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Supporting Information

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Construction of All-Carbon Quaternary Stereocenter by Broadly Effective Enantioselective and Diastereoselective Conjugate Addition of α-Substituted β-Ketoesters to α, β-Unsaturated Ketones with a Chiral Organic Catalyst

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General Information

^{1}H and ^{13}C NMR spectra were recorded on a Varian instrument (400 MHz and 100 MHz, respectively) and internally referenced to tetramethylsilane signal or residual proton solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift(δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), intergration, coupling constant(Hz). Data for ^{13}C NMR are reported in terms of chemical shift(δ, ppm). Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer and are reported in frequency of absorption. Low resolution mass spectra for all the new compounds done by either 20 eV, CH_4/CI or NH_3/CI were recorded on a Hewlett-Packard 5989A GC/MS, and exact mass spectra on a VG 7070 high resolution mass spectrometer. Specific rotations were measured on a Jasco Digital Polarimeter.

High performance liquid chromatography(HPLC) analysis was performed on a Hewlett-Packard 1100 Series instrument equipped with a quaternary pump, using a Daicel Chiralcel OJ, OD Column(250 x 4.6 mm); Chiralpak AD, AS Column (250 x 4.6 mm); or REGIS(R,R)Whelk-O 1, UV detection was monitored at 220 nm or at 215 nm.

Materails

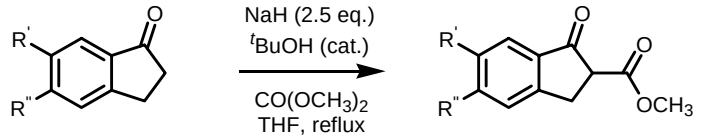
α,β-unsaturated ketone **3a**, **5a**, **5b** were purchased from Aldrich Inc. **3b** was purchased from Acros. **3a**, **3b** were used without further purifications. **5a**, **5b** were freshly

distilled before use. CH_2Cl_2 was freshly distilled over CaH_2 prior to use.

Preparation of β-ketone esters 2A-2H

β-ketone esters **2A**[1], **2B**[1], **2E**[2] were prepared according to literature procedures.

β-ketone esters **2C, 2D** were prepared with a modified literature procedure as described here:[1]



R' = OMe, R'' = H
R' = H, R'' = Cl

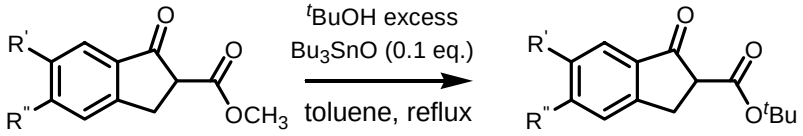
7C R' = OMe, R'' = H
7D R' = H, R'' = Cl

An oven-dried three-neck flask was charged with NaH (60% suspension in mineral oil, 100 mg, 2.5 mmol) and dry THF(5.0 mL) under N_2. The suspension was stirred at room temperature for 5 min and stood for another 5 min. The liquid phase was removed by a syringe and the residue was subjected to vacuum for 15 min. The resulting fine white powder was then suspended in THF(5.0 mL). To this suspension dimethyl carbonate(900 mg, 10.0 mmol) was added via a syringe. The resulting mixture was heated at reflux while a solution of indanone(1.0 mmol) in THF(5.0 mL) was introduced dropwise through a dropping funnel over 30 min. The resulting brown mixture was heated at reflux for an additional 15 min. The resulting green mixture was cooled to 0°C, to which acetic acid(2 mL) was added dropwise via a syringe. The resulting mixture was further acidified by addition of an aqueous solution of HCl(1.0 N, 2.0 mL). The mixture was extracted with EtOAc(10.0 mL×3). The combined organic phase was washed with water, 5% $NaHCO_3$(aq.), brine, drived over Na_2SO_4 and concentrated. The residue was subjected to silica gel chromatography(hexanes/EtOAc, 20/1) to give β-keto methyl esters **7**.

Methyl 6-methoxy-1-oxo-2-indanecarboxylate (**7C**) was obtained in 90% yield as a white solid.
^{1}H NMR($CDCl_3$, 400 MHz)(90% of keto form): δ ppm 7.39(d, ***J*** = 8.4 Hz, 1H), 7.23(dd, ***J*** = 8.4, 2.8 Hz, 1H), 7.19(d, ***J*** = 2.8 Hz, 1H), 3.84(s, 3H), 3.80(s, 3H), 3.77(dd, ***J*** = 8.4, 4.0 Hz, 1H), 3.48(dd, ***J*** = 16.8, 4.0 Hz, 1H), 3.31(dd, ***J*** = 16.8, 4.0 Hz, 1H). ^{1}H NMR ($CDCl_3$, 400 MHz)(10% of enol form): δ ppm

10.40(br s, 1H), 7.35(d, ***J*** = 8.4 Hz, 1H), 7.16(d, ***J*** = 2.0 Hz, 1H), 7.00(d, ***J*** = 8.4, 2.0 Hz, 1H), 3.862(s, 3H), 3.859(s, 3H), 3.45(s, 2H).

Methyl 5-chloro-1-oxo-2-indanecarboxylate(**7D**) was obtained in 95% yield as a white solid.
^{1}H NMR ($CDCl_3$, 400 MHz)(67% of keto form): δ ppm 7.71(d, ***J*** = 8.0 Hz, 1H), 7.51(s, 1H), 7.38(d, ***J*** = 8.0 Hz, 1H), 3.81(s, 3H), 3.76(dd, ***J*** = 8.4, 4.0 Hz, 1H), 3.56(dd, ***J*** = 17.6, 4.0 Hz, 1H), 3.36(dd, ***J*** = 17.6, 8.4 Hz, 1H). ^{1}H NMR ($CDCl_3$, 400 MHz)(33% of enol form): δ ppm 10.35(br s, 1H), 7.56(d, ***J*** = 8.0 Hz, 1H), 7.46(s, 1H), 7.37(d, ***J*** = 8.0 Hz, 1H), 3.86(s, 3H), 3.51(s, 2H).



7C R' = OMe, R" = H
7D R' = H, R" = Cl

2C R' = OMe, R" = H
2D R' = H, R" = Cl

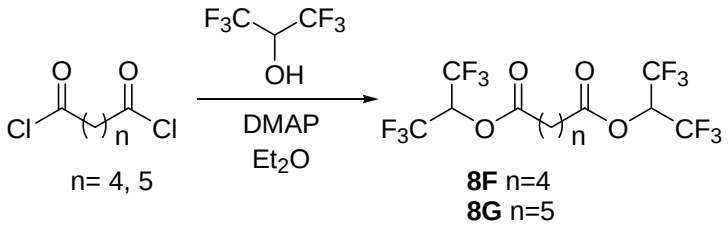
An oven-dried flask was charged with β-keto methyl ester **7**(1.0 mmol), Bu_2SnO(26.0 mg, 0.1 mmol), ^{t}BuOH(5.0 mL, 52.0 mmol) and toluene(15 mL). The resulting mixture was heated at reflux in a flask connected to a Dean-Star trap. Methanol and ***t***-butanol collected in the Dean-Star trap was released every hour, after which a portion of ^{t}BuOH(2.0 mL) was added. The mixture was heated at reflux for a total of 4 hours. The resulting yellow solution was concentrated. The residue was subjected to silica gel chromatography(hexanes/EtOAc, 20/1) to give the desired β-keto ^{t}butylesters **2**.

2C was obtained in 80% yield as a white solid.
^{1}H NMR ($CDCl_3$, 400 MHz)(90% keto ester form): δ ppm 7.38(d, ***J*** = 8.0 Hz, 1H), 7.20(m, 2H), 3.83(s, 3H), 3.64(dd, ***J*** = 8.0, 3.6 Hz, 1H), 3.40(dd, ***J*** = 16.8, 3.6 Hz, 1H), 3.26(dd, ***J*** = 16.8, 8.0 Hz, 1H), 1.49(s, 9H). (10 % enol form): δ ppm 10.52(br s, 1H), 7.32(d, ***J*** = 8.4 Hz, 1H), 7.13(d, ***J*** = 2.0 Hz, 1H), 6.96(dd, ***J*** = 8.4, 2.0 Hz, 1H), 3.85(s, 3H), 3.40(s, 2H), 1.57(s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz)(keto and enol forms): δ ppm 199.94, 168.32, 159.53, 146.53, 136.56, 127.11, 124.64, 105.48, 81.92, 55.53, 55.04, 29.62, 28.41, 27.94. IR ν): 2980(m), 1709(s, with a shoulder at 1740), 1645(m), 1494(m), 1277(m), 1149(s), 1028cm^{-1}.

2D was obtained in 84% yield as a purple solid.

^{1}H NMR ($CDCl_3$, 400 MHz) (85% keto ester form): δ ppm 7.68(d, ***J*** = 8.0 Hz, 1H), 7.49(s, 1H), 7.36(d, ***J*** = 8.0 Hz, 1H), 3.63(dd, ***J*** = 8.0, 4.0 Hz, 1H), 3.48(dd, ***J*** = 17.2, 4.0 Hz, 1H), 3.31(dd, ***J*** = 17.2, 4.0 Hz, 1H), 1.49(s, 9H). (15 % enol form): δ ppm 10.25(br s, 1H), 7.53(d, ***J*** = 7.6 Hz, 1H), 7.42 (s, 1H), 7.35(d, ***J*** = 7.6 Hz, 1H), 3.46(s, 2H), 1.57(s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) (keto and enol forms): δ ppm 198.46, 167.85, 155.07, 141.77, 133.88, 128.50, 127.18, 126.70, 125.59, 125.01, 121.38, 82.28, 54.39, 32.71, 29.99, 28.42, 27.96. IR ν 2980(m), 2933(w), 1716(s, with a shoulder at 1745), 1649(m), 1601(m), 1369(m), 1260(m), 1154 (s)cm^{-1}.

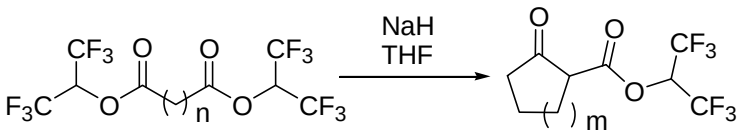
β-ketone esters **2F**, **2G** were prepared by a modified literature procedure as described here:[2, 3]



A solution of bisacid chloride(32.6 mmol) in anhydrous diethyl ether(5.0 mL) was added dropwise over 5 min to a stirred mixture of ***N***, ***N***-dimethylaniline(13.0 mL, 102.5 mmol) and hexafluoroisopropanol(11.0 mL, 106.0 mmol) in anhydrous ether(5.0 mL) at 0°C. The resulting mixture was stirred vigorously for an additional 20 h at room temperature, after which it was diluted with aqueous NaCl(10%w/v, 100 mL) The product was isolated by extraction with ether(100 mL x 2). The organic layer was washed with aqueous HCl(2 N)-brine solution(3:1v/v, 100 mL x 3), aqueous NaOH(1 N)–brine solution(3:1v/v, 100 mL X 2),and brine(100 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was subjected to silica gel chromatograghy(hexanes/EtOAc, 10/1) to afford the desired diester **8**.

8F was obtained in 82% yield as a colorless oil.
^{1}H NMR(400 MHz, $CDCl_3$) δ 5.82-5.73(m, 2H), 2.60-2.55(m, 4H), 1.81-1.74(m, 4H).

8G was obtained in 82% yield as a colorless oil.
^{1}H NMR(400 MHz, $CDCl_3$) δ 5.82-5.72(m, 2H), 2.54(t,***J***= 7.2 Hz, 4H), 1.78-1.70(m, 4H), 1.46-1.38(m, 2H).



