Supporting Information

Stereoselective Synthesis of Epoxyisoprostanes: An Organocatalytic and "Pot-economy" Approach

Jiang Weng,*[a] Sheng Wang,[a] Lin-Jie Huang,[a] Zhang-Yi Luo,[a] and Gui Lu*[a,b]

[a] Institute of Medicinal Chemistry, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006, People's Republic of China
Fax: (+86)-20-3994-3048; E-mail: wengj2@mail.sysu.edu.cn, lugui@mail.sysu.edu.cn

[b] Institute of Human Virology, Sun Yat-sen University, Guangzhou 510080, People's Republic of China

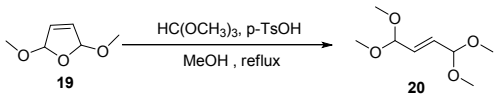
Table of Contents

General remarks

All the commercial reagents were used as such without further purification unless otherwise stated. All solvents were used as commercial reagent grade without further purification. Reactions requiring anhydrous solvents and inert atmosphere were mentioned in the experimental procedure. The flash column chromatography was carried out over silica gel (230-400 mesh). TLC analysis was performed on precoated silica gel GF254 slides, and visualized by either UV irradiation or $KMnO_4$ staining. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 MHz spectrometer. Chemical shifts in ^1H NMR spectra were reported in parts per million (ppm, δ) downfield from the internal standard Me_4Si (TMS, δ = 0 ppm). Chemical shifts in ^{13}C NMR spectra were reported relative to the central line of the chloroform signal (δ = 77.0 ppm). Peaks were labeled as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). High resolution mass spectra were obtained with a Shimadzu LCMS-IT-TOF mass spectrometer. Enantiomeric excesses of compounds were determined by HPLC using a Daicel chiral column. Optical rotations were measured using a 5 mL cell with 1 dm path length on a digital polarimeter and were reported as follows: (*c* in gram per 100 mL of solvent).

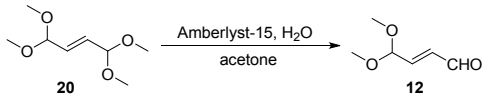
Experimental details and characterization data

(*E*)-1,1,4,4-tetraMethoxybut-2-ene (20)[1]



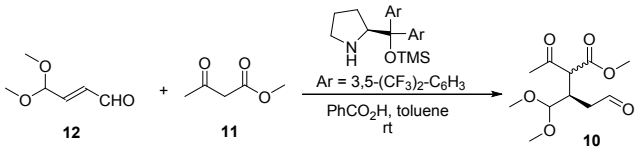
To a solution of 2,5-dimethoxy-2,5-dihydrofuran (**19**, 8.00 g, 61.5 mmol) in methanol (80 mL) was added trimethyl orthoformate (26.1 g, 246 mmol, 4.0 equiv.) and *p*-TsOH (1.06 g, 6.15 mmol, 10 mol%). After the solution was refluxed for 1 h, potassium carbonate (849 mg) was added and stirred for 10 mins. Then the mixture was concentrated and dissolved in dichloromethane. After filtration and concentration, the crude product was purified by flash column chromatography to give compound **20** (7.25 g, 67% yield) as a colorless oil. TLC: Rf = 0.36 (hexane/EtOAc, 6:1, I_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.79 (s, 2 H), 4.83 (s, 2 H), 3.30 (s, 12 H).

(*E*)-4,4-diMethoxybut-2-enal (12)[2]



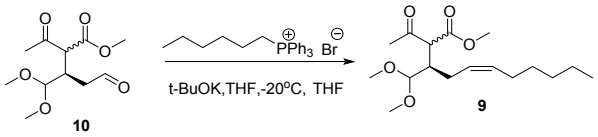
To a solution of **20** (6.34 g, 36.0 mmol) in acetone (120 mL) at 0 °C was added water (1.94 mL, 108 mmol, 3.0 equiv.) and Amberlyst-15 (1.39 g). The mixture was stirred at 0 °C for about 2.5 h. Then the mixture was filtered and treated with water (80 mL) and CH_2Cl_2 (80 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layer was washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford compound **12** as light yellow oil (3.02 g, 65% yield). TLC: Rf = 0.32 (hexane/EtOAc, 6:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 9.63 (d, *J* = 7.8 Hz, 1H), 6.64 (dd, *J* = 15.9, 3.9 Hz, 1H), 6.37 (m, 1H), 5.06 (dd, *J* = 3.9, 1.2 Hz, 1H), 3.37 (s, 6H).

Methyl (3*R*)-2-acetyl-3-(dimethoxymethyl)-5-oxopentanoate (10)



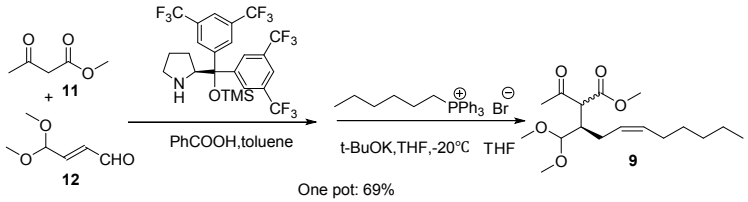
To a solution of **12** (1.30 g, 10.0 mmol) in toluene (17 mL) was added methyl acetoacetate **11** (2.32 g, 20.0 mmol, 2.0 equiv.), benzoic acid (122 mg, 1.0 mmol, 10 mol%) and (*S*)-2-(bis(3,5-bis(trifluoromethyl)phenyl)((trimethylsilyloxy)methyl)pyrrolidine (597 mg, 1.0 mmol, 10 mol%). The mixture was stirred for about 16 h at room temperature. Then the mixture was concentrated under vacuum and purified by flash column chromatography to give product **10** as colorless oil (2.12 g, 86% yield, 96% ee). TLC: Rf = 0.33 (hexane/EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78-9.51 (m, 1H), 4.33 (m, 1H), 3.70 (m, 3H), 3.45 (m, 1H), 3.32 (m, 6H), 3.16-3.03 (m, 1H), 2.71-2.40 (m, 2H), 2.26-2.21 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.5/202.0 ($CH_3\underline{C}OCH$-), 200.8/200.5 (-CH$\underline{C}$HO), 169.4/169.1 (-CH$\underline{C}O_2CH_3$), 129.9/128.3 (-$\underline{C}H(OCH_3)_2$), 64.9/64.2/58.3/57.9 (-CHO($\underline{C}H_3)_2$), 55.7 (-CO$\underline{C}HCO_2CH_3$), 52.4 (-$CO_2\underline{C}H_3$), 36.6/36.4 (-$\underline{C}H_2CHO$), 30.4/30.2 ($\underline{C}H_3CO$-), 20.1/20.0 (-$\underline{C}HCH_2CHO$). HRMS (ESI): calcd. for $C_{11}H_{18}O_6Na$ $[M+Na]^+$: 269.0996, found: 269.0988. $[a]_D^{20}$ = + 9.1 (c = 0.80, CH_2Cl_2) Enantiomeric purity was determined after aldehyde **10** was transformed to compound **26** *via* subsequent Wittig reaction and cyclization.

Methyl (3*R*,*Z*)-2-acetyl-3-(dimethoxymethyl) undec-5-enoate (9)



To a solution of hexyltriphenylphosphonium bromide (8.33 g, 19.5 mmol, 4.0 equiv.) in anhydrous THF (60 mL) at -20 °C was added *t*-BuOK (2.08 g, 18.5 mmol, 3.8 equiv.) under nitrogen atmosphere. After 1 h, aldehyde **10** (1.20 g, 4.87 mmol, 1.0 equiv.) in anhydrous THF (22 mL) was added dropwise via a syringe and the mixture was stirred for 1 h at -20 °C and another 12 h at room temperature. Then the reaction was quenched with water (30 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 70 mL), the combined organic layer was washed with brine (90 mL), dried over Na_2SO_4, concentrated under vacuum, and purified by flash column chromatography to give product **9** as colorless oil (1.10 g, 72% yield). TLC: Rf = 0.45 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): 5.52-5.38 (m, 1H), 5.37-5.25 (m, 1H), 4.50 (d, *J* = 6.0 Hz, 1H), 4.28 (d, *J* = 5.0 Hz, 1H), 3.70 (m, 3H), 3.63 (d, *J* = 5.8 Hz, 1H), 3.37-3.27 (m, 6H), 2.61 (m, 1H), 2.28 (m, 1H), 2.22 (s, 3H), 2.16 (m, 1H), 2.05-1.92 (m, 2H), 1.37-1.23 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.0/202.6 ($CH_3\underline{C}O$-), 169.9/169.6 (-$\underline{C}O_2CH_3$), 132.7/132.4 (-CH=$\underline{C}$H-C_5H_{11}), 126.3 (-$\underline{C}$H=CH-C_5H_{11}), 106.0 (-$\underline{C}H(OCH_3)_2$), 58.6/58.5/56.2/55.9 (-CH(O$\underline{C}H_3)_2$), 54.3/54.0 (-CO$\underline{C}HCO_2CH_3$), 52.0 (-COO$\underline{C}H_3$), 42.6/42.1 (-$\underline{C}$HCH(OCH$_3)_2$), 31.5 ($\underline{C}H_3CO$-), 30.4 (-$\underline{C}H_2CH_2CH_2CH_3$), 29.5/29.2 (-CH$\underline{C}H_2$CH=CH-), 27.1 (-$\underline{C}H_2C_4H_9$), 25.8/25.6 (-$\underline{C}H_2CH_2CH_3$), 22.5 (-$\underline{C}H_2CH_3$), 14.0 (-$\underline{C}H_3$). HRMS (ESI): calcd. for $C_{17}H_{30}O_5K$ $[M+K]^+$: 353.1725, found: 353.1710. $[a]_D^{20}$ = + 5.5 (*c* = 0.38, CH_2Cl_2).

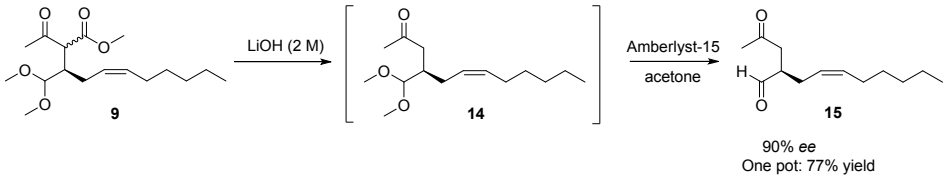
One-pot operation for the synthesis of 9



To a solution of **12** (1.04 g, 8.0 mmol) in toluene was added methyl acetoacetate **11** (1.21 g, 10.4 mmol, 1.3 equiv.), benzoic acid (98 mg, 0.8 mmol, 10 mol%) and (*S*)-2-(bis(3,5-bis(trifluoromethyl)phenyl)((trimethylsilyloxy)methyl)pyrrolidine (480 mg, 0.8 mmol, 10 mol%). After the solution was stirred at room temperature for 16 h, the mixture was concentrated under vacuum to afford the crude aldehyde **10** (2.10 g).

To a suspension of hexyltriphenylphosphonium bromide (13.7 g, 40.0 mmol, 4.0 equiv.) in anhydrous THF (100 mL) was added *t*-BuOK (3.40 g, 30.4 mmol, 3.8 equiv.) at -20 °C under N_2, the resulting orange mixture was stirred at -20 °C for 1 h. Then crude aldehyde **10** (2.10 g) in THF (30 mL) was added dropwise *via* a syringe. The mixture was stirred at -20 °C for 1 h and another 10 h at room temperature. The reaction was quenched with water (50 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 100 mL), the combined organic layer was washed with brine (140 mL), dried over Na_2SO_4, concentrated under vacuum and purified via flash column chromatography to afford compound **9** as colorless oil (1.74 g, 69% yield for two steps).

One-pot preparation of (*R*,*Z*)-2-(2-oxopropyl) dec-4-enal (15)



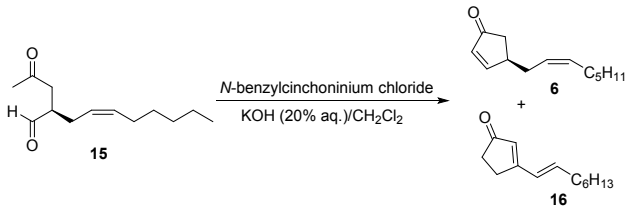
To a solution of aldehyde **9** (1.08 g, 3.44 mmol) in THF (120 mL) was added aqueous solution of LiOH (2 M, 35.0 mL). The mixture was refluxed for 10 h. Then the solution was cooled to room temperature and H_2O (65.0 mL) was added. After extraction with ether (2 × 120 mL), the combined organic layer was washed subsequently with saturated aqueous NH_4Cl (30 mL), H_2O (2 × 90 mL) and brine (60 mL), dried over Na_2SO_4, concentrated *in vacuo* to give the crude product **14** (875 mg) as light yellow oil. TLC: Rf = 0.48 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.49-5.39 (m, 1H), 5.30 (m, 1H), 4.18 (d, *J* = 5.1 Hz, 1H), 3.35 (s, 3H), 3.34 (s, 3H), 2.55 (dd, *J* = 16.2, 5.7 Hz, 1H), 2.41-2.25 (m, 2H), 2.21-2.14 (m, 1H), 2.13 (s, 3H), 2.07 (m, 1H), 2.01 (m, 2H), 1.30 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 208.4 ($CH_3\underline{C}O$-), 132.2 (-CH=$\underline{C}HC_5H_{11}$), 126.7 (-$\underline{C}H$=CHC_5H_{11}), 107.1 (-$\underline{C}H$ (OCH_3)$_2$), 55.2/54.4 (-$CH(O\underline{C}H_3)_2$,2H), 42.6 ($CH_3CO\underline{C}H_2$-), 37.4 (-$\underline{C}HCH(OCH_3)_2$), 31.5 (-$\underline{C}H_2CH_2CH_3$), 30.4 ($\underline{C}H_3CO$-), 29.3 (-$\underline{C}H_2C_3H_7$), 27.4 (-$\underline{C}H_2C_4H_9$), 27.2 (-$\underline{C}H_2CH$=$CHC_5H_{11}$), 22.5 (-$\underline{C}H_2CH_3$), 14.0 (-$\underline{C}H_3$). HRMS (ESI): calcd. for $C_{15}H_{28}O_3Na$ $[M+Na]^+$: 279.1931, found: 279.1917. $[a]_D^{20}$ = + 14.1 (*c* = 0.34, CH_2Cl_2).

To the crude **14** (875 mg) in acetone (20 mL) was added water (0.38 mL) and amberlyst-15 (2.53

g). Then the mixture was stirred for 16 h at room temperature. The mixture was filtered and the filtrate was treated with water (30 mL) and CH_2Cl_2 (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was washed with brine (60 mL), dried over Na_2SO_4, concentrated under vacuum and purified via flash column chromatography to afford compound **15** as colorless oil (556 mg, 77% yield from **9**, 90% *ee*). TLC: Rf = 0.44 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.72 (d, *J* = 1.4 Hz, 1H), 5.52 (m, 1H), 5.28 (m, 1H), 2.99-2.81 (m, 2H), 2.46 (m, 2H), 2.26 (m, 1H), 2.18 (s, 3H), 2.00 (m, 2H), 1.38-1.23 (m, 6H), 0.89 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 206.5 ($CH_3\underline{C}O$-), 203.0 (-$\underline{C}HO$), 133.4 (-CH=$\underline{C}H$-C_5H_{11}), 124.7 (-$\underline{C}H$=CH-C_5H_{11}), 46.7 (-$\underline{C}HCHO$), 41.5 ($CH_3CO\underline{C}H_2$-), 31.4 (-$\underline{C}H_2CH_2CH_3$), 30.0 ($\underline{C}H_3CO$-), 29.1 (-$\underline{C}H_2C_3H_7$), 27.2 (-$\underline{C}H_2C_4H_9$), 26.1 (-$\underline{C}H_2CHCHO$), 22.5 (-$\underline{C}H_2CH_3$), 14.0 (-$\underline{C}H_3$). HRMS (ESI): calcd. for $C_{13}H_{23}O_2$ $[M+H]^+$: 211.1693, found: 211.1681. $[a]_D^{20}$ = + 44.6 (*c* = 0.50, CH_2Cl_2).

To determine the enantiomeric purity, aldehyde **15** was transformed to compound **27** *via* Wittig reaction with (ethoxycarbonylmethylene)triphenylphosphorane.

(*R*,*Z*)-4-(Oct-2-en-1-yl) cyclopent-2-en-1-one (6)



To a solution of aldehyde **15** (250 mg, 1.19 mmol) in CH_2Cl_2 (50 mL) was added aqueous solution of KOH (20%, 40 mL) and *N*-benzylcinchoninium chloride (1.30 g, 3.09 mmol, 2.6 equiv.). The mixture was stirred for about 10 h at room temperature. Then the solution was extracted with CH_2Cl_2 (3 × 30 mL), dried over Na_2SO_4 and concentrated. The residue was dissolved in excess diethyl ether and filtered. The filter residue was washed with ether and dried to recover the crude phase-transfer catalyst (0.93 g). The filtrate was concentrated under vacuum and purified via flash column chromatography to give product **6** (68 mg, 30% yield, 87% ee) and byproduct **16** (75 mg, 33% yield) as colorless oil.

Compound 6:

TLC: Rf = 0.49 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 5.6, 2.5 Hz, 1H), 6.15 (dd, *J* = 5.6, 2.0 Hz, 1H), 5.58-5.41 (m, 1H), 5.39-5.24 (m, 1H), 2.99 (m, 1H), 2.50 (dd, *J* = 18.9, 6.4 Hz, 1H), 2.34-2.15 (m, 2H), 2.05-1.92 (m, 3H), 1.35-1.19 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 209.8 (-$\underline{C}O$-), 168.0 (-$\underline{C}H$=CHCO-), 134.0 (-CH=$\underline{C}H$CO-), 132.9 (-CH=$\underline{C}H$-C_5H_{11}), 125.4 (-$\underline{C}H$=CH-C_5H_{11}), 41.4 (-CO$\underline{C}H_2$-), 40.5 (-$COCH_2\underline{C}H$-), 31.9 (-$\underline{C}H_2CH$=CH-C_5H_{11}), 31.5 (-$\underline{C}H_2CH_2CH_3$), 29.2 (-$\underline{C}H_2C_3H_7$), 27.3 (-$\underline{C}H_2C_4H_9$), 22.5 (-$\underline{C}H_2CH_3$), 14.0 (-$\underline{C}H_3$). $[a]_D^{20}$ = + 14.4 (*c* = 0.16, CH_2Cl_2).

