First Total Synthesis of (±)-Prelunularin

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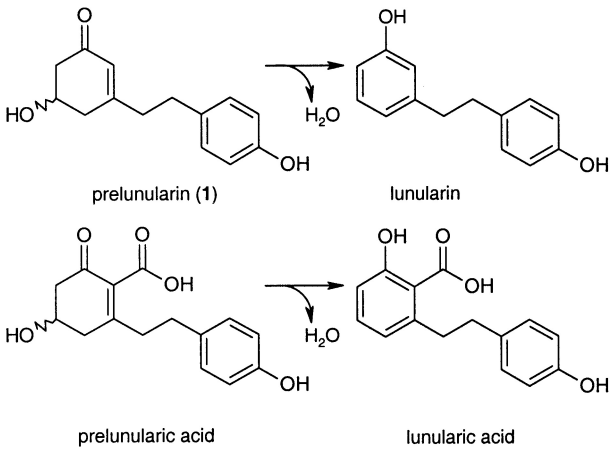
Abstract: The first total synthesis of (±)-prelunularin is described employing an intramolecular aldol addition/sulfinate elimination tandem reaction. Investigations on the mechanism of the one-pot cyclization reaction using time-dependent NMR spectroscopy suggested that the sulfinate elimination took place before the intramolecular ring-closing aldol addition.

Key words: tandem reactions, natural products, intramolecular cyclization

Bryophytes contain a large number of structurally novel natural compounds.[1,2] In particular, we focused on the synthesis of cyclic and acyclic bisbibenzylic structures with biological activities.[3–5]

In 1994 Kunz and Becker[6] reported for the first time the isolation of prelunularin (**1**) from the acetone extract of *Ricciocarpos natans*, a liverwort found in Central Europe. Later, prelunularin was also isolated from *Conocephalum conicum*, [7] one of the most widespread liverwort species in Japan. The authors suggested that this secondary metabolite plays an important biochemical role as a genuine precursor of lunularin (Scheme 1), a bibenzylic compound found in many liverwort species.[8,9]

Prelunularin (**1**) is, to the best of our knowledge, the only reported natural product containing a 3-substituted 5-hydroxycyclohex-2-enone skeleton. Not only this unique structural feature, but also the difficulty to obtain such a structure, prompted us to attempt the total synthesis of **1**. Prelunularin and prelunularic acid were easily converted into the corresponding aromatic compounds lunularin and lunularic acid[1,6] under mild basic as well as acidic conditions. These results suggested the difficulties to synthesize and handle these natural products.



Scheme 1 Suggested biogenesis of lunularin and lunularic acid.

In our preliminary studies, aimed at the preparation of the model structures 3-alkyl-5-hydroxycyclohex-2-enones, we attempted an intramolecular cyclization of a 1,5-dicarbonyl compound to obtain the central core of the molecule in the last step of our synthesis. We chose this strategy due to the easy elimination of the hydroxyl group.[10] Herein we report the first total synthesis of racemic prelunularin (**1**) via aldol addition/sulfinate elimination tandem reactions.

Starting with the aldehyde **2**, available from 3-(4-hydroxyphenyl)propionic acid by a known procedure,[11] Wittig reaction with acetonyltriphenylphosphonium chloride was performed under Boden's conditions[12] to yield **3** as a single *E*-isomer. Michael type addition of *p*-toluenesulfinic acid sodium salt to the α,β-unsaturated ketone **3** was performed in acetic acid/ethanol medium affording **4** in 90% yield. The carbonyl group of the δ-oxosulfone was protected as a ketal using ethylene glycol in the presence of catalytic amount of *p*-toluenesulfonic acid to give **5** in 80% yield. At this point, our synthetic strategy was based on the formation of α-sulfonylcarbanion from **5** using *tert*-butyllithium in anhydrous tetrahydrofuran. Further addition of allyl bromide provided the alkylated compound **6**, which was treated under reductive ozonolysis to afford aldehyde **7** in 60% overall yield. Our strategy called for the protection of the carbonyl group with 1,2-ethanedithiol in presence of $BF_3{\cdot}OEt_2$ to prevent aldehyde decomposition in acidic conditions, according to our previously report.[10] This treatment afforded thioacetal **8**, where the removal of the ketal group took place simultaneously to the formation of the dithiolane (Scheme 2).

