Intramolecular [2+2] Photocycloaddition-Fragmentation: Facile Entry to a Novel Tricyclic 5-6-7 Ring System

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An expeditious route to a novel 5-6-7 tricyclic ring system is described. The chemistry capitalizes on an enantioselective glyoxylate-ene reaction, enzymatic resolution as well as a [2+2] photocycloaddition-fragmentation.

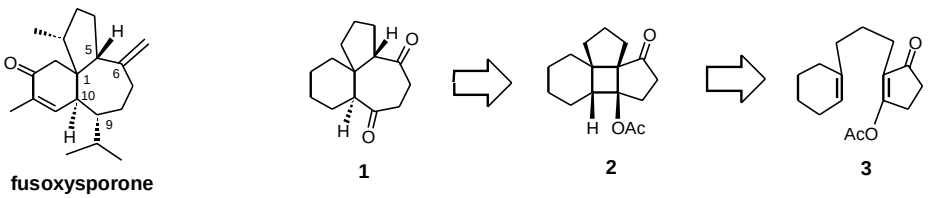
Keywords: Intramolcular; Photocycloaddition; Fragmentation; Synthesis.

The application of intramolecular enone-olefin photocycloadditions to the synthesis of natural products has received much attention over the years.[1] Recently, a photocycloaddition was employed in the synthesis of hetisine alkaloids and functionalized 5-8-5 ring systems.[2] Fusoxysporone was first isolated from liquid cultures of the fungus *Fusarium oxysporum*[3] in 1992. *Fusarium oxysporum* is an economically important soilborne plant pathogen and to date over 120 formae species have been described.[4] From *Fusarium* species, a number of secondary metabolites have been isolated including terpenes, polyketides and compounds derived from amino acid metabolism.[5] Some of the compounds isolated from these species exhibit interesting biological activity (e.g. chlorofusin, mangicol, apicidin, saricandin, subglutinol, vomitoxin, gibberellic acid). The unique tricyclic[8.4.0.0^{1,4}] tetradecen system of fusoxysporone has received much attention and a number of synthetic approaches have been reported.[6]

Herein, we report our recent studies directed at the construction of a spiro 5-6-7 tricyclic ring system[7] based on the core of fusoxysporone via an intramolecular [2+2] photocycloaddition-fragmentation strategy. The retro-synthetic analysis of this route is outlined in Scheme I. As shown, the fusoxysporone diketone precursor **1** that contains both the C-10 and C-5 hydrogens of fusoxysporone may be obtained *via* the photocycloaddition of enone **3** and fragmentation of the resulting adduct **2** (approximately a 1:1 isomeric mixture). Preparation of enone **3** was accomplished according to Scheme II. Ene reaction of methylenecyclohexane and methyl α-chloroacrylate catalyzed by $EtAlCl_2$ in benzene at 25 °C for 20 h gave **4** in 95% yield.[8] Chloroester **4** was hydrolyzed to hydroxy acid **5** in refluxing aqueous Na_2CO_3 solution (89% yield) and oxidized with $Pb(OAc)_4$ in pyridine for 2 h at 25 °C to give aldehyde **6** in 81% yield.[9] The difficulty of the aldol condensation of 1,3-cyclopentanediones and alkyl aldehyde[10] prompted us to employ a modified Knoevenagel reaction[11] in the subsequent step. Hence, a mixture of cyclopentane-1,3-dione, aldehyde **6**, thiophenol and silica gel in CH_2Cl_2 was stirred at ambient temperature to afford thiol ether **7** in 75% yield. Radical reductive deprotection of the thiol group of **7** (Ph_3SnH, *cat.* AIBN, C_6H_6) followed by acetylation (Ac_2O, NaOAc; 70%) gave the desired enone **3**.

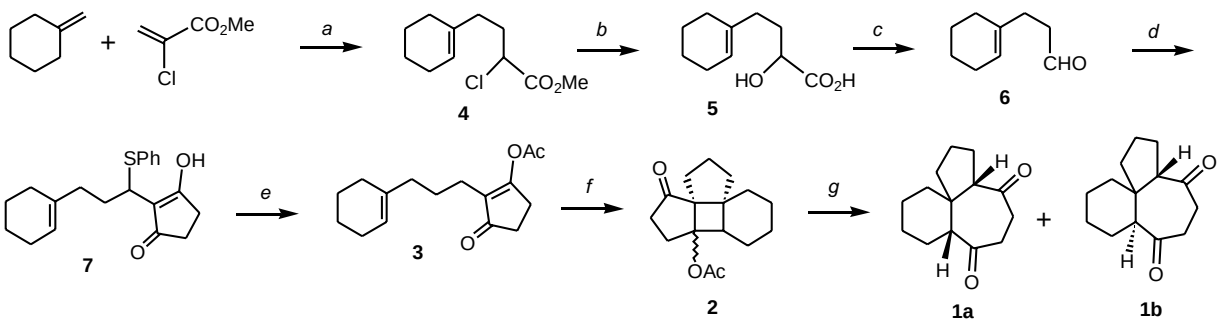
With **3** in hand, we were poised to examine our photocycloaddition. Irradiation of a 2 mM solution of **3** (acetonitrile; 450 W medium pressure Hg arc lamp; Pyrex immersion well) led to the formation of a single photoadduct **2**

Scheme I



fusoxysporone **1** **2** **3**

Scheme II

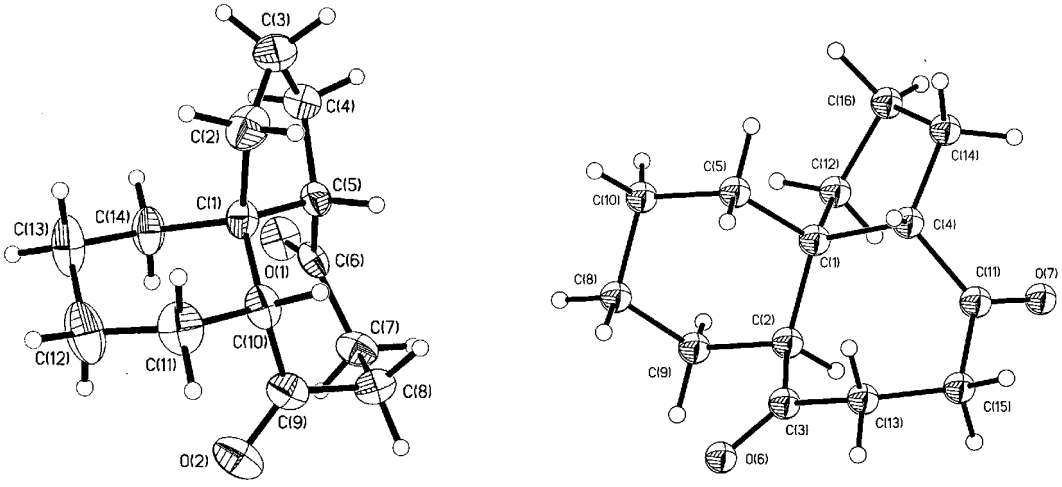


a. $AlEtCl_2$, C_6H_6; 95%. *b.* Na_2CO_3, H_2O; 89%. *c.* $Pb(OAc)_4$, pyridine; 81%. *d.* 1,3-cyclopentadione, thiophenol, silica gel, CH_2Cl_2; 75%. *e.* (1) Ph_3SnH, AIBN, C_6H_6; 76%. (2) Ac_2O, NaOAc; 70%. *f.* hυ, CH_3CN; 70%. *g,* KOH, MeOH; 85%.

