C), 132.0, 133.4, 135.1, 166.1, 168.6, 168.7.

Elemental analysis calcd (%) for $C_{21}H_{23}NO_6$: C 65.44, H 6.02, N 3.63; found: C 65.33, H 6.10, N 3.52.

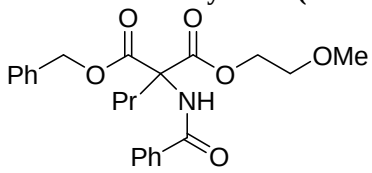
rac-2-Benzoylamino-2-ethylmalonic acid benzyl ester (2-methoxyethyl) ester (_rac_-2h)



Colorless oil (90%).

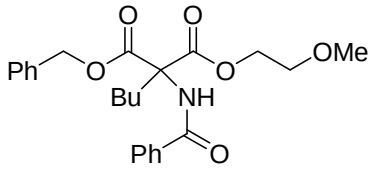
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, 3H, *J* = 7.5 Hz), 2.53 (q, 2H, *J* = 7.6 Hz), 3.25 (s, 3H), 3.42-3.52 (m, 2H), 4.24-4.35 (m, 2H), 5.22 (d, 1H, *J* = 12.4 Hz), 5.26 (d, 1H, *J* = 12.4 Hz), 7.26-7.35 (m, 5H), 7.44 (dd, 2H, *J* = 7.6, 7.3 Hz), 7.50 (brs, 1H), 7.52 (t, 1H, *J* = 7.3 Hz), 7.82 (d, 2H, *J* = 7.3 Hz)
^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.9, 25.7, 58.9, 65.4, 67.5, 68.1, 70.0, 127.2 (2C), 128.3 (2C), 128.57, 128.63 (2C), 128.7 (2C), 132.0, 133.5, 135.1, 166.1, 168.1, 168.2.
Elemental analysis calcd (%) for $C_{22}H_{25}NO_6$: C 66.15, H 6.31, N 3.51; found: C 66.06, H 6.41, N 3.36.

rac-2-Benzoylamino-2-propylmalonic acid benzyl ester (2-methoxyethyl) ester (_rac_-2i)



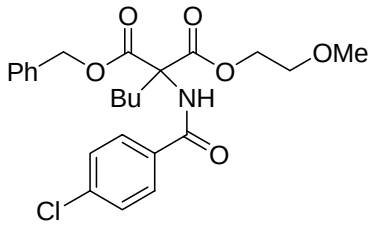
Colorless oil (95%).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, 3H, *J* = 7.3 Hz), 1.10-1.30 (m, 2H), 2.46 (t, 2H, *J* = 8.5 Hz), 3.24 (s, 3H), 3.44-3.52 (m, 2H), 4.24-4.35 (m, 2H), 5.21 (d, 1H, *J* = 12.4 Hz), 5.25 (d, 1H, *J* = 12.4 Hz), 7.29-7.33 (m, 5H), 7.44 (dd, 2H, *J* = 7.3, 8.2 Hz), 7.50 (brs, 1H), 7.52 (t, 1H, *J* = 7.3 Hz), 7.80 (d, 2H, *J* = 8.2 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 17.1, 34.4, 58.9, 65.4, 67.0, 68.1, 70.0, 127.2 (2C), 128.3 (2C), 128.56, 128.62 (2C), 128.7 (2C), 132.0, 133.5, 135.1, 166.0, 168.15, 168.23.
Elemental analysis calcd (%) for $C_{23}H_{27}NO_6$: C 66.81, H 6.58, N 3.39; found: C 66.89, H 6.72, N 3.07.

rac-2-Benzoylamino-2-butylmalonic acid benzyl ester (2-methoxyethyl) ester (_rac_-2j)



Colorless oil (89%).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, 3H, *J* = 7.3 Hz), 1.01-1.20 (m, 2H), 1.27 (tt, 2H, *J* = 7.3, 8.7 Hz), 2.47 (t, 2H, *J* = 8.7 Hz), 3.25 (s, 3H), 3.43-3.52 (m, 2H), 4.23-4.34 (m, 2H), 5.21 (d, 1H, *J* = 12.4 Hz), 5.28 (d, 1H, *J* = 12.4 Hz), 7.29-7.32 (m, 5H), 7.45 (dd, 2H, *J* = 7.3, 7.8 Hz), 7.51 (brs, 1H), 7.53 (t, 1H, *J* = 7.3 Hz), 7.82 (d, 2H, *J* = 7.8 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 22.5, 25.9, 32.1, 58.9, 65.4, 67.0, 68.1, 70.0, 127.2 (2C), 128.4 (2C), 128.58, 128.62 (2C), 128.7 (2C), 132.0, 133.5, 135.1, 166.0, 168.19, 168.23.
Elemental analysis calcd (%) for $C_{24}H_{29}NO_6$: C 67.43, H 6.84, N 3.28; found: C 67.39, H 6.81, N 3.25.

rac-2-(4-Chlorobenzoylamino)-2-butylmalonic acid ethyl ester (2-methoxyethyl) ester (_rac_-2k)



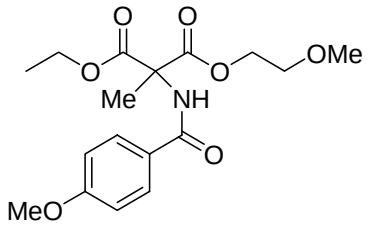
Colorless oil (62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, 3H, *J* = 7.1 Hz), 0.99-1.18 (m, 2H), 1.27 (tt, 2H, *J* = 7.1, 8.7 Hz), 2.46 (t, 2H, *J* = 8.7 Hz), 3.25 (s, 3H), 3.42-3.51 (m, 2H), 4.23-4.34 (m, 2H), 5.21 (d, 1H, *J* = 12.3 Hz), 5.26 (d, 1H, *J* = 12.3 Hz), 7.28-7.35 (m, 5H), 7.42 (d, 2H, *J* = 8.3 Hz), 7.46 (brs, 1H), 7.75 (d, 2H, *J* = 8.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 22.4, 25.7, 31.9, 58.8, 65.3, 66.9, 68.1, 69.8, 128.3 (2C), 128.5 (3C), 128.6 (2C), 128.9 (2C), 131.8, 134.9, 138.2, 164.9, 167.97, 168.00.