8F n=4
8G n=5

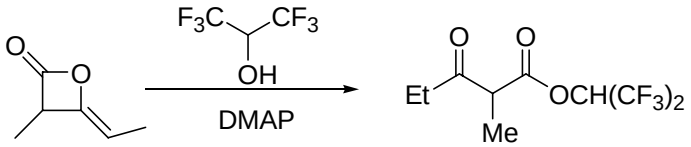
2F m=1
2G m=2

A solution of **8**(8.7 mmol) in THF(10.0 mL) was added to a suspension of NaH(60% in mineral oil, 750 mg, 18.7 mmol) in THF (10 mL). The resulting mixture was heated to 50°C (oil bath temperature) and kept at that temperature for 18 hours, and then cooled to 0°C. To the reaction mixture, HCl(2.0 N aq.) was added dropwise until pH=1. The resulting mixture was extracted with EtOAc(30 mL x 3). The organic layer was collected, washed with brine, dried over Na_2SO_4 and concentrated. The residue was subjected to silica gel chromatography(hexanes/EtOAc, 50/1) to furnish **2.**

2F was obtained in 65% yield as a colorless oil. ^{1}H NMR(400 MHz, $CDCl_3$)(14% of it was in the enol form and 86% was in the ketone form) δ 9.80(s, 0.14H, enol-H), 5.90-5.84(m, 0.14H), 5.83-5.74(m, 0.86H), 3.39-3.34(m, 0.86H), 2.63-1.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 166.4, 120.2(q, $^1J_{C,F}$ = 277.1 Hz), 98.2, 66.9(hept, $^2J_{C,F}$ = 34.2 Hz), 65.6(hept, $^2J_{C,F}$ = 34.9 Hz), 53.8, 37.7, 33.0, 27.2, 26.3, 20.8, 19.1.

2G was obtained in 25% yield as a colorless oil. ^{1}H NMR(400 MHz, $CDCl_3$))(80% of it was in the enol form and 20% ketone was in the ketone form) δ 11.41(s, 0.8H, enol-H), 5.91-5.79(m, 1H), 3.62-3.59 (m, 0.2H), 2.57-1.63 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 168.5, 148.9, 140.0, 120.5(q, $^1J_{C,F}$ = 283.9 Hz), 96.0, 65.9(hept, $^2J_{C,F}$ = 34.9 Hz), 61.7, 56.7, 41.5, 29.5, 27.0, 22.0, 21.8, 21.5.

β-ketone ester **2H** was prepared by a modified literature procedure:[4]



2H

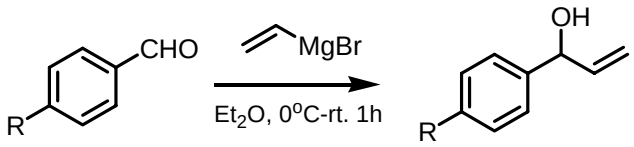
4-[(*Z*)-Ethylidene]-3-methyloxetan-2-one(448 mg, 4 mmol) was dissolved in hexafluoroisopropanol(1.0 mL), then DMAP(61 mg, 0.5 mmol) was added in one portion at 0°C. The

resulting mixture was allowed to stand at room temperature overnight, after which the whole mixture was subjected silica gel chromatography(hexanes/EtOAc, 10/1) to afford **2H** as a colorless oil (10 g, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81-5.75 (m, 1H), 3.73(q, ***J*** = 7.2 Hz, 1H), 2.65-2.52(m, 2H), 1.44(d, ***J*** = 7.2 Hz, 3H), 1.11(t, ***J*** = 7.8 Hz, 3H).

Preparation of enones 3c-d, 5c

5c was prepared according to a literature prodcedure.[6]

Preparation of vinyl aryl ketones **3c** and **3d**:

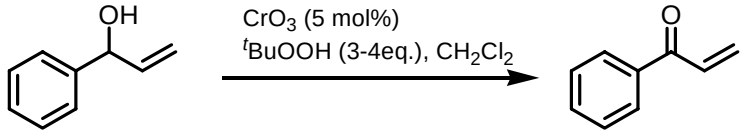


9c R = H
9d R = OMe

An oven-dried three-neck flask was charged with aldehyde(30.0 mmol) and anhydrous ether (100 mL) under the protection N_2. Vinylmagnesium bromide(1.0 M in THF, 45 mL, 45.0 mmol) was added into the aldehyde solution through a dropping funnel over 30 min at 0°C. The resulting white suspension was stirred at 0°C for 1 hour and then allowed to warm up to room temperature, afterwhich it was stirred for another 30 min. The reaction was quenched with slow addition of an aqueous solution of HCl(1 N, 50 mL) at 0°C. The organic layer was collected and the aqueous layer was extracted with ether(100 mL x 2). The combined organic phases were washed with water, brine, dried over Na_2SO_4 and concentrated. The residue was subjected to silica gel chromatography(hexanes/EtOAc, 10/1) to give allylic alcohol **9**.

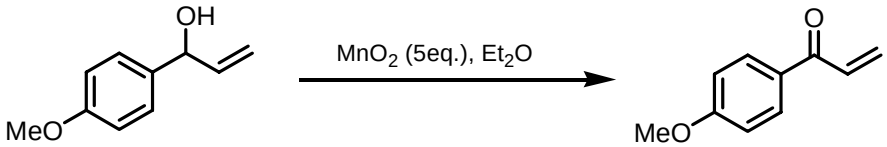
9c was obtained in 87% yield as a light yellow oil. ^{1}H NMR($CDCl_3$, 400 MHz): δ ppm 7.30-7.40(m, 5H), 6.04(ddd, ***J*** = 17.2, 10.4, 6.8 Hz, 1H), 5.34(dd, ***J*** = 17.2, 1.6 Hz, 1H), 5.18(d, ***J*** = 9.6 Hz, 1H), 5.18(brs, 1H), 4.66(s, 1H).

9d was obtained in 95% yield as a light yellow oil. ^{1}H NMR($CDCl_3$, 400 MHz): δ ppm 7.30(d, ***J*** = 8.8 Hz, 2H), 6.89(d, ***J*** = 8.8 Hz, 2H), 6.05(ddd, ***J*** = 17.2, 10.4, 6.0 Hz, 1H), 5.34(dt, ***J*** = 17.2, 1.2 Hz, 1H), 5.19(dt, ***J*** = 10.4, 1.2 Hz, 1H), 5.17(brs, 1H), 3.81(s, 3H).



9c **3c**

To a solution of allylic alcohol **9c**(3.0 g, 22.4 mmol) in CH_2Cl_2(50 mL) was added CrO_3(112 mg, 1.12 mmol, 5 mol%). ^{t}BuOOH(70%, 7.2 M in H_2O, 10.0 mL, 3.2 eq.) was added via a dropping funnal at 0°C over 1 h. The resulting brown mixture was stirred at room temperature overnight. The resulting yellow suspension was cooled to 0°C, at which $Na_2S_2O_3$(20 g) was added in portions. The resulting mixture was vigorously stirred at room temperature for 30 min. The solvent CH_2Cl_2 was removed by vacumn, the residue was extracted with ether(30 mL × 3). The combined extracts were washed with water(30 mL), brine(30 mL) and dried over Na_2SO_4 and concentrated. The residue was subjected to silica gel chromatography(hexanes/EtOAc, 20/1) to give **3c** (1.6 g, 55% yield) as a light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.93(dd, ***J*** = 8.0, 1.0 Hz, 2H), 7.42-7.46(m, 3H), 7.14(dd, ***J*** = 17.2, 10.4 Hz, 1H), 6.43(dd, ***J*** = 17.2, 1.0 Hz, 1H), 5.92(dd, ***J*** = 10.4, 1.0 Hz, 1H).

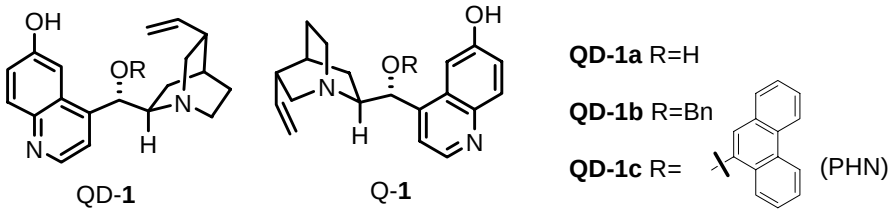


9d **3d**

To a solution of allylic alcohol **9d** (1.0 g, 6.1 mmol) in Et_2O (20.0 mL) was added MnO_2 (activated, 3.5 g, 40.2 mmol, 6.6 eq.) in portions at room temperature over 1h. The reaction mixture was vigorously stirred at room temperature for 30 min. The resulting black suspension was concentrated to ***ca***. 5 mL of liquid left and directly subjected to silica gel chromatography (pure hexanes and subsequently hexanes/EtOAc, 10/1) to afford **3d** as a colorless oil(0.40 g, 41% yield). The allylic alcohol **9d** was recycled(0.57 g, 57% yield). ^{1}H NMR($CDCl_3$, 400 MHz): δ ppm 7.97(d, ***J*** = 9.2 Hz, 2H), 7.18(dd, ***J*** = 17.2, 10.4 Hz, 1H), 6.96(d, ***J*** = 9.2 Hz, 2H), 6.43(dd, ***J*** = 17.2, 2.0 Hz, 1H), 5.88(dd, ***J*** = 10.4, 2.0 Hz, 1H), 3.88(s, 3H).

Structure of the catalysts

6′-OH cinchona alkaloid catalysts Q-**1** and QD-**1** were prepared according to literature.[5]

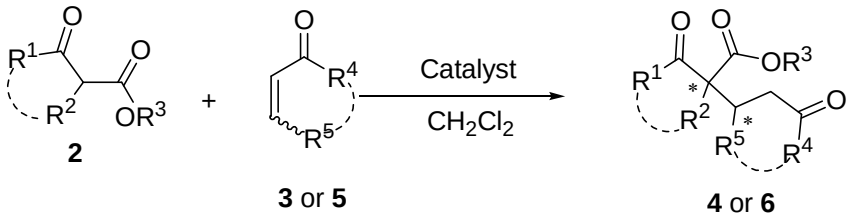


Preparation of Racemic 1, 4-adducts 4 and 6

To a solution of β-ketone ester **2**(0.3 mmol) in CH_2Cl_2(0.6 mL) was added DABCO(3 mg, 0.03 mmol) at room temperature. Then **3** or **5**(0.75 mmol, 2.5 eq.) was added to the resulting solution dropwise. After the reaction went to completion, as indicated by TLC or ^{1}H NMR analysis, the reaction mixture was directly subjected to silica gel chromatography(hexanes/EtOAc, 10/1) to afford the racemic 1,4-adduct **4** or **6**.

General procedure for enantioselective/diastereoselective Michael addition

General procedure for **1**-catalyzed Michael addition of β-ketone esters **2** to α,β-unsaturated ketone **3** or **5** with catalyst recovery:



Modified 6′-OH cinchona alkaloid catalyst **1**(0.03-0.06 mmol) was added to the solution of β -ketone ester **2**(0.3 mmol) in CH_2Cl_2(0.6 mL). To the resulting solution, α,β-unsaturated ketone **3** or **5**(0.75 mmol) was added dropwsie at the temperature indicated in tables 2 and 3. The reaction was monitored by TLC or ^{1}H NMR analysis. After **2** was consumed, the reaction mixture was directly subjected to silica gel chromatography(Hexanes/EtOAc, 10/1) to afford the desired 1, 4-adduct **4** or **6**.

After the 1, 4-adduct was collected, the column was washed with methanol to allow the recovery of 6′-OH cinchona alkaloid catalyst **1** in NMR pure form(>95% yield).