Compound 16:

TLC: Rf = 0.36 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.54 (d, *J* = 15.8 Hz, 1H), 6.34 (m, 1H), 5.97 (s, 1H), 2.75 (m, 2H), 2.45 (m, 2H), 2.24 (m, 2H), 1.52-1.41 (m, 2H), 1.39-1.28 (m, 6H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 209.6 (-$\underline{C}O$-), 172.8 (-

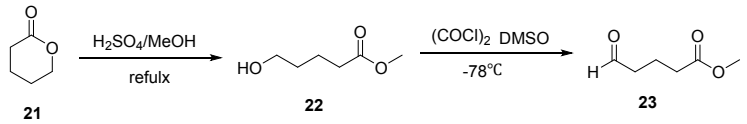
COCH=CH-), 141.2 (-COCH=CH-), 129.0 (-CH=CH-C_6H_{13}), 126.5 (-CH=CH-C_6H_{13}), 34.8 (-CH_2CO-), 33.2 (-$CH_2C_5H_{11}$), 31.6 (-$CH_2CH_2CH_3$), 28.9 (-$CH_2C_4H_9$), 28.6 (-$CH_2C_3H_7$), 27.1 (-CH_2CH_2CO-), 22.5 (-CH_2CH_3), 14.0 (-CH_3).

Procedure for the recycling of catalyst:

The filter residue was dried to give the crude catalyst, which was directly used in the next cyclization reaction.

To a solution of aldehyde **15** (40 mg, 0.19 mmol) in CH_2Cl_2 (7.0 mL) was added aqueous solution of 20% KOH (3.0 mL) and *N*-benzylcinchoninium chloride (210 mg, 0.50 mmol, 2.6 equiv.). The mixture was stirred overnight at room temperature. Then the mixture was extracted with CH_2Cl_2 (3 × 5 mL), dried over Na_2SO_4 and concentrated. The residue was dissolved in excess ether and filtered. The filtrate was concentrated *in vacuo* and purified via flash column chromatography to give product **6** (6 mg, 16% yield, 81% ee) and byproduct **16** (10 mg, 27% yield).

Methyl 5-oxopentanoate (23)[3]



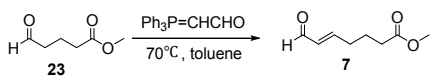
To a flask charged with δ-valerolactone **21** (15.0 g, 150 mmol) in MeOH (300 mL) was added concentrated sulphuric acid (0.8 mL, 15.0 mmol, 0.1 equiv.), the reaction mixture was refluxed for 21 h. Solid $NaHCO_3$ was added, and the solution was filtered and partially concentrated under vacuum. Then water (100 mL) was added, the mixture was extracted with EtOAc, dried over Na_2SO_4, filtered and concentrated under vacuum. The desired hydroxyester **22** was obtained as colorless oil (16.9 g, 85% yield).

TLC: Rf = 0.29 (hexane/EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 3 H), 3.65 (s, 2 H), 2.36 (t, *J* = 7.3 Hz, 2 H), 1.92 (s, 1 H), 1.78-1.66 (m, 2 H), 1.65-1.53 (m, 2 H).

To a solution of oxalylchloride (1.40 mL, 15.0 mmol, 1.1 equiv.) in CH_2Cl_2 (15.0 mL) at -78 °C was added a solution of DMSO (2.30 mL, 29.9 mmol, 2.2 equiv.) in CH_2Cl_2 (15.0 mL) dropwise. The reaction mixture was stirred for 10 min, then a solution of alcohol **22** (1.80 g, 13.6 mmol) in CH_2Cl_2 (15.0 mL) was added. The solution was stirred for 30 min, then Et_3N (10.1 mL, 72.5 mmol, 5.3 equiv.) was added and the reaction mixture was allowed to warm to room temperature. The mixture was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic phase was dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was distilled under vacuum to give aldehyde **23** (1.68 g, 95% yield) as a colorless oil.

TLC: Rf = 0.41 (hexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (s, 1 H), 3.70-3.62 (m, 3 H), 2.53 (d, *J* = 6.9 Hz, 2 H), 2.37 (d, *J* = 7.2 Hz, 2 H), 2.00-1.89 (m, 2 H).

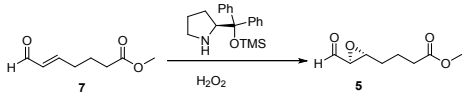
***E*-Methyl 7-oxohept-5-enoate (7)**[4]



The aldehyde **23** (7.09 g, 54.5 mmol) was added to a solution of 2-(triphenylphosphoranylidene)acetaldehyde (34.82 g, 114 mmol, 2.1 equiv.) in toluene (150 mL), and the mixture was stirred at 70 °C for 12 h. Then the solution was cooled to room temperature, poured into petrol ether (300 mL) and stirred until a clear yellow solution was formed. The

mixture was filtered, the filtrate was concentrated under vacuum and purified via flash column chromatography to give enal **7** (4.67 g, 55% yield) as a pale yellow oil with a 5:1 *E/Z* ratio. TLC: Rf = 0.31 (hexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.52 (d, *J* = 7.8 Hz, 1H), 6.83 (m, 1H), 6.14 (dd, *J* = 15.7, 7.8 Hz, 1H), 3.69 (s, 3H), 2.44-2.32 (m, 4H), 1.91-1.82 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.7 (-CHO), 173.3(-COOCH$_3$), 157.0 (HCOCH=CH-), 133.4 (HCOCH=CH-), 51.5 (-COOCH$_3$), 33.1 (-CH$_2$COOCH$_3$), 31.8 (-CH=CH-CH$_2$-), 22.9 (-CH$_2$CH$_2$COOCH$_3$).

Methyl 4-((2*R*,3*S*)-3-formyloxiran-2-yl) butanoate (5)[4]

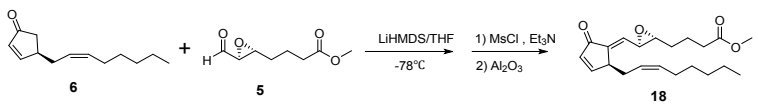


To a solution of enal **7** (1.9 g, 12.2 mmol, 1.0 equiv.) and (*S*)-2-(diphenyl ((trimethylsilyloxy)methyl)pyrrolidine (0.396 g, 1.2 mmol, 0.1 equiv.) in CH_2Cl_2 (30.0 mL) was added H_2O_2 (30% aqueous solution, 1.6 mL, 15.8 mmol, 1.3 equiv.) at 0 °C. The mixture was stirred at room temperature for 5 h, then saturated aqueous solutions of $NaHCO_3$ and $Na_2S_2O_3$ (V/V = 1/1, 30 mL) were added. The mixture was stirred for 30 min, then the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried over $MgSO_4$, concentrated under vacuum and purified via flash column chromatography (SiO_2, CH_2Cl_2/MeOH 98:2) to give epoxy aldehyde **5** (1.07 g, 10:1 *E/Z*, 51% yield, 92% ee) as a colorless oil.

TLC: Rf = 0.28 (hexane/EtOAc, 4:1).^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.02 (d, *J* = 6.2 Hz, 1H), 3.69 (s, 3H), 3.25 (m, 1H), 3.15 (dd, *J* = 6.2, 1.9 Hz, 1H), 2.40 (td, *J* = 7.1, 1.9 Hz, 2H), 1.88-1.74 (m, 3H), 1.70-1.61 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.3 (-CHO), 173.5 (-COOCH$_3$), 59.0 (HCOCH-), 56.4 (-OCH-CH$_2$-), 51.8 (-COOCH$_3$), 33.4 (-CH$_2$COOCH$_3$), 30.7 (-CH$_2$CH$_2$CH$_2$COOCH$_3$), 21.3 (-CH$_2$CH$_2$COOCH$_3$). $[a]_D^{20}$ = -25.2 (*c* = 0.43, $CHCl_3$).

To determine the enantiomeric purity, the epoxy aldehyde **5** was reduced with $NaBH_4$ and benzoylated.

Methyl-4-((2*R*,3*R*)-3-((*E*)-2-((*Z*)-oct-2-en-1-yl)-5-oxocychopent-3-en-1-ylidene) methyl) oxiran-2-yl) butanoate (18)[4]



Cyclopentenone **6** (57 mg, 0.3 mmol, 1.0 equiv.) in THF (1 mL) was added to a solution of LiHMDS (60 mg, 0.36 mmol, 1.2 equiv.) in THF (3 mL) at -78 °C. The mixture was stirred for 20 min, then a solution of epoxy aldehyde **5** (103 mg, 0.60 mmol, 2.0 equiv.) in THF (1 mL) was added. The solution was stirred at -78 °C for 2 h, then quenched at -78 °C with saturated NH_4Cl (4 mL) and warmed to room temperature. The mixture was extracted with ether (2 × 8 mL), the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by flash column chromatography to yield a mixture of the aldol product.

The mixture was dissolved in CH_2Cl_2 (3 mL) and treated with Et_3N (0.25 mL, 1.8 mmol, 6.0

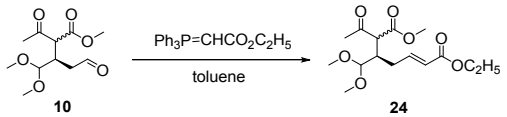
equiv.) and methanesulfonyl chloride (70 µL, 0.89 mmol, 3.0 equiv.) at 0 °C. The resulting solution was stirred at 0 °C for 1 h, then quenched with saturated $NaHCO_3$ solution and EtOAc. After vigorous stirring, the organic layer was separated, extracted with EtOAc, dried over $MgSO_4$ and concentrated. The crude product was passed through a short column of silica gel (hexane/EtOAc) to afford the corresponding mesylate, which was used for the next step without further purification.

To the resulting solution of the mesylate was added neutral aluminum oxide (0.30 g, 3.0 mmol, 10.0 equiv.). The mixture was vigorously stirred at room temperature for 15 h, then filtered through a plug of celite. The mixture was concentrated under vacuum and purified by flash column chromatography to give the EC methyl ester **18** (53 mg, 63% yield) as a yellow oil.

The spectral data (^{1}H NMR, ^{13}C NMR, HRMS, and optical rotation) of **18** was in excellent agreement with the published data.[4]

TLC: Rf = 0.52 (hexane/EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 3.9 Hz, 1H), 6.35 (d, *J* = 6.0 Hz, 1H), 6.19 (d, *J* = 8.1 Hz, 1H), 5.52 (m, 1H), 5.32 (m, 1H), 3.68 (s, 3H), 3.39 (d, *J* = 8.0 Hz, 1H), 2.98 (m, 1H), 2.55 (m, 1H), 2.43-2.31 (m, 3H), 1.98 (m, 2H), 1.79 (m, 3H), 1.61 (m, 2H), 1.28 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.9 (-CO-), 173.6 (-$\underline{C}OOCH_3$), 162.1 (-$\underline{C}H$=CH-CO-), 141.2 (-CO-C=$\underline{C}H$-), 134.6 (-CH=$\underline{C}H$-CO-), 133.5 (-CO-$\underline{C}$=CH-), 131.1 (-CH=$\underline{C}H$-C_5H_{11}), 124.5 (-$\underline{C}H$=CH-C_5H_{11}), 60.0 (-O-$\underline{C}H$-CH_2-), 55.1 (-CO-C=CH-$\underline{C}H$-), 51.8 (-COO$\underline{C}H_3$), 43.5 (-$\underline{C}H_2COOCH_3$), 33.6 (-$\underline{C}H_2$-CH=CH-C_5H_{11}), 32.0 (-$\underline{C}H_2CH_2CH_3$), 31.7 (-CO-CH=CH-$\underline{C}H$-), 31.4 (-$\underline{C}H_2CH_2CH_2COOCH_3$), 29.3 (-$\underline{C}H_2C_3H_7$), 27.5 (-$\underline{C}H_2C_4H_9$), 22.7 (-$\underline{C}H_2CH_3$), 21.5 (-$\underline{C}H_2CH_2COOCH_3$), 14.2 (-$\underline{C}H_3$). HRMS (ESI): calcd. for $C_{17}H_{31}O_5$ $[M+H]^+$: 347.2217, found: 347.2221. $[a]_D^{20}$ = + 165.7 (*c* = 0.19, $CHCl_3$).

1-Ethyl 7-methyl (*E*)-6-acetyl-5-(dimethoxymethyl)hept-2-enedioate (24)

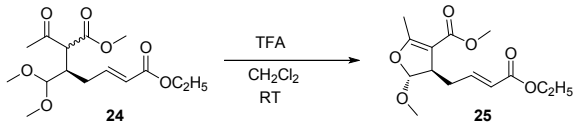


10 **24**

To a solution of aldehyde **10** (30 mg, 0.1 mmol, 1.0 equiv.) in toluene at room temperature was added ethyl (triphenylphosphoranylidene) acetate (51 mg, 0.18 mmol, 64 mg). After stirring overnight, the mixture was concentrated under vacuum and the residue was purified by column chromatography to give product **24** (25 mg, 65% yield) as colorless oil.

TLC: Rf = 0.35 (hexane/EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90 (m, 1H), 5.82 (m, 1H), 4.33 (m 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.75-3.69 (m, 3H), 3.69-3.59 (m, 1H), 3.40-3.26 (m, 6H), 2.80-2.62 (m, 1H), 2.50-2.29 (m, 2H), 2.22 (m, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.5/202.0 ($CH_3\underline{C}O$-), 169.6/169.2 (-$\underline{C}OOCH_3$), 166.2 (-$\underline{C}OOC_2H_5$), 146.4 (-$\underline{C}H$=CH-COO-), 123.5/123.2 (-CH=$\underline{C}H$-$COOCH_3$), 105.7 (-$\underline{C}H(OCH_3)_2$), 60.3 (-COO$\underline{C}H_2CH_3$), 58.4/57.9 (-CH(O$\underline{C}H_3)_2$,2H), 56.1/55.9 (-CO$\underline{C}HCOOCH_3$), 54.8/54.5 (-COO$\underline{C}H_3$), 52.3 (-$\underline{C}HCH(O\underline{C}H_3)_2$), 41.3/41.0 ($\underline{C}H_3CO$-), 30.8/30.4 (-$\underline{C}H_2CH$=CH-), 14.2(-$COOCH_2\underline{C}H_3$). $[a]_D^{20}$ = -11.4 (*c* = 0.50, CH_2Cl_2).

Methyl (*E*)-4-(4-ethoxy-4-oxobut-2-en-1-yl)-5–methoxy-2-methyl-4,5-dihydrofuran-3-carboxylate (25)

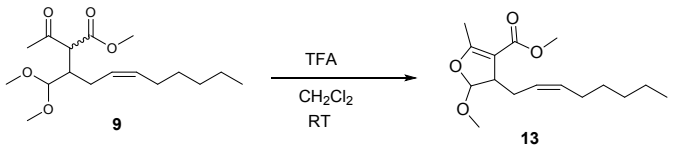


24 **25**

To a solution of **24** (25 mg, 0.16 mmol, 1.0 equiv.) in dichloromethane at room temperature was added TFA (5 mg, 0.08 mmol, 0.5 equiv.). After stirring for about 1 h, the mixture was purified by coloumn chromatography to give product **25** (19 mg, 84% yield, 95% *ee*) as colorless oil.

TLC: Rf = 0.39 (hexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (m, 1H), 5.87 (d, *J* = 15.7 Hz, 1H), 5.00 (d, *J* = 1.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 3H), 3.45 (s, 3H), 3.19-3.00 (m, 1H), 2.74-2.50 (m, 1H), 2.35-2.26 (m, 1H), 2.23 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.4 (-$\underline{C}OOCH_3$), 166.2 (-O-$\underline{C}$=C-), 165.6 (-$\underline{C}OOC_2H_5$), 145.2 (-$\underline{C}H$=$CHCOOC_2H_5$), 123.4 (-CH=$\underline{C}HCOOC_2H_5$), 109.9 (-O-C=$\underline{C}$-), 104.9 (-$\underline{C}H$-OCH_3), 60.3 (-$COO\underline{C}H_2CH_3$), 55.8 (-CH-O$\underline{C}H_3$), 50.9 (-$COO\underline{C}H_3$), 50.7 (-C=C-$\underline{C}H$-), 47.5 (-$\underline{C}HCH$=CH-), 33.8 ($\underline{C}H_3C$=C-), 14.3 (-$COOCH_2\underline{C}H_3$). $[a]_D^{20}$ = - 1.4 (*c* = 0.42, CH_2Cl_2).

Methyl-(*Z*)-5-methoxy-2-methyl-4-(oct-2-en-1-yl)-4,5-dihydrofuran-3-carboxylate (13)



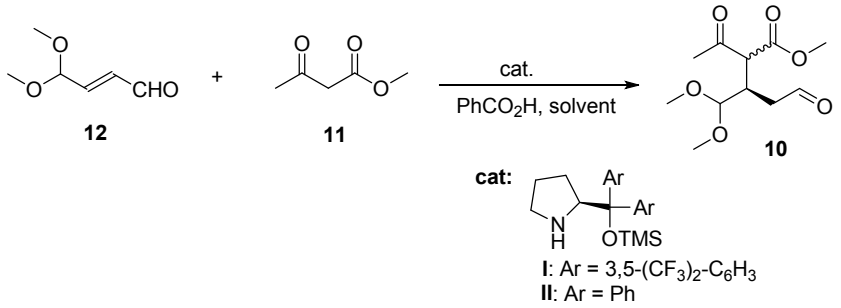
9 **13**

To a solution of **9** (30 mg, 0.10 mmol, 1.0 equiv.) in dichloromethane at room temperature was added TFA (5 mg, 0.05 mmol, 0.5 equiv.). After stirring for about 1 h, the mixture was purified by coloumn chromatography to give product **13** (23 mg, 85% yield) as colorless oil.

TLC: Rf = 0.59 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.57-5.41 (m, 1H), 5.35-5.23 (m, 1H), 5.00 (d, *J* = 1.9 Hz, 1H), 3.71 (s, 3H), 3.44 (s, 3H), 2.99 (m, 1H), 2.54-2.37 (m, 1H), 2.25 (s, 3H), 2.20-2.10 (m, 1H), 2.02 (dd, *J* = 14.2, 7.0 Hz, 2H), 1.39-1.23 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.8 (-$\underline{C}OOCH_3$), 165.9 ($CH_3\underline{C}$=C-), 132.7 (-CH=$\underline{C}$H-C_5H_{11}), 125.2 (-$\underline{C}$H=CH-C_5H_{11}), 110.4 (-C=$\underline{C}$-$COOCH_3$), 105.7 (-$\underline{C}$H-O-CH_3), 55.6 (-CH-O$\underline{C}H_3$), 50.7 (-$COO\underline{C}H_3$), 48.7 (-C=C-$\underline{C}$H-), 31.5 (-$\underline{C}H_2CH_2CH_3$), 29.3 (-$\underline{C}H_2C_3H_7$), 28.7 (-$\underline{C}H_2C_4H_9$), 27.3 (-$\underline{C}H_2CH_3$), 22.5 (-$CH\underline{C}H_2$-CH=CH-), 14.3 ($\underline{C}H_3$-C=C-), 14.0 (-$CH_2\underline{C}H_3$). HRMS (ESI): calcd. for $C_{17}H_{30}O_5Na$ $[M+Na]^+$: 305.1723, found: 305.1727. $[a]_D^{20}$ = - 116.2 (*c* = 0.74, CH_2Cl_2).