Elemental analysis calcd (%) for $C_{24}H_{28}NO_6Cl$: C 62.40, H 6.11, N 3.03; found: C 62.52, H 6.22, N 2.96.

***rac*-2-(4-Methoxybenzoylamino)-2-methylmalonic acid ethyl ester (2-methoxyethyl) ester (*rac*-2l)**



Colorless oil (95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, 3H, *J* = 7.1 Hz), 1.86 (s, 3H), 3.29 (s, 3H), 3.52-3.60 (m, 2H), 3.84 (s, 3H), 4.27 (q, 2H, *J* = 7.1 Hz), 4.35 (t, 2H, *J* = 4.8 Hz), 6.92 (d, 2H, *J* = 8.7 Hz), 7.45 (brs, 1H), 7.77 (d, 2H, *J* = 8.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 21.1, 55.5, 58.9, 62.8, 63.1, 65.4, 70.1, 113.8 (2C), 125.8, 129.1 (2C), 162.6, 165.6, 168.9, 169.0.

elemental analysis calcd (%) for $C_{17}H_{23}NO_7$: C 57.78, H 6.58, N 3.96; found: C 57.89, H 6.57, N 3.85.

Cu(OAc)$_2$/DTBM-SEGPHOS catalyzed alcoholytic kinetic resolution of (1a–l)

The value of theoretical conversion was calculated by the equation, convn = $ee_s/(ee_s + ee_p)$. The value of experimental conversion was determined as isolated yield of product **2** because **2** is quite stable under the condition of silica-gel column chromatography while small part of **1** is decomposed during the chromatographic isolation. (We confirmed rapid elution suppresses the decomposition in the least amount)**.** The differences in the values between theoretical conversions and experimental conversions were within ±2% in all cases, and the total yields of **1** and **2** were between 90–100%. In Table S-1, the k_{rel} values calculated from theoretical conversion and experimental conversion by using eqs (1), (2), (4), and (5) (equations in Figure 1) are listed in 3 digit number. The k_{rel} values calculated from theoretical

conversion by using eq (1), (4) and the k_{rel} values calculated from theoretical conversion by using eq (2), (5) became exactly same. However, the k_{rel} values calculated from experimental conversion by using eq (1), (4) and the k_{rel} values calculated from theoretical conversion by using eq (2), (5) were varied slightly.

Table S-1. Asymmetric alcoholysis of azlacone **1** with Cu-DTBM-SEGPHOS catalysts [a] (expressed as 3-digit numbers).

entry	sub-strate	time /h	convn [b] /%	% ee of **1**	k_{rel} [c,g] (0th)	k_{rel} [d,g] (1st)	% ee of **2**	k_{rel} [e,g] (0th)	k_{rel} [f,g] (1st)
1	**1a**	67	57.4(55.4)	99.4	6.66(9.01)	36.8(50.5)	73.9	6.66(6.66)	36.8(21.2)
2	**1b**	8	21.0(20.3)	21.5	9.58(11.8)	11.8(14.6)	81.1	9.58(9.58)	11.8(11.7)
3		17	31.5(30.3)	37.5	9.81(13.6)	14.1(19.5)	81.5	9.81(9.81)	14.1(13.8)
4		30	48.0(46.8)	74.0	9.05(11.6)	19.9(25.6)	80.1	9.05(9.05)	19.9(18.9)
5		52	55.8(55.3)	93.2	6.60(7.11)	22.1(23.8)	73.7	6.60(6.60)	22.1(20.6)
6	**1c**	37	16.6(17.6)	15.4	7.85(6.17)	9.12(7.17)	77.4	7.85(7.85)	9.12(9.22)
7		61	30.0(31.1)	33.2	7.81(6.56)	10.8(9.04)	77.3	7.81(7.81)	10.8(10.9)
8		52	33.9(33.5)	39.5	7.66(8.26)	11.2(12.1)	76.9	7.66(7.66)	11.2(11.1)
9		72	54.9(55.5)	94.1	7.77(7.15)	27.1(24.8)	77.2	7.77(7.77)	27.1(30.3)
10	**1d**	51	54.7(55.6)	89.2	6.69(5.95)	19.6(17.4)	74.0	6.69(6.69)	19.6(21.9)
11 [h]	**1e**	76	57.1(57.3)	92.8	5.60(5.48)	18.3(17.9)	69.7	5.60(5.60)	18.3(18.8)
12	**1f**	8	15.4(17.4)	15.2	11.3(6.18)	13.1(7.17)	83.7	11.3(11.3)	13.1(13.4)
13		16	31.5(32.7)	39.5	13.0(9.69)	19.1(14.2)	85.7	13.0(13.0)	19.1(19.5)
14		22	38.8(39.5)	52.9	11.1(9.54)	18.8(16.1)	83.5	11.1(11.1)	18.8(19.1)
15		50	53.4(53.8)	88.8	7.93(7.42)	23.2(21.7)	77.6	7.93(7.93)	23.2(24.2)
16	**1g**	8	18.4(19.2)	18.5	10.2(8.03)	12.3(9.61)	82.2	10.2(10.2)	12.3(12.4)
17		18	38.8(38.9)	51.9	10.1(9.82)	16.9(16.4)	82.0	10.1(10.1)	16.9(17.0)
18		24	44.1(43.7)	64.9	10.2(11.2)	19.8(21.8)	82.1	10.2(10.2)	19.8(19.5)
19		49	53.7(53.0)	88.9	7.55(8.45)	22.1(24.8)	76.6	7.55(7.55)	22.1(20.8)
20 [h]	**1h**	100	56.8(58.2)	93.4	5.87(5.08)	19.7(16.9)	70.9	5.87(5.87)	19.7(28.2)
21 [h]	**1i**	122	48.0(48.9)	71.3	7.77(6.85)	16.4(14.4)	77.2	7.77(7.77)	16.4(17.0)
22 [h]	**1j**	118	47.2(47.4)	56.0	4.36(4.28)	7.54(7.40)	62.7	4.36(4.36)	7.54(7.58)
23 [h]	**1k**	74	54.7(54.6)	95.9	8.76(8.72)	33.5(33.4)	79.5	8.76(8.76)	33.5(33.7)
24 [h]	**1l**	12	13.9(16.0)	13.5	11.0(5.87)	12.5(6.69)	83.3	11.0(11.0)	12.5(12.8)
25 [h]		20	25.1(25.8)	28.2	11.5(9.58)	15.1(12.6)	84.0	11.5(11.5)	15.1(15.3)
26 [h]		28	47.4(48.1)	74.2	10.4(9.03)	22.9(19.9)	82.4	10.4(10.4)	22.9(23.7)
27 [h]		48	52.6(53.8)	83.5	7.06(6.07)	18.2(15.6)	75.2	7.06(7.06)	18.2(20.0)