which on treatment with 2N aqueous KOH in methanol afforded the desired tricyclic diones **1a** and **1b** in approximately a 1:1 ratio. Treatment of **1a** or **1b** with 2N aqueous KOH in methanol afforded a 1:1 mixture of **1a** and **1b**. This observation is supported by MM2 calculations suggesting that **1a** and **1b** have similar energies. The structure of **1b** was established by ^1H, ^{13}C NMR, COSY, DEPT, HMQC and HRMS.[12] The *trans* relationship of the bridghead hydrogens in **1b** was unequivocally established by single crystal X-ray crystallographic analysis, as depicted in Fig. 1.

With the proof of concept in hand, we next turned our attention to an enantioselective route that would allow the introduction of various substituents around the tricyclic core. To this end, we decided to use a carbonyl-ene reaction[13] in order to incorporate a methyl group at the C-2 position of the fusoxysporone skeleton. Our first option was to use a catalytic enantioselective glyoxylate-ene reaction[14] of ethylidenecyclohexane and ethyl glyoxalate (Scheme II). We screened a number of reported conditions (BINOL-Ti,[15] $[Pd(CH_3CN)_2$-(S)-Tol-BINAP$]\cdot(SbF_6)_2$,[16] Taddol-Ti,[15] Cu(II)-bisoxazoline,[17]), but unfortunately, we only observed moderate stereo- and enantioselectivities (Table 1).

Our back up strategy to the catalytic enantioselective glyoxylate-ene reaction was an enzymatic resolution of the α-hydroxy intermediate **8**. After some experimentation, we opted to use an acyltransferase enzyme (ALTUS 20 CLEC catalyst[18]) to resolve racemic 8-*syn*. Using this route, we were able to recover (2*S*,3*S*)-**8**-*syn* and acylated (2*R*,3*R*)-**8**-*syn* in > 99.5% *ee* and 46% and 47% yield respectively.[19] Similarly, we were able to resolve racemic **8**-*anti* into acylated (2*R*,3*S*)-**8**-*anti* and (2*S*,3*R*)-**8**-*anti* in 46% and 43% yield and > 99.5% *ee* (Scheme IV). With (-)-(2*S*,3*S*)-**8**-*syn* in hand, the elabora-



1a **1b**

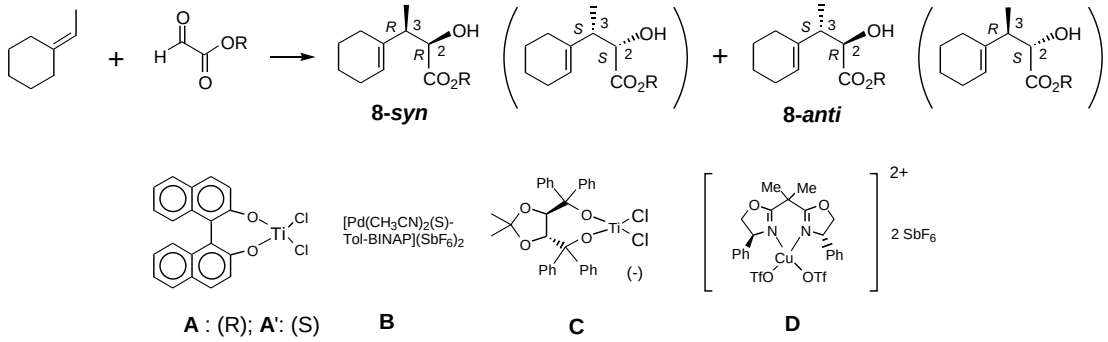
Fig. 1. ORTEP plots for X-ray crystal structures of **1a** and **1b**.

Table 1. Enantioselective Glyoxylate-Ene Reaction with Ethylidenecyclohexane

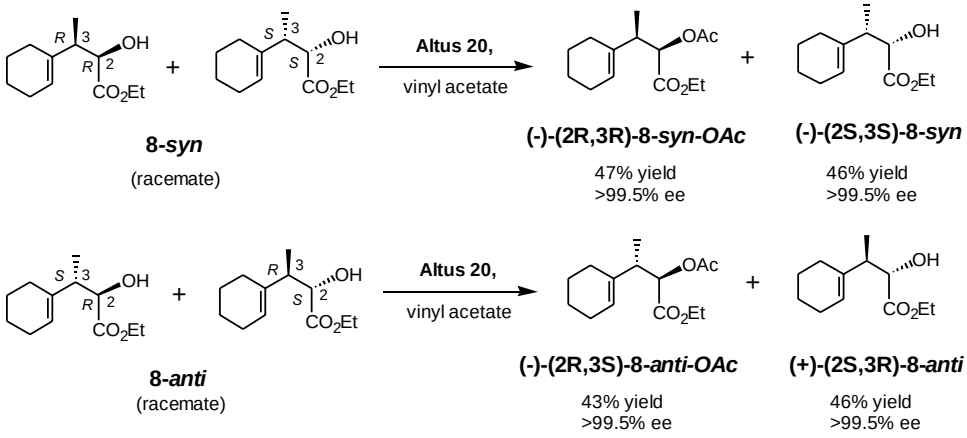
Entry	R	catalyst	Mol% catalyst	Time (h)	Solvent	Temp, (°C)	*syn/anti* ratio[b] (ee%)	Yield[a,] (%)
							2*R*3*R*/2*R*3*S*	
1	CH_3	**A**	10	2	CH_2Cl_2	0	84 (68) : 16	42[14]
2	CH_3	**A**	10	2	toluene	0	93 (69) : 7	61[14]
3	C_2H_5	**B**	10	4	1:2 toluene-$(ClCH_2)_2$	60	69 (81) : 31	94[15]
4	C_2H_5	**B**	10	4	1:2 toluene-$(ClCH_2)_2$	25	85 (75) : 15	83[15]
5	C_2H_5	**A**	10	2	CH_2Cl_2	0	85 (50) : 15 (23)	60
6	C_2H_5	**A**	10	2	toluene	0	83 (83) : 17 (83)	65
7	C_2H_5	**A'**	10	2	CH_2Cl_2	0	79 (27)[c] : 21 (17)[d]	61
8	C_2H_5	**A'**	10	2	toluene	0	93 (80)[c] : 7 (84)[d]	66
9	C_2H_5	**C**	10	2	toluene	0	69 (15) : 31 (10)	81
10	C_2H_5	**D**	10	12	CH_2Cl_2	0	71 (15) : 29 (55)	80
11	C_2H_5	$TiCl_2$ $(O\text{-}i\text{-}Pr)_2$	0	2	CH_2Cl_2	0	69 : 31	88

[a] Isolated yields based on ethylidenecyclohexane; [b] Determined by chiral GC using Astec γ-cyclodextrin column (G-TA trifluoroacetyl, 30 m × 0.25 mm); [c] e.e. ratio favors 2*S*,3*S*; [d] e.e. ratio favors 2*S*,3*R*.