Investigation on the Michael reaction of (*E*)-4,4-dimethoxybut-2-enal with methyl acetoacetate

Table S1. Optimization of the reaction conditions[a]

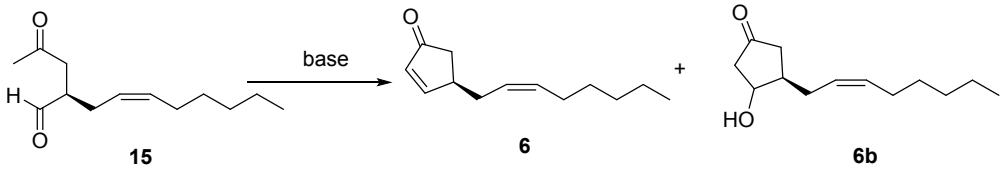


Entry	catalyst	solvent	yield (%)[b]	ee (%)[c]
1	I	$CHCl_3$	19	N.D
2	I	toluene	83	96
3	I	H_2O	45	88
4	II	$CHCl_3$	15	N.D.
5	II	toluene	32	90

[a]All reactions were carried out with **12** (0.5 mmol), **11** (1.0 mmol), catalyst (10 mol%), and $PhCO_2H$ (10 mol%) in the indicated solvent (1 mL) at room temperature for 24 h. [b] Product was isolated by flash chromatography. [c] The *ee* value was determined by chiral HPLC after **10** was converted to compound **26**.

Investigation on the intramolecular aldol/dehydration reaction

Table S2. Optimization of the cyclization reaction promoted by bases[a]



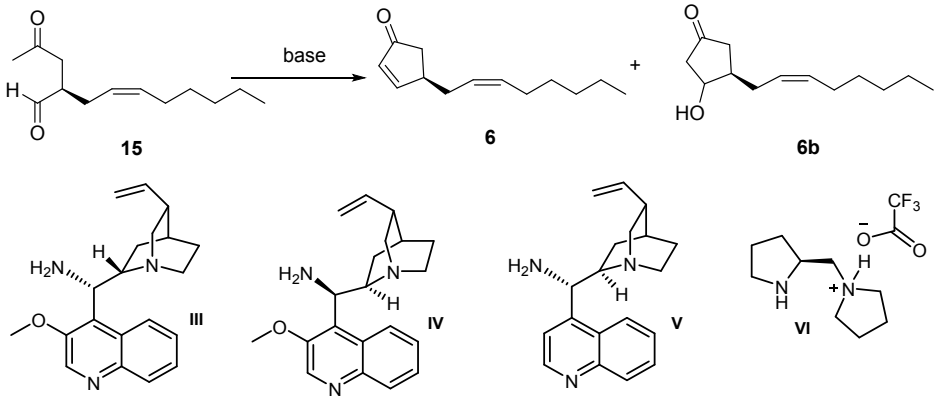
Entry	base	solvent	T (°C)	product	yield (%)[b]	ee (%)[c]
1[d]	NaOH (aq.)	Et_2O	RT	**6**	**63**	3
2[e]	$Ba(OH)_2$	MeOH	RT	**6**	11	28
3[f]	NaOMe	MeOH/THF	0	**6**	15	4
4[g]	LDA	THF	-78	**6b**	trace	-
5[h]	LiHMDS	THF	-78	**6b**	trace	-
6[i]	DBU	THF	RT	complex	-	-
7[j]	DIPEA/TMSCl/$TiCl_4$	DCM	0	complex	-	-
8[k]	DIPEA/TMSOTf/TiCl	DCM	0	complex	-	-

4

[a] Unless otherwise specified, all reactions were carried out with reactant (0.25 mmol) in the indicated solvent at room temperature. [b] Isolated yield. [c] The *ee* value was determined by chiral HPLC. [d] NaOH (5%, 2 mL), Et_2O (2 mL). [e] $Ba(OH)_2$ (0.15 mmol), MeOH (10 mL). [f] NaOMe (0.75 mmol), MeOH (1 mL), THF (4 mL). [g] LDA (0.275 mmol), THF (4 mL). [h] LiHMDS (0.275 mmol), THF (4 mL). [i] DBU (0.10 mmol), THF (2 mL). [j] DIPEA

(0.75 mmol), TMSCl (0.125 mmol), $TiCl_4$ (0.275 mmol), DCM (6 mL). [k] DIPEA (0.75 mmol), TMSOTf (0.125 mmol), $TiCl_4$ (0.275 mmol), DCM (5 mL).

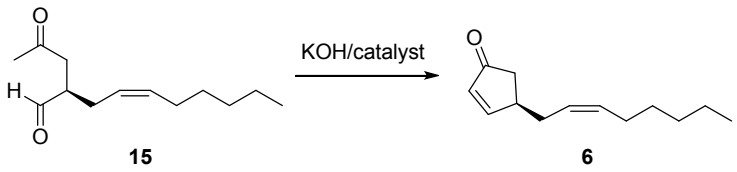
Table S3. Screening of the cyclization reaction promoted by various amine organocatalysts



Entry	catalyst	solvent	T (°C)	product	yield (%)[b]	ee (%)[c]
1[d]	Piperidine/HOAc	toluene	RT	NR	NR	-
2[e]	Bn_2NH/CF_3COOH	THF	RT	NR	NR	-
3[f]	**III**	toluene	RT	NR	NR	-
4[f]	**IV**	toluene	RT	NR	NR	-
5[f]	**V**	toluene	RT	NR	NR	-
6[f]	**VI**	DCM	RT	NR	NR	-

[a] Unless otherwise specified, all reactions were carried out with reactant (0.25 mmol) in the indicated solvent at room temperature. [b] Isolated yield. [c] The *ee* value was determined by chiral HPLC. [d] Catalyst (20 mol%), toluene (3.0 mL). [e] Catalyst (30 mol%), THF (1.5 mL). [f] Catalyst (20 mol%), solvent (3.0 mL)

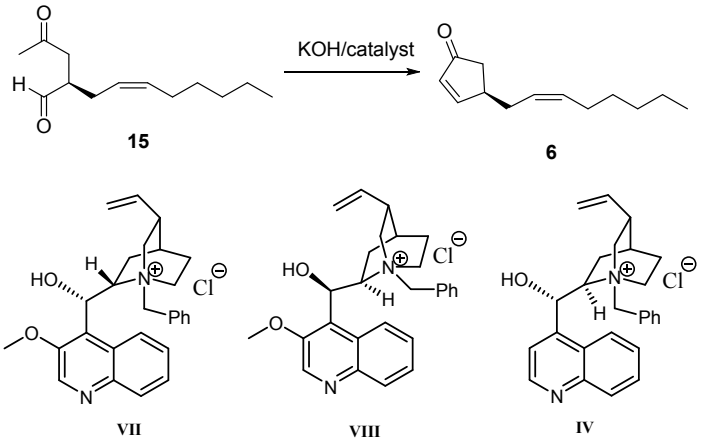
Table S4. Screening of the cyclization reaction under phase-transfer conditions[a]



Entry	catalyst	solvent	T (°C)	product	yield (%)[b]	ee (%)[c]
1	*n*-Bu_4NOH	$THF/Et_2O/H_2O$ (2:1:1)	RT	**6**	27	3
2	*n*-Bu_4NOH	$THF/Et_2O/H_2O$ (2:1:1)	0	**6**	14	7
3	*n*-Bu_4NI	Et_2O/H_2O (2:1)	RT	**6**	30	5
4	*n*-Bu_4NBr	Et_2O/H_2O (2:1)	RT	**6**	24	3

[a] Unless otherwise specified, all reactions were carried out with reactant (0.25 mmol), aq. KOH (5%, 4 mL), PTC catalyst (0.25 mmol), in the indicated solvent at room temperature. [b] Isolated yield. [c] The *ee* value was determined by chiral HPLC.

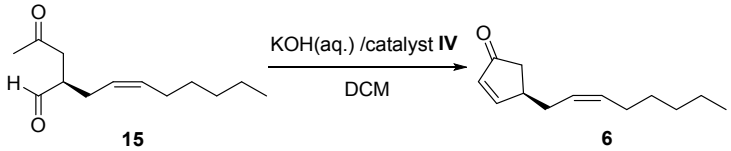
Table S5. Optimization of the cyclization reaction under phase-transfer conditions[a]



Entry	catalyst	solvent	yield (%)[b]	ee (%)[c]
1	**VII** (1.0 equiv.)	DCM	13	48
2	**VII** (1.0 equiv.)	Et_2O	24	7
3	**VII** (1.0 equiv.)	toluene	12	33
4	**VII** (2.5 equiv.)	DCM	14	85
5	**VII** (2.5 equiv.)	Et_2O	41	13
6	**VII** (2.5 equiv.)	toluene	24	33
7	**VII** (2.5 equiv.)	DCM/Et_2O (1:1)	17	63
8	**VII** (2.5 equiv.)	DCM/toluene (1:1)	11	72
9	**VIII** (2.5 equiv.)	DCM	10	61
10	**IV** (2.5 equiv.)	DCM	24	85
11[d]	**IV** (2.5 equiv.)	DCM	8	55
12[e]	**IV** (2.5 equiv.)	DCM	21	64
13[f]	**IV** (2.5 equiv.)	DCM	22	82

[a] Unless otherwise specified, all reactions were carried out with reactant **15** (0.25 mmol), aq. KOH (20%, 4 mL), PTC catalyst, in the indicated solvent (9 mL) at room temperature. [b] Isolated yield. [c] The *ee* value was determined by chiral HPLC. [d] At 0 °C. [e] aq. LiOH (20%, 4 mL) instead of aq. KOH. [f] aq. NaOH (20%, 4 mL) instead of aq. KOH.

Table S6. Effects of concentrations under phase-transfer conditions[a]



Entry	KOH (aq.)	DCM	Yield (%)[b]	Ee (%)[c]
1	5% / 4 mL	10 mL	19	41
2	20% / 4 mL	10 mL	24	85
3	40% / 4 mL	10 mL	trace	ND
4	10% / 4mL	10 mL	26	85
5	**10% / 8 mL**	**10 mL**	**30**	**87**
6	10% / 2 mL	10 mL	6	ND
7	10% / 8 mL	5 mL	8	ND
8	10% / 8 mL	15 mL	15	82
9	10% / 12 mL	10 mL	13	85

[a] Unless otherwise specified, all reactions were carried out with reactant **15** (0.25 mmol), aq. KOH, catalyst **IV** (2.5 equiv.), CH_2Cl_2 as solvent at rt. [b] Isolated yield. [c] The *ee* value was determined by chiral HPLC.

References

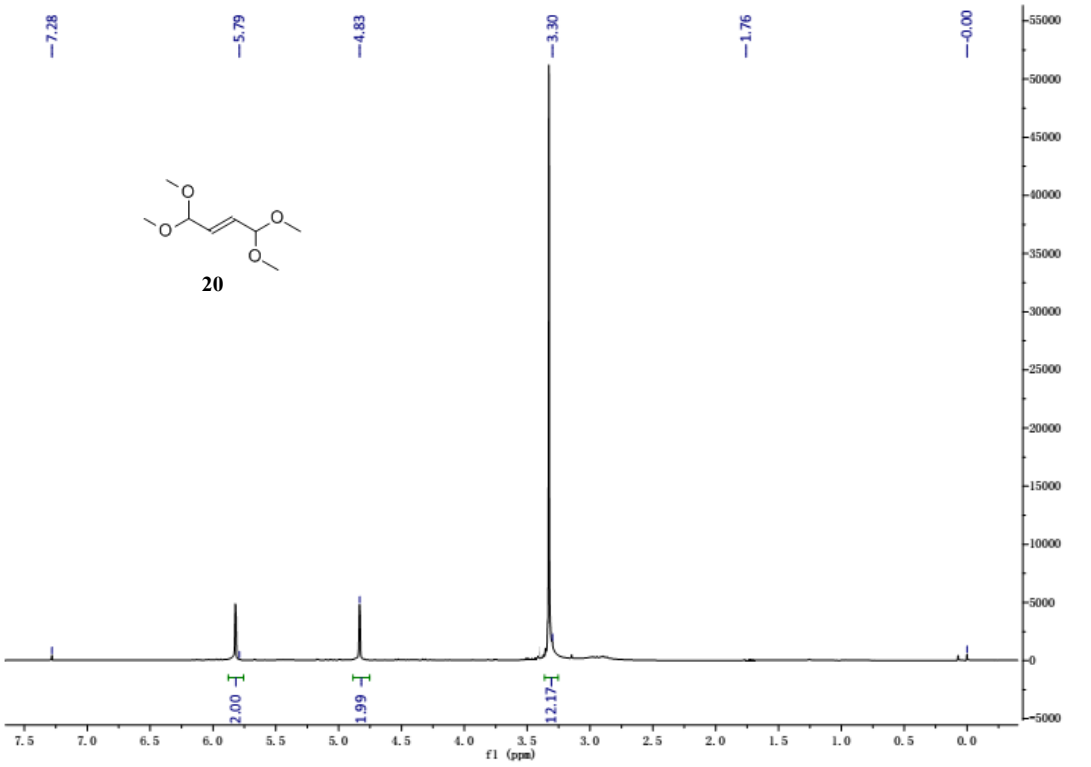
[1] K. Wolfgang, P. Joachim, Preparation of *E*,*Z*-butenedial bis(dialkyl aetals). Patent US5338888A.

[2] B. M. Trost, M. J. Bartlett, A. H. Weiss, A. J. von Wangelin V. S. Chan, *Chem. Eur. J.,* **2012**, *18*, 16498.

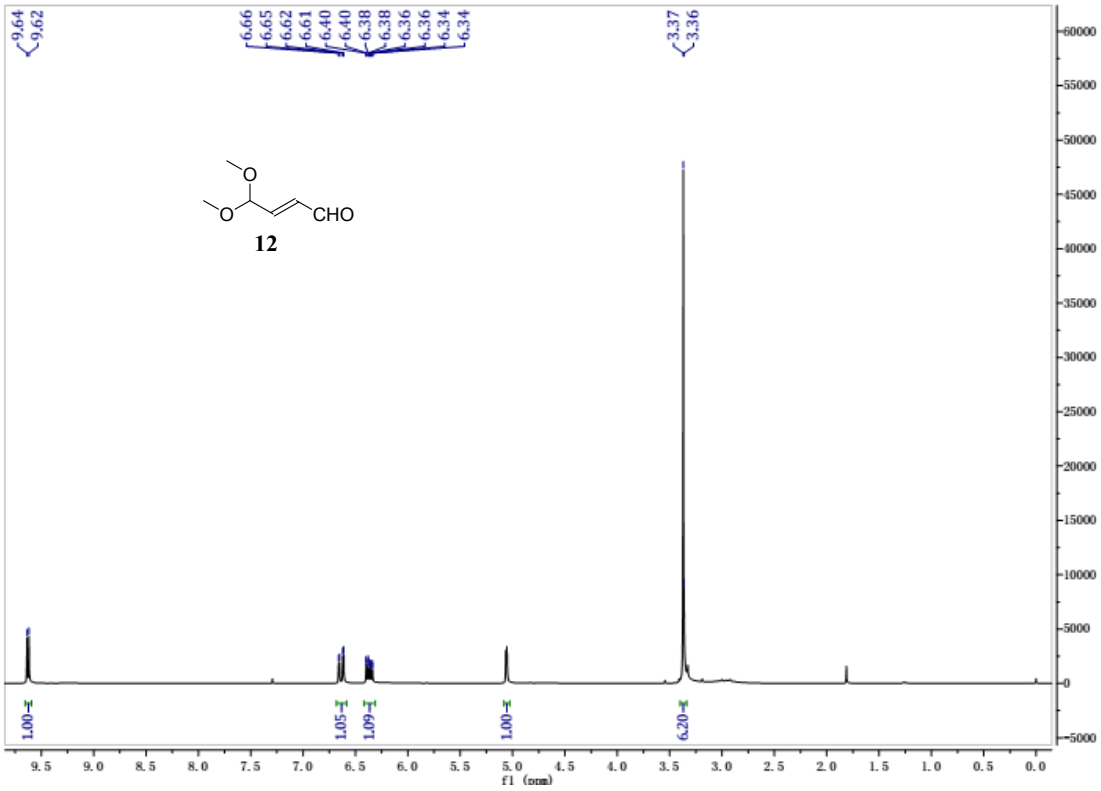
[3] C. Cook, F. Liron, X. Guinchard, E. Roulland, *J. Org. Chem*., **2012**, *77*, 6728.

[4] J. Egger, P. Bretscher, S. Freigang, M. Kopf, E. M. Carreira, *Angew. Chem., Int. Ed.*, **2013**, *52*, 5382.