[a] Conditions: see scheme 2. [b] Conversion was calculated by convn = $ee_s/(ee_s + ee_p)$, experimentally determined value is in parenthesis. [c] Calculated by eq (1). [d] Calculated by eq (2). [e] Calculated by eq (4). [f] Calculated by eq (5). [g] Calculated using experimentally determined conversion value in parenthesis. [h] 5 mol% $Cu(OAc)_2$ and 5 mol% DTBM-SEGPHOS were used.

Typical procedure for 1a, 1b, 1c, 1d, 1f, and 1g (2 mol% catalyst loading)

A dried 20 mL Schrenk flask was placed $Cu(OAc)_2$ (1.9 mg, 0.010 mmol), then the solid was heated 80 °C under vacuum for 3 minutes, then the flask was filled with Ar. To this was added (*S*)-DTBM-SEGPHOS (14.2 mg, 0.012 mmol) and toluene (1.0 mL), then the mixture was stirred at 45 °C for 1 h. The mixture was cooled to room temperature, and toluene (1.0 mL) solution of **1a** (116.6 mg, 0.500 mmol) and 2-methoxyethanol (80 μL, 1.0 mmol) was added. The mixture was stirred at 20 °C in incubator. The reaction was monitored by TLC or GLC. The product **2a** and the substrate **1a** were isolated by silica-gel column chromatography (elution: Hexane/Et_2O 10/1→1/1→1/2) to afford **1a** (40.9 mg, 35.1%, 99.4% ee) and **2a** (85.7 mg, 55.4%, 73.9% ee).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid methyl ester (1a)

1a (99.4% ee): GC (Chiraldex G-TA (Aztec) 120 ℃, T_R = 34.2 min (major), T_R = 35.5 min (minor)), $[\alpha]_D^{29}$ = -142.0° (c = 1.06, benzene).

2a (73.9% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 9/1, 1.0 mL/min, T_R = 19.6 min (major), T_R = 21.1 min (minor)).

Specific optical rotation of **2a** derived from **1a** (99.4% ee) was $[\alpha]_D^{27}$ = -21.2° (c = 1.12, benzene).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid ethyl ester (1b)

1b (52.0 mg, 42.1%, 93.2% ee) and **2b** (89.7 mg, 55.3%, 73.7% ee).

1b (86.6 mg, 69.7%, 37.5% ee) and **2b** (49.3 mg, 30.3%, 81.5% ee).

1b (93.2% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 200/1, 0.50 mL/min, T_R = 24.1 min (minor), T_R = 26.6 min (major)), $[\alpha]_D^{29}$ = -110.9° (c = 4.53, benzene).

2b (81.5% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min T_R = 8.9 min (major), T_R = 11.5 min (minor)), $[\alpha]_D^{26}$ = +9.0° (c = 1.00, benzene).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid propyl ester (1c)

1c (52.3 mg, 40.0%, 94.1% ee) and **2c** (93.7 mg, 55.5%, 77.2% ee).

1c (94.1% ee): the ee was determined by HPLC analysis of **2c** which was derived from **1c** obtained by the kinetic resolution, conversion of **1c** into **2c** was carried out with $Sc(OTf)_3$ as catalyst, HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 8.2 min (minor), T_R = 10.8 min (major), $[\alpha]_D^{29}$ = -108.0° (c = 1.11, benzene).

2c (77.2% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 8.0 min (major), T_R = 10.6 min (minor)).

Specific optical rotation of **2c** derived from **1c** (94.1% ee) was $[\alpha]_D^{27}$ = -10.0° (c = 0.860, benzene).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid allyl ester (1d)

1d (52.9 mg, 40.7%, 89.2% ee) and **2d** (93.5 mg, 55.6%, 74.0% ee).