Deprotection of **8** with $HgCl_2/CaCO_3$ in aqueous acetonitrile afforded keto aldehyde **9** in 50% yield after six hours. According to studies on kinetics and mechanism, dithiolane hydrolysis proceeds much faster at lower chloride ion concentration.[13,14] We found an efficient method by adding silver nitrate to the reaction mixture in order to decrease the chloride ion concentration. Under this new procedure the reaction occurred quantitatively to render keto aldehyde **9** in one hour.

Compound **9** was conceived as a structural entity, called *holosynthon*, specifically designed to make the subse-

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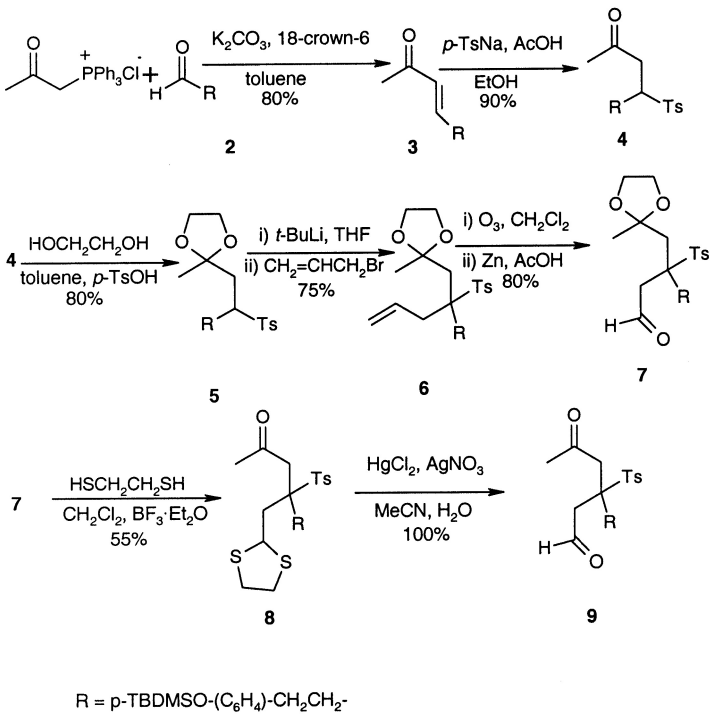
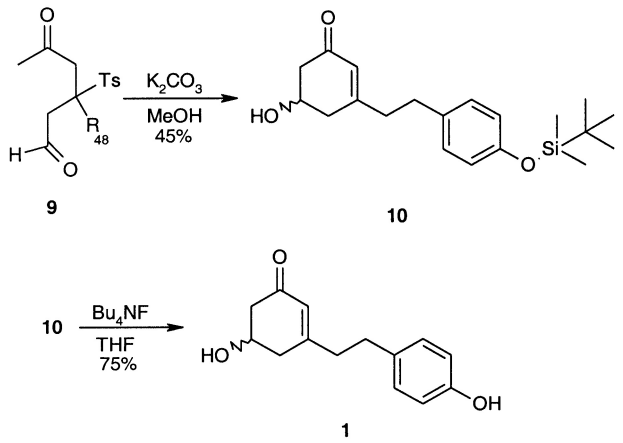


Scheme 2 Preparation of compound **9** from **3**.

quent tandem reactions.[15] In particular intramolecular cyclization was accomplished as shown in Scheme 3 by means of aldol addition/sulfinate elimination tandem reactions.

Using the optimized conditions, **9** was stirred with potassium carbonate in methanol at 0 °C for three hours and then the reaction mixture was left in a freezer overnight, affording **10** in 45% yield as a racemic mixture. Deprotection of *tert*-butyldimethylsilyloxy ether using tetrabutylammonium fluoride proceeded straightforward giving prelunularin (**1**) in 75% yield.