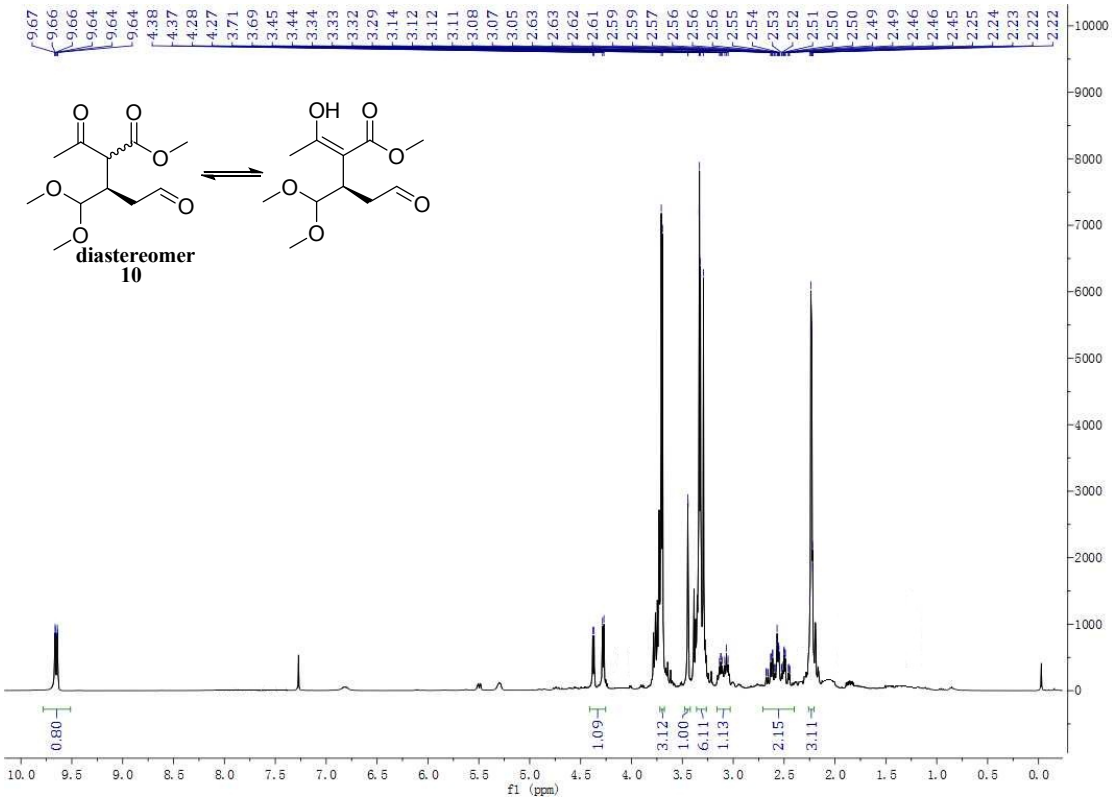
Copies of ^{1}H NMR and ^{13}C NMR spectra

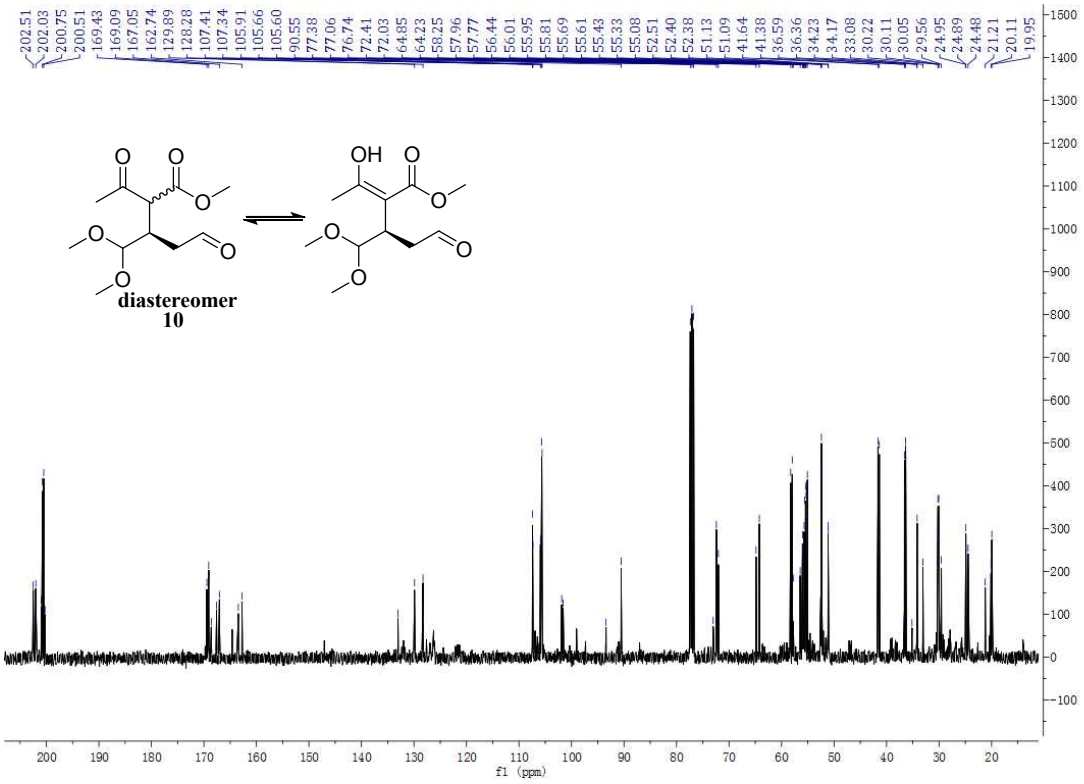


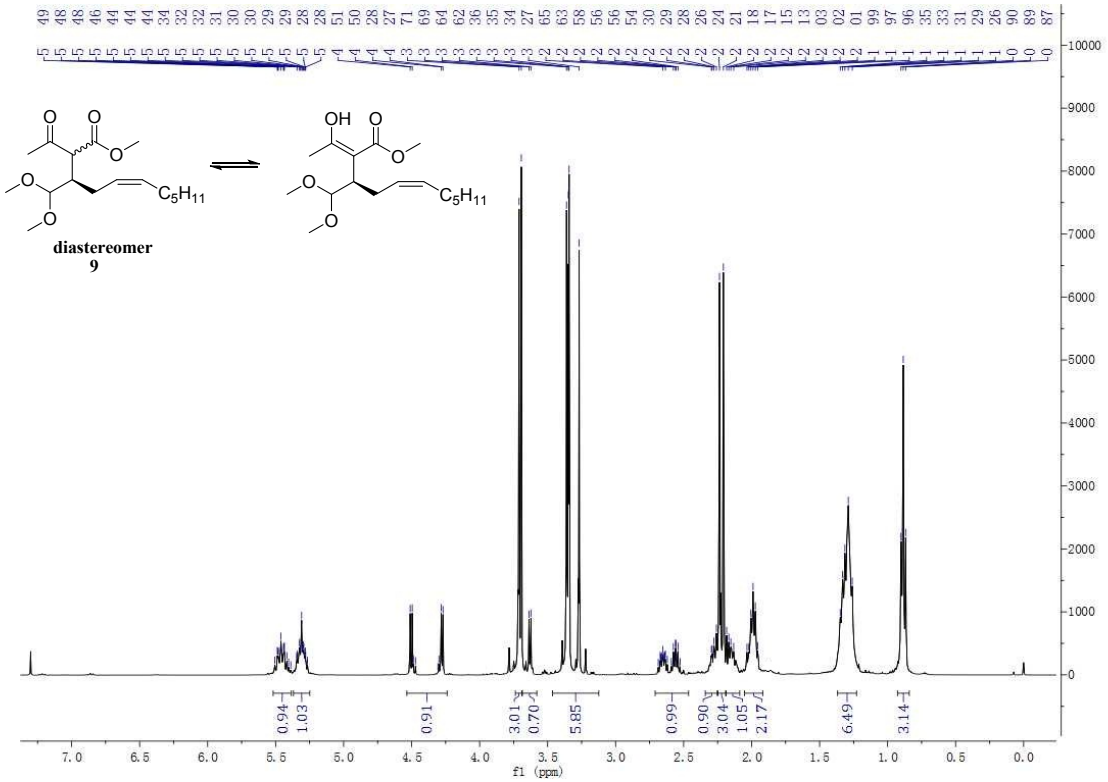
20

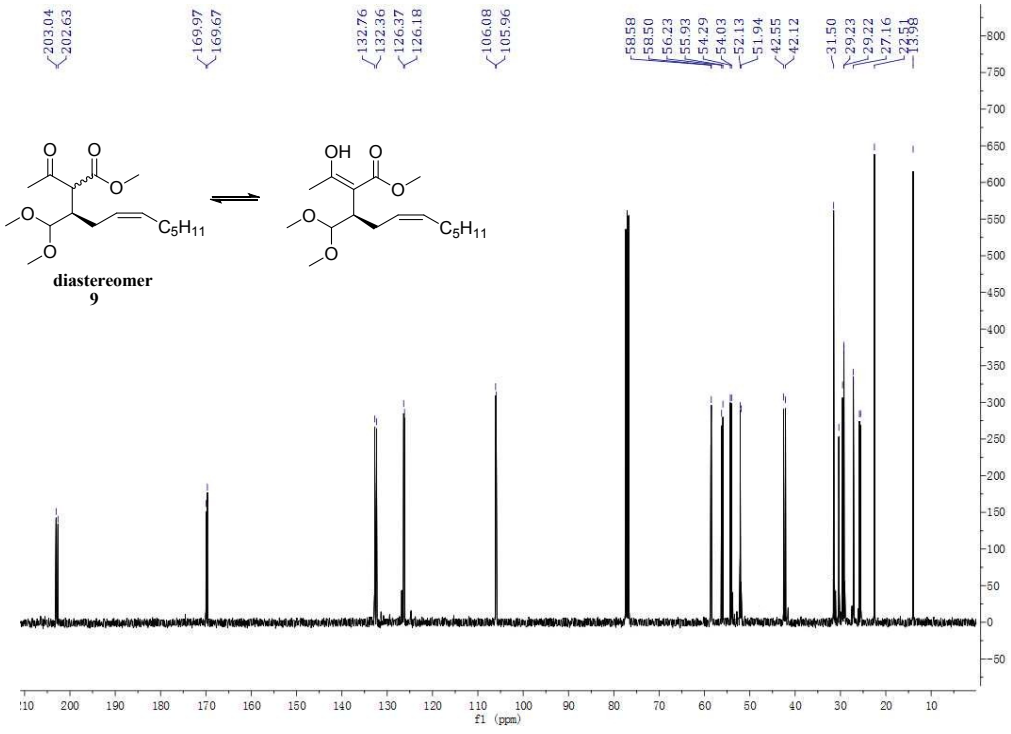


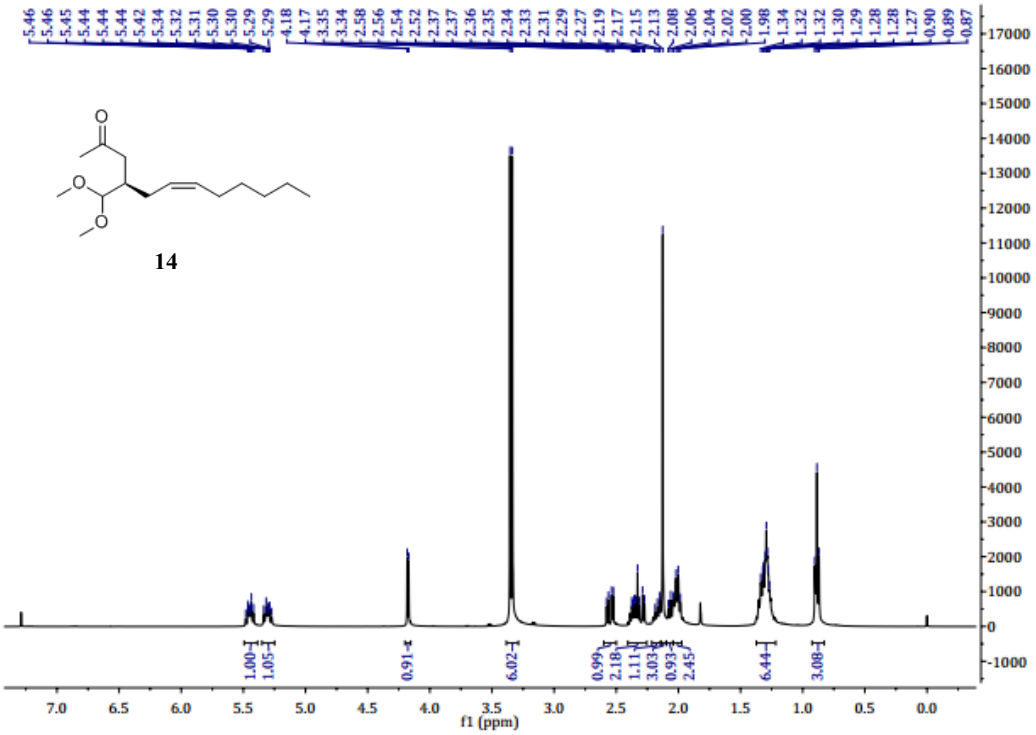
12

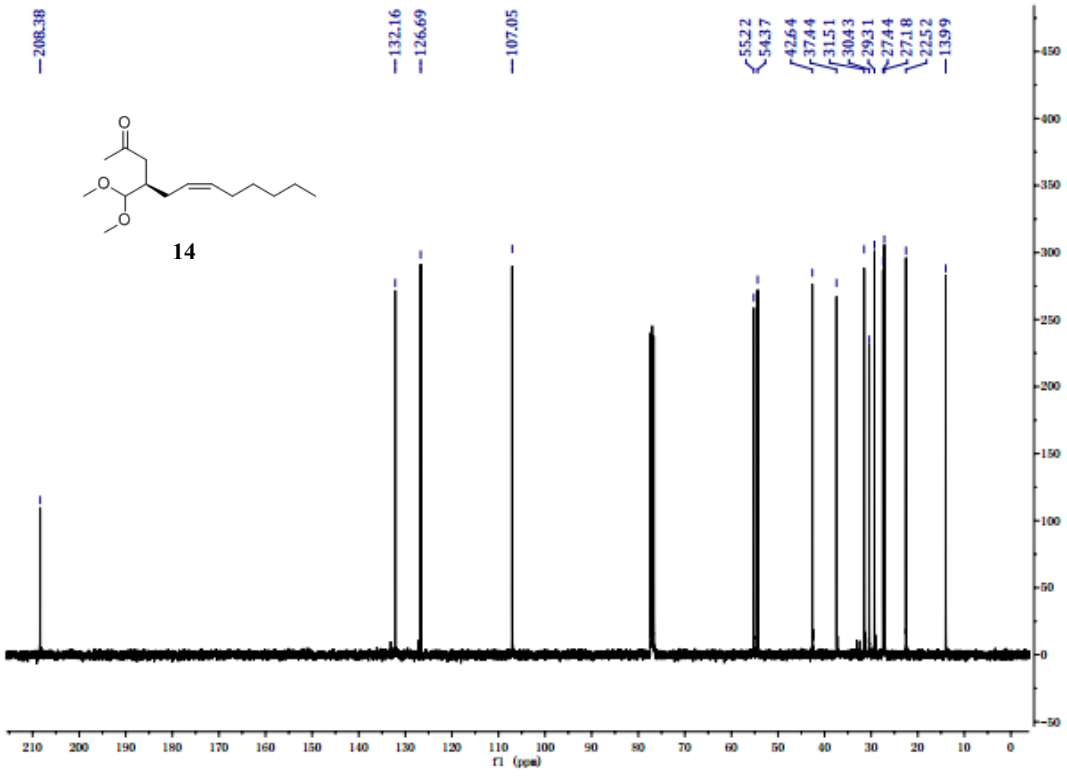

diastereomer
10
0.80
1.09
3.12
1.00
6.11
1.13
2.15
3.11
f1 (ppm)

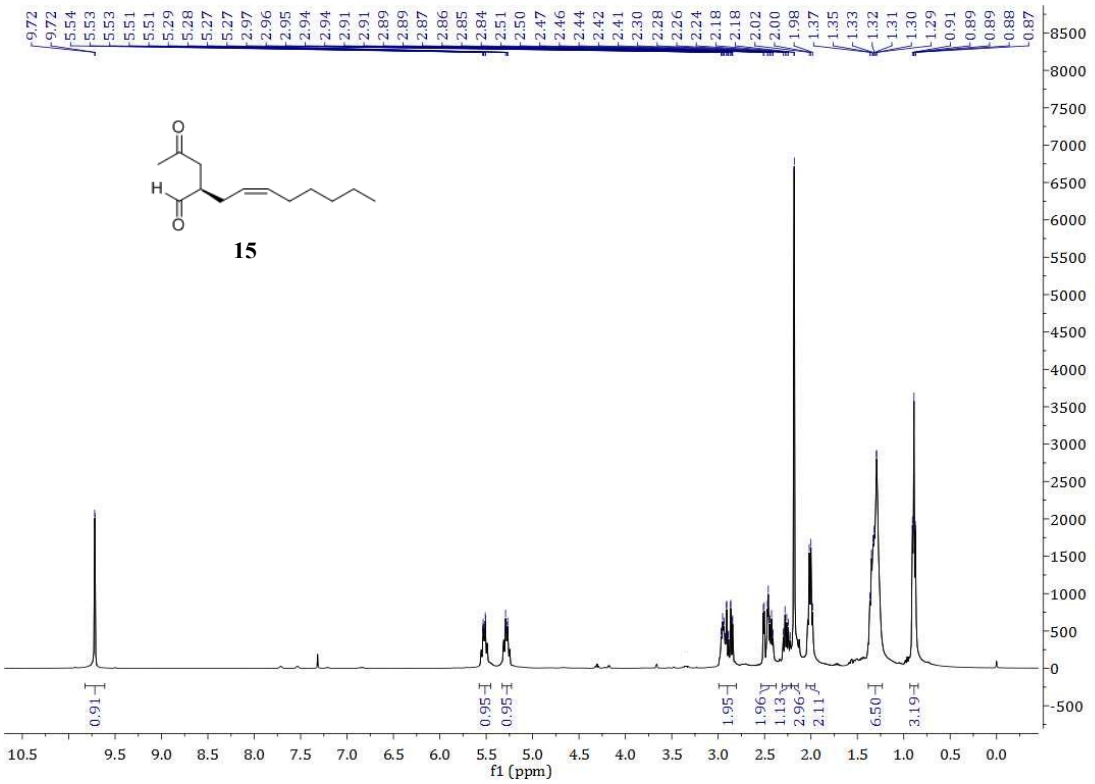

diastereomer
10
f1 (ppm)

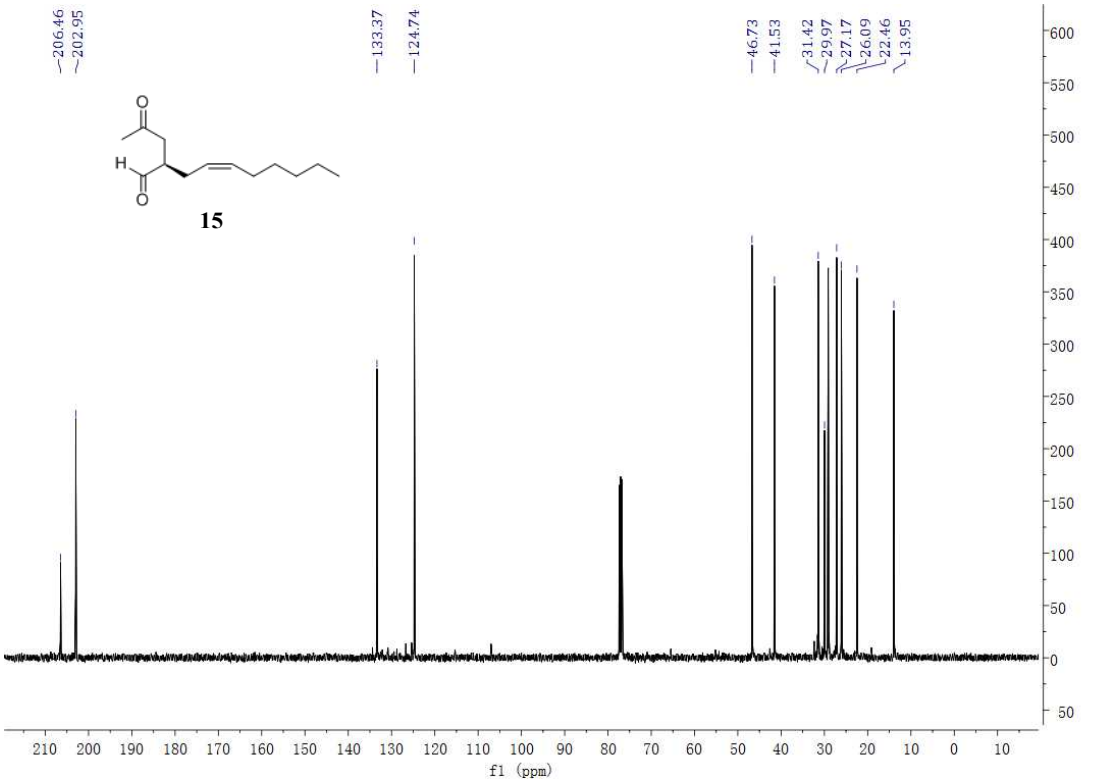

diastereomer
9
f1 (ppm)