1d (89.2% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 100/1, 0.50 mL/min T_R = 17.6 min (minor), T_R = 20.3 min (major)), $[\alpha]_D^{29}$ = -103.8° (c = 1.20, benzene).
2d (74.0% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 9.6 min (major), T_R = 12.6 min (minor)), $[\alpha]_D^{26}$ = +4.6° (c = 1.18, benzene).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid (2-methyl-propyl) ester (1f)
1f (63.6 mg, 46.2%, 88.8% ee) and **2f** (96.6 mg, 54.9%, 77.6% ee).
1f (91.9 mg, 66.3%, 39.5% ee) and **2f** (57.8 mg, 32.7%, 85.7% ee).
1f (88.8% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 200/1, 1.0 mL/min, T_R = 10.1 min (major), T_R = 11.8 min (minor)), $[\alpha]_D^{25}$ = -21.5° (c = 1.01, benzene).
2f (85.7% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 7.8 min (major), T_R = 10.8 min (minor)), $[\alpha]_D^{26}$ = +7.8° (c = 1.04, benzene).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1g)
1g (76.1 mg, 48.8%, 88.9% ee) and **2g** (103.0 mg, 53.0%, 76.6% ee).
1g (82.1 mg, 53.4%, 64.9% ee) and **2g** (83.8 mg, 43.7%, 82.1% ee).
1g (88.9% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 200/1, 1.0 mL/min, T_R = 25.2 min (minor), T_R = 30.3 min (major)), $[\alpha]_D^{24}$ = -74.1° (c = 1.07, benzene).
2g (82.1% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 12.6 min (major), T_R = 16.1 min (minor)), $[\alpha]_D^{29}$ = -4.9°(c = 1.12, benzene).

Typical procedure for 1e, 1h, 1i, 1j, 1k, and 1l (5 mol% catalyst loading)

A dried 20 mL Schrenk flask was placed $Cu(OAc)_2$ (3.7 mg, 0.020 mmol), then the solid was heated 80 °C under vacuum for 3 minutes, then the flask was filled with Ar. To this was added (*S*)-DTBM-SEGPHOS (23.6 mg, 0.0200 mmol) and toluene (1.0 mL), then the mixture was stirred at 45 °C for 1 h. The mixture was cooled to room temperature, and toluene (1.0 mL) solution of **1e** (110.1 mg, 0.4000 mmol) and 2-methoxyethanol (63.9 μL, 0.800 mmol) was added. The mixture was stirred at 20 °C in incubator. The reaction was monitored by TLC or GLC. The product **2a** and the substrate **1a** were isolated by silica-gel column chromatography (elution: Hexane/Et_2O 10/1→1/1→1/2) to afford **1e** (47.1 mg, 42.7%, 92.8% ee) and **2e** (84.2 mg, 59.9%, 69.7% ee).

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid butyl ester (1e)
1e (92.8% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 800/1, 1.0 mL/min, T_R = 25.3 min (major), T_R = 30.5 min (minor)), $[\alpha]_D^{24}$ = -93.4° (c = 1.01, benzene).
2e (69.7% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 7.4 min (major), T_R = 9.0 min (minor)), $[\alpha]_D^{26}$ = +6.5° (c = 1.04, benzene).

4-Ethyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1h)

1h (49.6 mg, 38.1%, 93.4% ee) and **2h** (93.5 mg, 58.2%, 70.9% ee).

1h (93.4% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 100/1, 1.0 mL/min, T_R = 12.9 min (minor), T_R = 15.2 min (major)), $[\alpha]_D^{26}$ = -72.4° (c = 1.03, benzene).

2h (70.9% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, , T_R = 14.1 min (major), T_R = 16.1 min (minor)), $[\alpha]_D^{26}$ = +1.8° (c = 1.05, THF).

4-Propyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1i)

1i (69.4 mg, 51.1%, 71.3% ee) and **2i** (88.9 mg, 53.5%, 77.2% ee).

1i (71.3% ee): the ee was determined by HPLC analysis of **2i** which was derived from **1i** obtained by the kinetic resolution, conversion of **1i** into **2i** was carried out with $Sc(OTf)_3$ as catalyst, HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 13.8 min (minor), T_R = 15.7 min (major)), $[\alpha]_D^{24}$ = -49.4° (c = 1.22, benzene).

2i (77.2% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 13.8 min (major), T_R = 15.7 min (minor)), $[\alpha]_D^{26}$ = -2.3° (c = 1.10, benzene).

4-Butyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1j)

1j (70.3 mg, 49.8%, 56.0% ee) and **2j** (81.5 mg, 47.4%, 62.7% ee).

1j (56.0% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 100/1, 0.50 mL/min, T_R = 20.6 min (minor), T_R = 22.5 min (major)), $[\alpha]_D^{30}$ = -40.6° (c = 1.00, benzene).

2j (62.7% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 11.8 min (major), T_R = 13.4 min (minor)), $[\alpha]_D^{30}$ = -1.1° (c = 1.60, THF).

4-Butyl-5-oxo-2-(4-chlorophenyl)-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (1k)

1k (72.3 mg, 45.4%, 95.9% ee) and **2k** (104.0 mg, 54.6%, 79.5% ee).

1k (95.9% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 200/1, 1.0 mL/min, T_R = 13.9 min (minor), T_R = 25.2 min (major)), $[\alpha]_D^{27}$ = -49.5° (c = 1.02, benzene).

2k (79.5% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 15.4 min (major), T_R = 17.8 min (minor)), $[\alpha]_D^{27}$ = +3.6° (c = 1.11, benzene).

4-Methyl-5-oxo-2-(4-methoxyphenyl)-4,5-dihydrooxazole-4-carboxylic acid ethyl ester (1l)

1l (42.9 mg, 38.7%, 83.5% ee) and **2l** (76.0 mg, 53.8%, 75.2% ee).