General procedure for **1**-catalyzed Michael addition of β-ketone esters **2** to α,β-unsaturated ketone **3** with 1.0 mol% catalyst:

A vial was charged with β-keto ester **2**(0.2 mmol) and a solution of 6'-OH cinchona alkaloid catalyst **1**(5.0 mM in CH_2Cl_2, 0.4 mL). The resulting mixture was shaked at room temperature for 1 min, then vinyl ketone **3**(0.5 mmol) was added to this solution via a syringe. The resulting mixture was occasionally shaked at room temperature until reaction went to completion. The reaction mixture was directly subjected to silica gel chromatography (hexanes/EtOAc, 10/1) to afford the desired 1, 4-adduct **4**.

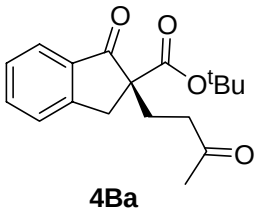
1-catalyzed Michael addition of β-ketone ester **2D** to α,β-unsaturated ketone **3d:**

6'-OH cinchona alkaloid catalyst **1**(0.02 mmol) was added to a solution of β-ketone ester **2D**(53.3 mg, 0.2 mmol) in CH_2Cl_2(0.4 mL). A solution of α,β-unsaturated ketone **3d** (81 mg, 0.5 mmol) in CH_2Cl_2(0.4 mL) was added via a syringe pump(0.07 mL/h) at -27°C. After the addition of **3d** was completed, the reaction was monitored by TLC analysis. After **2** was consumed, the reaction mixture was directly subjected to silica gel chromatography(hexanes/EtOAc, 10/1) to afford **4Dd**. The reaction time in table 2 included the time of slow addition of **3d**. The catalyst was recycled by washed down from the column using methanol with a recycling yield above 95% in NMR pure form.

1-catalyzed Michael addition of β-ketone ester **2B** to α,β-unsaturated ketone **3a** on gramm scale:

Modified 6'-OH cinchona alkaloid catalyst QD-**1c**(24 mg, 0.05 mmol) was added to the solution of β -ketone ester **2B**(1.16 g, 5.0 mmol) in CH_2Cl_2(10.0 mL). To the resulting solution, α,β-unsaturated ketone **3a** (1.02 mL, 12.5 mmol) was added dropwsie at room temperature. The resulting clear solution was stirred at room temperature for 3 hours until **2B** was consumed as monitored by TLC analysis. The reaction mixture was concentrated under vacuum and subjected to silica gel chromatography(Hexanes/EtOAc, 10/1). The 1, 4-adduct **4Ba** (1.51 g, quantitative yield) was obtained as a colorless oil in 97% ee. After the 1, 4-adduct was collected, the column was washed with methanol to allow the

recovery of 6′-OH cinchona alkaloid catalyst QD-**1c** in NMR pure form(23 mg, 96% yield).

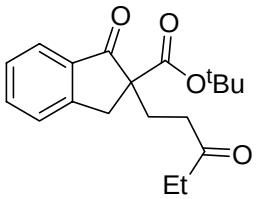


4Ba

(*R*)-(+)-*tert*-Butyl 1-oxo-2-(3-oxobutyl) 2-indancarboxylate 4Ba This product was obtained as a colorless oil in 96% yield and 96% ee from a reaction catalyzed by **Q-1c** (1.0 mol%) at room temperature for 3 hour. The enantiomer excess was determined by HPLC analysis [Daicel chiralcel OJ, Hexanes:IPA, 90:10, 1.00 ml/min, λ 220 nm, t_r(major)=33.4 min, t_r(minor)= 29.4 min]. $[\alpha]_D^{25}$ = +30.9°(c 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76(d, ***J*** = 8.0 Hz, 1H), 7.62(td, ***J*** = 7.2 Hz, ***J*** = 1.2 Hz, 1H), 7.47(d, ***J*** = 8.0 Hz, 1H), 7.40(t, ***J*** = 7.2 Hz, 1H), 3.61(d, ***J*** = 17.2 Hz, 1H), 3.01(d, ***J*** = 17.2 Hz, 1H), 2.68-2.47(m, 2H), 2.21-2.16(m, 2H), 2.13(s, 3H), 1.39(s, 9H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 207.6, 202.7, 170.1, 152.6, 135.2, 127.7, 126.3, 124.6, 81.9, 59.8, 38.8, 37.9, 29.8, 28.3, 27.2; IR($CHCl_3$) ν 2978, 2932, 1733, 1715, 1607, 1368, 1153cm^{-1}.

The absolute configuration of (+)-4Ba was determined to be *R* isomer by comparing the specific optical rotation with literature value.[1] $[\alpha]_D^{25}$ = +43.2°(c 2.50, benzene) for 96% ee. Lit.$[\alpha]_D^{25}$ = +44.7°(c 1.23, benzene) for 84% ee.

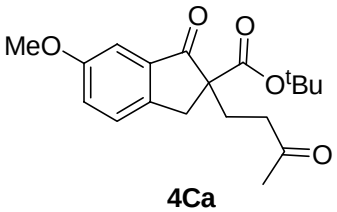
(*S*)-(-)-*tert*-Butyl 1-oxo-2-(3-oxobutyl) 2-indancarboxylate 4Ba (gramm scale)This product was obtained as a colorless oil in 100% yield and 97% ee from a reaction catalyzed by **QD-1c**(1 mol%) at r.t. for 3h.



4Bb

(+)-*tert*-Butyl 1-oxo-2-(3-oxopentyl) 2-indancarboxylate 4Bb. This product was obtained as a colorless oil in 94% yield after flash chromatography and 94% ee from a reaction catalyzed by **Q-1c**(1 mol%) at room temperature for 5 hours. The enantiomer excess was determined by HPLC analysis[Daicel chiralcel OJ, hexanes:IPA, 90:10, 1.00 ml/min, λ 220 nm, t_r(major) = 9.5 min, t_r(minor) = 7.2 min]. $[\alpha]_D^{25}$ = +35.7°(c 1.46, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.76(d, ***J*** = 7.6 Hz, 1H), 7.62(td, ***J*** = 7.2 Hz, ***J*** = 1.2 Hz, 1H), 7.47(d, ***J*** = 8.0 Hz, 1H), 7.40(t, ***J*** = 7.6 Hz, 1H), 3.61(d, ***J*** = 17.6 Hz, 1H),

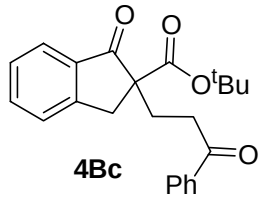
3.01(d, ***J*** = 16.8 Hz, 1H), 2.63-2.56(m, 1H), 2.51-2.38(m, 2H), 2.26-2.13(m, 3H), 1.39(s, 9H), 1.03(t, ***J*** = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.3, 202.7, 170.1, 152.6, 135.3, 135.2, 127.7, 126.3, 124.6, 81.9, 60.0, 37.8, 37.5, 35.8, 28.5, 27.8, 7.7; IR($CHCl_3$) ν 2977, 2936, 1733, 1713, 1608, 1368, 1153cm^{-1}; HRMS(CI) m/z calcd. for($C_{19}H_{24}O_4$ + H^+): 317.1753, found 317.1756.



4Ca

(+)-4Ca This product was obtained as a colorless oil in 98% yield and 96% ee from a reaction catalyzed by **Q-1c**(1 mol%) at room temperature for 5 hours. The enantiomer excess was determined by HPLC analysis [Daicel chiralcel OJ, hexanes:IPA, 90:10, 1.00 ml/min, λ 220 nm, t_r(major)=31.3 min, t_r(minor)=10.3 min]. $[\alpha]_D$= +35.4°(***c*** 0.63, $CHCl_3$); ^{1}H NMR($CDCl_3$, 400 MHz): δ ppm 7.35(d, ***J*** = 8.0 Hz, 1H), 7.21(dd, ***J*** = 8.0, 2.0 Hz, 7.18(d, ***J*** = 2.0 Hz, 1H), 3.84(s, 3H), 3.51(d, ***J*** = 16.8 Hz, 1H), 2.92(d, ***J*** = 16.8 Hz, 1H), 2.44-2.66(m, 2H), 2.18(m, 2H), 2.13(s, 3H), 1.40(s, 9H); ^{13}C NMR($CDCl_3$, 100 MHz): δ ppm 207.67, 202.69, 170.20, 159.61, 145.45, 136.48, 126.97, 124.68, 105.62, 81.92, 60.60, 55.54, 38.82, 37.28, 29.87, 28.40, 27.78; IR($CHCl_3$) 2978, 2935, 1750, 1712, 1618, 1494, 1279, 1155, 1027, 847, 766cm^{-1}; HRMS(CI) m/z calcd. for($C_{19}H_{24}O_5$ + H^+): 333.1701, found 333.1694.

(-)-4Ca This product was obtained as a colorless oil in 99% yield and 96% ee from a reaction catalyzed by **QD-1c**(1 mol%) at r.t. for 5h.

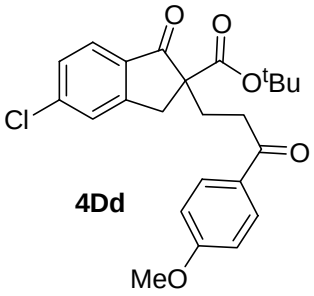


4Bc

(+)-4Bc This product was obtained as a white solid in 94% yield and 96% ee from a reaction catalyzed by **Q-1c** (10 mol%) at -24°C for 30 min. The enantiomer excess was determined by HPLC analysis [Daicel chiralpak AS, hexanes:IPA, 90:10, 1.00 ml/min, λ 220 nm, t_r(major)= 15.8 min, t_r(minor)= 19.4 min]. $[\alpha]_D^{25}$ = +4.2°(c 1.14, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.96-7.94(m, 2H), 7.78(d, ***J*** = 7.2 Hz, 1H), 7.63(td, ***J*** = 7.6 Hz, ***J*** = 1.2 Hz, 1H), 7.57-7.53(m, 1H), 7.49-7.39(m, 4H), 3.67(d, ***J*** = 17.6 Hz, 1H), 3.01(d, ***J*** = 17.6 Hz, 1H), 3.23-3.02(m, 2H), 2.43-2.27(m, 2H), 1.41(s, 9H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 202.7, 199.3, 170.1, 152.7, 136.6, 135.3, 135.2, 133.0, 128.5, 128.1, 127.7, 126.3, 124.7, 82.0, 60.2, 37.9, 34.1, 29.2, 27.8; IR($CHCl_3$) ν 2978, 2932, 1736, 1710, 1686,

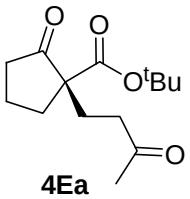
1607, 1449, 1368, 1255, 1212, 1152 cm^{-1}; HRMS(CI) m/z calcd. for($C_{23}H_{24}O_4$ + H^+):365.1752, found 365.1759.

(-)-4Bc This product was obtained as a colorless oil in 94% yield and 93% ee from a reaction catalyzed by **QD-1c**(10 mol%) at -24°C for 30 min.



(-)-4Dd This product was obtained as a white solid in 94% yield and 96% ee from a reaction catalyzed by **Q-1c** (10 mol%) at -24°C for 8h with slow addition of **3d**. The enantiomer excess was determined by HPLC analysis[Daicel chiralcel OD, hexanes:IPA, 90:10, 1.00 ml/min, λ 220 nm, t_r(major)= 12.2 min, t_r(minor)= 19.2 min]. $[\alpha]_D^{25}$ = -10.6°(c 0.70, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.93(d, ***J*** = 8.4 Hz, 2H), 7.71(d, ***J*** = 8.0 Hz, 1H), 7.46(s, 1H), 7.39(dd, ***J*** = 8.0 Hz, ***J*** = 1.2 Hz, 1H), 6.92(d, ***J*** = 9.2 Hz, 2H), 3.87(s, 3H), 3.64(d, ***J*** = 18.0 Hz, 1H), 3.07(d, ***J*** = 17.6 Hz, 1H), 3.14-2.93(m, 2H), 2.43-2.26(m, 2H), 1.41(s, 9H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 201.2, 197.7, 169.7, 163.5, 154.2, 141.8, 133.8, 130.4, 129.7, 128.6, 126.6, 125.8, 113.7, 82.3, 60.6, 55.4, 37.5, 33.6, 29.3, 27.8; IR($CHCl_3$) ν 2978, 1737, 1712, 1600, 1258, 1170, 1153cm^{-1}; HRMS(CI) m/z calcd. for($C_{24}H_{25}ClO_5$ + H^+): 429.1468, found 429.1475.