Scheme III



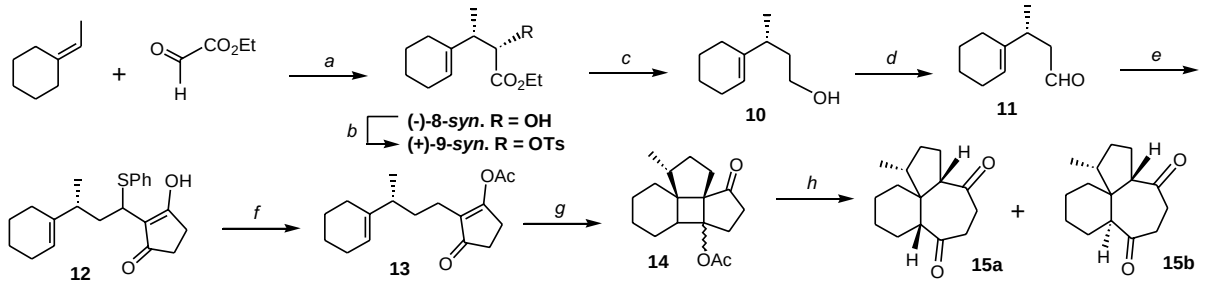
Scheme IV



tion of ethylidenecyclohexane to the Fusoxysporone analog tricycle **15** was then completed. The reaction sequence is outlined in Scheme V.

Alcohol (-)-(2*S*,3*S*)-**8**-*syn* was transformed into tosylate (+)-**9**-*syn*, (TsCl, pyridine, CH_2Cl_2, 12 h; 91%), and then reduced with $LiAlH_4$ to give alcohol (-)-**10** ($LiAlH_4$, THF; 89%). Alcohol (-)-**10** was also obtained from (-)-(2*R*,3*S*)-**8**-*anti*-OAc via acetate hydrolysis (K_2CO_3, MeOH), tosylation

Scheme V



a. (1) $TiCl_2(O\text{-}i\text{-}Pr)_2$. (2) Altus 20, vinyl acetate, as shown in **Scheme II**. *b.* TsCl, pyridine, CH_2Cl_2; 91%. *c.* $LiAlH_4$, THF; 89%. *d.* PCC, CH_2Cl_2; 84%. *e.* 1,3-cyclopentadione, thiophenol, silica gel, CH_2Cl_2; 73%. *f.* (1) Ph_3SnH, AIBN, C_6H_6; 77%. (2) Ac_2O, NaOAc; 71%. *g.* hυ, CH_3CN; 69%. *h,* KOH, MeOH; 85%.

and reduction as before. Oxidation of (-)-**10** by pyridinium chlorochromate (PCC, CH_2Cl_2; 84%), followed by the modified Knoevenagel reaction in the presence of thiophenol (cyclopentane-1,3-dione, thiophenol, silica gel, CH_2Cl_2; 73%), reductive deprotection (Ph_3SnH, *cat.* AIBN, C_6H_6; 77%) and acylation (Ac_2O, NaOAc; 71%) afforded ketoacetate (-)-**13**. Irradiation of a 2 mM solution of (-)-**13** (acetonitrile; 450 W medium pressure Hg arc lamp; Pyrex immersion well) led to the formation of a single photoadduct (-)-**14** in 69% yield, which on treatment with 2N aqueous KOH in methanol afforded the desired tricyclic diones (-)-**15a** and (-)-**15b**, (approximately a 1:1 ratio 85% yield).

In summary, we have described a rapid and enantioselective synthesis of a novel 5-6-7 tricyclic skeleton via a sequence of enantioselective ene reaction, enzymatic resolution and photocycloaddition-fragmentation. Work is in progress to use this methodology for the total synthesis of fusoxysporone as well as other complex skeletons bearing 5-6-7 ring systems (e.g. yuzurimine).

EXPERIMENTAL SECTION

General Procedure

All solvents were reagent grade. All chemicals were purchased from Aldrich Chemical Co. Reactions were normally carried out under argon atmosphere in flame-dried glassware. Merck silica gel 60 (particle size 0.04-0.063 mm) was employed for flash chromatography. HPLC was equipped with the ultraviolet and refractive index detectors. The sample was analyzed and/or separated on a μ-Porasil column (25 cm × 1.0 cm) by elution with gradient of ethyl acetate and hexane. The flow rate of the indicated elution solvent is maintained at 5 mL/min, and the retention time of a compound is recorded. Melting points are uncorrected. ^{1}H NMR and COSY spectra were obtained in $CDCl_3$ unless otherwise noted at 400 MHz. ^{13}C NMR spectra, HMBC, HMQC and DEPT experiments were obtained at 100 Hz MHz.

Preparation of chloroester 4

To a solution of methylenecyclohexane (1.59 g, 16.5 mmol) and methyl alpha-chloroacrylate (1.8 g, 15 mmol) in benzene (40 mL) was slowly added a solution of $AlEtCl_2$ in hexane (1 M, 20 mL, 20 mmol) at 25 °C and the resulting solution was stirred for 24 hours at the same temperature. The reaction was quenched by the addition of water (10 mL) into the solution. The solution was extracted with ether (50 mL × 2), and the organic solution was dried over $MgSO_4$, concentrated in vacuo to give the crude product. The reside was purified by flash column chromatography with 5% Et_2O-hexane (R_f = 0.60 in 10% Et_2O-hexane) to give chloroester **4** as a yellow oil (3.08 g, 95% yield). IR (neat): 2937, 1744, 1442 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.42 (br.s, 1H), 4.23 (dd, *J* = 7.8, 5.1 Hz, 1H), 3.75 (s, 3H), 2.15-1.80 (m, 8H), 1.60-1.40 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 170.28 (C), 135.28 (C), 122.69 (CH), 56.75 (CH), 52.83 (CH_3), 34.09 (CH_2), 32.85 (CH_2), 28.08 (CH_2), 25.16 (CH_2), 22.84 (CH_2), 22.34 (CH_2); MS (*m/z*, relative intensity): 216 (M^+, 30), 180 (79), 120 (90), 108 (100); exact mass calculated for $C_{11}H_{17}O_2Cl$ (M^+): 216.0918; found 216.0910.