1l (73.3 mg, 66.5%, 28.2% ee) and **2l** (36.3 mg, 25.8%, 84.0% ee).

1l (83.5% ee): HPLC (CHIRALCEL OD (DAICEL), hexane/2-propanol = 100/1, 1.0 mL/min, T_R = 12,2 min (minor), T_R = 16.6 min (major)), $[\alpha]_D^{27}$ = -90.8° (c = 1.01, benzene).

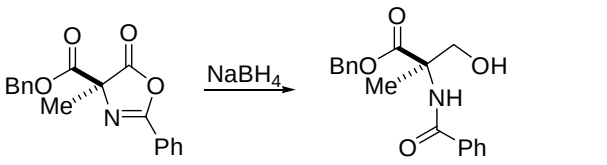
2l (84.0% ee): HPLC (CHIRALPAK AD-H (DAICEL), hexane/2-propanol = 4/1, 1.0 mL/min, T_R = 17.7 min (major), T_R = 22.6 min (minor)), $[\alpha]_D^{26}$ = +9.6° (c = 1.02, benzene).

Determination of absolute configuration of the azlactones and alcoholized products

The absolute configurations of 8 compounds ((-)-**1a**, (-)-**1k**, (-)-**1g**, (-)-**1d**, (-)-**2a**, (+)-**2d**, (-)-**2g**, and (+)-**2k**) were determined. The results suggest optically active unreacted substrates **1** obtained by the present kinetic resolution employing (S)-DTBM-SEGPHOS have *S* configuration. On the other hand, optically active products **2** have *R* configuration.

The absolute configuration of (-)-**1a** and (-)-**1k** was determined as *S* by comparison of the retention time of chiral GLC of **1a** and chiral HPLC of **1k** with that reported in the literature[2].

Derivatization of (-)-1g into *N*-benzoyl-α-methylserine benzyl ester

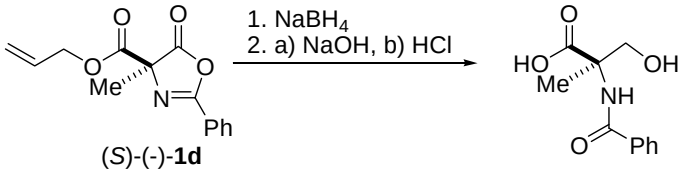


(*S*)-(-)-**1g** (*R*)-(-)-*N*-benzoyl-α-methylserine

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid benzyl ester (40.0 mg, 0.129 mmol, 80% ee, (-)-**1g**) was dissolved in THF (1.0 mL), then cooled to 0 ℃. To this was added $NaBH_4$ (3.0 mg, 0.0711 mmol) and the reaction mixture was stirred at 0 ℃ for 45 min. To this was added saturated aqueous $NaHCO_3$ (1 mL), then the mixture was extracted with CH_2Cl_2 (10 mL x 3), dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel column chromatography (Hexane/Et_2O = 1/2) to give the product (23.7 mg, 59%, $[\alpha]_D^{27}$ = -4.6° (c = 2.37, $CHCl_3$)) as colorless oil.

Comparison of the optical rotation of the product with that reported in the literature (81% ee, $[\alpha]_D^{20}$ = -4.5° (c = 1.00, $CHCl_3$) [2]) confirmed that the absolute configuration is *R*. Consequently, (-)-**1g** was determined as *S*.

Derivatization of (-)-1d into *N*-benzoyl-α-methylserine



(*S*)-(-)-**1d** (+)-(*R*)-*N*-benzoyl-α-methylserine

4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazole-4-carboxylic acid allyl ester (53.1 mg, 0.205 mmol, 82.7% ee, (-)-**1d**) was dissolved in THF (1.6 mL). Then, this solution was cooled to 0 ℃, $NaBH_4$ (4.7 mg, 0.113 mmol) was added. The reaction mixture was stirred at 0 ℃ for 45 min, then saturated aqueous $NaHCO_3$ (1 mL) was added. The mixture was extracted with CH_2Cl_2 (10 mL x 3), dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The residue was purified by silica-gel

column chromatography (Hexane/Et_2O = 1/2) to give *N*-benzoyl-α-methylserine allyl ester (23.3 mg, 43%, $[\alpha]_D^{27}$ = -1.3° (c = 2.33, $CHCl_3$)) as colorless oil.
Then, 2 M solution of NaOH (44.3 mL, 0.0885 mmol) was added to a solution of this product (23.3 mg, 0.0885 mmol) in methanol (1 mL). This mixture was stirred for 3.5 h at room temperature. H_2O (5 mL) was then added, and the methanol was removed by rotary evaporation. The water layer was washed with CH_2Cl_2 (10 mL x 3) and then acidified with 1 M HCl (0.5 mL). The product was extracted into CH_2Cl_2 (10 mL x 3) and dried by Na_2SO_4. The solvent was removed by rotary evaporation, the crude was purified by recycling preparative HPLC to give *N*-benzoyl-α-methylserine (1.1 mg, 5%, $[\alpha]_D^{27}$ = +5.8° (c = 0.11, EtOH)) as white solid.
Comparison of the optical rotation of the product with that reported in the literature ((+)-(*R*)-*N*-benzoyl-α-methylserine, $[\alpha]_D^{20}$ = +1.9° (c = 1.00, EtOH) [3]) confirmed that the absolute configuration is *R*. Consequently, (-)-**1d** was determined as *S*.