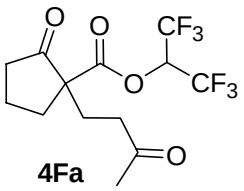
(+)-4Dd. This product was obtained as a colorless oil in 93% yield and 93% ee from a reaction catalyzed by **QD-1c**(10 mol%) at -24°C for 8h with slow addition of **3d.**



(*S*)-(-)-*tert*-Butyl 2-oxo-1-(3-oxobutyl) cyclopentanecarboxylate 4Ea This product was obtained as a colorless oil in 95% yield and 96% ee from a reaction catalyzed by **Q-1c** (10 mol%) at room temperature for 84 hr. The enantiomer excess was determined by HPLC analysis [Daicel chiralpak AS, hexanes:IPA, 99:1, 0.44 ml/min, λ 215 nm, t_r(major)= 47.6 min, t_r(minor)= 40.4 min]. $[\alpha]_D^{25}$ = -5.9°(c 0.53, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 2.78-2.71(m, 1H), 2.50-2.35(m, 3H), 2.31-2.22(m, 1H), 2.14(s, 3H), 2.07-1.81(m, 5H), 1.44(s, 9H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 215.3, 208.1, 170.7, 82.0, 59.4, 38.9, 38.0, 34.6, 29.9, 27.9, 27.0, 19.6; IR($CHCl_3$) ν 2975, 1747, 1716, 1368, 1146cm^{-1}.

The absolute configuration of (-)-4Ea was determined to be *S* isomer by comparing the specific optical rotation with

literature value.[7] Lit. $[\alpha]_D^{25}$ = +8.7°(c 0.41, $CHCl_3$)(92% ee for ***R*** isomer).

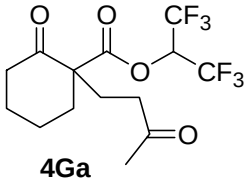


4Fa

Hexafloroisopropyl 2-oxo-1-(3-oxobutyl) cyclopentane carboxylate 4Fa This product was obtained as a colorless oil in 93% yield and 96% ee from a reaction catalyzed by **Q-1c** (10 mol%) at room temperature for 30 min. The enantiomer excess was determined by HPLC analysis [REGIS(R,R) Whelk-O1, hexanes:IPA, 99:1, 1.00 ml/min, λ 215 nm, t_r(major) = 11.5 min, t_r(minor)= 13.6 min]. ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.81-5.72(m, 1H), 2.75-2.67(m, 1H), 2.52-2.41(m, 4H), 2.23-1.98(m, 5H), 2.14(s, 3H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 212.1, 207.1, 168.5, 120.1(q, $^1J_{C,F}$ =280.8 Hz), 66.7(hept, $^2J_{C,F}$ =34.2 Hz), 58.6, 38.2, 37.6, 34.1, 29.8, 26.6, 19.5; IR($CHCl_3$) ν 2971, 1779, 1742, 1716, 1386, 1359, 1289, 1234, 1201, 1167, 906cm^{-1}. HRMS(CI) m/z calcd. for($C_{13}H_{14}F_6O_4$ + H^+): 349.0875, found 349.0880.

Hexafloroisopropyl 2-oxo-1-(3-oxobutyl) cyclopentane carboxylate 4Fa This product was obtained as a colorless oil in 90% yield and 95% ee from a reaction catalyzed by **QD-1c**(10 mol%) at r.t. for 30 min.

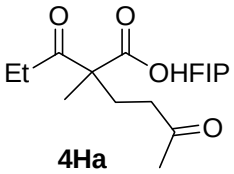
(+)-Hexafloroisopropyl 2-oxo-1-(3-oxobutyl) cyclopentane carboxylate (+)-4Fa This product was obtained as a colorless oil in 92% yield and 94% ee from a reaction catalyzed by **Q-1c**(1 mol%) at r.t. for 24h.



4Ga

(-)-Hexafloroisopropyl 2-oxo-1-(3-oxobutyl) cyclopentane carboxylate (-)-4Ga This product was obtained as a colorless oil in 89% yield and 98% ee from a reaction catalyzed by **Q-1c** (10 mol%) at room temperature for 24h. The enantiomer excess was determined by HPLC analysis[REGIS(R,R) Whelk-O1, hexanes:IPA, 99:1, 0.90 ml/min, λ 215 nm, t_r(major)= 5.6 min, t_r(minor)= 14.3 min]. $[\alpha]_D^{25}$ = -46.1°(c 3.67, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.87-5.78(m, 1H), 2.61-2.42(m, 4H), 2.38-2.30 (m, 1H), 2.26-2.18(m, 1H), 2.05-1.94(m, 2H), 1.86-1.61(m, 4H), 2.13(s, 3H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 206.7, 250.7, 169.4, 120.2(q, $^1J_{C,F}$ =280.8 Hz), 66.7(hept, $^2J_{C,F}$ =34.2 Hz), 60.2, 40.4, 38.2, 36.4, 29.8, 27.8, 27.2, 21.9; IR($CHCl_3$) ν 2953, 2872, 1770, 1716, 1721, 1386, 1359, 1288, 1233, 1202, 1110, 906cm^{-1}. HRMS(CI) m/z calcd. for($C_{14}H_{16}F_6O_4$ + H^+): 363.1031, found 363.1028.

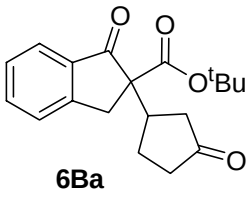
(+)-Hexafloroisopropyl 2-oxo-1-(3-oxobutyl) cyclopentane carboxylate (+)-4Ga This product was obtained as a colorless oil in 86% yield and 96 % ee from a reaction catalyzed by **QD-1c** (10 mol%) at r.t. for 24h. $[\alpha]_D^{25}$ = + 44.4°(c 3.45, $CHCl_3$).



4Ha

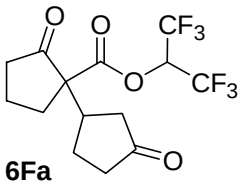
(+)-Hexafloroisopropyl 2-propionyl-2-Methyl-5-oxohexanoate (+)-4Ha This product was obtained as a colorless oil in 82% yield and 90% ee from a reaction catalyzed by **Q-1c** (10 mol%) at -24°C for 20 hours. The enantiomer excess was determined by HPLC analysis[Daicel chiralcel OJ, hexanes:IPA, 99:1, 1.00 ml/min, λ 215 nm, t_r(major) = 15.8 min, t_r(minor)= 8.5 min]. $[\alpha]_D^{25}$ = +4.3°(c 0.67, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.84-5.75(m, 1H), 2.52-2.40(m, 4H), 2.26-2.10(m, 2H), 2.15(s, 3H), 1.44(s, 3H), 1.07(t, ***J*** = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 206.4, 170.2, 120.4(q, $^1J_{C,F}$ =280.9 Hz), 67.0(hept, $^2J_{C,F}$ =34.9 Hz), 58.9, 38.3, 31.8, 30.1, 28.5, 19.5, 8.0; IR($CHCl_3$) ν 2974, 1771, 1717, 1386, 1288, 1233, 1110, 907cm^{-1}. HRMS(CI) m/z calcd. for($C_{13}H_{16}F_6O_4$ + H^+): 351.1031, found 351.1036.

(-)-Hexafloroisopropyl 2-propionyl-2-Methyl-5-oxohexanoate (-)-4Ha This product was obtained as a colorless oil in 85% yield after flash chromatography and 90% ee from a reaction catalyzed by **QD-1c**(10 mol%) at -24°C for 40 hours.



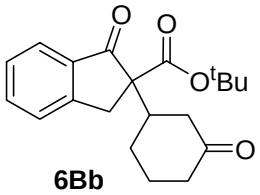
6Ba

6Ba This product was obtained as a white solid in 99% yield and 96:4 diastereomer ratio(dr) from a reaction catalyzed by **QD-1b** (10 mol%) at room temperature for 12 hours. dr was determined by ^{1}H NMR analysis of the crude product. ee of the major diastereomer was determined to be 98% by HPLC analysis [Daicel chiralpak AS, hexanes:IPA, 95:5, 1.00 ml/min, λ 220 nm, major isomer: t_r(major) =29.8 min, t_r(minor) =58.3 min]. ^{1}H NMR (400 MHz, $CDCl_3$)(major isomer) δ 7.76(d, ***J*** = 7.6 Hz, 1H), 7.63(t, ***J*** = 7.2 Hz, 1H), 7.49(d, ***J*** = 8.0 Hz, 1H), 7.40(t, ***J*** = 7.6 Hz, 1H), 3.67(d, ***J*** = 17.2 Hz, 1H), 3.24-3.15(m, 1H), 3.08(d, ***J*** = 18.0 Hz, 1H), 2.36-2.16(m, 4H), 1.94-1.86(m, 1H), 1.68-1.57(m, 1H), 1.41(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$)(major isomer) δ 217.3, 201.8, 169.2, 152.8, 135.6, 135.4, 127.9, 126.2, 124.7, 82.4, 62.9, 40.7, 39.6, 38.3, 34.0, 27.8, 25.3; IR($CHCl_3$) ν 2976, 2933, 1739, 1706, 1606, 1276, 1149cm^{-1}. HRMS(CI) m/z calcd. for($C_{19}H_{22}O_4$ + H^+): 315.1596, found 315.1594.



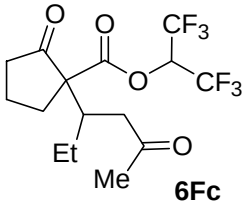
6Fa

6Fa This product was obtained as colorless oil in 95% yield and 93:7 diastereomer ratio from a reaction catalyzed by **Q-1c** (20 mol%) at room temperature for 2 hours. dr was determined by HPLC analysis. ee of the major diastereomer was determined to be 95% by HPLC analysis[Daicel chiralcel OD, hexanes:IPA, 90:10, 1.00 ml/min, λ 215 nm, major isomer: t_r(major) = 11.3 min, t_r(minor) = 13.3 min; minor isomer: t_r(major) = 15.0 min, t_r(minor) = 10.5 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84-5.75(m, 1H), 3.02-2.93(m, 1H), 2.58-2.49(m, 2H), 2.42-2.19(m, 5H), 2.13-2.04(m, 4H), 1.67-1.55(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.0, 211.4, 167.6, 120.1(q, $^1J_{C,F}$ = 281.6Hz), 66.8(hept, $^2J_{C,F}$ =34.9 Hz), 61.2, 40.0, 39.5, 38.3, 38.1, 30.3, 24.9, 19.5; IR($CHCl_3$) ν 2969, 1787, 1741, 1732, 1403, 1378, 1358, 1294, 1195, 1110, 906cm^{-1}. HRMS(CI) m/z calcd. for($C_{14}H_{14}F_6O_4$ + H^+): 361.0875, found 361.0875.