Preparation of hydroxyester 5

To a solution of **4** (400 mg, 1.86 mmol) in water (50 mL) was added $Na_2CO_3 \cdot 10\ H_2O$ (2.7 g, 9.4 mmol) and the suspension was heated to reflux for 17 hours and cooled down to room temperature. A solution of 10% aqueous HCl solution was added into the reaction mixture until the PH value of the reaction solution reach to 2. The solution was extracted with $CHCl_3$ (50 mL × 2), the extract was dried over $MgSO_4$, concentrated in vacuo and the residue was purified

by filter the solution through a small silica gel column to give hydroxyester **5** as a white solid (304 mg, 89% yield). mp. 87-89 °C; IR (neat): 3100-3600, 2931, 1725, 1217, 1095 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.45 (br.s, 1H), 4.26 (dd, *J* = 7.5, 3.6 Hz, 1H), 1.82-2.10 (m, 7H), 1.65-1.80 (m, 1H), 1.40-1.60 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 179.85 (C), 137.09 (C), 122.99 (CH), 70.70 (CH), 33.80 (CH_2), 32.78 (CH_2), 28.87 (CH_2), 25.90 (CH_2), 23.60 (CH_2), 23.11 (CH_2); MS (*m/z*, relative intensity): 185 (M^++1, 15), 184 (M^+, 28), 109 (70), 81 (85), 66 (100); exact mass calculated for $C_{10}H_{16}O_3$ (M^+): 184.1099; found 184.1094.

Preparation of aldehyde 6

A solution of **5** (100 mg, 0.54 mmol) in pyridine (10 mL) was treated with $Pb(OAc)_4$ (240 mg, 0.54 mmol) and stirred for 2.5 h at room temperature. A solution of aqueous oxalic acid (2 M, 5 mL) was added into the reaction mixture and produced precipitate immediately. The solution was filtered through filter paper, washed with Et_2O (100 mL). Aqueous 10% HCl solution was added into the filtrate until the solution turned acidic. The organic solution was washed with brine (50 mL), dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography with 15% EtOAc-hexane (R_f = 0.65 in 25% EtOAc-hexane) to give aldehyde **6** as a pale yellow oil (60 mg, 81% yield). IR (neat): 2928, 1720, 1446, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.67 (t, *J* = 1.8 Hz, 1H), 5.30-5.35 (m, 1H), 2.40-2.45 (m, 2H), 2.10-2.20 (m, 2H), 1.80-2.00 (m, 4H), 1.40-1.60 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 203.14 (CH), 136.25 (C), 122.37 (CH), 42.38 (CH_2), 30.71 (CH_2), 28.95 (CH_2), 25.68 (CH_2), 23.37 (CH_2), 22.90 (CH_2); MS (*m/z*, relative intensity): 138 (M^+, 3), 137 (M^+-1, 10), 123 (8), 94 (50), 70 (100); exact mass calculated for $C_9H_{14}O$ (M^+): 138.1045; found 138.1031.

Preparation of thiolether 7

To a solution of **6** (800 mg, 5.8 mmol) in CH_2Cl_2 (40 mL) was added 1,3-cyclopentadione (681 mg, 6.9 mmol), benzenethiol (6.4 g, 58 mmol), silica gel (12 g), sequentially and stirred for 24 h at 25 °C. The reaction mixture was filtered through filter paper, concentrated in vacuo and the residue was purified by flash column chromatography with 40% EtOAc-hexane (R_f = 0.51 in 50% EtOAc-hexane) to give thiolether **7** as a yellow oil (1.42 g, 75% yield). IR (neat): 3100-3500, 2925, 2728, 1572, 1408, 746, 663 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30-7.10 (m, 5H), 5.41 (br.s, 1H), 4.23 (dd, *J* = 7.0, 6.7 Hz, 1H), 2.50-2.30 (m, 4H), 2.10-1.75 (m, 9H), 1.60-1.40 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 137.05 (C), 134.08 (C), 131.06 (two CH), 129.78 (two CH), 129.73 (C), 128.28 (C), 127.96 (CH), 127.85 (C), 122.53 (CH), 117.18 (C), 43.14 (CH), 36.08 (CH_2), 32.57 (CH_2), 28.95 (CH_2), 25.96 (CH_2), 23.65 (CH_2), 23.17 (CH_2), one C not evident because of tautomeric exchange, for similar example, see: Fuchs, K.; Paquette, L. A. *J. Org. Chem.* **1994**, *59*, 528-532; MS (*m/z*, relative intensity): 328 (M^+, 4), 326 (12), 298 (12), 218 (85), 189 (80), 97 (100); exact mass calculated for $C_{20}H_{24}O_2S$ (M^+): 328.1498; found 328.1491.

Preparation of acetate 3

To a solution of **7** (4.0 g, 12 mmol) in benzene (50 mL) was added Ph_3SnH (5.1 g, 14 mmol), AIBN (148 mg, 0.9 mmol), sequentially. The solution was heated to reflux for 1 h, cooled down to room temperature, concentrated in vacuo and the residue was purified by flash column chromatography with 40% EtOAc-hexane (R_f = 0.28 in 50% EtOAc-hexane) to give thiolether **7.5** as a yellow oil (2.0 g, 76% yield). IR (neat): 3100-3600, 2929, 1719, 1445 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.55 (br.s, 1H), 5.33 (br.s, 1H), 2.60-2.45 (m, 4H), 2.20-1.80 (m, 8H), 1.60-1.40 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 198.70 (C), 137.63 (C), 120.58 (CH), 118.38 (C), 37.93 (CH_2), 30.49 (CH_2), 28.25 (CH_2), 26.02 (CH_2), 25.19 (CH_2), 22.99 (CH_2), 22.54 (CH_2), 20.81 (CH_2), two C not evident because of tautomeric exchange; MS (*m/z*, relative intensity): 220 (M^+, 20), 124 (45), 111 (100); exact mass calculated for $C_{14}H_{20}O_2$ (M^+): 220.1463; found 220.1459.

To a solution of thiolether **7.5** (3.0 g, 13 mmol) in Ac_2O (50 mL) was added NaOAc (372 mg, 4.5 mmol) and the reaction solution was stirred at 25 °C for 2 h. The solution was concentrated in vacuo and the residue was diluted with Et_2O (200 mL). The organic solution was washed with saturated aqueous $NaHCO_3$ solution (50 mL × 2), brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography with 10% EtOAc-hexane (R_f = 0.66 in 20% EtOAc-hexane) to give acetate **3** as a yellow oil (2.4 g, 70% yield). IR (neat): 2929, 1774, 1705, 1650, 1440, 1400, 1180, 735, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.35 (br.s, 1H), 2.81 (dd, *J* = 4.4, 4.7 Hz, 2H), 2.50-2.45 (m, 2H), 2.25 (s, 3H), 2.14-2.04 (m, 2H), 1.98-1.82 (m, 6H), 1.65-1.40 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 205.86 (C), 175.94 (C), 166.76 (C), 137.15 (C), 130.27 (C), 121.13 (CH), 37.75 (CH_2), 34.50 (CH_2), 28.17 (CH_2), 26.90 (CH_2), 25.24 (CH_2), 25.12 (CH_2), 23.00 (CH_2), 22.58 (CH_2), 21.43 (CH_2), 21.03 (CH_3); MS (*m/z*, relative intensity): 262 (M^+, 3), 234 (4), 220 (39), 149 (36), 124 (50), 111 (100); exact mass calculated for $C_{16}H_{22}O_3$ (M^+): 262.1569; found 262.1564.