Optically active (-)-**1a**, (-)-**1d**, (-)-**1g**, and (-)-**1k** ((*S*)-isomers) were converted to **2a**, **2d**, **2g**, **2k** by $Sc(OTf)_3$ as catalyst, then retention time of chiral HPLC was compared with (-)-**2a**, (+)-**2d**, (-)-**2g**, and (+)-**2k**, which were obtained by the kinetic resolution. All the charts showed opposite enantiomer is major isomer. Consequently, the absolute configuration of (-)-**2a**, (+)-**2d**, (-)-**2g**, and (+)-**2k** was determined as *R*.

Introduction of Equations and Graphic Drawing

Equations were derived essentially the same way of Kagan.[4]

$$S_R \xrightarrow{k_R} P_R$$

$$S_S \xrightarrow{k_S} P_S$$

For first order reaction, differential equation becomes as follows.

$$\left.\begin{aligned} -\frac{d[S_R]}{dt} &= k_1[S_R] \\ -\frac{d[S_S]}{dt} &= k_2[S_S] \end{aligned}\right\} \qquad (S1)$$

Integration of eqs (S1) gives eqs (S2).

$$\left.\begin{aligned} [S_R] &= [S_R]_0 e^{-k_1 t} \\ [S_S] &= [S_S]_0 e^{-k_2 t} \end{aligned}\right\} \qquad (S2)$$

The combination of eqs (S2) leads to eq (S3).

$$\frac{k_1}{k_2} = \frac{\ln ([S_R]/[S_R]_0)}{\ln ([S_S]/[S_S]_0)} \qquad \text{(S3)}$$

For zeroth order reaction, differential equation becomes as follows.

$$\left.\begin{aligned} -\frac{d[S_R]}{dt} &= k_1 \\ -\frac{d[S_S]}{dt} &= k_2 \end{aligned}\right\} \qquad \text{(S4)}$$

Integration of eqs (S4) gives eqs (S5).

$$\left.\begin{aligned} [S_R] &= [S_R]_0 - k_1 t \\ [S_S] &= [S_S]_0 - k_2 t \end{aligned}\right\} \qquad \text{(S5)}$$

The combination of eqs (S5) leads to eq (S6).

$$\frac{k_1}{k_2} = \frac{[S_R]_0 - [S_R]}{[S_S]_0 - [S_S]} \qquad \text{(S6)}$$

For second order reaction, differential equation becomes as follows.

$$\left.\begin{aligned} -\frac{d[S_R]}{dt} &= k_1[S_R]^2 \\ -\frac{d[S_S]}{dt} &= k_2[S_S]^2 \end{aligned}\right\} \qquad \text{(S7)}$$

Integration of eqs (S7) gives eqs (S8) and (S8').

$$\left.\begin{aligned} k_1 t &= \frac{[S_R]_0 - [S_R]}{[S_R][S_R]_0} \\ k_2 t &= \frac{[S_S]_0 - [S_S]}{[S_S][S_S]_0} \end{aligned}\right\} \qquad \text{(S8)}$$

$$\left.\begin{aligned} [S_R] &= \frac{[S_R]_0}{[S_R]_0\, k_1 t + 1} \\ [S_S] &= \frac{[S_S]_0}{[S_S]_0\, k_2 t + 1} \end{aligned}\right\} \qquad \text{(S8')}$$

The combination of eqs (S8) leads to eq (S9).

$$\frac{k_1}{k_2} = \frac{[S_S]([S_R]_0 - [S_R])}{[S_R]([S_S]_0 - [S_S])} \qquad (S9)$$

Following expressions are used for obtaining the equations.

$$1 - ee_s = \frac{2[S_R]}{[S_R] + [S_S]} \qquad 1 + ee_s = \frac{2[S_S]}{[S_R] + [S_S]} \qquad 1 - conv = \frac{[S_R] + [S_S]}{[S_R]_0 + [S_S]_0} \qquad (S10)$$

$$1 - ee_p = \frac{2[P_S]}{[P_R] + [P_S]} \qquad 1 + ee_p = \frac{2[P_R]}{[P_R] + [P_S]} \qquad convn = \frac{[P_R] + [P_S]}{[S_R]_0 + [S_S]_0} \qquad (S11)$$

$$[S_R]_0 = [S_R] + [P_R] \qquad [S_S]_0 = [S_S] + [P_S] \qquad (S12)$$

Introduction of Equations

From eqs (S3) and eqs (S9), eq (S13) is obtained.

$$k_{rel} = \frac{\ln[(1 - convn)(1 - ee_s)]}{\ln[(1 - convn)(1 + ee_s)]} \qquad (S13)$$

[1st order, substrate]

From eqs (S3), eqs (S10), and eqs (S11), eq (S14) is obtained.

$$k_{rel} = \frac{\ln[1 - convn(1 + ee_p)]}{\ln[1 - convn(1 - ee_p)]} \qquad (S14)$$

[1st order, product]

From eqs (S6) and eqs (S9), eq (S15) is obtained.

$$k_{rel} = \frac{1 - (1 - convn)(1 - ee_s)}{1 - (1 - convn)(1 + ee_s)} \qquad (S15)$$

[0th order, substrate]

From eqs (S6), eqs (S10), and eqs (S11), eq (S16) is obtained.

$$k_{rel} = \frac{1 + ee_p}{1 - ee_p} \qquad (S16)$$

[0th order, product]

From eqs (S9) and eqs (S9), eq (S17) is obtained.

$$k_{rel} = \frac{[1 - (1 - convn)(1 - ee_s)](1 + ee_s)}{[1 - (1 - convn)(1 + ee_s)](1 - ee_s)} \qquad (S17)$$

[2nd order, substrate]

From eqs (S9), eqs (S10), and eqs (S11), eq (S18) is obtained.

$$k_{rel} = \frac{[1 - convn(1 - ee_p)](1 + ee_p)}{[1 - convn(1 + ee_p)](1 - ee_p)} \qquad (S18)$$

[2nd order, product]

Graphic Drawing

Graphic drawings were performed with Mathematica program. Using eqs (S2), eqs (S5), and eqs (S8), parametrically plots were carried out where *t* was used as parameter.