6Bb

6Bb This product was obtained as a white solid in 87% yield and 93:7 diastereomer ratio from a reaction catalyzed by **QD-1b**(20 mol%) at room temperature for 5 days. dr was determined by HPLC analysis. ee of the major diastereomer was determined to be 85% by HPLC analysis[Daicel chiralcel OD, hexanes:IPA, 95:5, 1.00 ml/min, λ 220 nm, major isomer: t_r(major)= 21.5 min, t_r(minor)= 15.1 min; minor isomer: t_r(major = 12.0 min, t_r(minor)= 10.9 min]. ^{1}H NMR (400 MHz, $CDCl_3$)(major isomer) δ 7.73(d, ***J*** = 8.0 Hz, 1H), 7.62(td, ***J*** = 7.2 Hz, ***J*** = 1.2 Hz, 1H), 7.49(d, ***J*** = 8.0 Hz, 1H), 7.38(t, ***J*** = 7.2 Hz, 1H), 3.71(d, ***J*** = 18.0 Hz, 1H), 3.16(d, ***J*** = 17.6 Hz, 1H), 2.91-2.83(m, 1H), 2.41-2.37(m, 1H), 2.25-2.17(m, 2H), 2.12-2.04(m, 2H), 1.95-1.90(m, 1H), 1.74-1.62(m, 1H),1.47-1.37(m, 1H), 1.41(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$)(major isomer) δ 209.5, 201.3, 168.6, 152.9, 135.6, 135.3, 127.7, 126.0, 124.4, 82.2, 64.7, 42.4, 42.3, 41.0, 33.3, 27.7, 26.7, 24.6; IR($CHCl_3$) ν 2935, 1734, 1709, 1368, 1152cm^{-1}. HRMS(CI) m/z calcd. for($C_{20}H_{24}O_4$ + H^+): 329.1753, found 329.1755.



6Fc

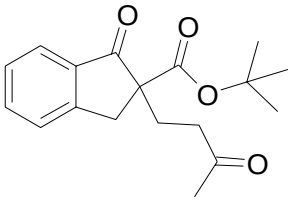
6Fc This product was obtained as a colorless oil in 83% yield and 86:14 diastereomer ratio from a reaction catalyst Q-**1c** (20 mol%) at room temperature for 20 hours. dr was determined by HPLC analysis. Methanol-deactivated silica gel was used in

chromatography. ee of the major diastereomer was determined to be 99% and ee of the minor diastereomer was determined to be 94% ee by HPLC analysis[REGIS, (R, R) Whelk-O1+ Daicel chiralpak AD, hexanes:IPA, 95:5, 0.80 mL/min, λ 215 nm, major isomer: t_r(major) = 11.1 min, t_r(minor) = 12.1 min; minor isomer: t_r(major) = 23.2 min, t_r(minor) = 27.1 min]. ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.78-5.69(m, 1H), 3.13-3.07(m, 1H), 2.61-2.50(m, 2H), 2.40-2.34(m, 4H), 2.19-1.92(m, 2H), 2.14(s, 3H), 1.49-1.27(m, 2H), 0.88(t, ***J***=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.0, 207.8, 167.4, 120.2(q, $^1J_{C,F}$ = 281.6Hz), 66.6(hept, $^2J_{C,F}$ =34.9 Hz), 63.4, 43.8, 38.9, 38.2, 32.4, 29.9, 24.3, 19.2, 12.6; IR ($CHCl_3$) ν 2970, 1782, 1742, 1716, 1386, 1359, 1288, 1234, 1198, 1110, 908cm^{-1}. HRMS(CI) m/z calcd. For($C_{15}H_{18}F_6O_4$ + H^+): 377.1187, found 377.1176.

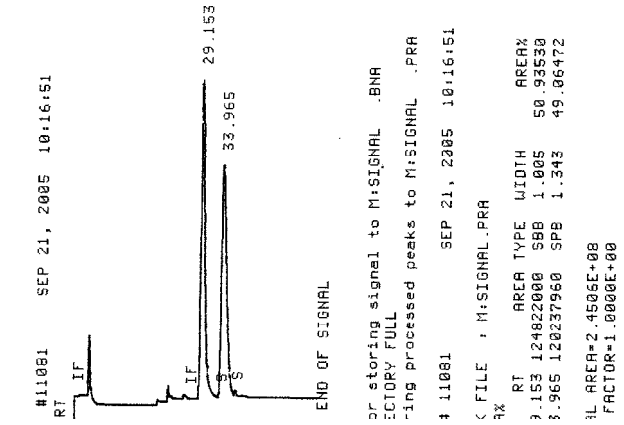
References for Supporting Information:

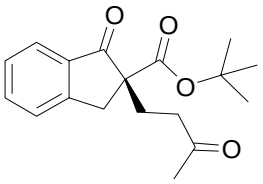
1. M. Nakajima, S. Yamamoto, Y. Yamaguchi, S. Nakamura, S. Hashimoto, *Tetrahedron* **2003**, *59*, 7307-7313.
2. D. Henderson, K. A. Richardson, R. J. K. Taylor, *Synthesis* **1983**, 996-997.
3. J. H. Babler, S. J. Sarussi, *J. Org. Chem.* **1987**, *52*, 3462-3464.
4. L. Hintermann, A. Togni, *Helv. Chim. Acta* **2000**, *83*, 2425-2435.
5. (a) H. Li, Y. Wang, L. Tang, L. Deng, *J. Am. Chem. Soc.* **2004**, *126*, 9906-9907. (b) X. Liu, H. Li, L. Deng, *Org. Lett*. **2005**, *7*, 167-169.
6. D. H. Grayson, M. R. J. Tuite, *J. Chem. Soc. Perkin Trans. I* **1986**, 2137-2142.
7. Y. Hamashima, D. Hotta, M. Sodeoka, *J. Am. Chem. Soc*. **2002**, *124*, 11240-11241.

HPLC Conditions: Daicel chiralcel OJ, Hexane:IPA, 90:10, 1.00 mL/min, λ 220 nm

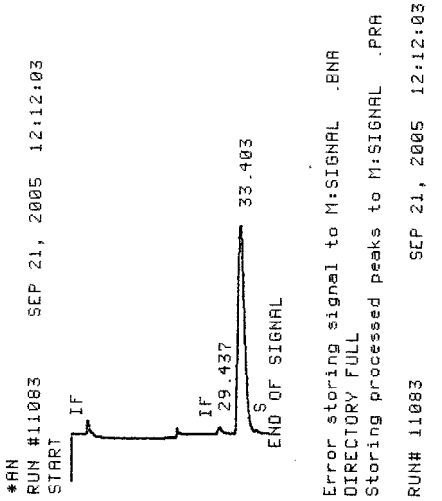


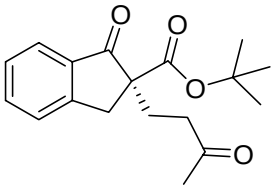
Racemic 4Ba



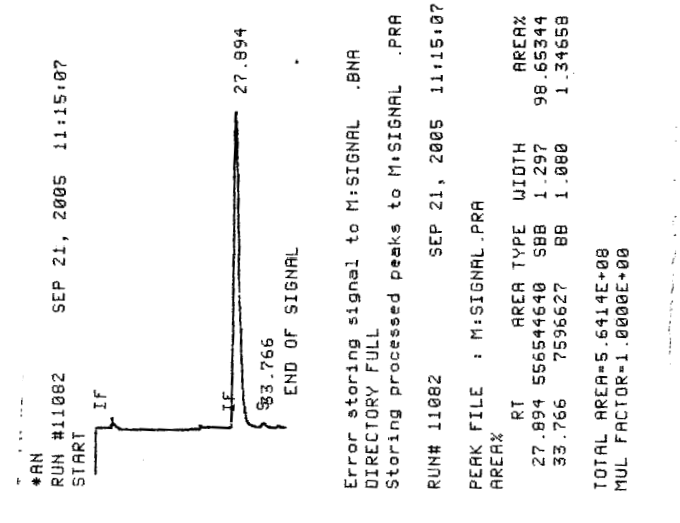


Asymmetric *R-(+)*- 4Ba, 96% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(1 mol%)

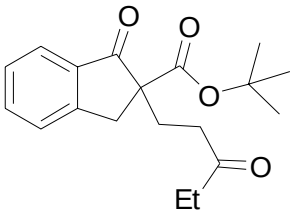




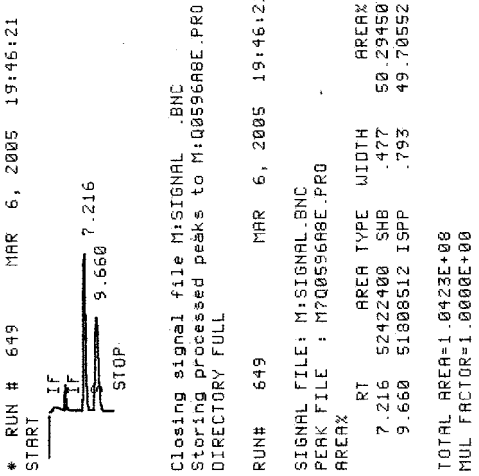
Asymmetric 4Ba, 97% ee, reaction catalyzed by QD-PHN-OH(QD-1c)(1 mol%) 5 mmol scale



HPLC Conditions: Daicel chiralcel OJ, Hexane:IPA, 90:10, 1.00 mL/min, λ 220 nm



Racemic4Bb



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                IF
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DIRECTORY FULL

RUN#   649          MAR  6, 2005  19:46:21

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                RT      AREA TYPE  WIDTH     AREA%
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             9.660  51808512 ISPP    .793   49.70552

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MUL FACTOR=1.0000E+00
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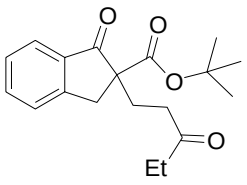
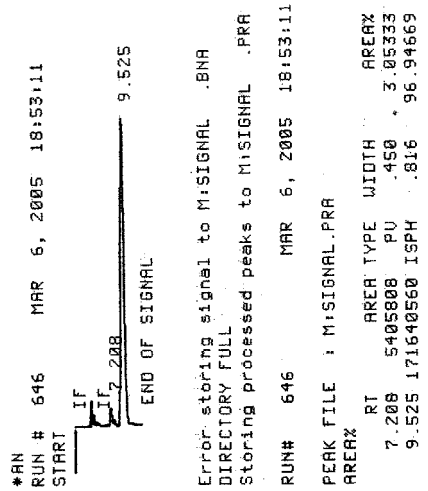


Asymmetric 4Bb, 94% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(1 mol%)



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*AN
RUN #  646      MAR  6, 2005  18:53:11
START
                IF
                IF
                S  7.208          9.525
                END OF SIGNAL

Error storing signal to M:SIGNAL   .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL   .PRA

RUN#   646          MAR  6, 2005  18:53:11

PEAK FILE  : M:SIGNAL.PRA
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                RT      AREA TYPE  WIDTH     AREA%
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             9.525 171640560 ISPH    .816  96.94669

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MUL FACTOR=1.0000E+00
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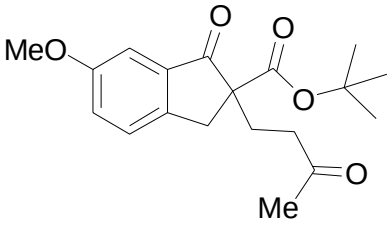
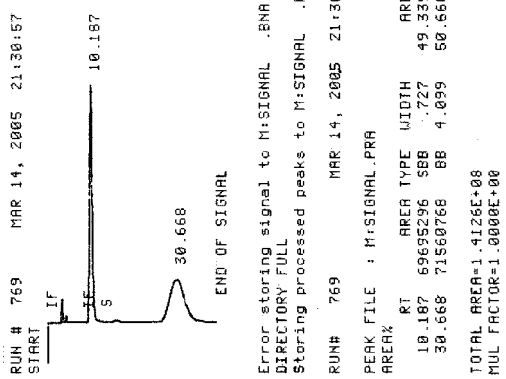
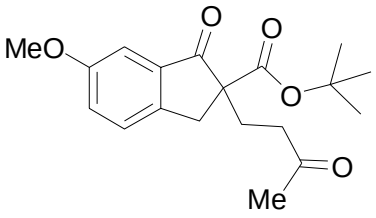
HPLC Conditions: Daicel chiralcel OJ, Hexane:IPA, 90:10, 1.00 mL/min, λ 220 nm