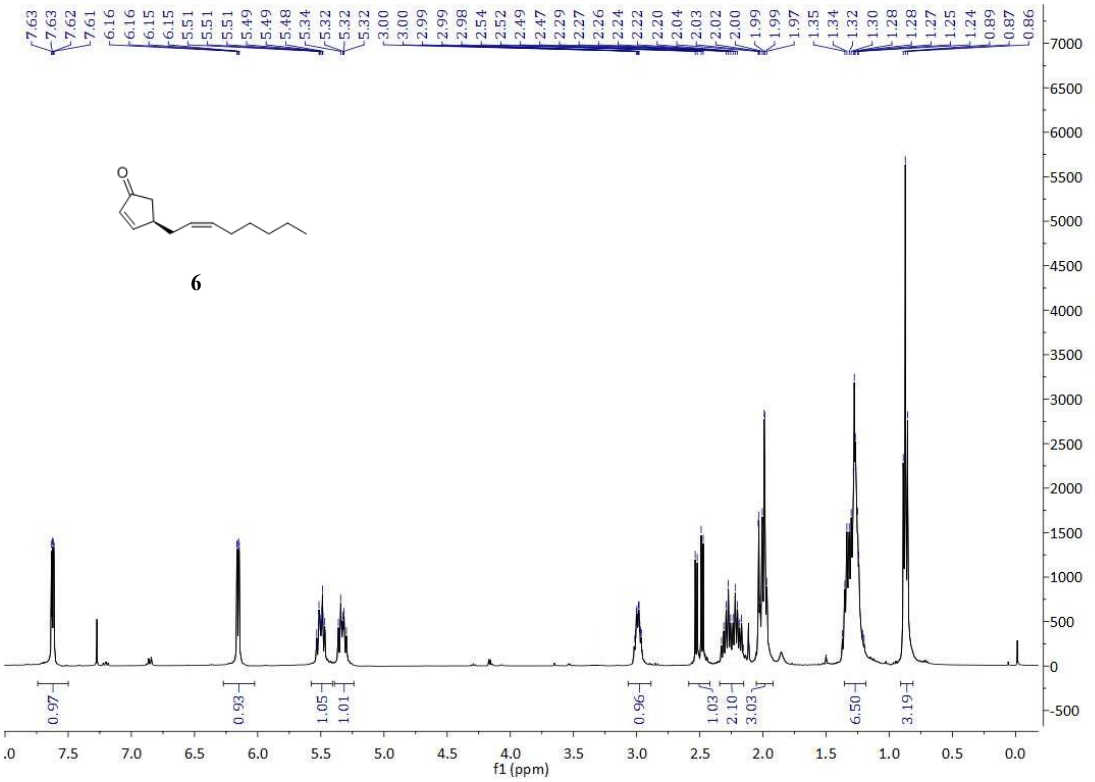

diastereomer
9
f1 (ppm)

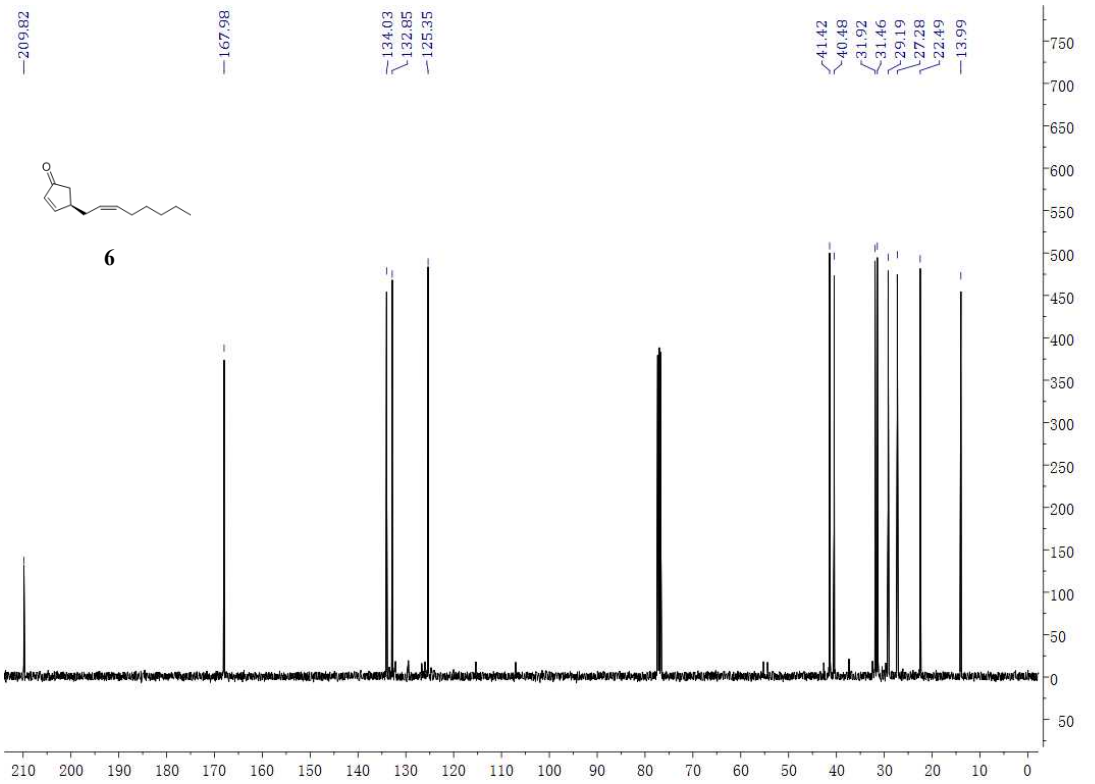

14
f1 (ppm)

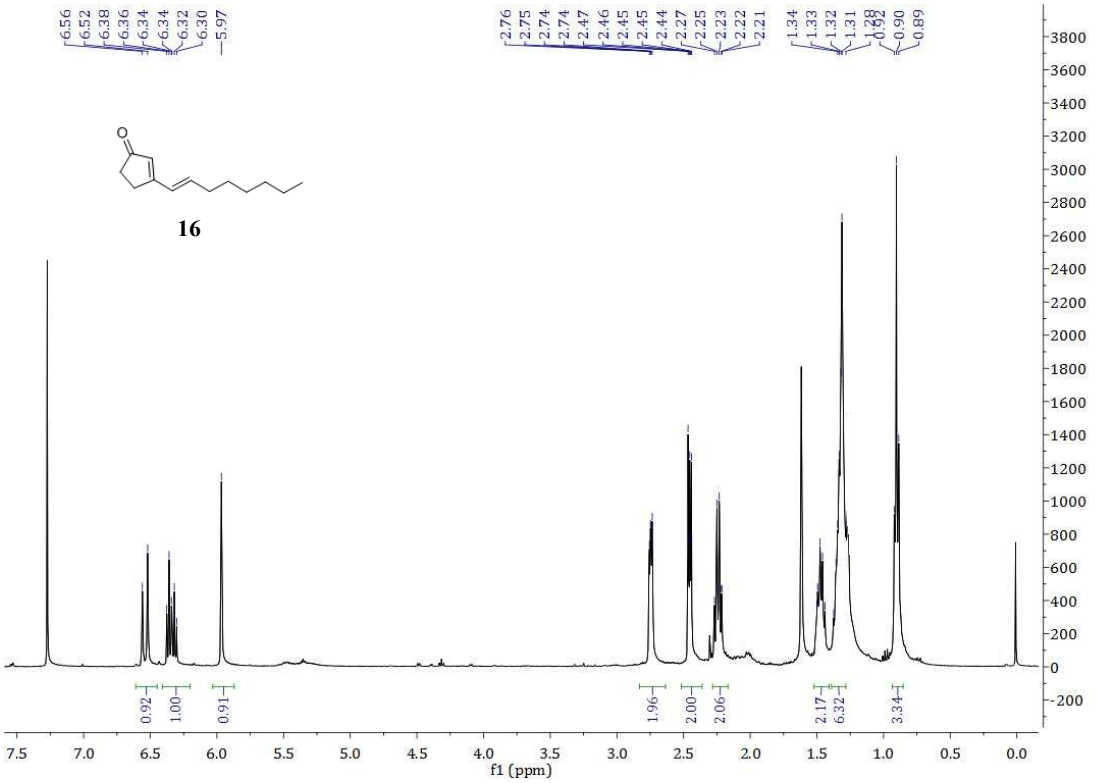

14
f1 (ppm)


9.72 9.72 5.54 5.53 5.53 5.51 5.51 5.29 5.28 5.27 5.27 2.97 2.96 2.95 2.94 2.94 2.91 2.91 2.89 2.89 2.87 2.86 2.85 2.84 2.51 2.50 2.47 2.46 2.44 2.42 2.41 2.30 2.28 2.26 2.24 2.18 2.18 2.02 2.00 1.98 1.37 1.35 1.33 1.32 1.31 1.30 1.29 0.91 0.89 0.89 0.88 0.87
15
0.91 0.95 0.95 1.95 1.96 1.13 2.96 2.11 6.50 3.19
f1 (ppm)

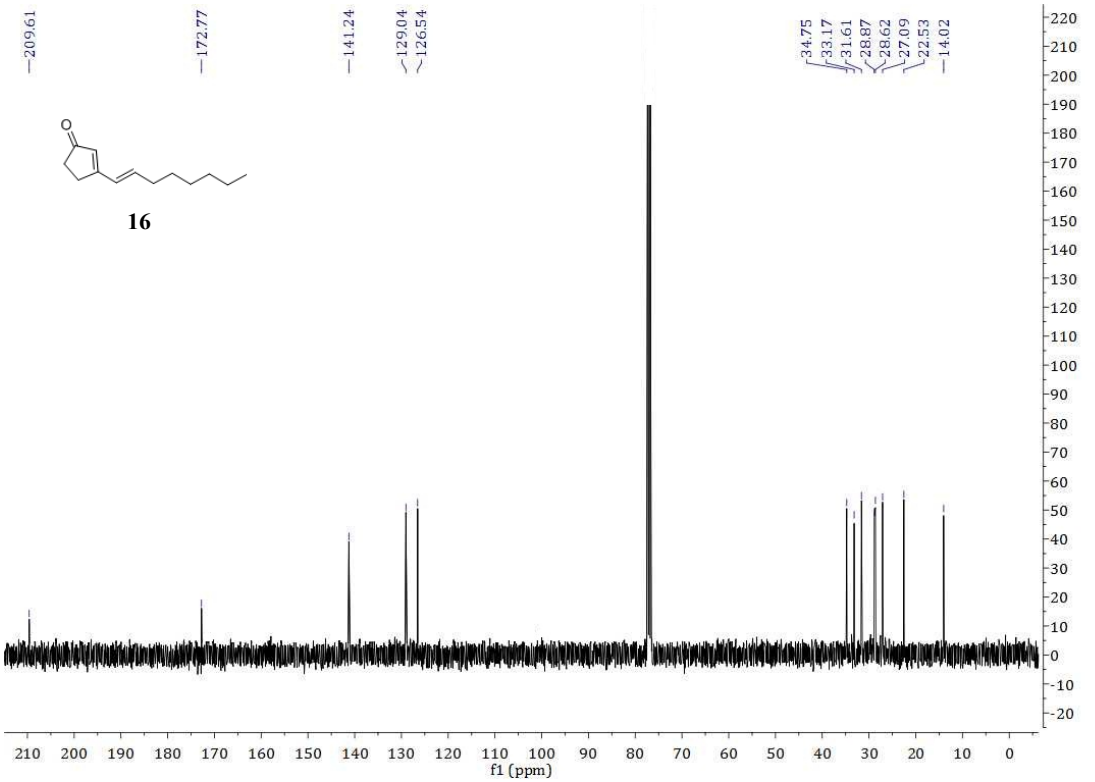

206.46 202.95 133.37 124.74 46.73 41.53 31.42 29.97 27.17 26.09 22.46 13.95
15
f1 (ppm)


7.63
7.63
7.62
7.61
6.16
6.16
6.15
6.15
5.51
5.51
5.51
5.49
5.49
5.48
5.34
5.32
5.32
5.32
3.00
3.00
2.99
2.99
2.98
2.54
2.52
2.49
2.47
2.29
2.27
2.26
2.24
2.22
2.20
2.04
2.03
2.02
2.00
1.99
1.99
1.97
1.35
1.34
1.32
1.30
1.28
1.28
1.27
1.25
1.24
0.89
0.87
0.86
6
0.97
0.93
1.05
1.01
0.96
1.03
2.10
3.03
6.50
3.19
f1 (ppm)

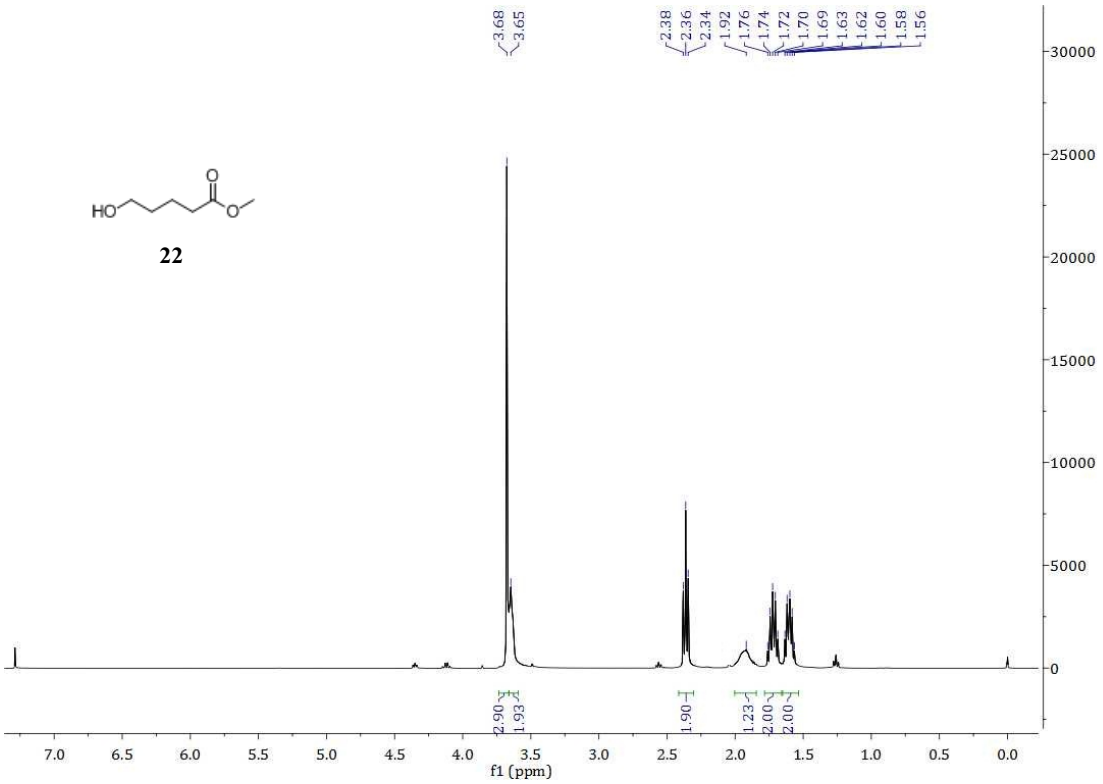

209.82
167.98
134.03
132.85
125.35
41.42
40.48
31.92
31.46
29.19
27.28
22.49
13.99
6

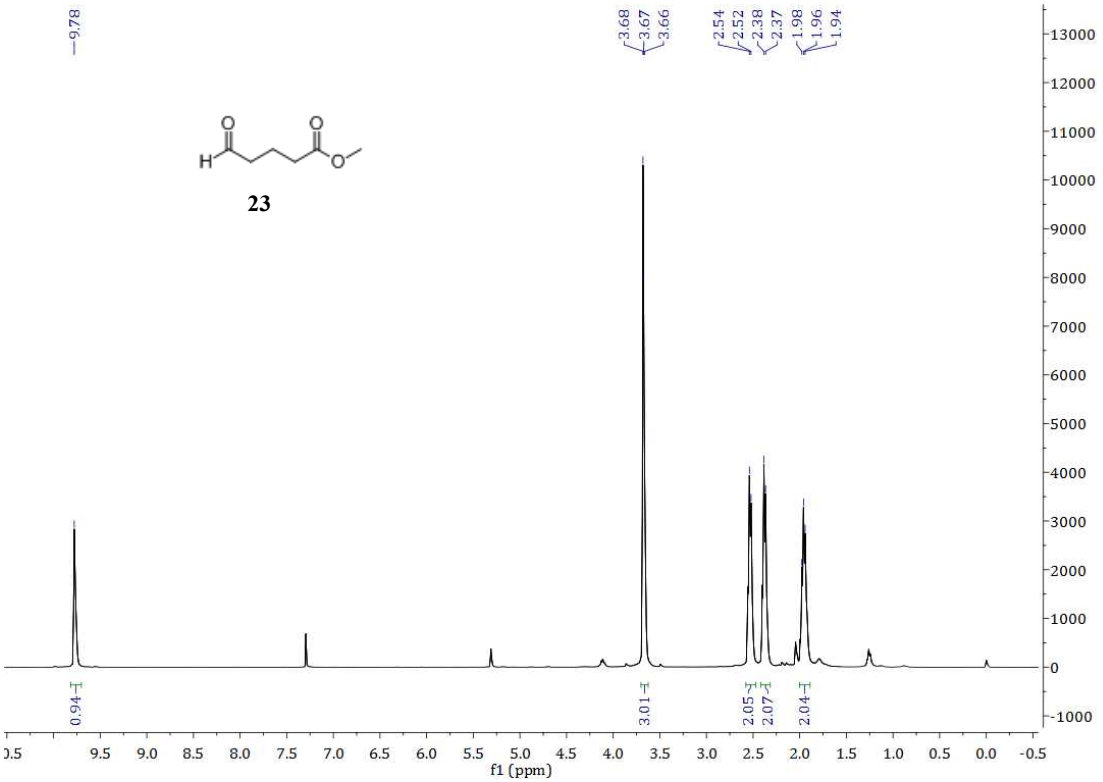

6.56
6.52
6.38
6.36
6.34
6.34
6.32
6.30
5.97
2.76
2.75
2.74
2.74
2.47
2.46
2.45
2.45
2.44
2.27
2.25
2.23
2.22
2.21
1.34
1.33
1.32
1.31
1.28
0.90
0.89
0.92
1.00
0.91
1.96
2.00
2.06
2.17
6.32
3.34
f1 (ppm)

