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First Total Syntheses of the Phytotoxins Solanapyrones D and E via the Domino Michael Protocol

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The phytotoxins solanapyrones D (**1**) and E (**2**) have been synthesized from the decalone prepared by the domino Michael reaction of the kinetic enolate of optically pure acetylcyclohexene with methyl crotonate. The decalone was transformed into a solanapyrone core by equilibration into thermodynamically stable *trans*-decalone (**11**), dehydroxylation, and dehydration. Condensation of a methyl acetoacetate equivalent followed by cyclization installed a pyrone moiety. Introduction of a formyl or hydroxymethyl unit into the pyrone ring via Pummerer related reactions furnished solanapyrones D (**1**) and E (**2**).

Introduction

Solanapyrones D (**1**)[1] and E (**2**)[2] are polyketide natural products isolated with solanapyrone A (**3**), B (**4**), or C (**5**)[3] by Oikawa and Ichihara from *Altenaria solani*, a causal fungus of early blight disease to tomato and potato plants. Subsequently, Strange et al.[4] discovered solanapyrones A (**3**) and C (**5**) from stationary cultures of *Ascochyta rabiet* on a Czapek−Dox medium, supplemented with an extract of chickpea seed. Those fungi are known to reduce large amounts of chickpea, tomato, or potato crops by infecting the plants when the weather of their growing season is cool and moist. Recently, during the course of examination of the antialgal effects of fungal metabolites, the isolation of *cis*-solanapyrones C (**5**), E (**6**),[5] F (**7**), and G (**8**), having an amino group in the pyrone nucleus, was reported by Fenical et al.[6] from the unidentified marine organism isolated from the surface of the green alga *Halimedia monile* (Figure 1). Distribution of solanapyrones in terrestrial as well as marine organisms is very interesting in view of the common biogenesis among the different organisms. Their biological activities are yet to be explored. Phytotoxic activities of solanapyrones A (**3**), B (**4**), C (**5**), D (**1**), and E (**2**) were assayed on the growth inhibition of lettuce seedlings,[2] and the formyl derivatives **1** and **3** exhibited complete inhibition at 250 ppm, stronger activity than those of the hydroxyl analogues **2** and **4**. In addition, solanapyrone C (**5**) exhibited substantial antialgal activity at a concentration of 300 μM against marine unicellular alga *Dunaliella* sp.

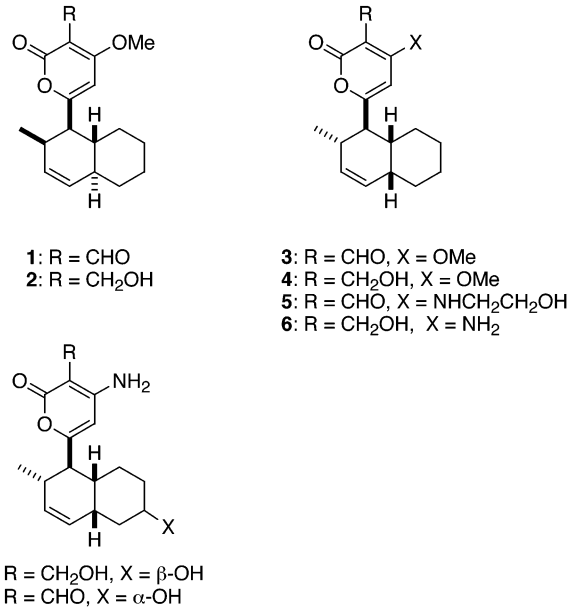

FIGURE 1.

Racemic solanapyrone A (**3**) has been synthesized by an intramolecular Diels−Alder reaction as a key step[7] in which solanapyrone D (**1**) was obtained as a byproduct

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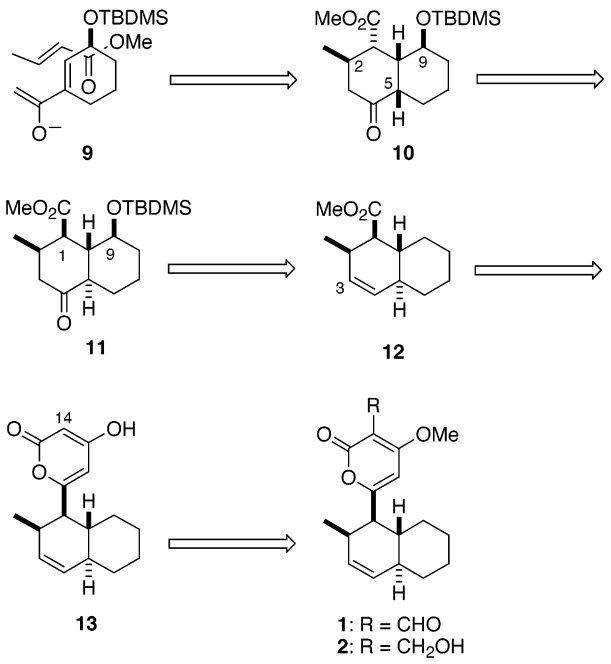
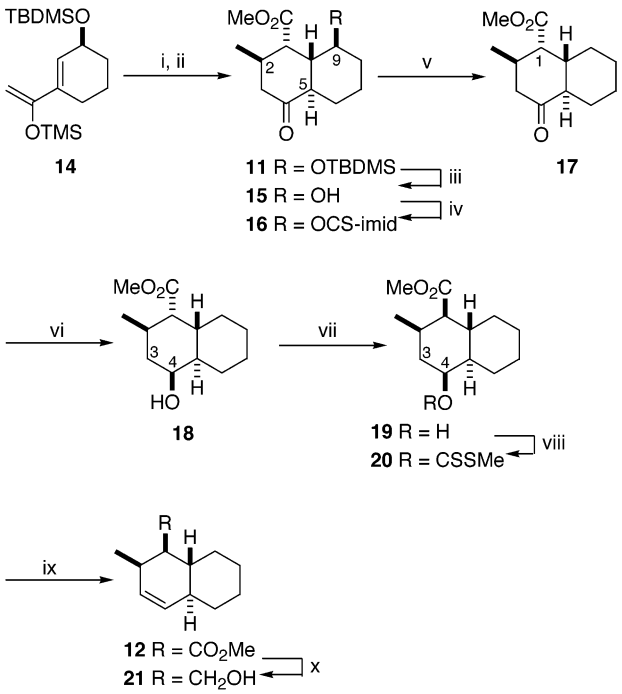
SCHEME 1



SCHEME 2[a]



[a] Reagents and conditions: (i) MeLi, methyl crotonate, HMPA, THF; (ii) MeONa, MeOH, 86% from **14**; (iii) aq HF, CH_3CN, 94%; (iv) 1,1′-thiocarbonyldiimidazole, 90%; (v) AIBN, Bu_3SnH, benzene, 93%; (vi) L-selectride, aq NaOH, H_2O_2, THF, 90%; (vii) *t*-BuOK, *t*-BuOH, DMSO, 78%; (viii) *t*-BuOK, CS_2, MeI, THF, 91%; (ix) 1-methylnaphthalene, 190 °C; (x) LAH, Et_2O, 89% from **20**.

prior to isolation from the fungus. This result implied the intervention of Diels−Alderase in the biosynthetic pathway, and Oikawa and co-workers unveiled the existence of Diels−Alderase for the first time through their study of the biosynthesis of solanapyrone A (**3**).[8] Actually, by incubation of the achiral triene precursor in the crude enzyme extract from *A. solani*, they obtained solanapyrone A (**3**) in 53% yield with 98% ee.