Preparation of acetate 2

A solution of **3** (500 mg, 1.9 mmol) in acetonitrile (300 mL) was degassed for 0.5 h, and the resulting solution was

cooled to 0 °C and irradiated through a Pyrex filter for 40 min. The solution was concentrated in vacuo and the residue was purified by flash column chromatography with 10% EtOAc-hexane (R_f = 0.64 in 20% EtOAc-hexane) to give acetate **2** as a colorless oil (348 mg, 70% yield). IR (neat): 2925, 1726, 1224, 757 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.55-2.72 (m, 2H), 2.29-2.31 (m, 1H), 2.15-2.24 (m, 1H), 2.01 (s, 3H), 2.00-1.10 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 219.25 (C), 170.05 (C), 84.47 (C), 66.67 (C), 49.23 (C), 44.19 (CH), 40.50 (CH_2), 39.14 (CH_2), 28.98 (CH_2), 28.38 (CH_2), 27.49 (CH_2), 25.41 (CH_2), 21.25 (CH_2), 20.50 (CH_3), 20.33 (CH_2), 19.83 (CH_2); MS (*m/z*, relative intensity): 262 (M^+, 12), 220 (100), 202 (30), 124 (70), 111 (95); exact mass calculated for $C_{16}H_{22}O_3$ (M^+): 262.1569; found 262.1563.

Preparation of dione 1a and 1b

To a solution of **2** (50 mg, 0.19 mmol) in MeOH (5 mL) was added KOH (2.66 mg, 0.19 mmol) and the resulting solution was stirred for 30 min at room temperature. The solution was diluted wit EtOAc (100 mL), washed with brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and purified by flash column chromatography with 10% EtOAc-hexane (For **1a**: R_f = 0.31; For **1b**: R_f = 0.37 in 15% EtOAc-hexane) to give dione **1a** (17.5 mg, 42% yield) and **1b** (17.9 mg, 43 yield) as the white solids.

For Dione **1a**: mp. 87-89 °C; IR (neat): 2940, 2866, 1702, 1443, 1355, 1160, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.47-3.40 (m, 1H), 3.10-3.01 (m, 1H), 2.80-2.20 (m, 6H), 2.10-1.85 (m, 1H), 1.80-1.10 (m, 11H); ^{13}C NMR ($CDCl_3$) δ 211.37 (C), 209.67 (C), 60.42 (CH), 59.36 (CH), 48.00 (C), 38.89 (CH_2), 38.59 (CH_2), 38.07 (CH_2), 27.78 (CH_2), 24.70 (CH_2), 23.61 (CH_2), 21.35 (CH_2), 21.27 (CH_2), 20.70 (CH_2); MS (*m/z*, relative intensity): 220 (M^+, 60), 165 (68), 135 (92), 124 (100); exact mass calculated for $C_{14}H_{20}O_2$ (M^+): 220.1463; found 220.1460.

Dione **1b**: mp. 90-92 °C; IR (neat): 2940, 2866, 1701, 1443, 1355, 1160, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.10-3.00 (m, 1H), 2.90-2.70 (m, 1H), 2.68-2.42 (m, 3H), 2.35-2.15 (m, 2H), 2.14-1.90 (m, 2H), 1.85-1.24 (m, 9H), 1.22-1.08 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 210.89 (C), 210.56 (C), 58.95 (C), 53.42 (CH), 48.40 (CH), 38.38 (CH_2), 38.20 (CH_2), 33.74 (CH_2), 32.42 (CH_2), 23.83 (CH_2), 23.44 (CH_2), 21.59 (CH_2), 21.42 (CH_2), 21.24 (CH_2); MS (*m/z*, relative intensity): 220 (M^+, 32), 165 (23), 135 (44), 124 (100); exact mass calculated for $C_{14}H_{20}O_2$ (M^+): 220.1463; found 220.1461.

Representative procedure for the enantioselective ene reaction

To a solution of $TiCl_2(O\text{-}iPr)_2$ (0.3 M in toluene, 0.33 mL, 0.10 mmol) in toluene (2 mL) was added **(*R*)-(+)-1,1′-bi-2-naphthol** (28.9 mg, 0.1 mmol) at ambient temperature and stirred for 1 h. The solution was cooled to -78 °C, followed by the sequential addition of ethylidenecyclohexane (100 mg, 0.91 mmol) and glyoxylic acid ethyl ester (100 mg, 0.99 mmol). The resulting solution was stirred for 1 h at -78 °C, then immediately warmed up to 0 °C and stirred at 0 °C for 2 h until the reaction completed, followed by the addition of EtOAc (100 mL), and then washed with saturated aqueous $NaHCO_3$ (50 mL × 2). The organic layer was dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography (10% EtOAc-hexane, ***8*-*syn***: R_f = 0.24, ***8*-*anti***: R_f = 0.25 in 10% EtOAc-hexane) to give the adduct ***8*-*syn*** (104 mg, 54% yield) and ***8*-*anti*** (21 mg, 11% yield) as colorless liquids.

Enzymatic resolution of (±)-8-*syn*

To a solution of **(±)-8-*syn*** (50 mg, 0.24 mmol) and Altus-20 (62 mg) in toluene (5 mL) was added vinyl acetate (0.1 mL). The reaction was agitated by a solid-phase synthesizer at ambient temperature for 10 h. The suspension was filtered, washed with toluene (10 mL), and the combined solution was concentrated in vacuo and the residue was purified by flash column chromatography with 10% EtOAc-hexane (**(-)-2*S*,3*S*-8-*syn*** : R_f = 0.24; **(-)-2*R*,3*R*-8-*syn*-OAc**: R_f = 0.36 in 10% EtOAc-hexane) to give **(-)-8-2*S*,3*S*-8-*syn*** (23 mg, 46% yield > 99.5% e.e.) and **(-)-8-2*R*,3*R*-*syn*-OAc** (28 mg, 47%, > 99.5% e.e.).

(-)-2*S*,3*S*-8-*syn*: $[\alpha]_D^{25}$ -2.6 (C 0.1, $CHCl_3$), IR (neat): 3100-3600, 2932, 1739, 1445, 1216, 757 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.51 (br.s, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.17 (d, *J* = 3.4 Hz, 1H), 2.60-2.32 (m, 2H), 2.10-1.90 (m, 4H), 1.70-1.45 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.81 (C), 138.05 (C), 123.01 (CH), 73.05 (CH), 61.45 (CH_2), 45.05 (CH), 26.77 (CH_2), 25.30 (CH_2), 22.97 (CH_2), 22.45 (CH_2), 14.24 (CH_3), 12.76 (CH_3); MS (*m/z*, relative intensity): 212 (M^+, 4), 194 (50), 139 (22), 121 (18), 110 (100); exact mass calculated for $C_{12}H_{20}O_3$ (M^+): 212.1412; found 212.1414.