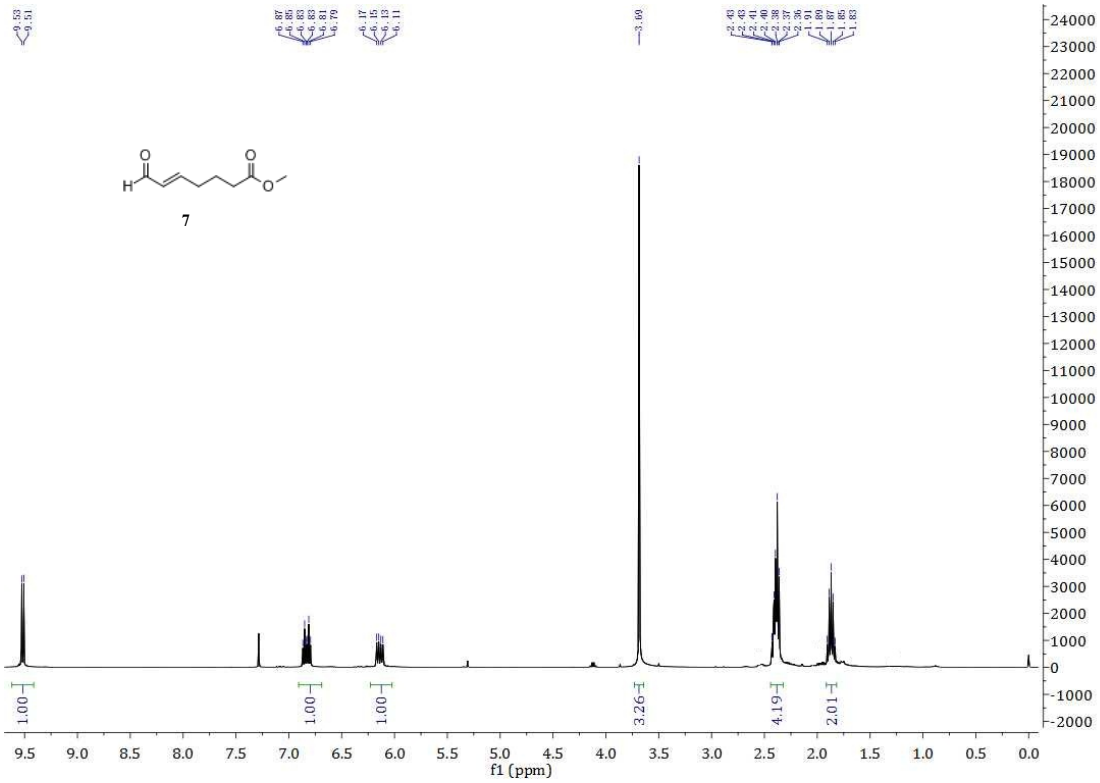
16

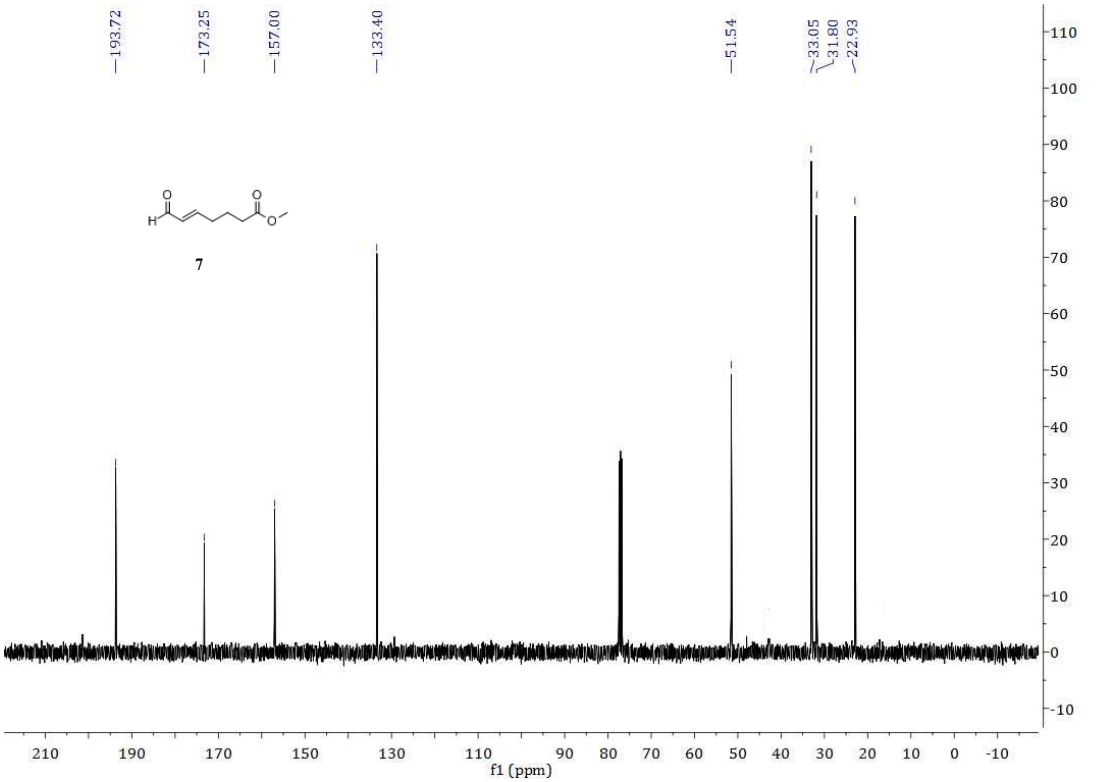

209.61
172.77
141.24
129.04
126.54
34.75
33.17
31.61
28.87
28.62
27.09
22.53
14.02
f1 (ppm)

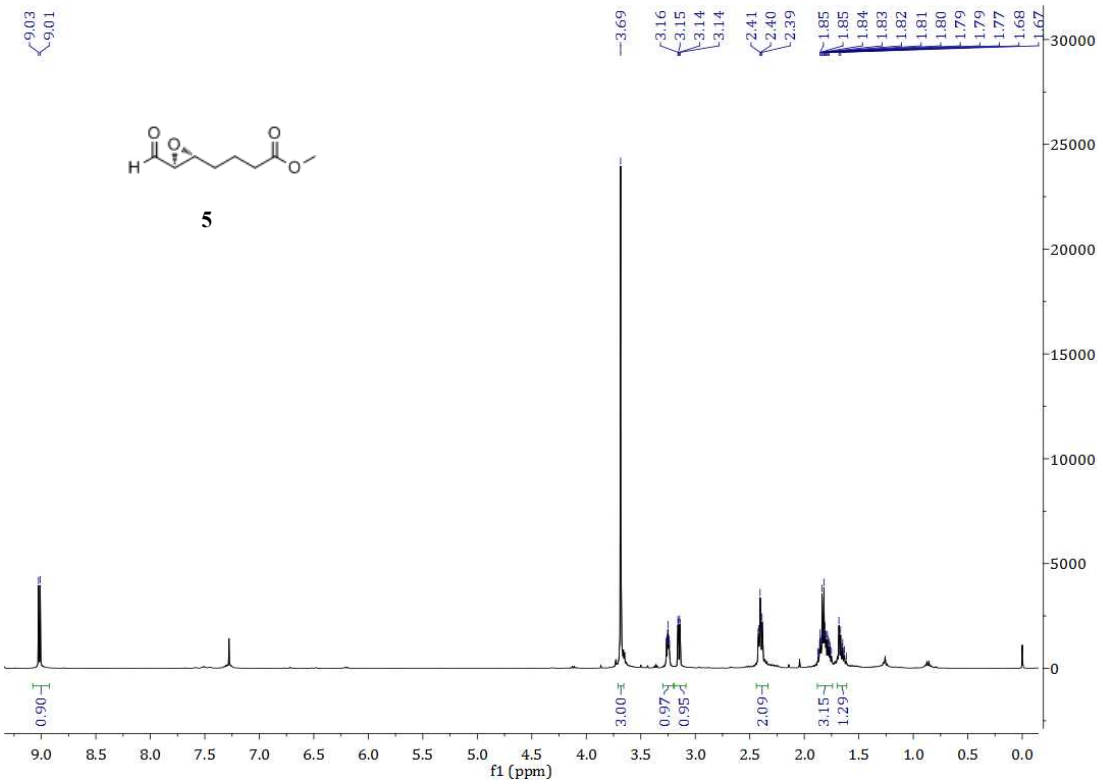
16


3.68
3.65
2.38
2.36
2.34
1.92
1.76
1.74
1.72
1.70
1.69
1.63
1.62
1.60
1.58
1.56
HO
O
O
22
2.90
1.93
1.90
1.23
2.00
2.00
f1 (ppm)

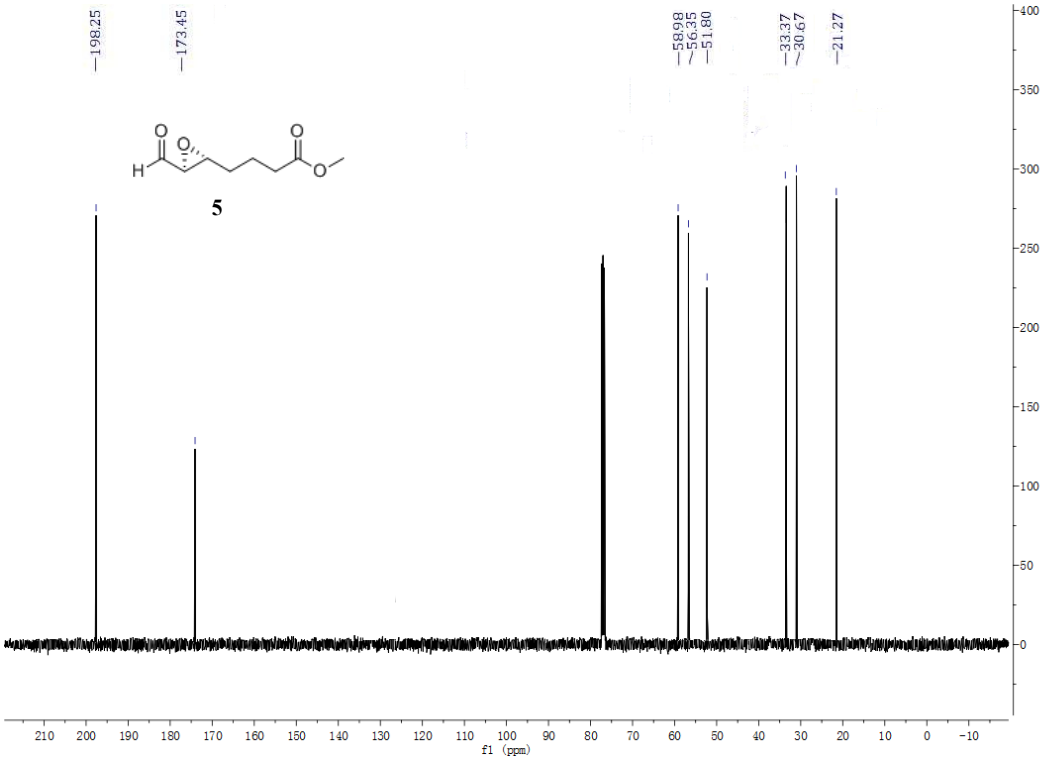

9.78
3.68
3.67
3.66
2.54
2.52
2.38
2.37
1.98
1.96
1.94
H
O
O
O
23
0.94
3.01
2.05
2.07
2.04
f1 (ppm)


9.53
9.51
6.87
6.85
6.83
6.81
6.79
6.17
6.15
6.13
6.11
3.69
2.43
2.41
2.40
2.38
2.37
1.91
1.89
1.87
1.85
1.83
7
1.00
1.00
1.00
3.26
4.19
2.01
f1 (ppm)

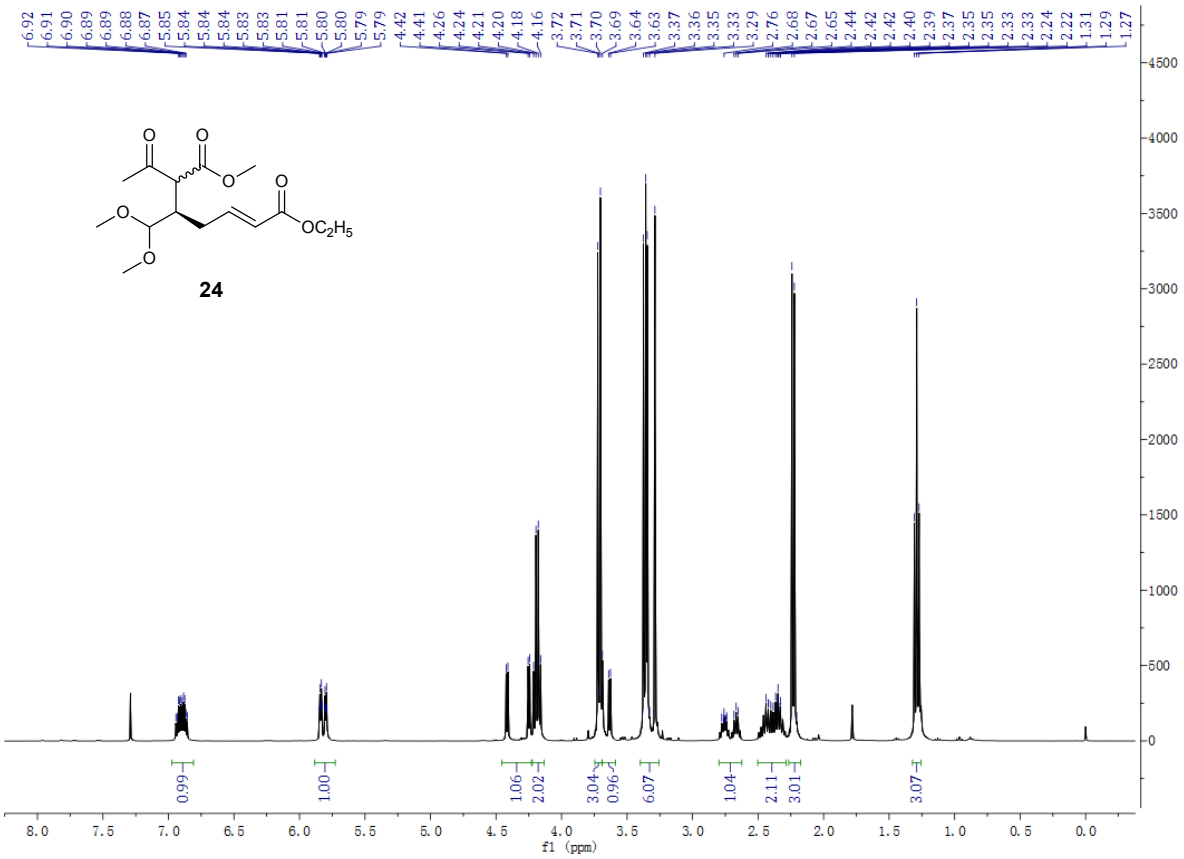

193.72
173.25
157.00
133.40
51.54
33.05
31.80
22.93
7
f1 (ppm)

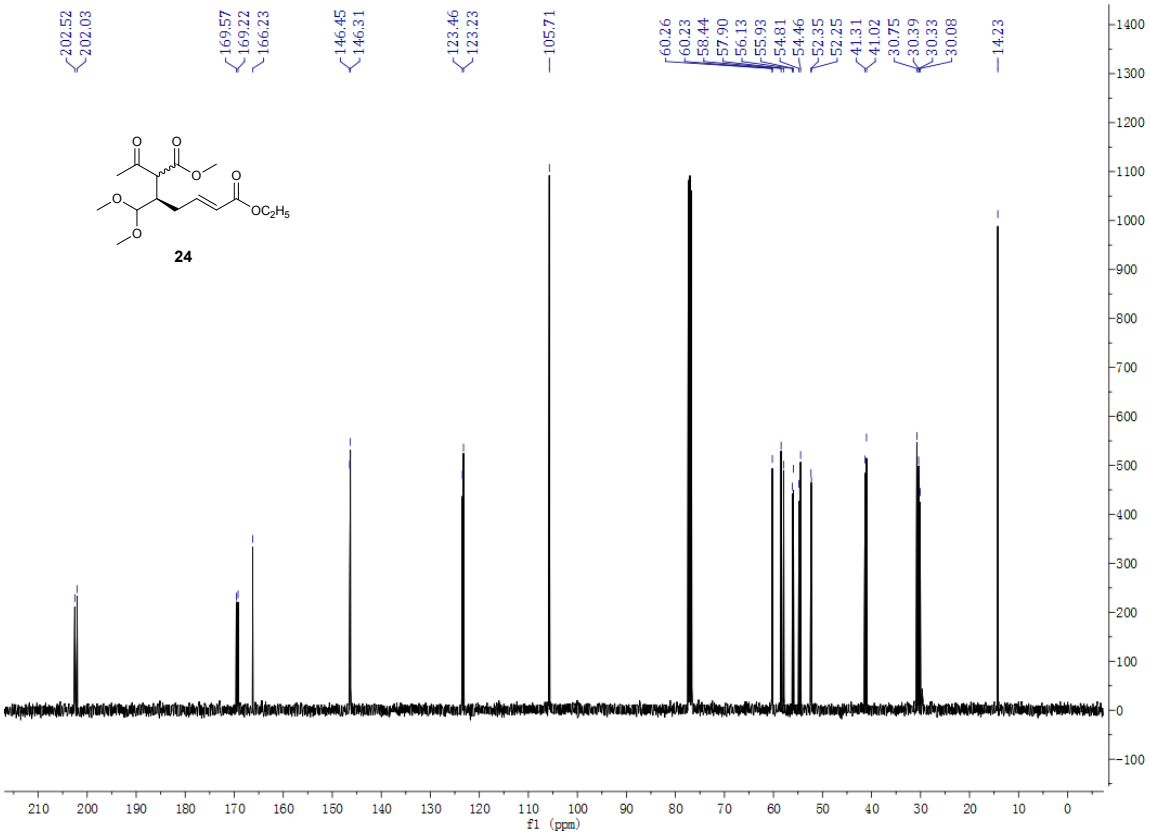

9.03
9.01
3.69
3.16
3.15
3.14
3.14
2.41
2.40
2.39
1.85
1.85
1.84
1.83
1.82
1.81
1.80
1.79
1.79
1.77
1.68
1.67
30000
25000
20000
15000
10000
5000
0
0.90
3.00
0.97
0.95
2.09
3.15
1.29
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