The success of the synthesis of natural solanapyrone A (**3**) by an enzymatic Diels−Alder reaction[8] prompted us to investigate chemical synthesis, and we describe herein the first total syntheses of solanapyrone D (**1**)[9] and E (**2**).

Results and Discussion

Our synthetic design is outlined in Scheme 1. The decaline framework of **10**, having requisite functionalities, would be obtained by a domino Michael reaction between acetylcyclohexene (**9**) and methyl crotonate. Base-catalyzed isomerization would lead to *trans*-decalone **11**, having a *β*-equatorial ester. After removal of the alkoxy group at C-9 (solanapyrone numbering) followed by introduction of a double bond at C-3, installation of a pyrone group at C-1 would furnish solanapyrone D (**1**) and E (**2**).

Synthesis of Decalin Portion. The synthesis was started from the enantiomerically pure trimethylsilyl enol ether (**14**) of (*S*)-acetylcyclohexene obtained by lipase-catalyzed enantioselective acylation (Scheme 2).[10] The domino Michael reaction between methyl crotonate and the kinetic enolate **9** generated by cleavage of the trimethylsilyl enol ether (**14**) by methyllithium provided decalone **10**, which was treated with base to ensure isomerization into more stable *trans*-decalone **11** (in 86% overall yield), whose relative structure was established by intensive NMR study.[11] In the decalone **11**, the ester group at C-1 still stayed in the α-axial position, contrary to our expectation. The double Michael reaction proceeded via chelation control between the enolate and Michael partners. Discussions on the reaction pathway have already been described in our earlier literature.[9]

Before the introduction of a double bond at C-3 of the decalone **11**, the chiral directing alkoxy group at C-9 was removed by radical cleavage. After deprotection of the TBDMS group by hydrogen fluoride in 94% yield, the solid-state reaction of the resulting alcohol **15** with thiocarbonyl diimidazole provided thiocarbonylimidazolide **16** in 90% yield. The reaction in THF or dichloromethane recovered a large amount of the alcohol **15**, even in the presence of DMAP. The present solid-state reaction was carried out by simply grinding a mixture of crystals of **15** and thiocarbonyldiimidazole with a mortar and pestle in a nitrogen bag.[12] All conventional attempts via alkoxide of the alcohol **15** to prepare xanthate resulted in decomposition, probably because of the proximity of the hydroxy group at C-9 to the ester group at

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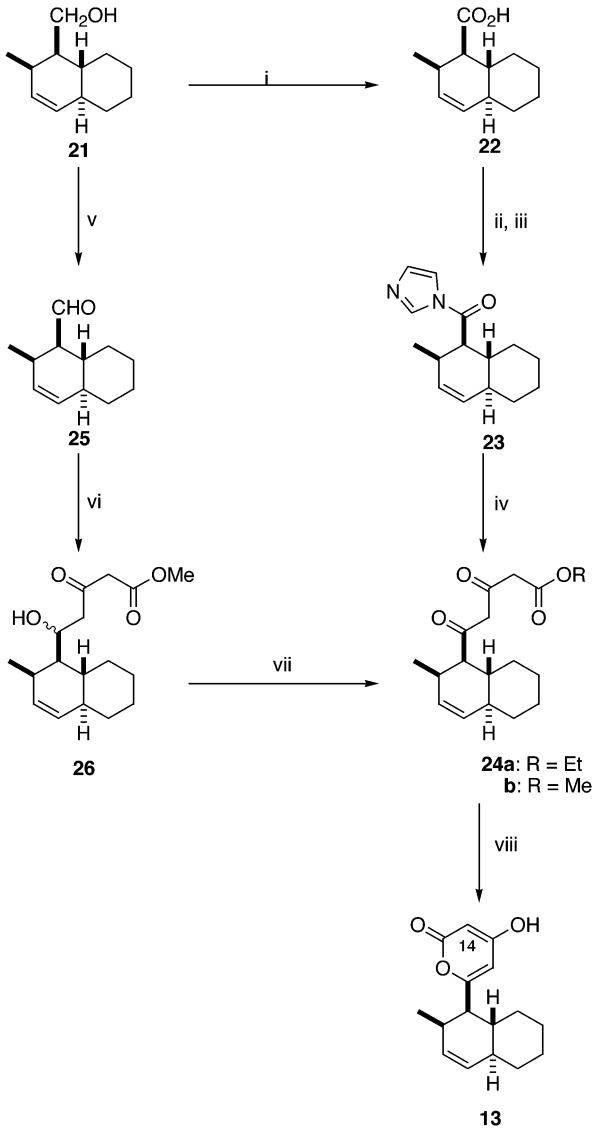
C-1. The imidazolide **16** was reduced with *n*-tetrabutyltin hydride to afford decalone **17** in 93% yield. To introduce a double bond selectively at C-3 by syn elimination, we reduced the carbonyl group at C-4 of the decalone **18** with L-selectride to give axial alcohol **19** in 90% yield. According to the MM2 calculations[13] of all plausible substrates for the isomerization at C-1, the calculated energy of stabilization of the decalone **19** was the largest after the isomerization. Then, the α-axial ester group of **17** was isomerized into the thermodynamically more stable *β*-equatorial orientation to furnish decalone **18**, having all the requisite stereochemistry of solanapyrones D (**1**) and E (**2**). The double bond was selectively introduced at C-3 by xanthate pyrolysis at 190 °C in 1-methylnaphthalene to afford the unsaturated ester **12**, which was reduced with lithium aluminumhydride in situ to enable easy separation from 1-methylnaphthalene. Alcohol **21** was obtained in 89% yield in two steps.

Installation of Pyrone Nucleus. The requisite pyrone moiety was installed by DBU-mediated cyclization of *β*,*δ*-diketoester **24** which was elaborated by two alternative routes (Scheme 3). The alcohol **21** was subjected to Jones oxidation to give carboxylic acid **22** in 91% yield. Treatment with thionyl chloride and subsequently with imidazole provided carbonylimidazolide **23**, which was condensed with a dianion of ethyl acetoacetate to furnish *β*,*δ*-diketoester **24** in 45% yield in three steps. However, this protocol lacked reproducibility, especially in the condensation of ethyl acetoacetate. Consequently, the alcohol **21** was oxidized by PCC to aldehyde **25**, which was reacted cleanly with the bis(trimethylsilyl) enol ether of methyl actoacetate[14] in the presence of titanium tetrachloride ($TiCl_4$) to give hydroxyketoester **26** in 75% overall yield. The Jones oxidation furnished in 74% yield the diketoester **24**, which was cyclized with DBU to pyrone **13** in 93% yield.[15]

Introduction of a Formyl or Hydroxymethyl Group to Pyrone: Total Syntheses of Solanapyrones D (1) and E (2). Introduction of the formyl group at C-14 (solanapyrone numbering) of the pyrone **13** was troublesome. We investigated the solution of this issue by model experiments (Scheme 4). Reaction of various 4-hydroxypyrone (pyrone numbering) derivatives **27** with paraformaldehyde in the presence of Lewis bases or acids afforded methylenebispyrone derivatives **28** in high yields.[16] Deprotonation of 4-methoxypyrone (**29**) with LDA was successful to give the carbanion **31**, as exemplified by the 79% deuterium take up after quenching with D_2O.[17] The carbanion **31** was reactive toward tributyltin chloride in the presence of TMEDA to give 3-tributyltinpyrone (**32**), which was lithiated back to the carbanion **31** by treatment with *n*-butyllithium. However, the nucleophilicity of **31** toward carbonyl compounds such as DMF, ethyl formate, or even formaldehyde was too low to result in the recovery of 4-methoxypyrone (**29**). An attempt at Pd-catalyzed CO insertion of tributyltin derivative **32** also failed. One of the literature precedents[18] for our purpose is the reaction of 4-methoxypyrone (**29**) with dichloromethyl methyl ether in the presence of $TiCl_4$ to give 3-formylpyrone (**30**), though we found that the procedure lacked reproducibility by our experiments.