(-)-2*R*,3*R*-8-*syn*-OAc: $[\alpha]_D^{27}$ -17.8 (C 0.06, $CHCl_3$), IR (neat): 2929, 1747, 1455, 1378, 1268, 1232, 1032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.48 (br.s, 1H), 4.95 (d, *J* = 6.5 Hz, 1H), 4.20-4.08 (m, 2H), 2.65-2.52 (m, 1H), 2.10 (s, 3H), 2.00-1.90 (m, 4H), 1.65-1.45 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 170.61 (C), 170.06 (C), 136.95 (C), 123.79 (CH), 75.14 (CH), 61.04 (CH_2), 42.97 (CH), 26.08 (CH_2), 25.30 (CH_2), 22.87 (CH_2), 22.37 (CH_2), 20.62 (CH_3), 14.20 (CH_3), 14.17 (CH_3); MS (*m/z*, relative intensity): 254 (M^+, 7), 194 (33), 148 (23), 121 (41), 109 (100);

exact mass calculated for $C_{14}H_{22}O_4$ (M^+): 254.1518; found 254.1516.

Enzymatic resolution of (±)-8-*anti*

To a solution of **(±)-8-*anti*** (50 mg, 0.24 mmol) and Altus-20 (62 mg) in toluene (5 mL) was added vinyl acetate (0.1 mL). The reaction was agitated by solid-phase synthesizer at ambient temperature for 48 h. The solution was filtered, Altus-20 was washed with toluene (10 mL), and the combined solution was concentrated in vacuo and purified by flash column chromatography with 10% EtOAc-hexane (**(-)-2*S*,3*R*-8-*anti*** : R_f = 0.25; **(+)-2*R*,3*S*-8-*anti*-OAc**: R_f = 0.37 in 10% EtOAc-hexane) to give **(-)-2*S*,3*R*-8-*anti*** (23 mg, 46% yield > 99.5% e.e.) and **(+)-2*R*,3*S*-8-*anti*-OAc** (26 mg, 43%, > 99.5% e.e.).

(+)-2*S*,3*R*-8-*anti*: $[\alpha]_D^{27}$ +6.7 (C 0.19, $CHCl_3$), IR (neat): 3050-3600, 2927, 1732, 1384, 1262, 1099 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.50 (br. s, 1H), 4.20 (q, *J* = 7.3 Hz, 2H), 4.05 (d, *J* = 4.0 Hz, 1H), 2.50-2.60 (m, 1H), 2.00-2.85 (m, 4H), 1.70-1.45 (m, 4H), 1.27 (t, *J* = 7.3 Hz, 3H), 1.09 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.34 (C), 137.41 (C), 124.39 (CH), 73.92 (CH), 61.22 (CH_2), 45.34 (CH), 26.64 (CH_2), 25.29 (CH_2), 22.91 (CH_2), 22.45 (CH_2), 15.53 (CH_3), 14.22 (CH_3); MS (*m/z*, relative intensity): 212 (M^+, 3), 194 (47), 139 (20), 110 (100); exact mass calculated for $C_{12}H_{20}O_3$ (M^+): 212.1412; found 212.1410.

(-)-2*R*,3*S*-8-*anti*-OAc: $[\alpha]_D^{26}$ -4.9 (C 0.18, $CHCl_3$), IR (neat): 2929, 1748, 1457, 1376, 1269, 1232, 1118, 1032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.47 (br.s, 1H), 494 (d, *J* = 6.5 Hz, 1H), 4.15 (q, *J* = 7.3 Hz, 2H), 2.55-2.65 (m, 1H), 2.09 (s, 3H), 2.05-1.90 (m, 4H), 1.70-1.40 (m, 4H), 1.23 (t, *J* = 7.3 Hz, 3H), 1.05 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 170.47 (C), 169.55 (C), 137.16 (C), 124.08 (CH), 75.63 (CH), 60.94 (CH_2), 42.88 (CH), 25.76 (CH_2), 22.92 (CH_2), 22.43 (CH_2), 20.63 (CH_3), 15.06 (CH_3), 14.17 (CH_3); MS (*m/z*, relative intensity): 254 (M^+, 8), 194 (34), 121 (43), 109 (100); exact mass calculated for $C_{14}H_{22}O_4$ (M^+): 254.1518; found 254.1519.

Prepration of (-)-2*R*,3*S*-8-*anti*

To a solution of **(-)-2*R*,3*S*-8-*anti*-OAc** (18 mg, 0.07 mmol) in EtOH (10 mL) was added K_2CO_3 (10 mg, 0.07 mol) and the solution was stirred at room temperature for 5 h. The solution was diluted with EtOAc (250 mL), washed with water (10 mL × 2), dried over $MgSO_4$, concentrated in vacuo and purified by flash column chromatography with 5% EtOAc-hexane (R_f = 0.25 in 10% EtOAc-hexane) to give **(-)-2*R*,3*S*-8-*anti*** (13 mg, 87% yield). $[\alpha]_D^{26}$ -7.3 (C 0.07, $CHCl_3$).

Preparation of (+)-9-*syn*

To a solution of **(-)-2*S*,3*S*-8-*syn*** (21 mg, 0.1 mmol), pyridine (25 mg, 0.3 mmol) and in CH_2Cl_2 (10 mL) was added TsCl (38 mg, 0.2 mmol) at 0 °C. The solution was stirred for 12 h at the same temperature and diluted with EtOAc (100 mL), washed with brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and purified by flash column chromatography with 5% EtOAc-hexane (R_f = 0.27 in 10% EtOAc-hexane) to give **(+)-9-*syn*** (33 mg, 91% yield). $[\alpha]_D^{25}$ +7.5 (C 0.22, $CHCl_3$), IR (neat): 2932, 1752, 1368, 1179, 1006, 841, 672 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 5.43 (br.s, 1H), 4.66 (d, *J* = 7.1 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 2.60-2.45 (m, 1H), 2.42 (s, 3H), 2.10-1.10 (m, 8H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.40 (C), 144.60 (C), 135.52 (C), 133.38 (C), 129.78 (two CH), 128.09 (two CH), 125.14 (CH), 80.58 (CH), 61.29 (CH_2), 43.88 (CH), 25.78 (CH_2), 25.18 (CH_2), 22.62 (CH_2), 22.11 (CH_2), 21.56 (CH_3), 14.12 (CH_3), 13.97 (CH_3); MS (*m/z*, relative intensity): 366 (M^+, 3), 321 (9), 194 (19), 121 (100); exact mass calculated for $C_{19}H_{26}O_5S$ (M^+): 366.1502; found 366.1505.