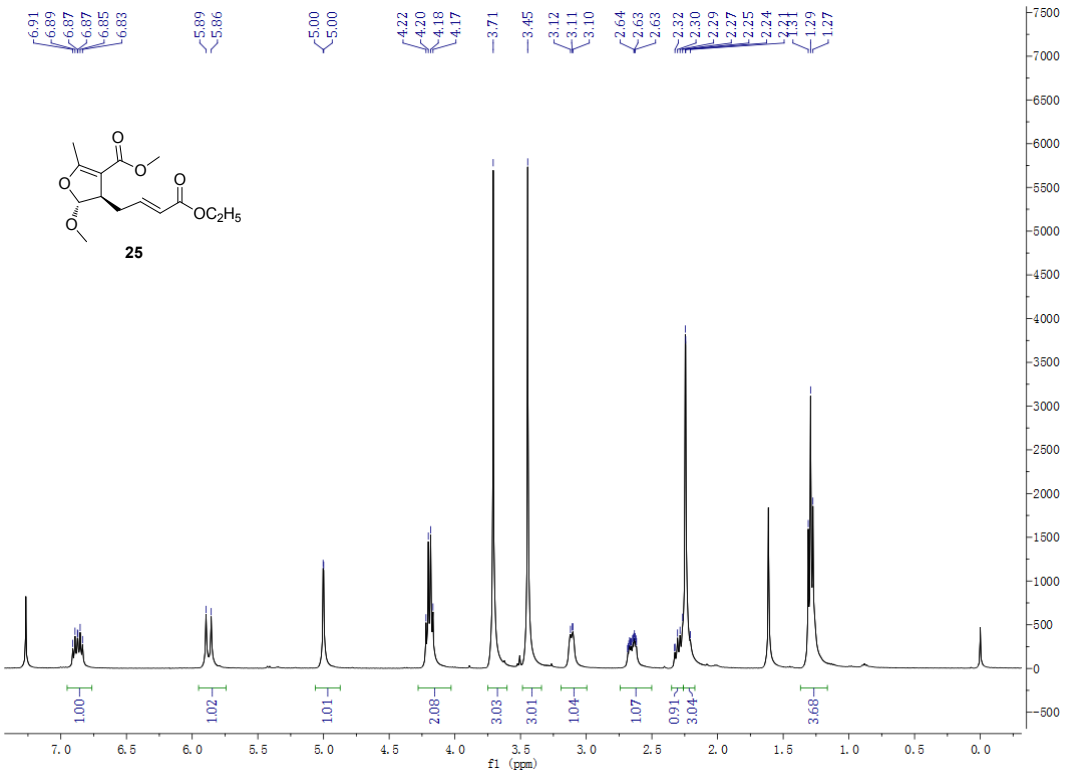
5

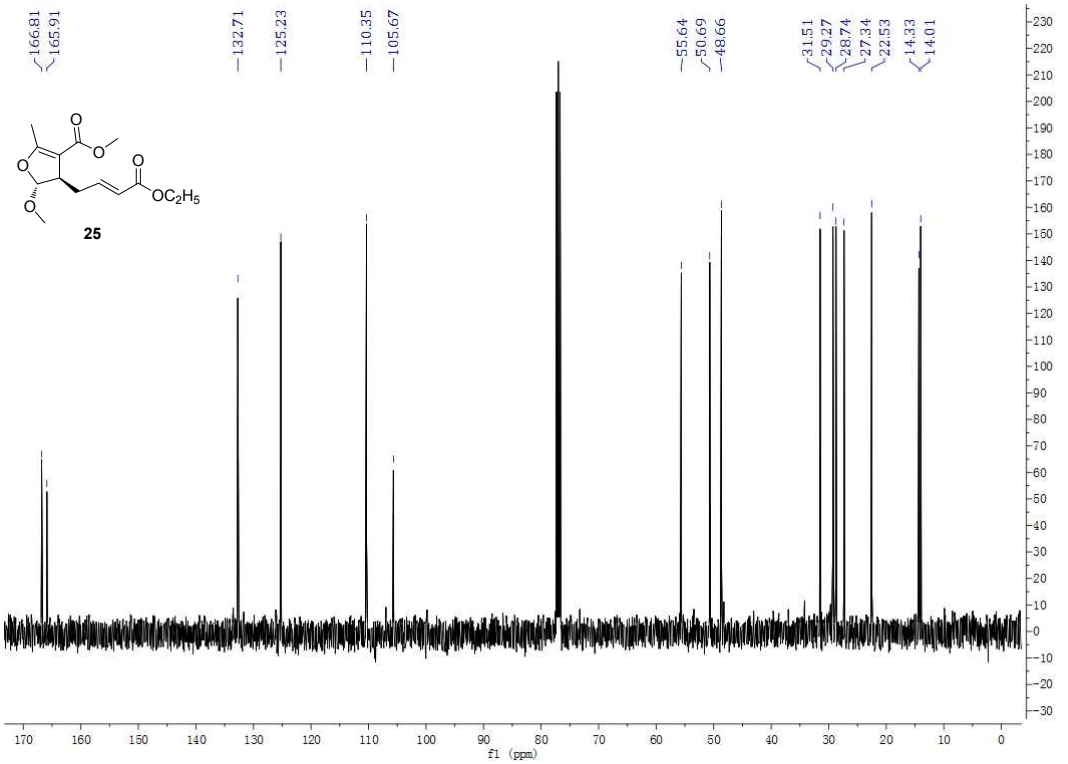

198.25
173.45
58.98
56.35
51.80
33.37
30.67
21.27
400
350
300
250
200
150
100
50
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

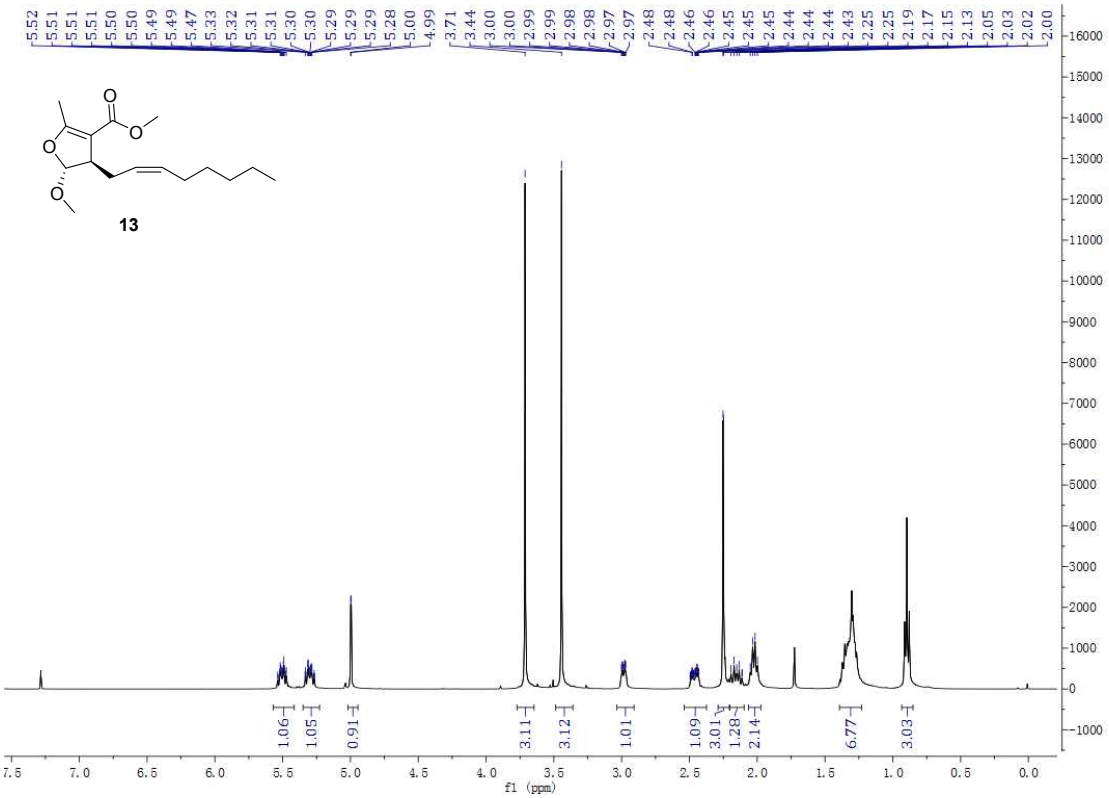
5

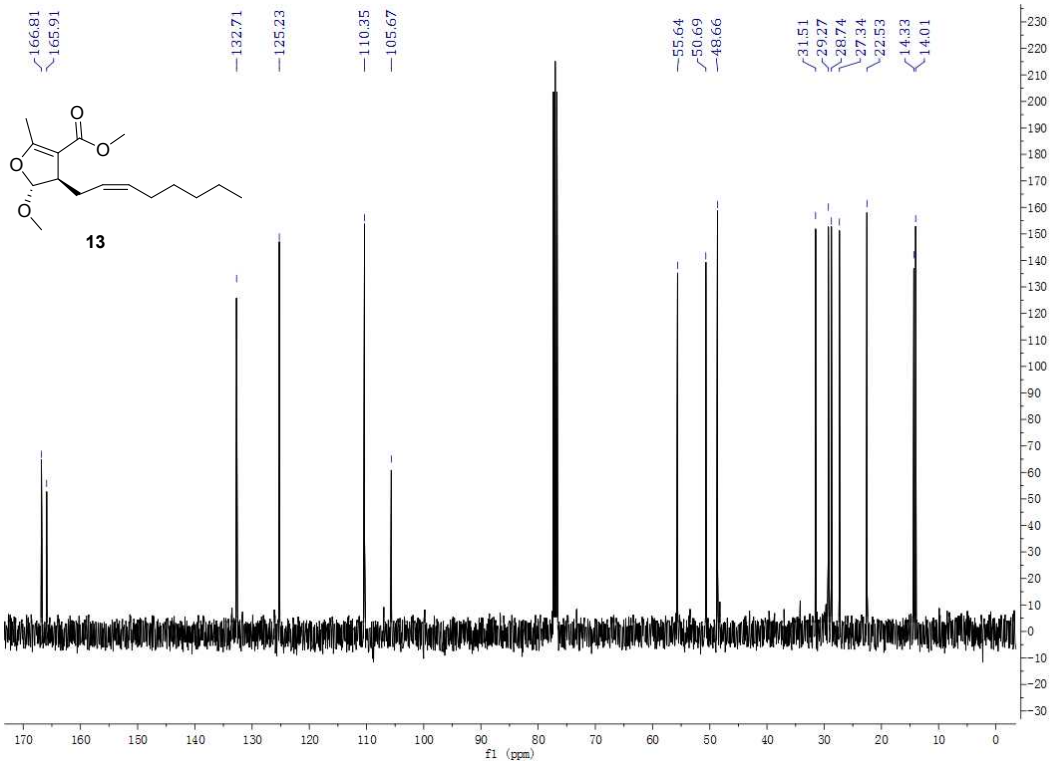

6.92 6.91 6.90 6.89 6.89 6.88 6.87 5.85 5.84 5.84 5.84 5.83 5.83 5.81 5.81 5.80 5.80 5.79 5.79 5.79
4.42 4.41 4.26 4.24 4.21 4.20 4.18 4.16
3.72 3.71 3.70 3.69 3.64 3.63 3.37 3.36 3.35 3.33 3.29 2.76 2.68 2.67 2.65 2.44 2.42 2.42 2.40 2.39 2.37 2.35 2.35 2.33 2.24 2.22 1.31 1.29 1.27
O
O
O
O
O
O
OC_2H_5
24
0.99 1.00 1.06 2.02 3.04 0.96 6.07 1.04 2.11 3.01 3.07
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
4500 4000 3500 3000 2500 2000 1500 1000 500 0

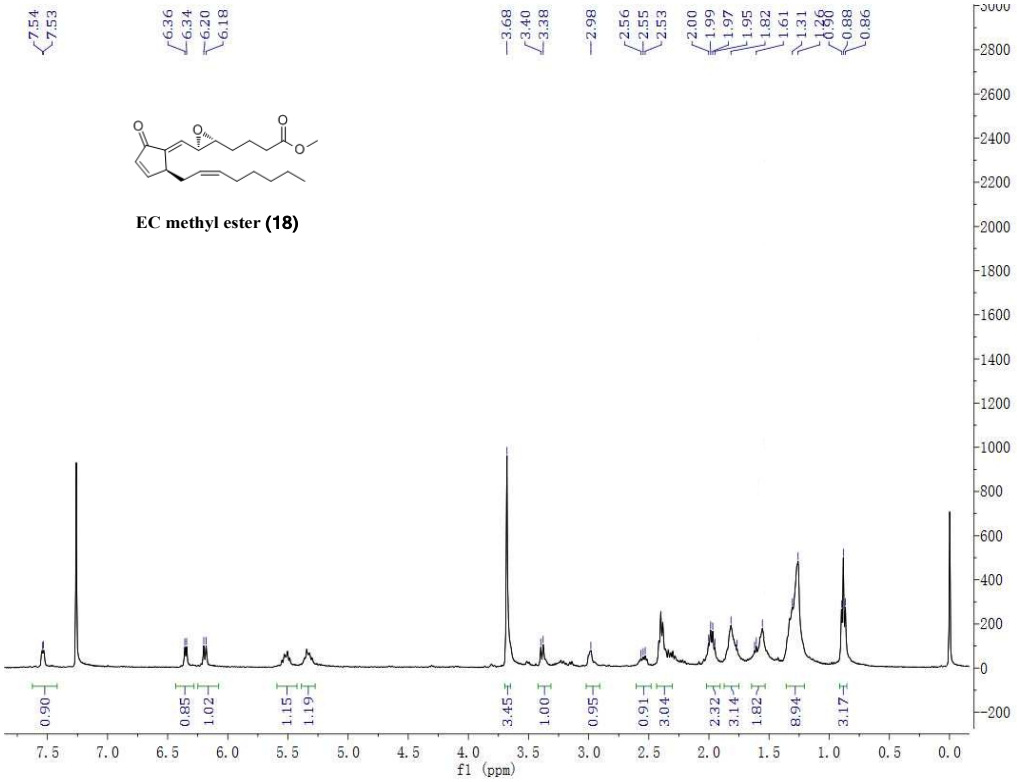

202.52 202.03
169.57 169.22 166.23
146.45 146.31
123.46 123.23
105.71
60.26 60.23 58.44 57.90 56.13 55.93 54.81 54.46 52.35 52.25 41.31 41.02 30.75 30.39 30.33 30.08
14.23
O
O
O
O
O
OC_2H_5
24
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100


6.91
6.89
6.87
6.87
6.85
6.83
5.89
5.86
5.00
5.00
4.22
4.20
4.18
4.17
3.71
3.45
3.12
3.11
3.10
2.64
2.63
2.63
2.32
2.30
2.29
2.27
2.25
2.24
2.21
1.31
1.29
1.27
1.00
1.02
1.01
2.08
3.03
3.01
1.04
1.07
0.91
3.04
3.68
f1 (ppm)

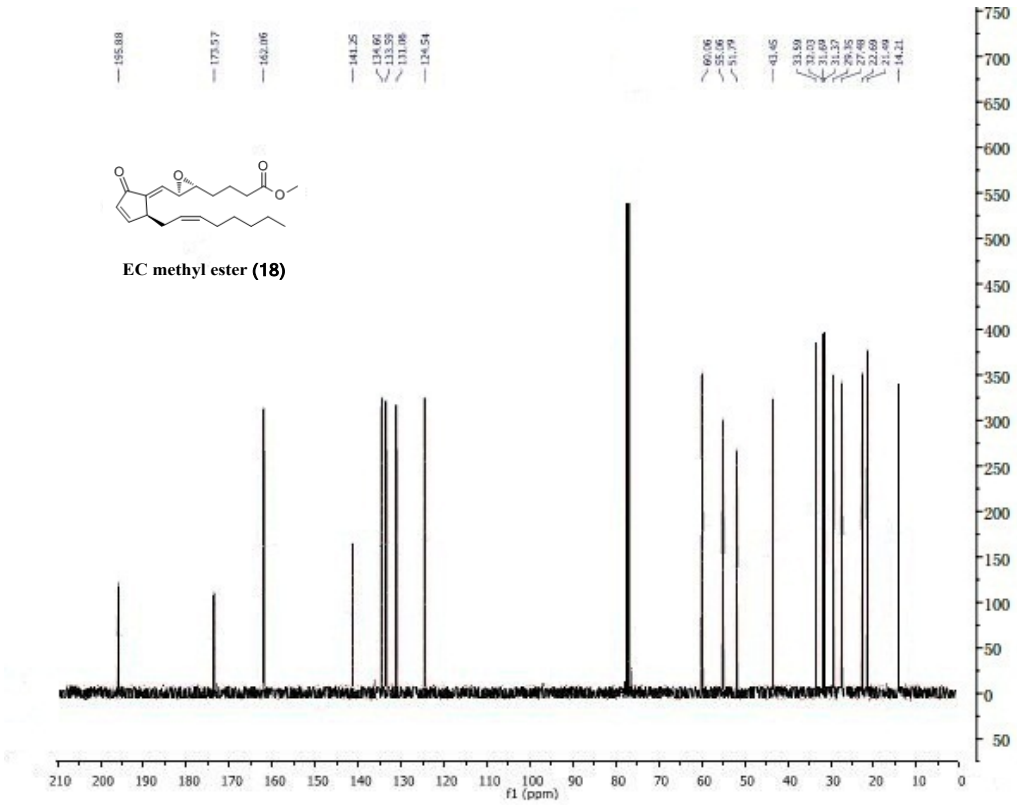

166.81
165.91
132.71
125.23
110.35
105.67
55.64
50.69
48.66
31.51
29.27
28.74
27.34
22.53
14.33
14.01
f1 (ppm)


13
f1 (ppm)


13
f1 (ppm)