Therefore, an alternative route was investigated by the introduction of a heteroatom substituted C-1 unit followed by the alteration of the oxidation state of the carbon. We have found that a phenylthiomethyl group was introduced according to the procedure of Moreno-Manas et al.[19] to afford phenylthiomethylpyrone **34** in reproducible yields (Scheme 5). *O*-Methylation followed

SCHEME 3[a]



[a] Reagents and conditions: (i) Jones reagent, acetone, 91%; (ii) $SOCl_2$; (iii) imidazole; (iv) NaH, *n*-BuLi, ethyl acetoacetate, 45% from **22**; (v) PCC, 4A-MS, CH_2Cl_2; (vi) methyl acetoacetate bis(TMS) enol ether, $TiCl_4$, CH_2Cl_2, 75% from **21**; (vii) Jones reagent, acetone, 74%; (viii) DBU, benzene, 93%.

(13) Molecular modeling was performed using PCMODEL (Serena Software, Bloomington, IN).

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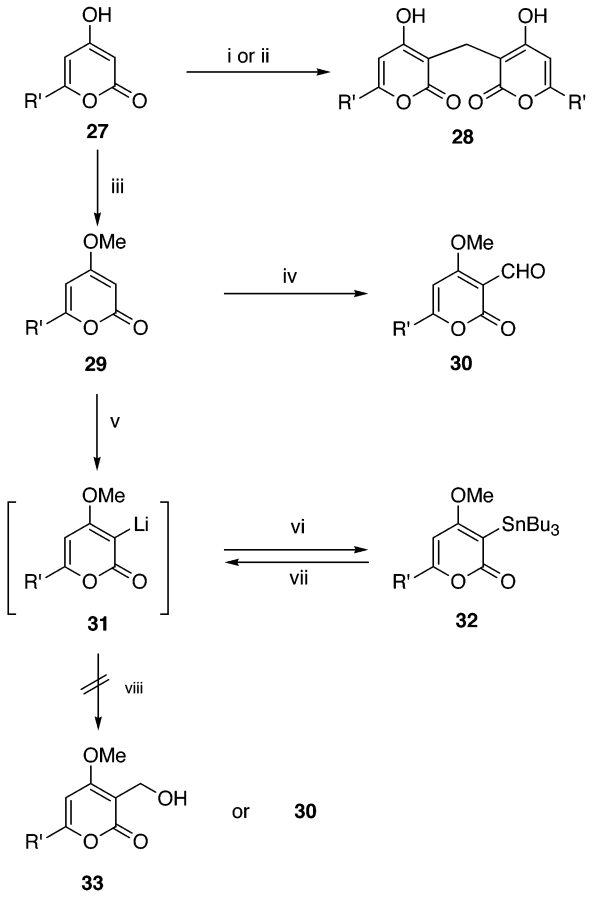
SCHEME 4[a]



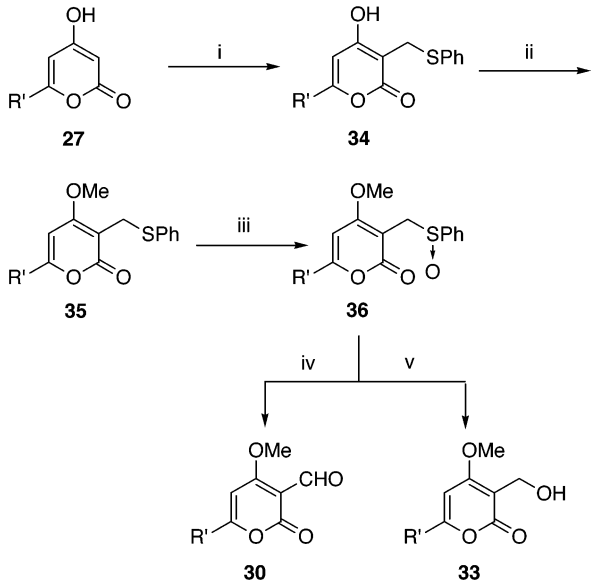
[a] Reagents and conditions: (i) paraformaldehyde, DBU; (ii) paraformaldehyde, Et_2AlCl; (iii) Me_2SO_4, K_2CO_3; (iv) Cl_2CHOMe, $TiCl_4$, 43% (R′ = cyclohexyl); (v) LDA, −78 °C; (vi) TMEDA, Bu_3SnCl, 100% (R′ = C_9H_{19}); (vii) *n*-BuLi, HMPA; (viii) DMF, HCO_2Et or HCHO.

by MCPBA oxidation gave sulfoxide **36**[20] in good yield. We envisaged that Pummerer rearrangement of the sulfoxide **36** followed by hydrolysis would enable the introduction of the formyl group at C-3 of the pyrone nucleus.

After screening numerous reagents to activate the phenylsulfinyl group, a combination of (trimethylsilyl)-trifluoromethanesulfonate (TMSOTf) as an *O*-silylating reagent and (diethylamino)trimethylsilane (DEATMS) as a mild base provided 3-formylpyrone (**30**) after treatment with tetrabutylammonium fluoride (Table 1). None of the other silylating or acylating reagents gave any of the desired products. Excess TMSOTf was required to get better yields, probably because of the coordination to the methyl ether at C-4, thus suppressing elimination of phenyltrimethylsiloxysulfide from the reaction intermediate. Such elimination leads to a substitution reaction to give hyroxymethylpyrone **33** (vide infra). DEATMS was a better base than triethylamine or diethylamine.

On the other hand, treatment of the sulfoxides **36** with trifluoroacetic anhydride followed by basic workup provided 3-hydroxymethylpyrone (**33**) in satisfactory yield, contrary to our anticipation. Pummerer rearrangement of the sulfoxides **36** did not proceed at all. This result is understood by the higher electron-donating ability of the methoxy group at C-4 to eliminate thiophenyl trifluoroacetate from the intermediate. Subsequent conjugate addition of the trifluoroacetoxy anion followed by basic hydrolysis furnished 3-hydroxymethylpyrone (**33**). A detailed discussion and the scope of the reaction have already been reported.[20]

SCHEME 5[a]



[a] Reagents and conditions: (i) paraformaldehyde, PhSH, AcOH, piperidine; (ii) Me_2SO_4, K_2CO_3; (iii) MCPBA; (iv) TMSOTf, TMS-NEt_2 then TBAF; (v) $(CF_3CO)_2O$ then aq NaOH.