The ^{1}H and ^{13}C NMR spectra of the natural and synthetic samples were compared. According to Kunz and Becker's assignment,[6] two proton and two carbon signals could be exchanged. Application of two-dimensional NMR techniques allowed the unambiguous assignment of all ^{1}H and ^{13}C signals, along with two reassignments (data available on request from authors).

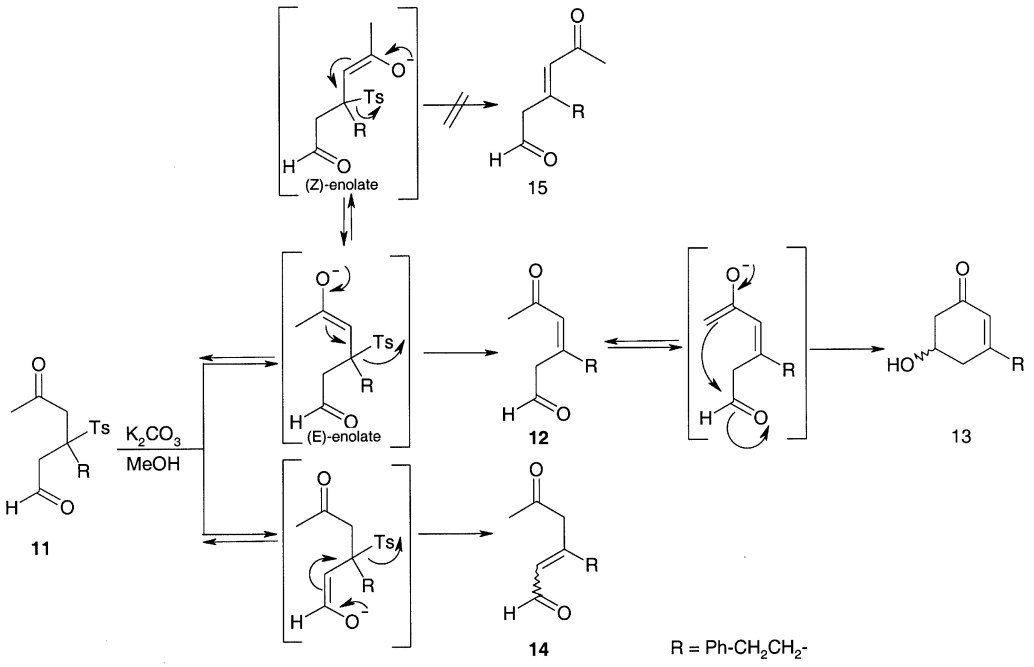


Scheme 3 Preparation of prelunularin (**1**) from keto aldehyde **9** via aldol addition/sulfinate elimination tandem reactions.

Having established the synthetic route to prelunularin (**1**), we turned our attention to study the mechanism of the intramolecular aldol addition/sulfinate elimination tandem reactions. In order to determine which of the two possible mechanisms (sulfinate elimination followed by intramolecular aldol addition, or the inverse pathway) is correct, these tandem reactions were monitored by ^{1}H NMR spectroscopy with a previously reported analogue molecule.[10]

When after 60 minutes the reaction was quenched and the mixture worked up, its ^{1}H NMR spectrum (Figure 1) revealed the presence of compounds, **12**, traces of **13** and **14** (mixture of *Z*/*E*-isomers). After 240 minutes (Figure 2) compound **12** was totally consumed and the signals of the final product **13** were easily identified (see experimental). The first step in this mechanism involves exclusively the formation of the thermodynamic (*E*)-enolate of **11** and the subsequent sulfinate elimination. Surprisingly, under these thermodynamic conditions, which normally permit equilibration between all the enolates, compound **15** was not detected. The second step can be regarded as the ring-closing aldol addition of the intermediate **12** according to Scheme 4.