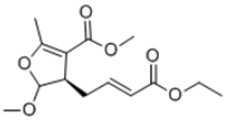


EC methyl ester (18)



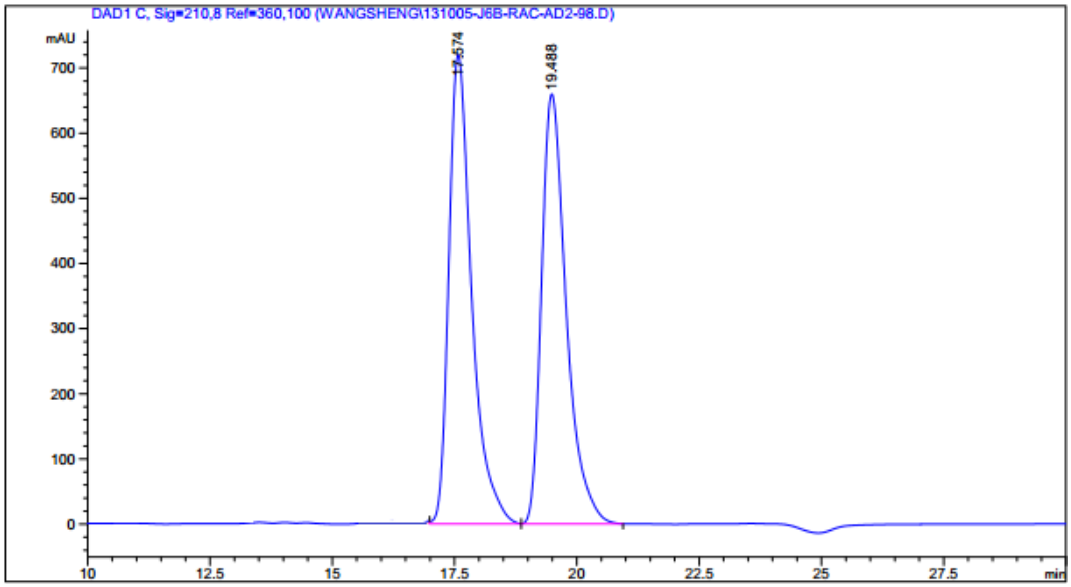
EC methyl ester (18)

Copies of HPLC spectra



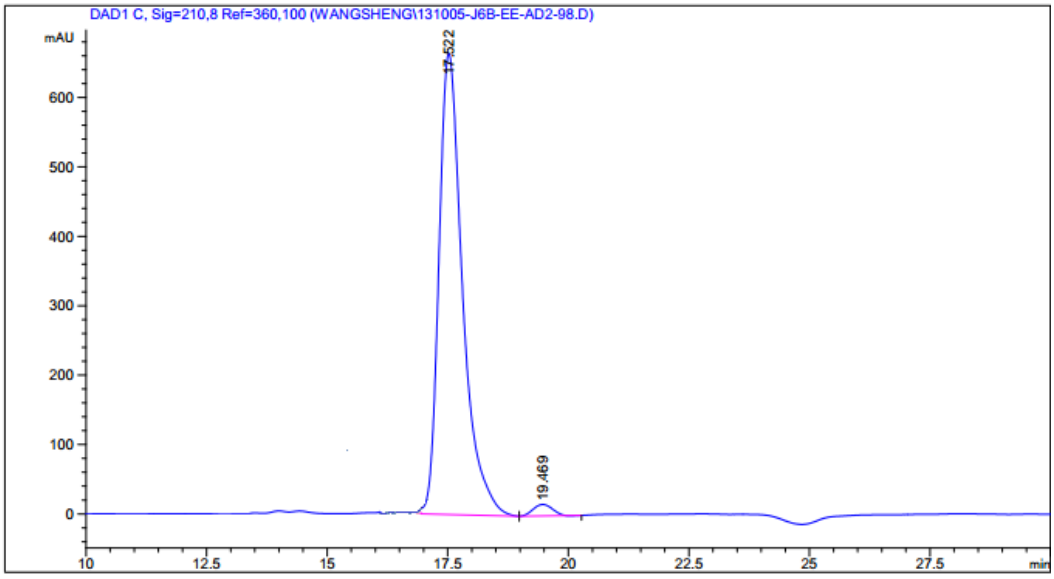
25

HPLC: (hexane: *i*-PrOH = 98:2, 0.8 mL/min, chiral AD-H)



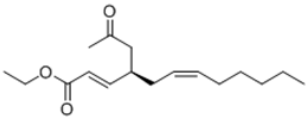
信号 1: DAD1 C, Sig=210,8 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	17.574	VV	0.4912	2.34163e4	720.45856	50.2432
2	19.488	VB	0.5359	2.31895e4	659.94635	49.7568



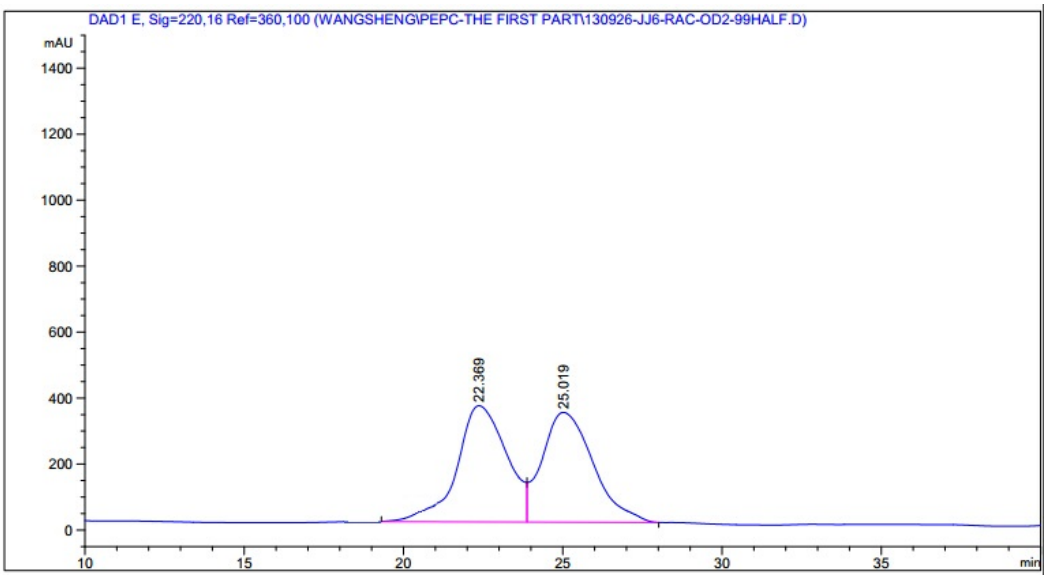
信号 1: DAD1 C, Sig=210,8 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	17.522	VB	0.5170	2.25997e4	664.16541	98.0473
2	19.469	BB	0.4393	450.10309	16.44554	1.9527



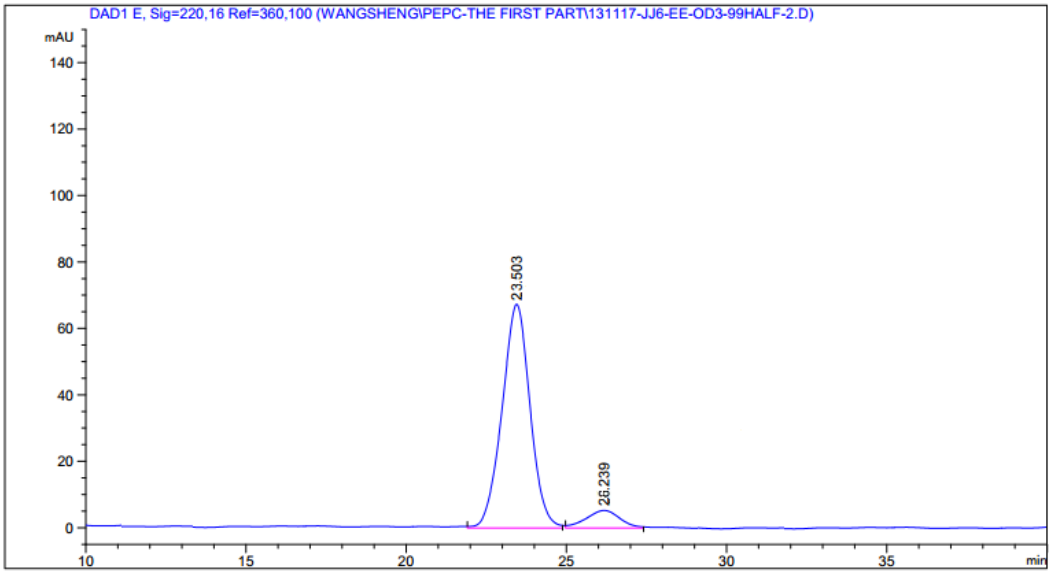
26

HPLC: (hexane: *i*-PrOH = 99.5:0.5, 0.8 mL/min, chiral OD-H)



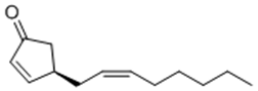
信号 1: DAD1 E, Sig=220,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	22.369	FM	1.7719	3.74743e4	352.49246	50.1825
2	25.019	VB	1.7333	3.72017e4	333.00885	49.8175

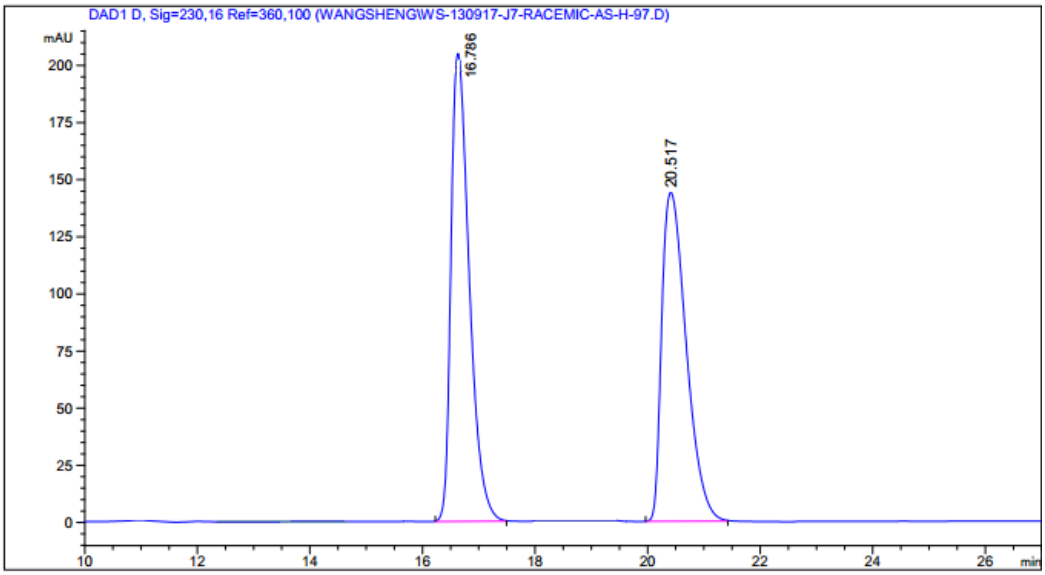


信号 1: DAD1 E, Sig=220,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	23.503	MF	1.0122	4152.28174	67.33751	95.0595
2	26.239	MF	1.2175	215.80429	5.27209	4.9405

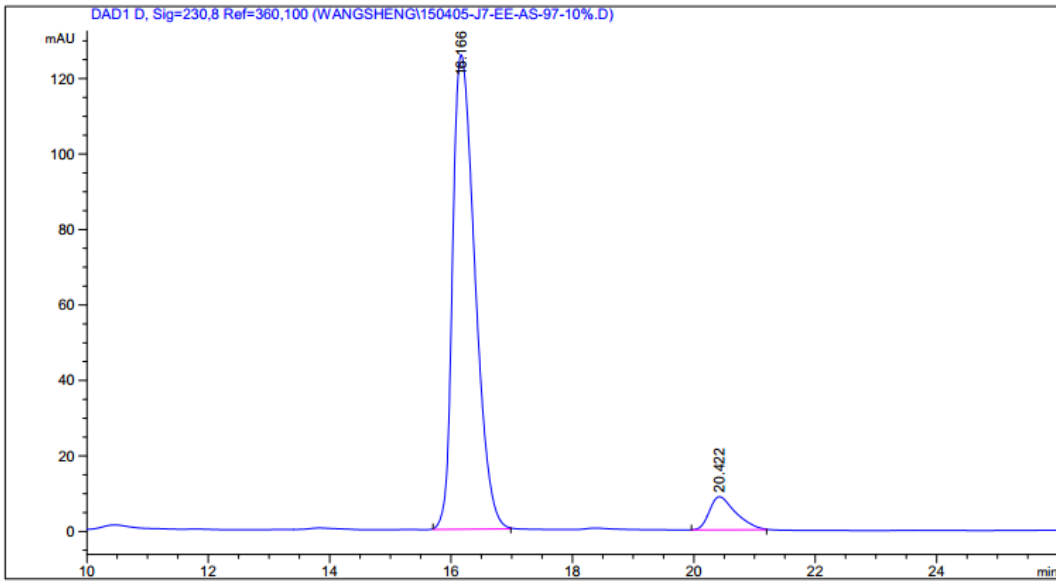


6 HPLC: (hexane: *i*-PrOH = 97:3, 0.8 mL/min, chiral AS-H)



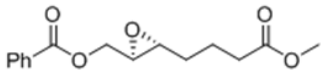
信号 1: DAD1 D, Sig=230,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.786	BB	0.3489	4612.56738	204.69792	51.5128
2	20.517	BB	0.4738	4341.65332	143.96176	48.4872



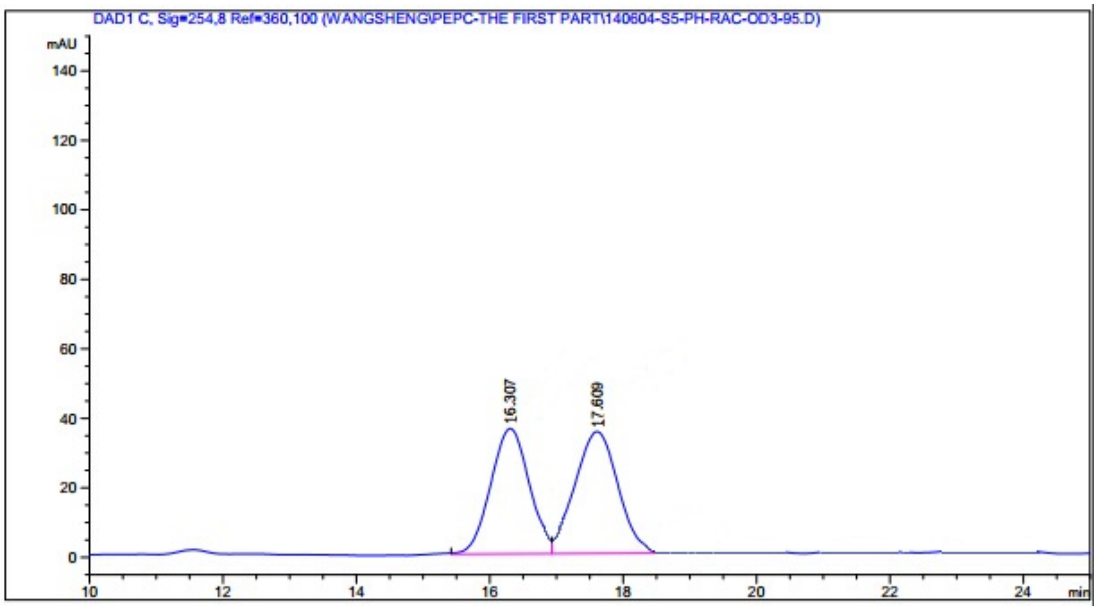
信号 1: DAD1 D, Sig=230,8 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.166	MM	0.4268	3221.41504	125.80131	93.2769
2	20.422	MM	0.4626	232.18980	8.36473	6.7231



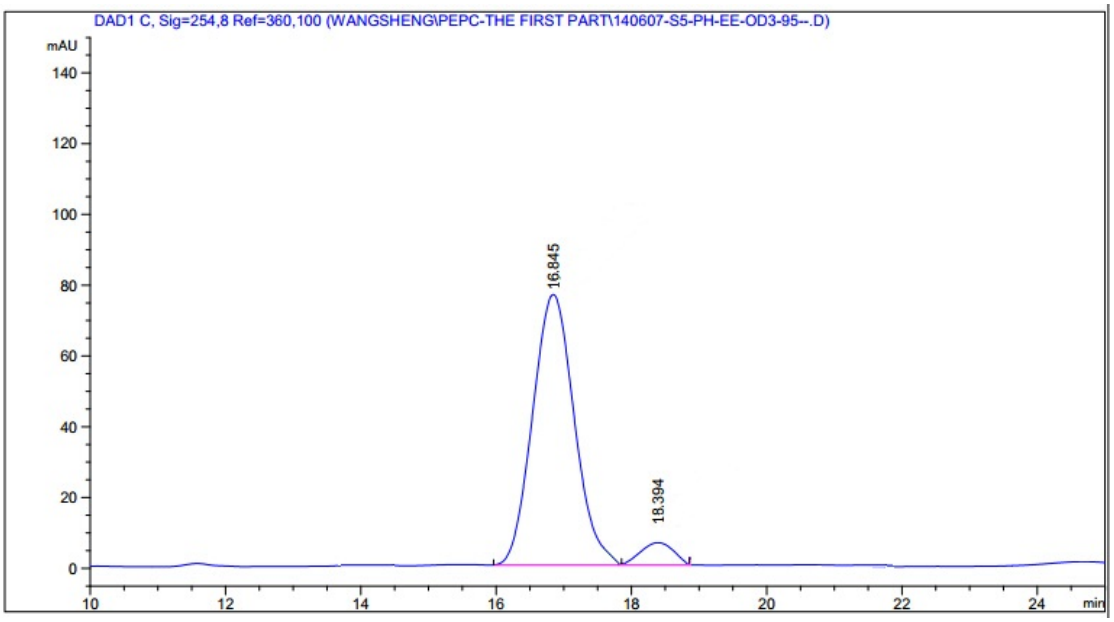
27

HPLC: (hexane: *i*-PrOH = 95:5, 0.8 mL/min, chiral OD-H)



信号 1: DAD1 C, Sig=254,8 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.307	MF	0.6754	1419.53955	36.07079	49.6425
2	17.609	MF	0.7605	1439.98242	35.07640	50.3575



信号 1: DAD1 C, Sig=254,8 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.845	MF	0.7157	3193.93872	76.47227	96.1309
2	18.394	MF	0.3851	128.55124	7.05336	3.8691