TABLE 1. Formylation of Pyrone 27

entry	formylpyrone **30**	yield (%)
1	**a**: R = $(CH_2)_8CH_3$	49
2	**b**: R = cyclohexyl	33
3	**c**: R = $(CH_2)_2Ph$	37

Since we have acquired new protocols to introduce a formyl or hydroxymethyl group at C-3 of a pyrone ring simply by changing reagents starting from the same sulfoxide **36**, our attention turned to completion of the total syntheses of the solanapyrones (Scheme 6). Introduction of the phenylthiomethyl group to the pyrone **13** proceeded smoothly to afford sulfide **37** in 82% yield. Conventional *O*-methylation with dimethyl sulfate proceeded in 77% yield, and subsequent MCPBA oxidation afforded sulfoxide **39** in 88% yield. Finally, treatment of the sulfoxide **39** with TMSOTf and DEATMS provided solanapyrone D (**1**) in 69% yield ($[\alpha]_D$ −148.7, lit.[1] $[\alpha]_D$ −125.2). On the other hand, treatment of the sulfoxide **39** with trifluoroacetic anhydride furnished solanapyrone E (**2**) in 62%yield {$[\alpha]_D$ −154.9, lit.[2] $[\alpha]_D$ −76.4}. The NMR data (500 MHz) were completely identical with those of the natural products kindly provided by Prof. Oikawa. The large difference in specific rotations in solanapyrone E (**2**) may be caused by impurities involved in the natural product (see Supporting Information of ref 9).

In summary, the first total syntheses of the phytotoxins solanapyrones D (**1**) and E (**2**) have been achieved by a

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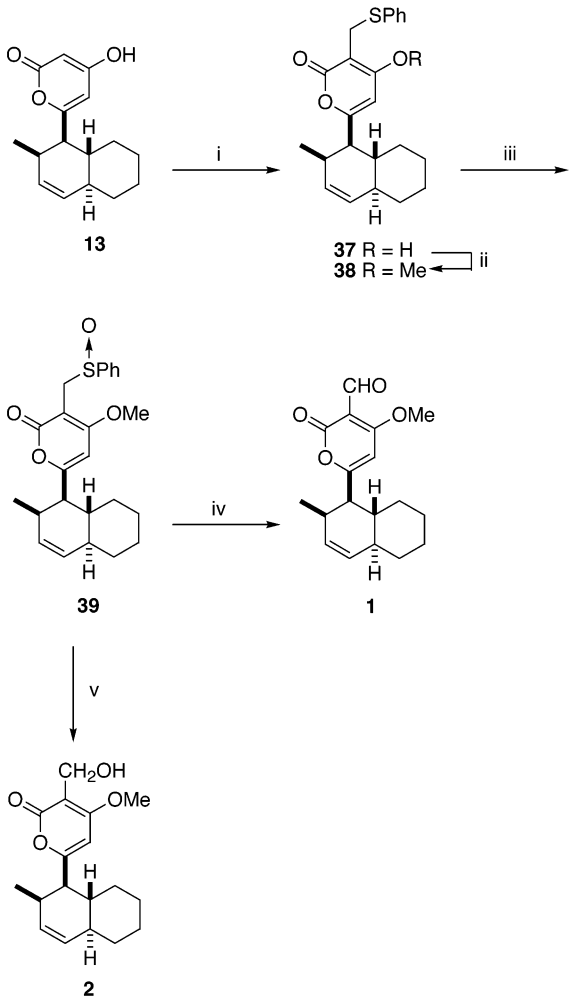
SCHEME 6[a]



[a] Reagents and conditions: (i) paraformaldehyde, PhSH, AcOH, piperidine, 82%; (ii) Me_2SO_4, K_2CO_3, acetone, 77%; (iii) MCPBA, CH_2Cl_2, 88%; (iv) TMSOTf, $TMSNEt_2$ then TBAF, 69%; (v) $(CF_3CO)_2O$, CH_2Cl_2 then aq NaOH, THF, 62%.

double Michael protocol for the synthesis of the decalin portion and by a Pummerer-related protocol for the introduction of an oxygenated methyl group of the pyrone moiety.

Experimental Section

General. Mp's are uncorrected. IR spectra and optical rotations were recorded for solutions in chloroform. ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were obtained for solutions in deuteriochloroform with tetramethylsilane as internal standard. ^{1}H NMR (500 MHz) spectra were run for solutions in deuteriochloroform. Mass spectra were measured under EI conditions.

Methyl (1*S*,2*R*,4a*R*,8*S*,8a*R*)-1,2,3,4a,6,7,8,8a-Octahydro-8-(*tert*-butyldimethylsiloxy)-2-methylnaphthalen-4(4a*H*)-one-1-carboxylate (11). To a stirred solution of TMS enol ether **14** (4.87 g, 14.9 mmol) in THF (20 mL) was added methyllithium (15.7 mL, 1.14 M in diethyl ether, 16.6 mmol) dropwise at −78 °C under nitrogen. After it was stirred at −78 °C for 30 min and at 0 °C for 35 min, a solution of HMPA (5.2 mL, 29.9 mmol) and methyl crotonate (2.4 mL, 22.3 mmol) in THF (15 mL) was added dropwise at −78 °C. The resulting solution was stirred at −78 °C for 50 min, at 0 °C for 35 min, and at room temperature for 70 min. The reaction was quenched by addition of H_2O, and the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with brine (×2) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue involving compound **10** was used in the next step without further purification.

To a stirred solution of sodium methoxide prepared from sodium (462 mg, 20 mmol) in methanol (15 mL) was added crude domino Michael product **10** at 0 °C under nitrogen. The resulting solution was heated at reflux for 5.5 h and cooled at 0 °C. After addition of 1 N aqueous HCl, the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with brine (×2), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Treatment with diazomethane followed by column chromatography (EtOAc/*n*-hexane 1:5) of the residue provided *trans*-decalone (**11**) (4.57 g, 86%) as a colorless oil: $[\alpha]_D^{20} = +43.05$ ($c = 1.01$); IR 2953, 1723, 1709, 1449, 1437, 1388, 1370, 1315, 1309, 1156, 1138, 1092, 1046, 1007 cm^{-1}; ^{1}H NMR (200 MHz) δ −0.07 (s, 6H), −0.03 (s, 3H), 0.80 (s, 9H), 0.98 (d, 3H, $J = 7.3$ Hz), 1.05−1.28 (m, 3H), 1.58−1.73 (m, 2H), 1.79−1.93 (m, 2H), 2.021 (m, 1H), 2.47−2.71 (m, 2H), 2.84−3.00 (m, 2H), 3.64 (s, 3H), 3.73 (m, 1H); ^{13}C NMR (50 MHz) δ −5.4, −3.7, 17.8, 19.8, 22.2, 24.8, 25.7, 33.7, 35.9, 44.1, 44.4, 47.2, 48.3, 51.1, 71.5, 174.4, 211.1.

Methyl (1*S*,2*R*,4a*R*,8*S*,8a*R*)-1,2,3,4a,6,7,8,8a-Octahydro-8-hydroxy-2-methylnaphthalen-4(4a*H*)-one-1-carboxylate (15). To a stirred solution of *trans*-decalone (**11**) (4.88 g, 14 mmol) in acetonitrile (40 mL) was added aqueous hydrogen fluoride (46%, 6 mL) at room temperature. After it was stirred for 2 h, the solution was neutralized with 2 N aqueous NaOH. The reaction mixture was extracted with EtOAc (×2), and the combined organic layers were washed with brine (×2) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc/*n*-hexane 2:3 then 2:1) to afford alcohol **15** (3.12 g, 94%) as crystals: mp = 88−89 °C; $[\alpha]_D^{20}$ +43.78 ($c = 1.00$); IR 3488, 2953, 1728, 1709, 1451, 1437, 1309, 1173, 1150, 1067, 1040 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.05 (d, 3H, $J = 7.3$ Hz), 1.12−1.32 (m, 3H), 1.77−1.82 (m, 2H), 1.87−2.00 (m, 2H), 2.09 (dd, 1H, $J = 13.9$, 2.7 Hz), 2.24 (d, 1H, $J = 4.7$ Hz), 2.62 (m, 1H), 2.69 (td, 1H, $J = 12.0$, 3.4 Hz), 3.03 (dd, 1H, $J = 13.9$, 6.1 Hz), 3.05 (d, 1H, $J = 5.1$ Hz), 3.58 (tdd, 1H, $J = 10.0$, 5.4, 4.7, Hz), 3.78 (s, 3H); ^{13}C NMR (125 MHz) δ 20.1, 22.3, 24.8, 33.1, 34.9, 44.1, 44.6, 47.3, 48.2, 51.7, 71.4, 174.5, 211.3; MS *m*/*z* 240 (M^+, 34%), 222 (53), 196 (34), 163 (100), 162 (53), 97 (63), 69 (45). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.82; H, 8.38.