Preparation of (-)-9-*anti*

To a solution of **(-)-2*R*,3*S*-8-*anti*** (19 mg, 0.09 mmol), pyridine (0.23 mg, 0.27 mmol) and in CH_2Cl_2 (10 mL) was added TsCl (34 mg, 0.18 mmol) at 0 °C. The solution was stirred for 12 h at the same temperature and diluted with EtOAc (100 mL), washed with brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and purified by flash column chromatography with 5% EtOAc-hexane (R_f = 0.28 in 10% EtOAc-hexane) to give **(-)-9-*anti*** (29 mg, 89% yield).

$[\alpha]_D^{26}$ -17.5 (C 0.15, $CHCl_3$), IR (neat): 2930, 1752, 1382, 1157, 1021, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 5.40 (br.s, 1H), 4.63 (d, *J* = 7.2 Hz, 1H), 4.04 (q, *J* = 7.2 Hz, 2H), 2.60-2.50 (m, 1H), 2.40 (s, 3H), 1.90-1.10 (m, 8H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 5.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.22 (C), 144.84 (C), 137.47 (C), 135.96 (C), 129.59 (two CH), 128.06 (two CH), 124.94 (CH), 80.60 (CH), 61.31 (CH_2), 43.66 (CH), 25.27 (CH_2), 25.18 (CH_2), 22.65 (CH_2), 22.19 (CH_2), 21.56 (CH_3), 14.75 (CH_3), 13.96 (CH_3); MS (*m/z*, relative intensity): 366 (M^+, 4), 321 (5), 211 (12), 121 (70), 79 (100); exact mass calculated for $C_{19}H_{26}O_5S$ (M^+): 366.1502; found 366.1499.

Preparation of alcohol 10

To a solution of **(+)-9-*syn*** (100 mg, 0.26 mmol) in THF

(10 mL) was added $LiAlH_4$ (30 mg, 0.78 mmol) at 0 °C. The suspension was stirred for 1 h and graduately warmed up to ambient temperature. The reaction was quenched by slow addition of H_2O (10 mL). The solution was diluted with EtOAc (100 mL), washed with brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography with 10% EtOAc-hexane (R_f = 0.42 in 20% EtOAc-hexane) to give alcohol **10** (37 mg, 89% yield). A similar procedure was applied to **(-)-9-*anti*** (80 mg, 0.21 mmol) and gave alcohol **10** (28 mg, 88% yield). $[\alpha]_D^{27}$ -3.1 (C 0.19, $CHCl_3$), IR (neat): 3100-3600, 2927, 1660, 1450, 1052 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.41 (br.s, 1H), 3.60-3.45 (m, 2H), 2.20-2.10 (m, 1H), 2.00-1.72 (m, 4H), 1.62-1.20 (m, 6H), 0.96 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 141.68 (C), 120.74 (C), 61.63 (CH_2), 38.36 (CH), 37.56 (CH_2), 25.15 (CH_2), 24.58 (CH_2), 22.96 (CH_2), 22.73 (CH_2), 19.67 (CH_3); MS (*m/z*, relative intensity): 154 (M^+, 20), 123 (20), 110 (98), 81 (100); exact mass calculated for $C_{10}H_{18}O$ (M^+): 154.1358; found 154.1355.

Preparation of aldehyde 11

To a solution of **10** (100 mg, 0.65 mmol) in CH_2Cl_2 (100 mL) was added PCC (210 mg, 0.97 mmol) at room temperature. The suspension was stirred for 2 h and was diluted with EtOAc (100 mL). The solution was washed with brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography with 5% EtOAc-hexane (R_f = 0.70 in 10% EtOAc-hexane) to give aaldehyde **11** (83 mg, 84% yield). $[\alpha]_D^{24}$ -11.3 (C 0.03, $CHCl_3$), IR (neat): 2925, 1458, 1217, 758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.66 (t, J = 2.2 Hz, 1H), 5.44 (br.s, 1H), 2.68-2.55 (m, 1H), 2.52-2.40 (m, 1H), 2.35-2.22 (m, 1H), 2.00-1.80 (m, 3H), 1.65-1.35 (m, 5H), 1.04 (d, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 202.99 (CH), 140.19 (C), 121.27 (CH), 48.86 (CH_2), 35.97 (CH), 25.72 (CH_2), 25.12 (CH_2), 22.90 (CH_2), 22.56 (CH_2), 19.58 (CH_3); MS (*m/z*, relative intensity): 153 (M^++1, 3), 151 (M^+-1, 12), 136 (29), 121 (32), 109 (48), 81 (100); exact mass calculated for $C_{10}H_{16}O$ (M^+): 152.1201; found 152.1209.

Preparation of thiolether 12

To a solution of **11** (800 mg, 5.26 mmol) in CH_2Cl_2 (40 mL) was added 1,3-cyclopentadione (612 mg, 6.2 mmol), benzenethiol (5.76 g, 52 mmol), silica gel (12 g), sequentially and stirred for 24 h at 25 °C. The reaction mixture was filtered through filter paper, concentrated in vacuo and the residue was purified by flash column chromatography with 40% EtOAc-hexane (R_f = 0.27 in 50% EtOAc-hexane) to give thiolether **12** as a yellow oil (1.31 g, 73% yield). $[\alpha]_D^{26}$ -1.6 (C 0.17, $CHCl_3$), IR (neat): 3100-3500, 2925, 2728, 1572, 1408, 746, 663 cm^{-1}; ^1H NMR ($CDCl_3$, * denonate minor isomer) δ 7.30-7.10 (m, 5H), 5.51 (br.s, 1H), 5.40* (br.s, 1H), 4.30-4.05 (m, 1H), 2.50-2.25 (m, 5H), 2.10-1.45 (m, 11H), 0.99* (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 140.81, 140.06, 133.52, 130.45, 129.05, 128.99, 127.56, 127.24, 127.14, 122.25, 121.12, 116.92, 116.84, 41.77, 39.28, 39.06, 238.70, 38.29, 25.38, 25.25, 25.19, 23.69, 23.03, 22.99, 22.81, 22.73, some C not evident because of tautomeric exchange; MS (*m/z*, relative intensity): 342 (M^+, 6), 326 (5), 246 (18), 231 (30), 217 (52), 149 (25), 108 (100); exact mass calculated for $C_{21}H_{26}O_2S$ (M^+): 342.1655; found 342.1654.

Preparation of acetate 13

To a solution of **12** (50 mg, 0.15 mmol) in benzene (10 mL) was added Ph_3SnH (56 mg, 0.16 mmol), AIBN (7 mg, 0.04 mmol), subsequently. The solution was heated to reflux for 1 h and cool down to room temperature, concentrated in vacuo and the residue was purified by flash column chromatography with 30% EtOAc-hexane (R_f = 0.37 in 60% EtOAc-hexane) to give thiolether **12.5** as a yellow oil (27 mg, 73% yield). $[\alpha]_D^{27}$ -3 (C 0.09, $CHCl_3$), IR (neat): 3100-3600, 2929, 2862, 1731, 1595, 1393, 1275, 1228, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.39 (br.s, 1H), 2.55-2.38 (m, 3H), 2.10-1.75 (m, 6H), 1.65-1.10 (m, 8H), 1.00-0.80 (m, 1H), 0.95 (d, J = 9.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 196.88 (C), 196.85 (C), 142.15 (C), 120.71 (CH), 118.65 (C), 41.33 (CH), 32.71 (CH_2), 30.45 (CH_2), 29.70 (CH_2), 25.28 (CH_2), 24.67 (CH_2), 23.10 (CH_2), 22.86 (CH_2), 19.67 (CH_3), 19.19 (CH_2); MS (*m/z*, relative intensity): 235 (M^++1, 22), 234 (M^+, 28), 233 (37), 216 (65), 125 (100); exact mass calculated for $C_{15}H_{22}O_2$ (M^+): 234.1620; found 234.1619.