In summary, we have achieved the first total synthesis of (±)-prelunularin (**1**) in 8 steps with 9% overall yield from **3**. We have shown the relevance of the '*holosynthon*' concept to access prelunularin using tandem aldol addition/sulfinate elimination reactions. Based on spectroscopic and experimental data, we proposed a mechanism for these reactions with a sulfinate elimination as the first step



Scheme 4 Proposed mechanistic pathway for the tandem reaction.

followed by intramolecular ring-closing by means of aldol addition.

Solvents were purified and dried by standard procedures before use. Petroleum ether used had bp 40–60 °C. Ozone was generated with Fisher Ozone 500. Melting points are uncorrected. IR spectra were recorded on Bomen, Hartman & Braun FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on Bruker AM 400 spectrometer. The chemical shifts are expressed in ppm (δ) downfield from TMS as internal standard. Mass spectra were obtained with a Shimadzu QP 1100 EX mass spectrometer. Elemental analyses were carried out on a Fision EA 1108 CHNS-O analyzer.

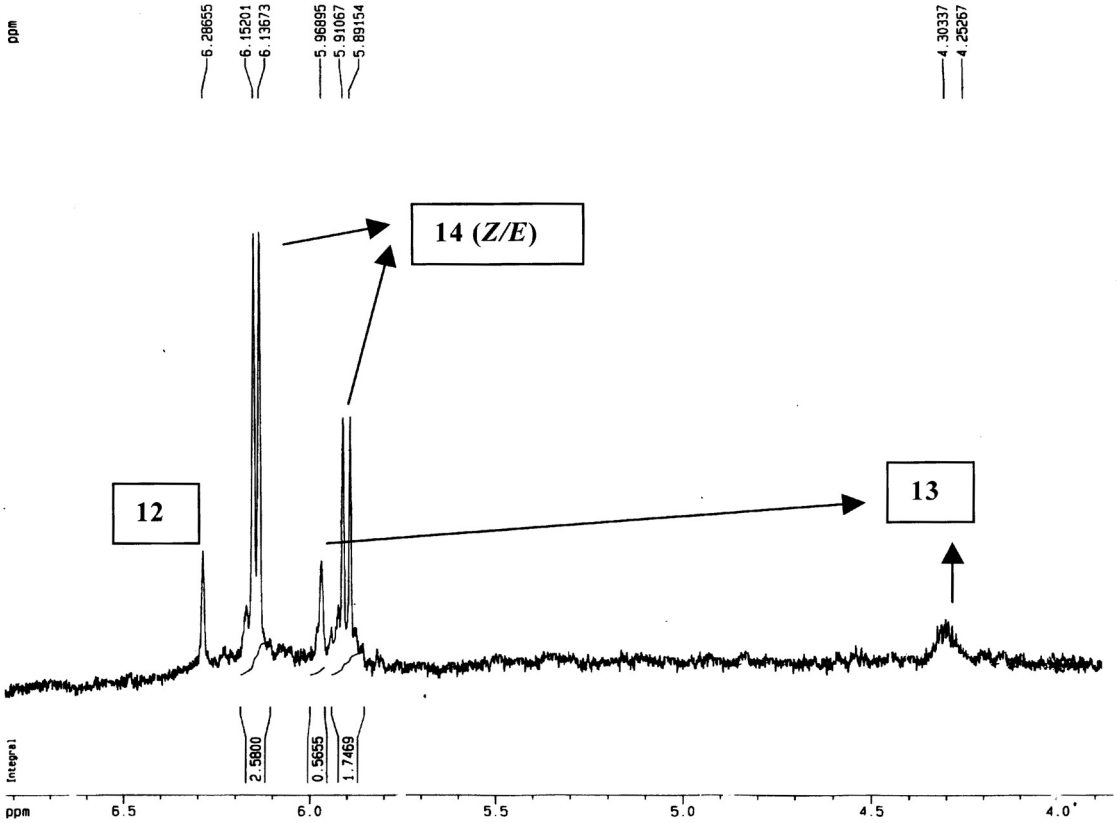


Figure 1 ^{1}H NMR spectrum after 60 minutes in $CDCl_3$

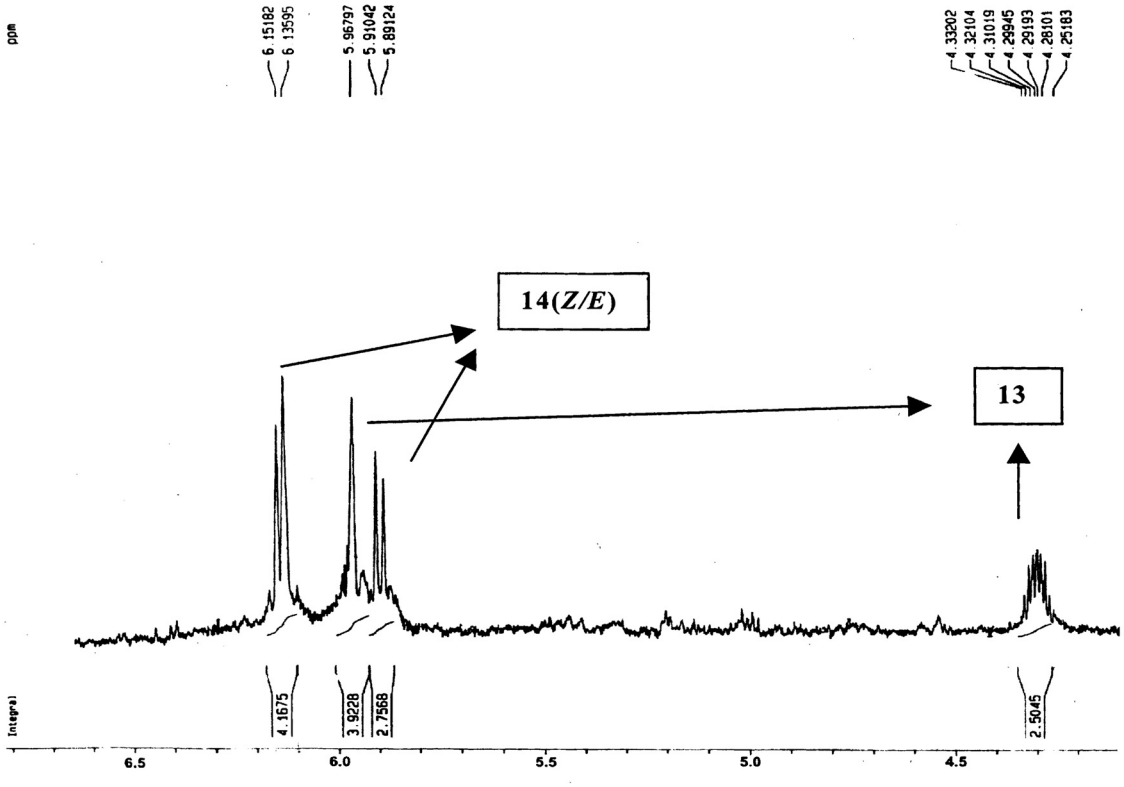


Figure 2 ^{1}H NMR spectrum after 240 minutes in $CDCl_3$

(3*E*)-6-[4-(*tert*-Butyldimethylsilyloxy)phenyl]hex-3-en-2-one (3)
To a stirred solution of **2** (1.50 g, 9.4 mmol) in toluene (50 mL), were added acetonyltriphenylphosphonium chloride (5.0 g, 14.1 mmol), K_2CO_3 (1.9g, 14.1 mmol) and 18-crown-6 ether (20 mg). The reaction mixture was refluxed for 2 h and poured into H_2O. The mixture was extracted with EtOAc (3 × 50 mL), the combined extracts were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, petroleum ether–EtOAc, 95:05) to afford 2.3 g (80%) of **3** as a colorless oil.