***O*-[(1*S*,2*R*,4a*R*,8*S*,8a*R*)-Methyl-1,2,3,4a,6,7,8,8a-octahydro-8-hydroxy-2-methylnaphthalen-4(4a*H*)-one-1-carboxylate-8-yl]thiocarboxyimidazolide (16).** A mixture of the alcohol **15** (4.40 g, 18.3 mmol) and 1,1′-thiocarbonyldiimidazole (97%, 5.06 g, 27.5 mmol) was ground well with a pestle in a mortar at room temperature under nitrogen. The reaction mixture was left for 2 h and diluted with EtOAc. Evaporation of EtOAc followed by purification of the residue by column chromatography (EtOAc/*n*-hexane 1:1) gave thiocarbonylimidazolide **16** (5.79 g, 90%) as crystals: mp = 112−113 °C; $[\alpha]_D^{20}$ = +20.25 ($c = 1.00$); IR 2868, 1726, 1713, 1462, 1389, 1333, 1283, 1100, 992 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.09 (d, 3H, $J = 7.3$ Hz), 1.12−1.48 (m, 3H), 1.84−2.42 (m, 6H), 2.61 (m, 1H), 2.78 (m, 1H), 2.90−3.09 (m, 2H), 3.64 (s, 3H), 5.53 (td, 1H, $J = 10.4$, 4.6 Hz), 7.06 (dd, 1H, $J = 1.6$, 0.9 Hz), 7.62 (d, 1H, $J = 1.6$ Hz), 8.32 (d, 1H, $J = 0.9$ Hz); ^{13}C NMR (50 MHz) δ 20.3, 21.8, 24.5, 30.5, 33.0, 44.0, 44.2, 44.8, 48.0, 52.1, 83.1, 117.8, 130.9, 136.6, 173.7, 183.3, 209.6; MS *m*/*z* 319 (M^+ − MeO, 3%), 223 (89), 222 (64), 163 (100), 121 (45), 69 (50). Anal. Calcd for $C_{17}H_{22}N_2O_4S$: C, 58.27; H, 6.33; N, 7.99. Found: C, 58.45; H, 6.28; N, 7.98.

Methyl *(1S,2R,4aR,8S,8aR)*-1,2,3,4a,6,7,8,8a-Octahydro-2-methylnaphthalen-4(4a*H*)-one-1-carboxylate (17). To a stirred solution of thiocarbonylimidazolide **16** (2.45 g, 7 mmol) in benzene (35 mL) were added AIBN (118 mg, 0.7 mmol) and

n-tributyltinhydride (2.8 mL, 11 mmol), and the solution was stirred at 60 °C for 1 h under nitrogen atmosphere. After addition of H_2O at 0 °C, the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, purification of the residue by column chromatography (EtOAc/*n*-hexane 1:1) afforded ketoester **17** (1.46 g, 93%) as a solid: mp = 42−43 °C; $[\alpha]_D^{20}$ = +27.09 (*c* = 1.00); IR 2936, 1725, 1703, 1449, 1440, 1352, 1321, 1308, 1169, 1138 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (d, 3H, *J* = 7.1 Hz), 1.12−1.32 (m, 4H), 1.65−1.79 (m, 3H), 1.82 (tdd, 1H, *J* = 12.0, 4.6, 3.2 Hz), 1.99 (m, 1H), 2.08 (ddd, 1H, *J* = 13.7, 3.4, 1.7 Hz), 2.48−2.55 (m, 2H), 2.73 (td, 1H, *J* = 11.2, 3.4 Hz), 3.06 (dd, 1H, *J* = 13.7, 5.9 Hz), 3.73 (s, 3H); ^{13}C NMR (125 MHz) δ 20.4, 25.0, 25.3, 26.0, 30.9, 33.5, 40.0, 44.4, 49.1, 49.7, 51.3, 174.8, 212.3; MS *m*/*z* 224 (M^+, 9%), 147 (15), 124 (23), 85 (68), 83 (100), 58 (15), 47 (23). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.40; H, 8.75.

Methyl (1*S*,2*R*,4a*R*,8*S*,8a*R*)-Decahydro-4-hydroxy-2-methylnaphthalene-1-carboxylate (18). To a stirred solution of ketoester **17** (1.04 g, 4.6 mmol) in THF (30 mL) was added L-selectride (1.0 M solution in THF, 7 mL, 7 mmol) at 0 °C under nitrogen, and stirring was continued for 1.5 h. After addition of 1 N aqueous NaOH (24 mL) and hydrogen peroxide (30 wt %, 10.5 mL, 93 mmol), the resulting solution was stirred at room temperature for 11.5 h. The solution was neutralized with 1 N aqueous HCl, and the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was treated with diazomethane and purified by column chromatography (EtOAc/*n*-hexane 1:5) to afford hydroxyester **18** (944 mg, 90%) as crystals: mp = 64−65 °C; $[\alpha]_D^{20}$ = +39.49 (*c* = 1.00); IR 3488, 2994, 1725, 1449, 1435, 1388, 1327, 1294, 1167, 1146, 1105, 1003 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (qd, 1H, *J* = 12.0, 3.7 Hz), 1.27 (d, 3H[a], *J* = 7.6 Hz), 1.20−1.38 (m, 4H[a]), 1.53 (m, 1H), 1.58−1.64 (m, 2H), 1.69−1.70 (m, 2H), 1.82−1.92 (m, 2H), 2.60 (qdt, 1H, *J* = 7.6, 5.9, 1.7 Hz), 2.21 (ddd, 1H, *J* = 14.6, 5.9, 3.4 Hz), 2.42 (dd, 1H, *J* = 2.7, 1.7 Hz), 3.63 (s, 3H), 3.84 (m, 1H); [a]total 4H; ^{13}C NMR (125 MHz) δ 22.7, 26.2, 26.6, 29.3, 29.9, 31.0, 31.1, 34.6, 39.6, 50.4, 50.8, 70.8, 175.7; MS *m*/*z* 208 ($M^+ - H_2O$, 25%), 176 (29), 149 (100), 148 (85), 108 (66), 93 (34), 79 (36). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.91; H, 9.83.