To a solution of thiolether **12.5** (30 mg, 0.13 mmol) in Ac_2O (10 mL) was added NaOAc (3.72 mg, 0.045 mmol) and the reaction solution was stirred at 25 °C for 2 h. The solution was concentrated in vacuo and the residue was diluted with Et_2O (100 mL). The organic solution was washed with saturated aqueous $NaHCO_3$ solution (50 mL × 2), brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography with 10% EtOAc-hexane (R_f = 0.85 in 20% EtOAc-hexane) to give acetate **3** as a yellow oil (25 mg, 71% yield). $[\alpha]_D^{26}$ -6.6 (C 0.08, $CHCl_3$); IR (neat): 2928, 1706, 1646, 1441, 1180, 734, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.36 (br.s, 1H), 2.78 (d, J = 4.9 Hz, 2H), 2.50-2.40 (m, 2H), 2.24 (s, 3H), 2.05-1.75 (m, 4H), 1.70-1.15 (m, 8H), 1.05-0.80 (m, 1H), 0.94 (d, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 205.83 (C), 175.66 (C), 166.76 (C), 141.13 (C), 130.61 (C), 120.79 (CH), 41.33 (CH), 34.51

(CH_2), 32.06 (CH_2), 26.90 (CH_2), 25.27 (CH_2), 24.61 (CH_2), 23.11 (CH_2), 22.88 (CH_2), 20.99 (CH_3), 19.98 (CH_2), 19.54 (CH_3); MS (*m/z*, relative intensity): 277 (M^++1, 11), 234 (36), 216 (36), 125 (100), 112 (100); exact mass calculated for $C_{17}H_{24}O_3$ (M^+): 276.1725; found 276.1721.

Preparation of acetate 14

A solution of **13** (100 mg, 0.36 mmol) in acetonitrile (300 mL) was degassed for 0.5 h, and the resulting solution was cooled to 0 °C and irradiated through a Pyrex filter for 40 min. The solution was evaporated and the residue was purified by flash column chromatography with 10% EtOAc-hexane (R_f = 0.53 in 20% EtOAc-hexane) to give acetate **14** as a colorless oil (ca. 3:1 mixture of stereoisomers, 69 mg, 69% yield).

$[\alpha]_D^{28}$ -5.75 (C 0.08, $CHCl_3$); IR (neat): 2935, 1730, 1231, 1033, 770 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.70-2.52 (m, 2H), 2.40-2.20 (m, 2H), 2.15-1.80 (m, 6H), 1.78-1.42 (m, 7H), 1.40-0.80 (m, 4H), 0.80 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 3:1 isomeric forms, * denotes major isomer) δ 219.39 (C), 219.08*(C), 170.17 (C), 170.02* (C), 84.87 (C), 84.03* (C), 67.74 (C), 66.67* (C), 51.63* (C), 49.85 (C), 47.74 (CH), 46.16* (CH), 41.29* (CH), 39.11* (CH_2), 38.99 (CH_2), 38.01 (CH), 27.45* (two of CH_2), 27.41 (CH_2), 27.02 (CH_2), 26.24* (CH_2), 23.39 (*CH_3 and CH_2), 22.72 (CH_2), 22.41 (CH_2), 21.84 (CH_2), 21.48* (CH_2), 21.26 (CH_3 and *CH_3), 19.91* (CH_2), 19.37 (CH_2 and *CH_2), 18.42* (CH_2), 16.57 (CH_3); MS (*m/z*, relative intensity): 277 (M^++1, 7), 276 (12), 233 (36), 216 (68), 125 (100); exact mass calculated for $C_{17}H_{24}O_3$ (M^+): 276.1725; found 276.1750.

Preparation of dione 15a and 15b

To a solution of **14** (50 mg, 0.18 mmol) in MeOH (5 mL) was added KOH (2.66 mg, 0.19 mmol) and the resulting solution was stirred for 30 min. at room temperature. The solution was diluted with EtOAc (100 mL), washed with brine (50 mL × 2), dried over $MgSO_4$, concentrated in vacuo and the residue was purified by flash column chromatography with 10% EtOAc-hexane (**15a**: R_f = 0.32; **15b**: R_f = 0.35 in 15% EtOAc-hexane) to give dione **15a** (19 mg, 43% yield) and **15b** (17 mg, 42 mmol) as white needles.

Spectroscopic data for **15a**: mp 82-84 °C; $[\alpha]_D^{27}$ -16.5 (C 0.04, $CHCl_3$); IR (neat): 2937, 2872, 1700, 1453, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.70-3.60 (m, 1H), 3.12-3.00 (m, 1H), 2.80-2.30 (m, 4H), 2.10-1.15 (m, 11H), 1.00-0.75 (m, 1H), 0.97 (d, J = 6.9 Hz, 3H), 0.65-0.50 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.40 (C), 210.22 (C), 56.29 (CH), 53.82 (CH), 50.46 (C), 39.00 (CH_2), 38.35 (CH), 38.27 (CH_2), 28.95 (CH_2), 28.87 (CH_2), 23.70 (CH_2), 20.99 (CH_2), 20.85 (two CH_2), 16.90 (CH_3); MS (*m/z*, relative intensity): 234 (M^+, 50), 161 (66), 149 (100); exact mass calculated for $C_{15}H_{22}O_2$ (M^+): 234.1620; found 234.1615.

Spectroscopic data for **15b**: mp 85-88 °C; $[\alpha]_D^{27}$ -16.8 (C 0.05, $CHCl_3$); IR (neat): 2937, 2872, 1700, 1453, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.10-3.00 (m, 1H), 2.85-2.70 (m, 1H), 2.65-2.35 (m, 3H), 2.10-1.15 (m, 14H), 0.91 (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.81 (C), 212.27 (C), 59.76 (CH), 59.64 (CH), 50.11 (C), 42.74 (CH), 36.90 (CH_2), 34.04 (CH_2), 31.63 (CH_2), 31.49 (CH_2), 27.11 (CH_2), 26.50 (CH_2), 25.69 (CH_2), 21.07 (CH_2), 12.49 (CH_3); MS (*m/z*, relative intensity): 234 (M^+, 100), 161 (50), 124 (41); exact mass calculated for $C_{15}H_{22}O_2$ (M^+): 234.1620; found 236.1618.

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