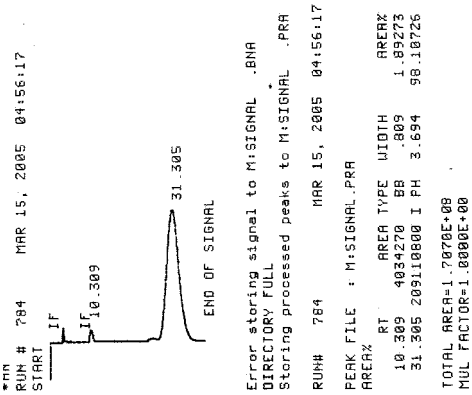


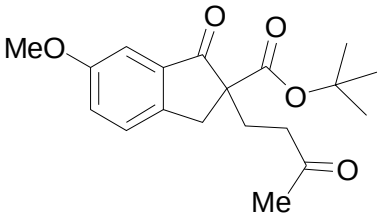
Racemic4Ca



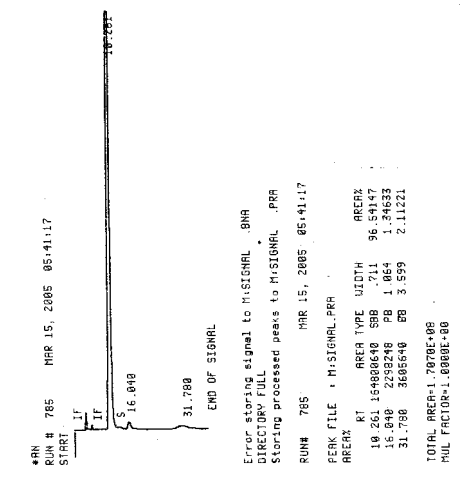


Asymmetric 4Ca, 96% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(1 mol%)

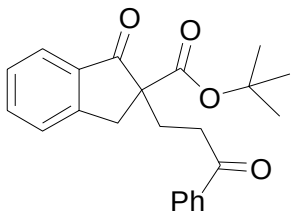




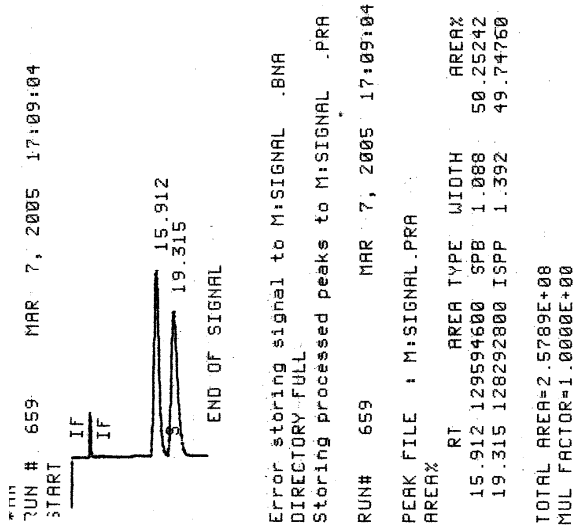
Asymmetric 4Ca, 96% ee, reaction catalyzed by QD-PHN-OH(QD-1c)(1 mol%)

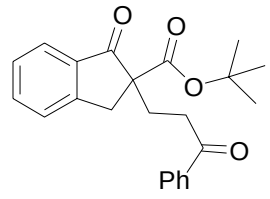


HPLC Conditions: Daicel chiralpak AS, Hexane:IPA, 98: 2, 1.00 mL/min, λ 220 nm

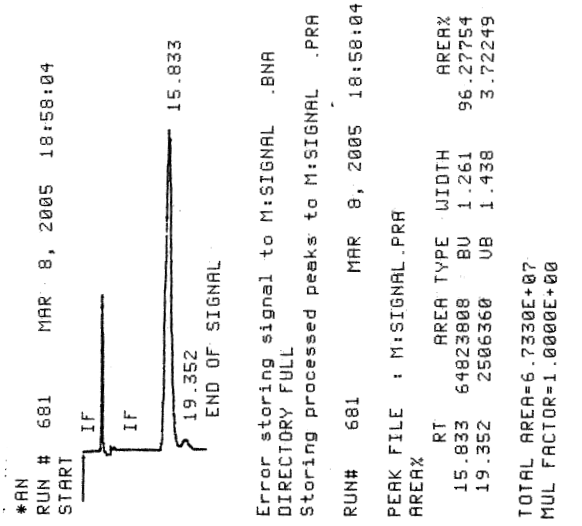


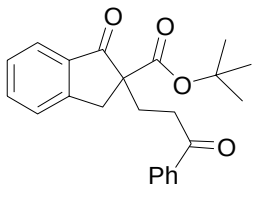
Racemic4Bc



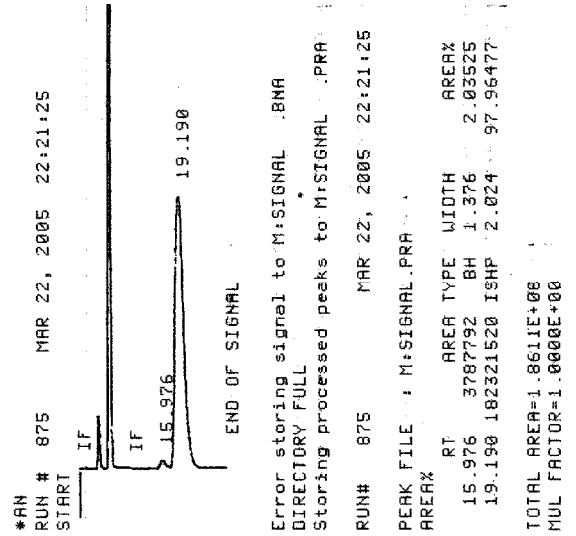


Asymmetric 4Bc, 96% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(10 mol%)

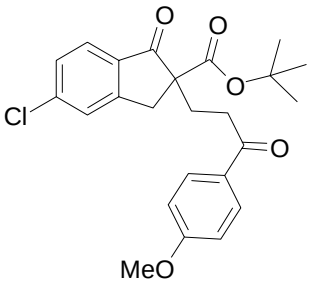




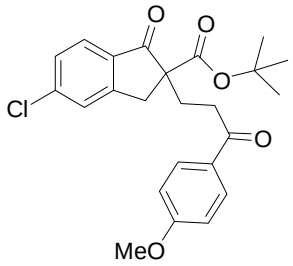
Asymmetric 4Bc, 93% ee, reaction catalyzed by QD-PHN-OH(QD-1c)(10 mol%)



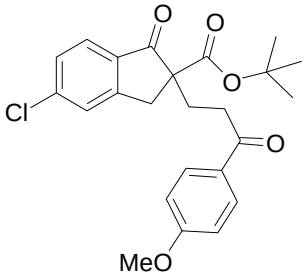
HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 90:10, 1.00 mL/min, λ 220 nm



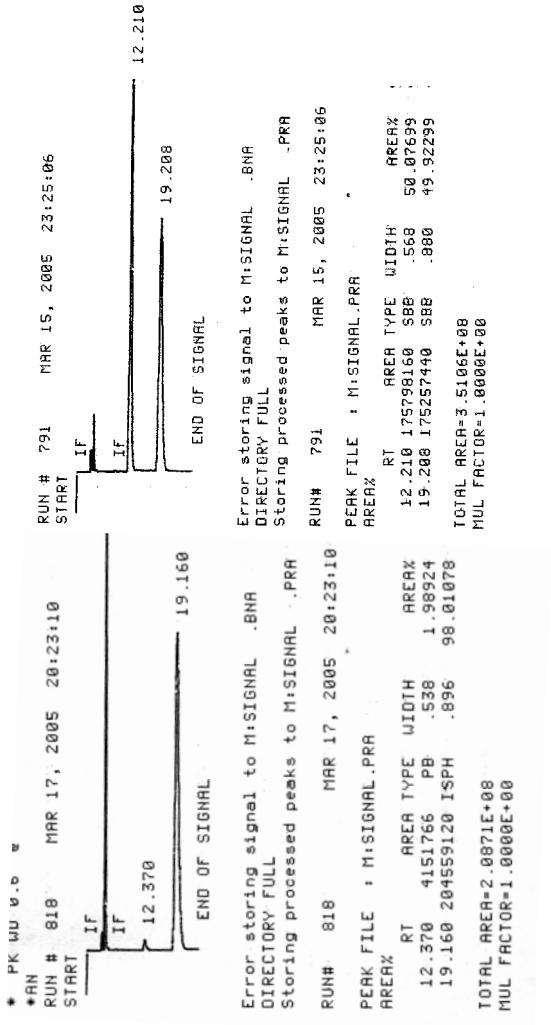
Racemic4Dd



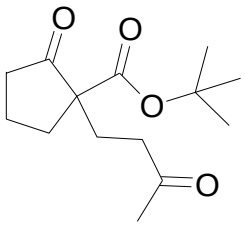
Asymmetric 4Dd, 96% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(10 mol%)



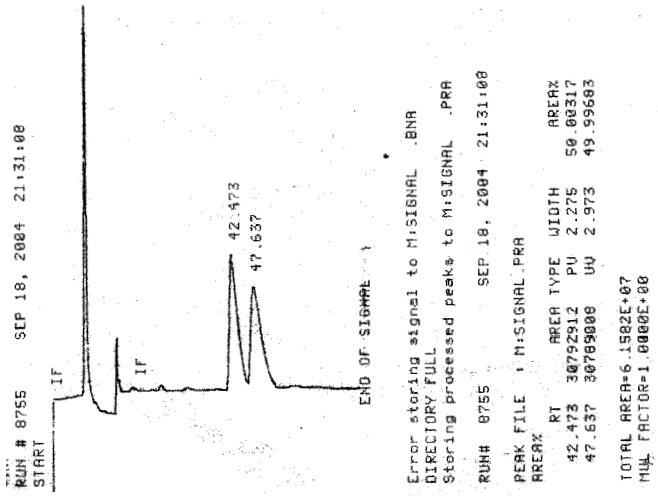
Asymmetric 4Dd, 93% ee, reaction catalyzed by QD-PHN-OH(QD-1c)(10 mol%)

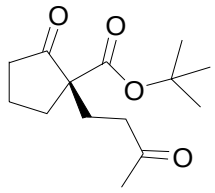


HPLC Conditions: Daicel chiralpak AS, Hexane:IPA, 99: 1, 0.44 mL/min, λ 215 nm

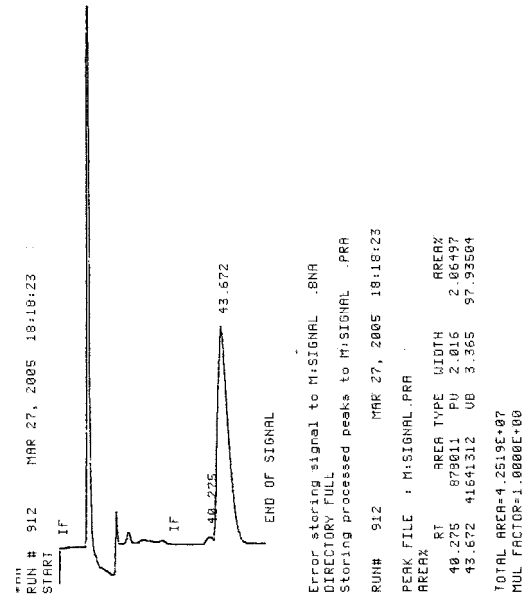


Racemic4Ea

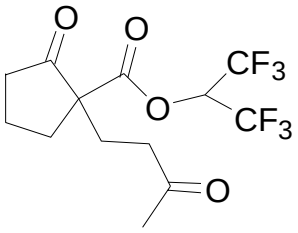




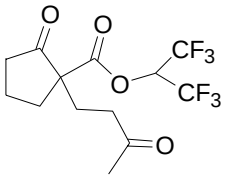
Asymmetric 4Ea, 96% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(10 mol%)