Methyl (1*R*,2*R*,4a*R*,8*S*,8a*R*)-Decahydro-4-hydroxy-2-methylnaphthalene-1-carboxylate (19). To a stirred solution of axial ester **18** (226 mg, 1 mmol) in DMSO (50 μL) were added potassium *tert*-butoxide (116 mg, 1 mmol) and *tert*-butyl alcohol (190 μL, 2 mmol) under nitrogen atmosphere, and stirring was continued at room temperature for 23 h. After addition of 1 N aqueous HCl, the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with H_2O and brine (×2), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Treatment with diazomethane followed by MPLC (EtOAc/*n*-hexane 2:3) of the residue provided isomeric equatorial ester **19** (178 mg, 78%) as a colorless oil: $[\alpha]_D^{20}$ = −31.16 (*c* = 1.00); IR 3488, 2857, 1730, 1449, 1437, 1298, 1265, 1169, 1146, 1009 cm^{-1}; ^1H NMR (500 MHz) δ 0.81 (qd, 1H, *J* = 12.3, 3.4 Hz), 1.09 (m, 1H[a]), 1.10 (d, 3H[a], *J* = 7.3 Hz), 1.22−1.34 (m, 2H), 1.38−1.44 (m, 2H), 1.54 (m, 1H), 1.70 (m, 1H), 1.74−1.82 (m, 2H), 1.84−1.94 (m, 3H), 2.23 (qddd, 1H, *J* = 7.3, 5.4, 4.9, 2.4 Hz), 2.28 (dd, 1H, *J* = 11.0, 4.9 Hz), 3.67 (s, 3H), 3.78 (m, 1H); [a]total 4H; ^{13}C NMR (125 MHz) δ 17.9, 26.1, 26.5, 29.4, 30.1, 31.8, 39.0, 46.0, 51.1, 53.2, 70.6, 174.8; MS *m*/*z* 226 (M^+, 7%), 208 (14), 149 (77), 148 (100), 81 (33), 43 (36), 41 (39). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.94; H, 9.69.

***O*-[Methyl (1*R*,2*R*,4a*R*,8*S*,8a*R*)-Decahydro-2-methylnaphthalene-1-carboxylate-4-yl] *S*-Methyl Dithiocarbonate (20).** To a stirred solution of the equatorial ester **19** (185 mg, 0.8 mmol) in THF (8.2 mL) was added potassium *tert*-butoxide (236 mg, 2.0 mmol) at −50 °C under nitrogen. After the resulting solution was stirred for 40 min, carbon disulfide (74 μL, 1.2 mmol) was added at −35 °C. After this solution was stirred for 50 min, methyl iodide (79 μL, 1.2 mmol) was added, and stirring was continued for 10 min. The reaction was quenched by aqueous ammonium chloride, and the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc/*n*-hexane 1:9) to afford xanthate **20** (258.1 mg, 91%) as a yellow oil: $[\alpha]_D^{20}$ = −29.87 (*c* = 1.10); IR 2936, 1730, 1449, 1435, 1298, 1252, 1169, 1144, 1055 cm^{-1}; ^1H NMR (200 MHz) δ 0.82 (m, 1H), 0.99 (d, 3H, *J* = 7.3 Hz), 1.20−2.08 (m, 11H), 2.18−2.40 (m, 2H), 2.58 (s, 3H), 3.68 (s, 3H), 5.70 (m, 1H); ^{13}C NMR (50 MHz) δ 17.1, 18.9, 25.9, 26.3, 29.0, 29.7, 31.7, 32.6, 35.1, 45.1, 51.3, 52.5, 82.8, 174.3, 215.6; MS *m*/*z* 316 (M^+, 0.5%), 285 (2), 209 (19), 208 (11), 150 (16), 149 (100). Anal. Calcd for $C_{15}H_{24}O_3S_2$: C, 56.93; H, 7.66; S, 20.26. Found: C, 57.15; H, 7.66; S, 20.10.

Methyl (1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methylnaphthalene-1-carboxylate (12). A stirred solution of the xanthate **20** (43.6 mg, 0.14 mmol) in 1-methylnaphthalene (0.7 mL) was heated at 190 °C for 3 h under nitrogen. After dilution with EtOAc, the solution was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was used in the next step without further purification.

(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methylnaphthalene-1-methanol (21). To a stirred solution of the ester **12** in diethyl ether (2.8 mL) was added lithium aluminumhydride (17 mg, 0.41 mmol, 3 equiv) at 0 °C under nitrogen. After this solution was stirred for 15 min, aq NH_4Cl was added. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by column chromatography (EtOAc/*n*-hexane 1:6) to afford alcohol **21** (22 mg, 89% from **20**) as an amorphous solid: mp = 89−90 °C; $[\alpha]_D^{20}$ = −126.82 (*c* = 1.07); IR 3488, 2928, 1448, 1095, 1017, 1001 cm^{-1}; ^1H NMR (200 MHz) δ 0.93 (d, 3H[a], *J* = 7.3 Hz), 0.89−1.48 (m, 6H[a]), 1.52−1.84 (m, 6H), 2.42 (m, 1H), 3.53 (td, 1H, *J* = 10.7, 5.6 Hz), 3.84 (td, 1H, *J* = 10.7, 5.4 Hz), 5.38 (d, 1H, *J* = 9.8 Hz), 5.60 (ddd, 1H, *J* = 9.8, 4.7, 2.4 Hz); [a]total 9H; ^{13}C NMR (50 MHz) δ 15.5, 26.5, 26.8, 29.3, 31.5, 33.2, 37.7, 43.6, 44.1, 63.0, 131.2, 132.25; MS *m*/*z* 180 (M^+, 13%), 162 (10), 150 (16), 149 (100), 147 (13), 107 (13), 105 (17), 91 (16), 81 (21), 79 (15). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.02; H, 10.98.

(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methylnaphthalene-1-carboxylic Acid (22). To a solution of the alcohol **21** (92 mg, 0.5 mmol) in acetone (2.6 mL) was added Jones reagent dropwise at 0 °C until the orange color persisted. After addition of H_2O, the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure followed by column chromatography (MeOH/$CHCl_3$ 1:10) of the residue afforded carboxylic acid **22** (90 mg, 91%) as crystals: mp = 142−143 °C; $[\alpha]_D^{20}$ = −141 (*c* = 0.2); IR 3099, 2920, 1709, 1448, 1292, 1222, 1143, 1111 cm^{-1}; ^1H NMR (200 MHz) δ 0.8−1.0 (m, 1H), 1.0 (d, 3H, *J* = 6.9 Hz), 1.05−1.5 (m, 5H), 1.68−1.85 (m, 4H), 1.95−2.10 (m, 1H), 2.55−2.70 (m, 2H), 5.4 (d, 1H, *J* = 9.8 Hz), 5.51−5.61 (m, 1H).

Ethyl 5-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methylnaphthyl]-3,5-dioxopentanoate (24a). A solution of the carboxylic acid **22** (23 mg, 0.12 mmol) in $SOCl_2$ (357 μL, 4.9 mmol) was heated at 55 °C for 2 h. After evaporation of $SOCl_2$ in vacuo, a solution of imidazole (16 mg, 0.23 mmol) in THF (0.23 mL) was added and the resulting solution was stirred at room temperature overnight. Evaporation of the solvent provided imidazolide **23** as a solid which was used immediately for the next reaction without further purification.

Sodium hydride (9.4 mg, 60%, 0.23 mmol) was washed with *n*-hexane twice. To a stirred suspension of NaH in THF (0.3 mL) was added ethyl acetoacetate (30 μL, 0.23 mmol) at 0 °C under nitrogen atmosphere. After this mixture was stirred for 10 min, a solution of *n*-BuLi (144 μL, 1.6 M in *n*-hexane, 0.23 mmol) was added. Subsequently, after 10 min, a solution of the imidazolide **23** in THF (0.26 mL) was added. Stirring was continued for 1.5 h, and the reaction was quenched by addition of aq NH_4Cl. The reaction mixture was extracted with EtOAc (×2). Combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure followed by column chromatography (EtOAc/*n*-hexane 1:3) and MPLC (EtOAc/*n*-hexane 1:3) gave β,δ-diketoester **24a** (16 mg, 45% from **22**) as an oil which was used immediately for the next transformation: IR 2967, 1736, 1599, 1448, 1376, 1311, 1158, 1033 cm^{-1}; ^1H NMR (200 MHz) δ 0.75−2.0 (m, 11H), 0.94 (d, 3H, J = 6.8 Hz), 1.29 (t, 3H, J = 7.0 Hz), 2.35−2.50 (m, 2H), 3.34 (d, 2H, J = 2.0 Hz), 4.2 (q, 2H, J = 7.0 Hz), 5.35−5.47 (brd, 1H), 5.5−5.65 (m, 2H).