Figure S-1 and S-2

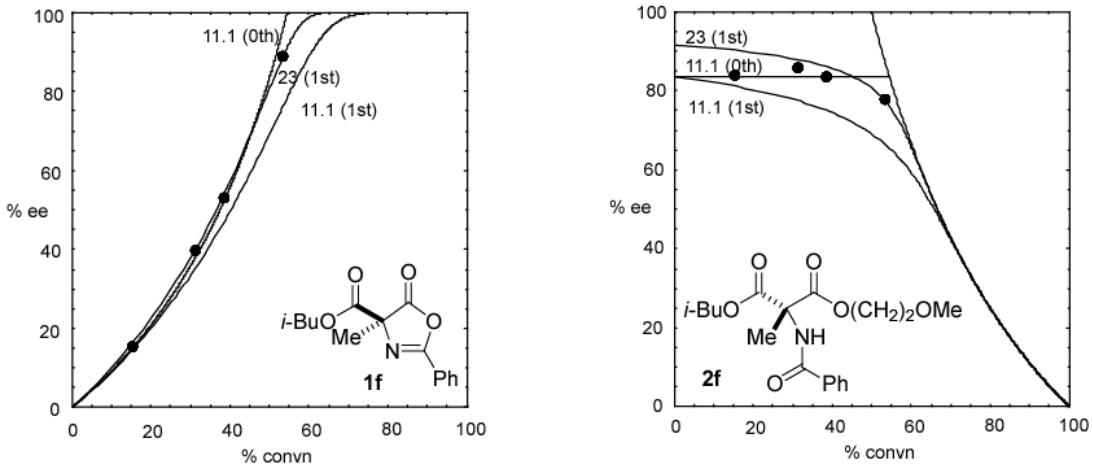


Figure S-1. Kinetic resolution of *rac*-**1f**: experimental values (dots), simulated lines as zeroth order reaction (k_{rel} = 11.1), and as first order reaction (k_{rel} = 11.1 and 23).

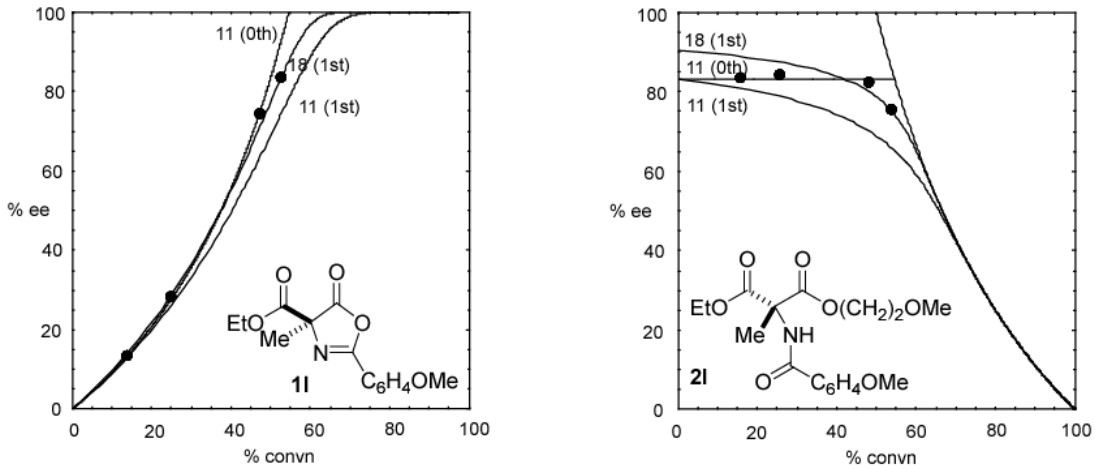


Figure S-2. Kinetic resolution of *rac*-**1l**: experimental values (dots), simulated lines as zeroth order reaction (k_{rel} = 11), and as first order reaction (k_{rel} = 11 and 18).