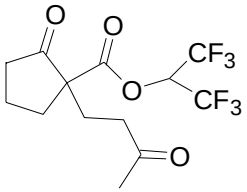
HPLC Conditions: REGIS, (R, R) Whelk-O1, Hexane:IPA, 99: 1, 1.00 mL/min, λ 215 nm



Racemic 4Fa

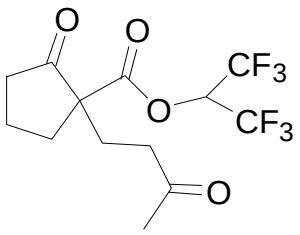


Asymmetric 4Fa, 96% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(10 mol%)

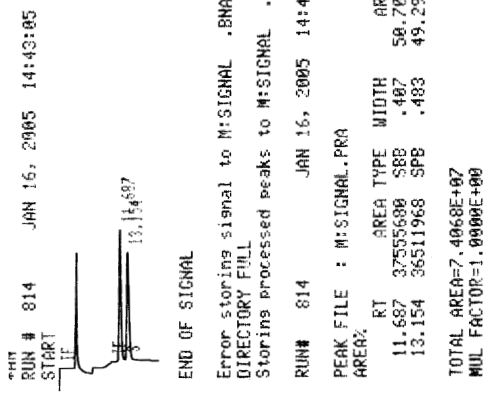


Asymmetric 4Fa, 95% ee, reaction catalyzed by QD-PHN-OH(QD-1c)(10 mol%)

HPLC Conditions: REGIS, (R, R) Whelk-O1, Hexane:IPA, 99: 1, 1.00 mL/min, λ 215 nm



Racemic 4Fa



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IF
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DIRECTORY FULL
Storing processed peaks to M:SIGNAL  .PRA

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      RT      AREA TYPE  WIDTH      AREA%
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  13.154   36511968 SPB    .483   49.29542

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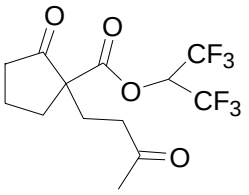
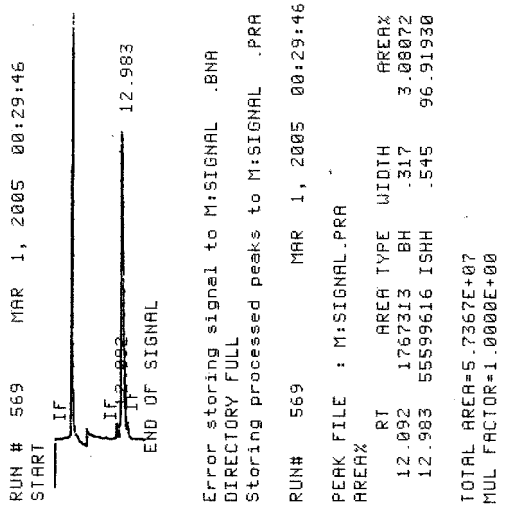


Asymmetric 4Fa, 94% ee, reaction catalyzed by 1 mol% Q-PHN-OH(Q-1c)



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IF
IF
IF
END OF SIGNAL

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DIRECTORY FULL
Storing processed peaks to M:SIGNAL  .PRA

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  12.983   55599616 ISHH   .545   96.91930

TOTAL AREA=5.7367E+07
MUL FACTOR=1.0000E+00
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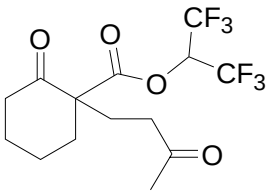
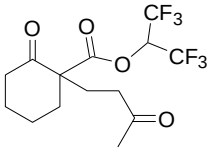
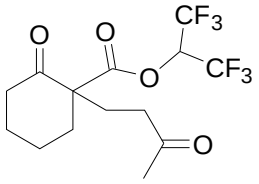
HPLC Conditions: REGIS, (R, R) Whelk-O1, Hexane:IPA, 99: 1, 0.90 mL/min, λ 215 nm



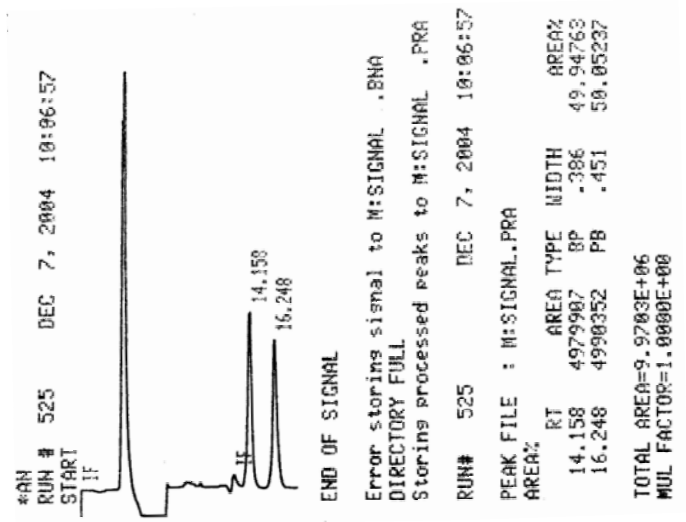
Racemic4Ga

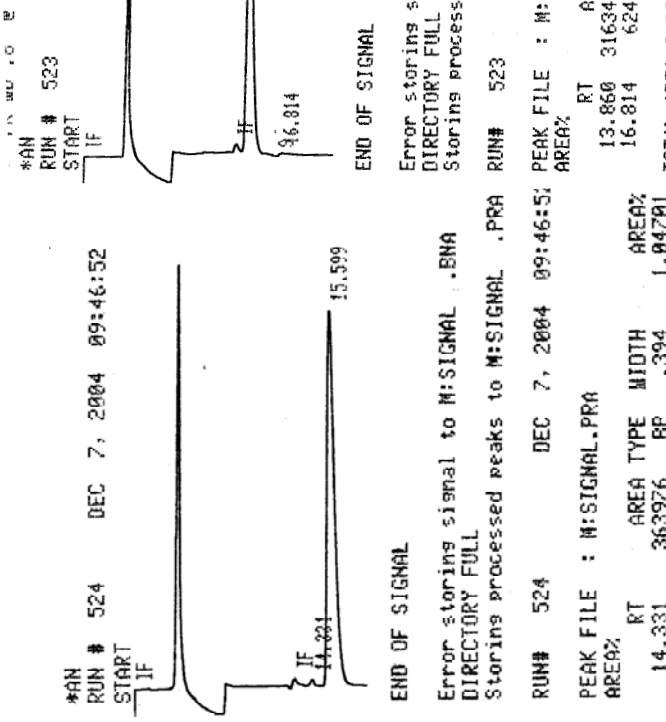


Asymmetric 4Ga, 98% ee, reaction catalyzed by Q-PHN-OH(Q-1c)(10 mol%)

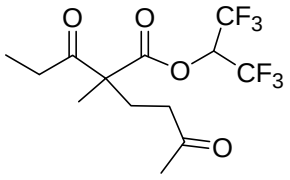


Asymmetric 4Ga, 96% ee, reaction catalyzed by QD-PHN-OH(QD-1c)(10 mol%)

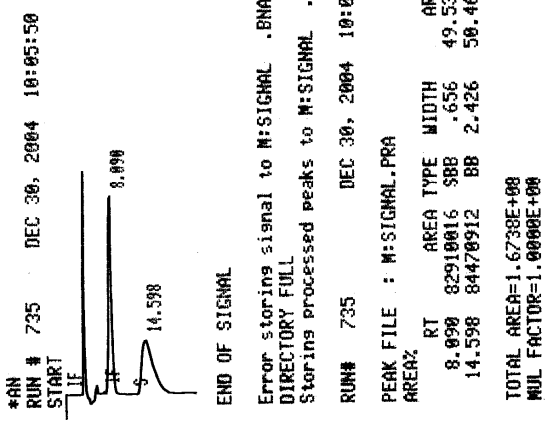


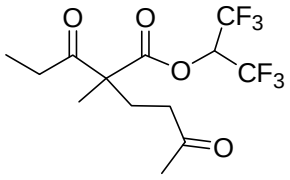


HPLC Conditions: Daicel chiralcel OJ, Hexane:IPA, 99:1, 1.00 mL/min, λ 215 nm

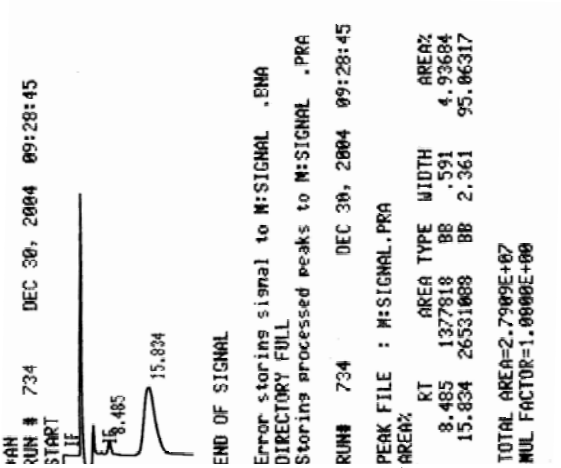


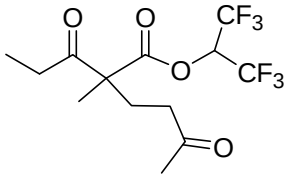
Racemic 4Ha



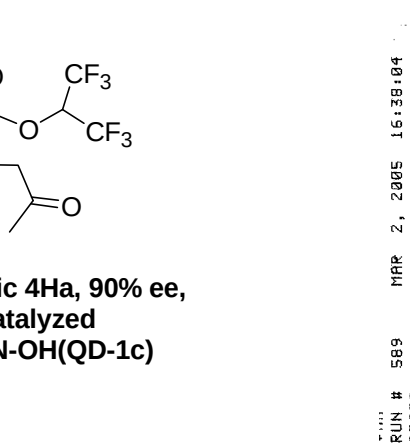


Asymmetric 4Ha, 90% ee, reaction catalyzed by Q-PHN-OH(Q-1c)

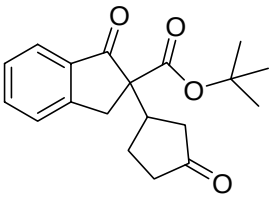




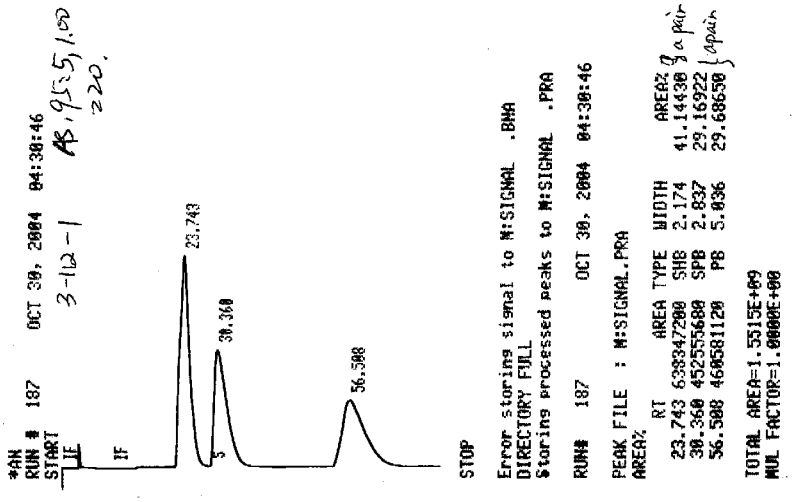
Asymmetric 4Ha, 90% ee, reaction catalyzed by QD-PHN-OH(QD-1c)