(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methylnaphthalene-1-carbaldehyde (25). To a suspension of PCC (65 mg, 0.3 mmol) and 4-Å molecular sieves powder (65 mg) in CH_2Cl_2 (2 mL) was added a solution of the alcohol **21** (18 mg, 0.1 mmol) in CH_2Cl_2 (3 mL) under nitrogen, and the resulting mixture was stirred at room temperature for 30 min. After dilution with EtOAc, the reaction mixture was subjected to column chromatography (EtOAc/*n*-hexane 1:6) to give aldehyde **25** (17 mg) which was immediately used for the next step: ^1H NMR (200 MHz) δ 1.05 (d, 3H[a], J = 7.0 Hz), 0.80−1.99 (m, 10H[a]), 2.38 (m, 1H), 2.59 (m, 1H), 5.42 (d, 1H, J = 10.0 Hz), 5.55 (ddd, 1H, J = 10.0, 4.2, 2.1 Hz), 9.75 (d, 1H, J = 4.4 Hz); [a]total 13H.

Methyl 5-Hydroxy-5-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-3-oxopentanoate (26). To a stirred solution of the aldehyde **25** (17 mg) in CH_2Cl_2 (2 mL) were added a solution of methyl acetoacetate bis(TMS) enol ether (127 μL, 0.5 mmol) in CH_2Cl_2 (3 mL) and $TiCl_4$ (1.0 M in CH_2Cl_2, 22 μL, 0.2 mmol) at −78 °C under nitrogen atmosphere, and the resulting solution was stirred for 1 h. After addition of H_2O, the reaction mixture was extracted with EtOAc (×2). The combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure followed by chromatography (EtOAc/*n*-hexane 1:4) of the residue afforded a mixture of methyl acetoacetate and hydroxyketoester **26** (22 mg, 75% from the alcohol **21**) which was used for the next step without further purification: IR 3568, 2957, 1746, 1712, 1450, 1440, 1323, 1153, 1007 cm^{-1}; ^1H NMR (200 MHz) δ 0.99 (d, 1.6H[a,b], J = 7.0 Hz), 1.08 (d, 1.4H[a,b], J = 7.0 Hz), 0.95−1.48 (m, 6H[b]), 1.50−1.88 (m, 4H), 2.03 (m, 1H), 2.22−2.50 (m, 2H), 2.58−2.99 (m, 2H), 3.51 (s, 1.1H[c]), 3.53 (s, 0.9H[c]), 3.75 (s, 3H), 4.25 (m, 0.55H[d]), 4.46 (m, 0.45[d]), 5.32 (d, 1H, J = 9.7 Hz), 5.64 (ddd, 1H, J = 9.7, 4.1, 2.0 Hz); [a]total 3H, [b]total 9H, [c]total 2H, [d]total 1H.

Methyl 4-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methylnaphthyl]-3,5-dioxobutanoate (24b). To a stirred solution of the hydroxyketoester **26** (27 mg, 0.09 mmol) in acetone (1 mL) was added Jones reagent dropwise at 0 °C until the orange color persisted. After addition of H_2O, the reaction mixture was extracted with EtOAc (×2). Combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure followed by column chromatography (EtOAc/*n*-hexane 1:8) gave β,δ-diketoester **24** (20 mg, 74%) as a yellow oil: IR 2959, 1742, 1610, 1593, 1450, 1439, 1321, 1156, 1130, 1015 cm^{-1}; ^1H NMR (200 MHz) δ 0.93 (d, 3H[a], J = 7.0 Hz), 0.80−1.95 (m, 11H[a]), 2.38−2.50 (m, 2H), 3.36 (s, 2H), 3.75 (s, 3H), 5.39 (d, 1H, J = 9.8 Hz), 5.55 (ddd, 1H[b], J = 9.8, 3.8, 2.5 Hz), 5.59 (s, 1H[b]); [a]total 14H, [b]total 2H.

4-Hydroxy-6-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-2*H*-pyran-2-one (13). To a stirred solution of β,δ-diketoester **24** (20 mg, 0.068 mmol) in benzene (1 mL) was added DBU (20 μL, 0.14 mmol) under nitrogen, and the solution was stirred at 60 °C for 2.5 h. The reaction was quenched by 1 N aqueous HCl at 0 °C, and the reaction mixture was extracted with CH_2Cl_2 (×3). The combined organic layers were washed with H_2O and brine. After they were dried over anhydrous Na_2SO_4, the solvent was removed under reduced pressure. The residue was purified by column chromatography (MeOH/$CHCl_3$ 0:1 then 1:10) to give 4-hydroxy-2-pyrone **13** (16.3 mg, 93%) as crystals: ^1H NMR (200 MHz) δ 0.85 (m, 1H[a]), 0.93 (d, 3H[a], J = 7.1 Hz), 1.02−1.82 (m, 10H), 2.47 (m, 1H), 2.68 (dd, 1H, J = 11.2, 6.0 Hz), 5.42 (d, 1H, J = 9.7 Hz), 5.52 (d, 1H[b], J = 2.1 Hz), 5.56 (ddd, 1H[b], J = 9.7, 4.2, 2.4 Hz), 5.94 (d, 1H, J = 2.1 Hz); [a]total 4H, [b]total 2H.

4-Hydroxy-6-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-3-phenylthiomethyl-2*H*-pyran-2-one (37). To a stirred suspension of paraformaldehyde (3.0 mg, 0.095 mmol), thiophenol (0.05 mL, 0.19 mmol), acetic acid (3 μL, 0.052 mmol), and piperidine (3 μL, 0.030 mmol) in EtOH (2 mL) was added a solution of 4-hydroxy-2-pyrone **13** (16 mg, 0.063 mmol) in EtOH (3 mL) at 55 °C under nitrogen. The resulting mixture was stirred for 17 h and concentrated under reduced pressure. Purification of the residue by column chromatography (MeOH/$CHCl_3$ 0:1 then 1:50) provided 3-phenylthiomethyl-2-pyrone **37** (19.7 mg, 82%) as an amorphous solid: ^1H NMR (200 MHz) δ 0.80 (m, 1H[a]), 0.85 (d, 3H[a], J = 7.2 Hz), 1.02−1.82 (m, 9H), 2.40 (m, 1H), 2.58 (dd, 1H, J = 11.1, 6.0 Hz), 4.11 (s, 2H), 5.39 (d, 1H, J = 9.9 Hz), 5.56 (ddd, 1H, J = 9.9, 4.1, 2.3 Hz), 5.86 (s, 1H), 7.12−7.54 (m, 5H), 8.84 (brs, 1H); [a]total 4H.