Figure S-3

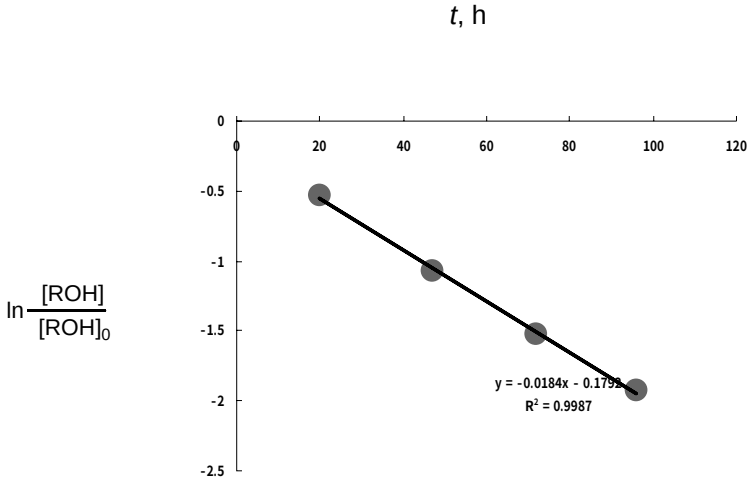
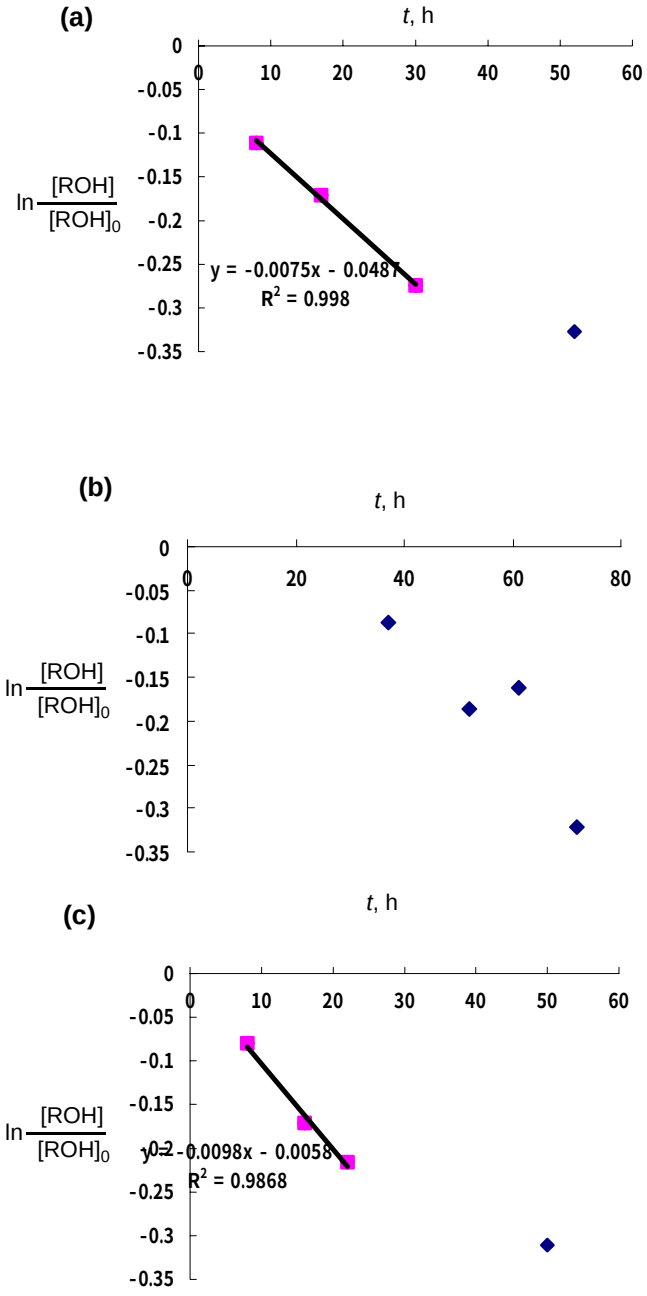


Figure S-3. First order plot for the Cu-catalyzed alcoholysis of rac-**1b** with 0.6 eq of 2-methoxyethanol.

Figure S-4


(a)
t, h
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
0
10
20
30
40
50
60
ln [ROH]/[ROH]0
y = -0.0075x - 0.0481
R2 = 0.998
(b)
t, h
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
0
20
40
60
80
ln [ROH]/[ROH]0
(c)
t, h
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
0
10
20
30
40
50
60
ln [ROH]/[ROH]0
y = -0.0098x - 0.0058
R2 = 0.9868

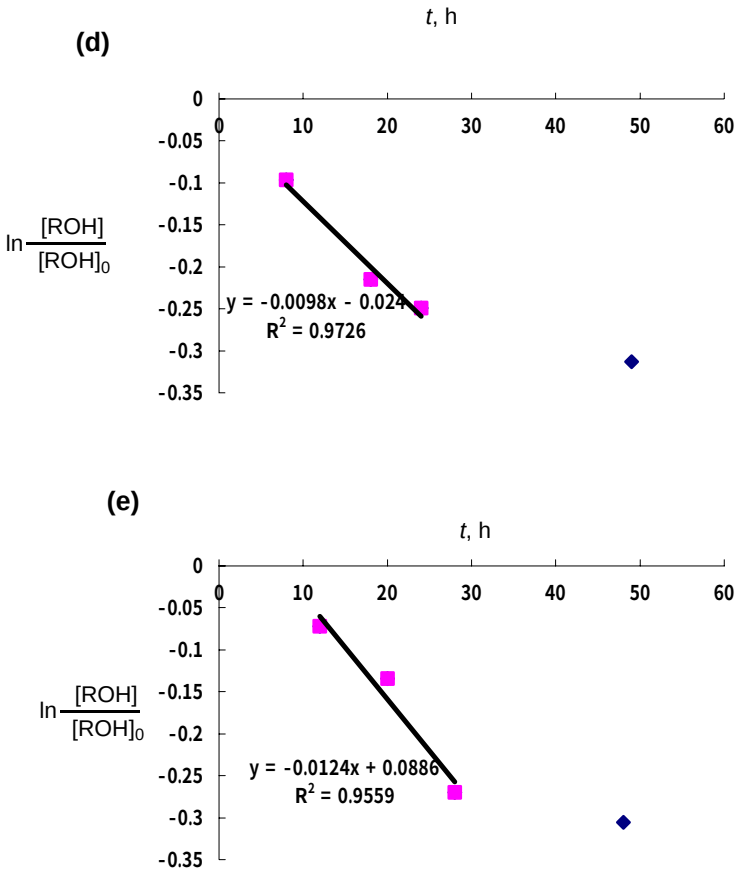


Figure S-4. First order plot of the data in Table 1: **(a) 1b** (entries 2-5), **(b) 1c** (entries 6-9), **(c) 1f** (entries 12-15), **(d) 1g** (entries 16-19), and **(e) 1l** (entries 24-27).

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