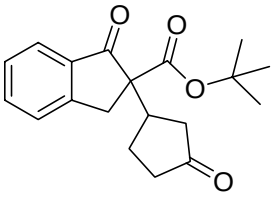


HPLC Conditions: Daicel chiralpak AS, Hexane:IPA, 95: 5, 1.00 mL/min, λ 220 nm

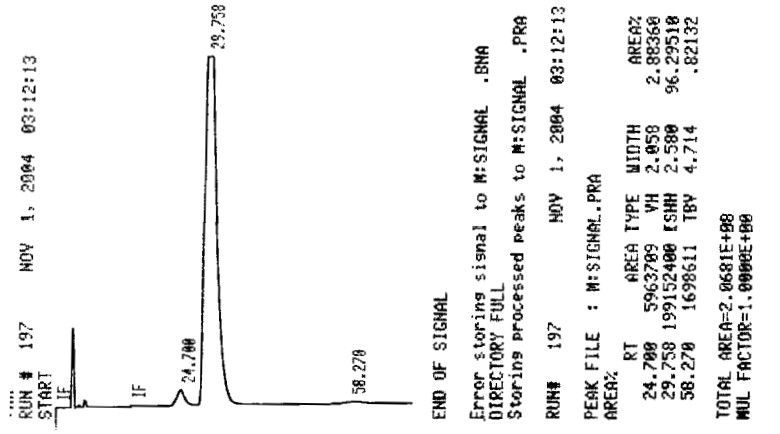


Recamic 6Ba

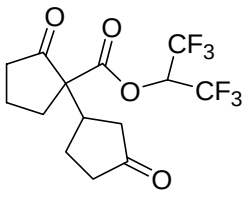




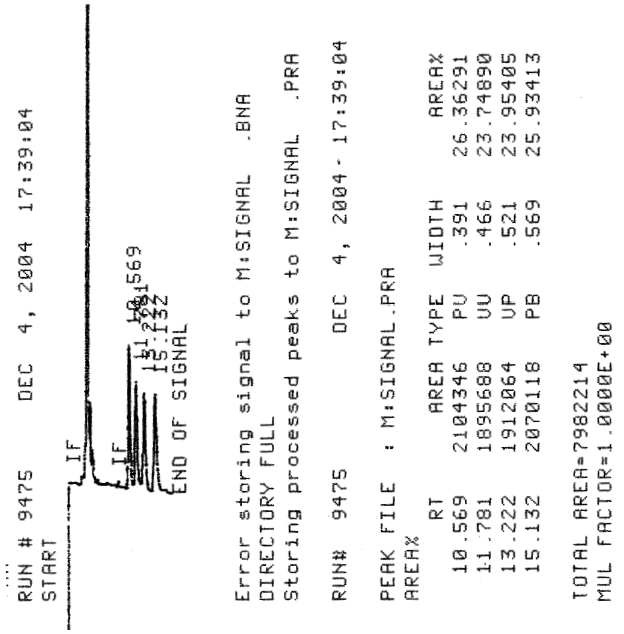
Asymmetric 6Ba, dr=96:4
98% ee of major isomer,
reaction catalyzed
by QD-1b



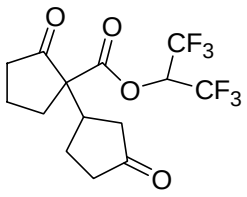
HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 90:10, 1.00 mL/min, λ 215 nm



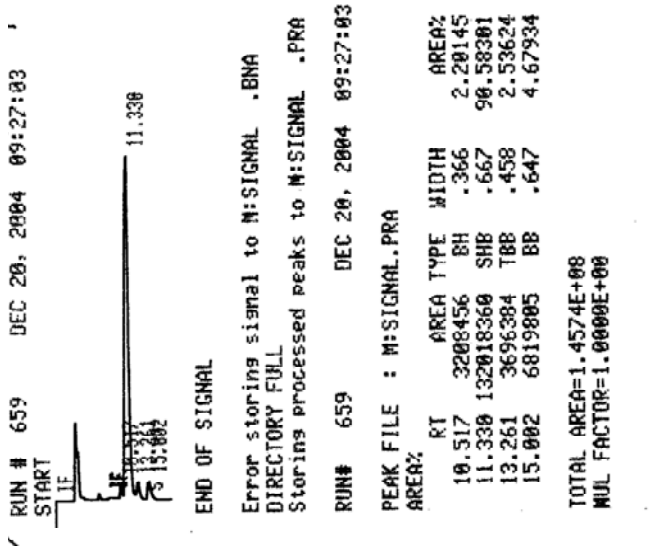
Recamic 6Fa



```
RUN # 9475      DEC  4, 2004  17:39:04
START
                                  10.569
                                  11.781
                                  13.222
                                  15.132
END OF SIGNAL

Error storing signal to M:SIGNAL  .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL  .PRA

RUN#  9475          DEC  4, 2004 - 17:39:04

PEAK FILE  : M:SIGNAL.PRA
AREA%
        RT      AREA TYPE  WIDTH      AREA%
    10.569   2104346  PU    .391   26.36291
    11.781   1895688  VV    .466   23.74890
    13.222   1912064  VP    .521   23.95405
    15.132   2070118  PB    .569   25.93413

TOTAL AREA=7982214
MUL FACTOR=1.0000E+00
```

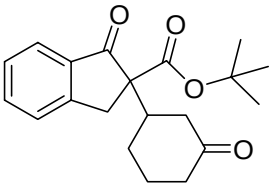


Asymmetric 6Fa, dr=93:7
95% ee of major isomer,
reaction catalyzed
by Q-1c

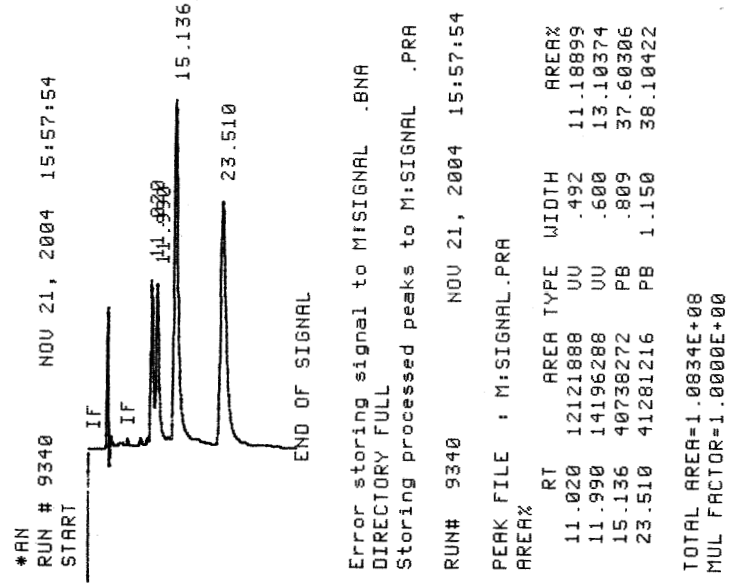


```
RUN #  659      DEC 20, 2004  09:27:03
START
                                  11.330
END OF SIGNAL

Error storing signal to M:SIGNAL  .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL  .PRA

RUN#  659          DEC 20, 2004  09:27:03

PEAK FILE  : M:SIGNAL.PRA
AREA%
        RT      AREA TYPE  WIDTH      AREA%
    10.517   3208456  BH    .366    2.20145
    11.330 132018360  SHB   .667   90.58301
    13.261   3696384  TBB   .458    2.53624
    15.002   6819805  BB    .647    4.67934

TOTAL AREA=1.4574E+08
MUL FACTOR=1.0000E+00
```

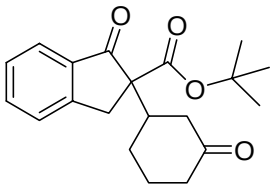
HPLC Conditions: Daicel chiralcel OD, Hexane:IPA, 95:5, 1.00 mL/min, λ 220 nm



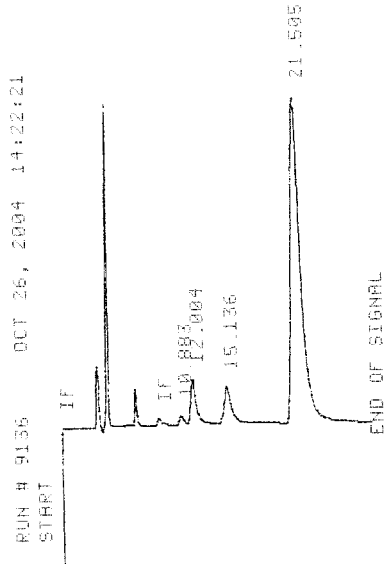
Racemic 6Bb




```
Error storing signal to M:SIGNAL  .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL  .PRA

RUN#  9340          NOV 21, 2004  15:57:54

PEAK FILE  : M:SIGNAL.PRA
AREA%
        RT        AREA TYPE  WIDTH      AREA%
    11.020    12121888  VV     .492   11.18899
    11.990    14196288  VV     .600   13.10374
    15.136    40738272  PB     .809   37.60306
    23.510    41281216  PB    1.150   38.10422

TOTAL AREA=1.0834E+08
MUL FACTOR=1.0000E+00
```

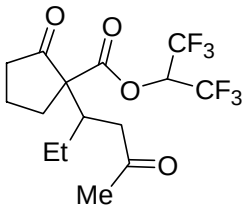


Asymmetric 6Bb, dr=93:7
85% ee of major isomer,
reaction catalyzed
by QD-1b

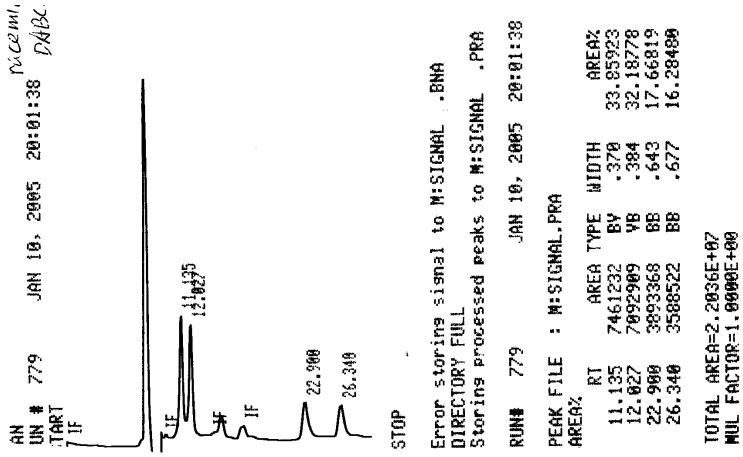


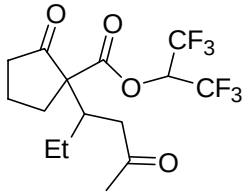

```
Error storing signal to M:SIGNAL  .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL  .PRA

RUN#  9136          OCT 26, 2004  14:22:21

PEAK FILE  : M:SIGNAL.PRA
AREA%
        RT        AREA TYPE  WIDTH      AREA%
    10.803     1349675  BV     .458    1.06653
    12.004     7768815  VB     .550    6.13901
    15.136     9903955  PB     .755    7.03601
    21.505   108525960  ISPH  1.076   85.75846

TOTAL AREA=1.2655E+08
MUL FACTOR=1.0000E+00
```

HPLC Conditions: REGIS, (R, R) Whelk-O1 + Daicel chiralpak AD, Hexane:IPA, 95:5, 0.80 mL/min, λ 215 nm



Recamic 6Fc





Asymmetric 6Fc, dr=86:14
99% ee of major isomer, 94% ee of minor isomer
reaction catalyzed by Q-1c