4-Methoxy-6-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-3-phenylthiomethyl-2*H*-pyran-2-one (38). A suspension of 4-hydroxypyrone **37** (127 mg, 0.33 mmol), dimethyl sulfate (157 mL, 1.66 mmol), and potassium carbonate (231 mg, 1.66 mmol) in acetone (3.3 mL) was stirred at room temperature for 30 min under nitrogen. H_2O (1.7 mL) was added, and the resulting solution was stirred at room temperature for 14.5 h. After addition of aqueous ammonium chloride, the reaction mixture was extracted with CH_2Cl_2 (×2). Combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by MPLC (EtOAc/*n*-hexane 1:2) of the residue provided 4-methoxy-2-pyrone **38** (101.5 mg, 77%) as a viscous oil: $[\alpha]_D^{20}$ = −121.67 (c = 0.98); IR 2932, 1703, 1640, 1563, 1464, 1406, 1358, 1261, 1125, 1026 cm^{-1}; ^1H NMR (200 MHz) δ 0.87 (m, 1H[a]), 0.95 (d, 3H[a], J = 7.1 Hz), 1.02−1.84 (m, 9H), 2.43 (m, 1H), 2.65 (dd, 1H, J = 10.9, 6.0 Hz), 3.72 (s, 3H), 3.98 (s, 2H), 5.42 (d, 1H, J = 9.9 Hz), 5.55 (ddd, 1H, J = 9.9, 4.2, 2.3 Hz), 5.93 (s, 1H), 7.10−7.31 (m, 3H), 7.40−7.48 (m, 2H); [a]total 4H; ^{13}C NMR (50 MHz) δ 17.8, 26.4, 26.6, 28.3, 30.2, 33.0, 35.5, 36.5, 43.1, 49.7, 56.3, 95.8, 101.3, 126.5, 128.5, 130.9, 131.1, 131.4, 167.9.

4-Methoxy-6-[(1*R*,2*R*,4a*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-3-phenylsulfinylmethyl-2*H*-pyran-2-one (39). To a stirred solution of the phenylthiomethylpyrone **38** (69 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added *m*-CPBA (80%, 37 mg, 0.17 mmol) at 0 °C under nitrogen atmosphere. After this solution was stirred for 15 min, aqueous sodium hydrogencarbonate was added and the reaction mixture was extracted with CH_2Cl_2 (×2). The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was purified by MPLC (EtOAc/*n*-hexane 6:1) to afford 3-phenylsulfinyl-2-pyrone **39** (less polar diastereomer 28 mg, more polar diastereomer 34 mg, total 88%) as a viscous oil. Less polar diastereomer: IR 2928, 1703, 1638, 1563, 1466, 1408, 1356, 1036 cm^{-1}; ^1H NMR (200 MHz) δ 0.90 (m, 1H), 0.95 (d, 3H, J = 7.2 Hz), 1.02−1.83 (m, 9H), 2.45 (m, 1H), 2.67 (dd, 1H, J = 10.8, 5.9 Hz), 3.75 (s, 3H), 3.90 (d, 1H, J = 12.1 Hz), 4.13 (d, 1H, J = 12.1 Hz), 5.42 (d, 1H, J = 9.9 Hz), 5.56 (ddd, 1H, J = 9.9, 4.1, 2.2 Hz), 5.97 (s, 1H), 7.42−7.51 (m, 3H), 7.60−7.68 (m,

2H). More polar diastereomer: IR 2857, 1703, 1638, 1563, 1466, 1408, 1356, 1256, 1037, 1030 cm^{-1}; ^1H NMR (200 MHz) δ 0.88 (m, 1H), 0.95 (d, 3H, J = 7.1 Hz), 1.03−1.89 (m, 9H), 2.48 (m, 1H), 2.67 (dd, 1H, J = 10.9, 5.9 Hz), 3.74 (s, 3H), 3.88 (d, 1H, J = 12.1 Hz), 4.13 (d, 1H, J = 12.1 Hz), 5.43 (d, 1H, J = 9.9 Hz), 5.56 (ddd, 1H, J = 9.9, 4.1, 2.2 Hz), 5.97 (s, 1H), 7.42−7.51 (m, 3H), 7.60−7.71 (m, 2H).

Solanapyrone D (1). To a stirred solution of the sulfoxide **39** (20 mg, 0.05 mmol) in CH_2Cl_2 (EtOH free, 3 mL) were added DEATMS (36 μL, 0.19 mmol) and TMSOTf (25 μL, 0.14 mmol) at −25 °C under nitrogen. After the solution was stirred for 90 min with gradual warming to −5 °C, TBAF (0.15 mL, 1 M solution in THF) was added and stirring was continued for 20 min. The solution was diluted with EtOAc and passed through a short column of silica gel. Evaporation of the solvent followed by MPLC (EtOAc) purification furnished solanapyrone D (**1**) (9.9 mg, 69%) as an oil: $[\alpha]_D^{22.5} = -148.66$ (c = 0.60); IR 2930, 2861, 1726, 1686, 1617, 1520, 1375, 1342, 1265 cm^{-1}; ^1H NMR (500 MHz) δ 0.90 (m, 1H), 0.99 (d, 3H, J = 7.1 Hz), 1.13 (m, 1H), 1.22−1.42 (m, 3H), 1.53−1.88 (m, 5H), 2.51 (m, 1H), 2.75 (dd, 1H, J = 11.2, 5.9 Hz), 4.06 (s, 3H), 5.44 (d, 1H, J = 9.9 Hz), 5.57 (ddd, 1H, J = 9.8, 4.4, 2.4 Hz), 6.12 (s, 1H), 10.15 (s, 1H); ^{13}C NMR (125 MHz) δ 17.7, 26.3, 26.4, 30.2, 32.9, 35.5, 36.5, 42.8, 50.7, 57.6, 95.9, 101.6, 130.6, 131.0, 162.3, 173.6, 176.2, 186.8.

Solanapyrone E (2). To a stirred solution of the sulfoxide **39** (4.7 mg, 0.01 mmol) in CH_2Cl_2 (EtOH free, 1.1 mL) was added trifluoroacetic anhydride (7 μL, 0.04 mmol) at 0 °C under nitrogen. After the solution was stirred for 30 min at 0 °C, 1 N aqueous NaOH (1 mL) and THF (2 mL) were added and stirring was continued for 40 min at room temperature. The reaction mixture was extracted with CH_2Cl_2 (×2), and the combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by MPLC (EtOAc/*n*-hexane 10:1) purification furnished solanapyrone E (**2**) (2.2 mg, 62%) as an amorphous solid: $[\alpha]_D^{20} = -154.88$ (c = 0.93); IR 3504, 2926, 2855, 1690, 1636, 1564, 1466, 1626, 1098, 1013 cm^{-1}; ^1H NMR (500 MHz) δ 0.88 (qd, 1H, J = 12.5, 3.2 Hz), 0.97 (d, 3H, J = 7.1 Hz), 1.12 (qd, 1H, J = 12.8, 3.1 Hz), 1.24−1.42 (m, 2H), 1.61−1.70 (m, 2H), 1.71−1.81 (m, 4H), 2.46 (m, 1H), 2.69 (dd, 1H, J = 11.2, 5.9 Hz), 2.97 (brs, 1H), 3.90 (s, 3H), 4.55 (s, 2H), 5.45 (d, 1H, J = 10.0 Hz), 5.55 (ddd, 1H, J = 10.0, 4.4, 2.6 Hz), 6.05 (s, 1H); ^{13}C NMR (125 MHz) δ 17.8, 26.4, 26.5, 30.2, 33.0, 35.5, 36.6, 43.1, 49.8, 54.7, 56.4, 96.2, 103.7, 130.9, 131.0, 165.3, 166.5, 168.6.

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Supporting Information Available: NMR spectra of compounds **1**, **2**, **13**, **24b**, **26**, **37**, **38**, and **39** as well as natural **1** and **2** (PDF, 19 pages). This material is available free of charge via the Internet at http://pubs.acs.org.

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