IR (KBr): 1676, 1611, 1509, 1253, 914 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.04 (d, 2 H, *J* = 8.4 Hz), 6.85–6.80 (m, 1 H), 6.78 (d, 2 H, *J* = 8.4 Hz), 6.09 (d, 1 H, *J* = 16.0 Hz), 2.72–2.76 (m, 2 H), 2.55–2.50 (m, 2 H), 2.23 (s, 3 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 198.8, 154.4, 147.6, 133.7, 132.0, 129.6 (2), 120.4 (2), 34.7, 34.0, 27.2, 26.1 (3), 18.6, –4.0.

MS (EI 20 eV): *m*/*z* (%) = 304 (M^+, 5), 247 (49), 221 (100), 141 (97).

Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 70.58, H, 9.52.

6-[4-(*tert*-Butyldimethylsilyloxy)phenyl]-4-[(4-methylphenyl)sulfonyl)]hexan-2-one (4)
To a stirred solution of **3** (3.0 g, 9.7 mmol) in EtOH (25 mL) was added AcOH (1.2 mL) and *p*-toluenesulfinic acid sodium salt dihydrate (4.2 g, 19.4 mmol). The mixture was stirred at r.t. for 48 h, diluted with Et_2O (100 mL) and washed with an aq sat. solution of $NaHCO_3$ (30 mL), followed by brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, petroleum ether–EtOAc, 7:3) to afford 4.0 g (90%) of **4** as a colorless oil.

IR (KBr): 1725, 1600, 1512, 1289, 1142, 1256, 912 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.75 (d, 2 H, *J* = 8.2 Hz), 7.35 (d, 2 H, *J* = 8.2 Hz), 6.91 (d, 2 H, *J* = 8.4 Hz), 6.72 (d, 2 H, *J* = 8.4 Hz), 3.78–3.70 (m, 1 H), 3.14 (dd, 1 H, *J* = 18.1, 5.3 Hz), 2.62 (dd, 1 H, *J* = 18.1, 5.3 Hz), 2.64–2.46 (m, 2 H), 2.46 (s, 3 H), 2.15 (s, 3 H), 2.15–2.05 (m, 1 H), 1.80–1.70 (m, 1 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 204.3, 254.4, 145.2, 135.1, 133.4, 130.3 (2), 129.5 (2), 129.2 (2), 120.4 (2), 59.6, 41.9, 32.4, 31.1, 30.5, 26.1 (3), 22.0, 18.6, –4.0.

MS (EI 70 eV): *m*/*z* (%) = 461 (M^+, 5), 286 (24), 247 (77), 221 (83), 141 (100).

Anal. Calcd for $C_{25}H_{36}O_4SSi$: C, 65.18; H, 7.88; S, 6.96. Found: C, 64.77; H, 7.89; S, 7. 10.

2-({4-[4-(*tert*-Butyldimethylsilyloxy)phenyl]}-2-[(4-methylphenyl)sulfonyl]butyl)-2-methyl-1,3-dioxolane (5)
To a solution of **4** (0.95 g, 2.1 mmol) in anhyd toluene (30 mL) was added ethylene glycol (0.4 mL, 7.2 mmol) and *p*-toluenesulfonic acid (20 mg). The solution was refluxed for 2.5 h using a Dean–Stark apparatus and allowed to cool. The reaction mixture was washed with an 10% aq solution of $NaHCO_3$ (20 mL), followed by brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, petroleum ether–EtOAc, 7:3) to afford 0.85 g (80%) of **5** as a colorless oil.

IR (KBr): 1609, 1510, 1256, 1144, 916 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.78 (d, 2 H, *J* = 8.0 Hz), 7.36 (d, 2 H, *J* = 8.0 Hz), 7.01 (d, 2 H, *J* = 8.2 Hz), 6.75 (d, 2 H, *J* = 8.0 Hz), 3.95–3.80 (m, 2 H), 3.75–3.60 (m, 2 H), 3.25–3.15 (m, 1 H), 2.90–2.75 (m, 1 H), 2.75–2.60 (m, 1 H), 2.46 (s, 3 H), 2.32 (d, 1 H, *J* = 14.7 Hz),

2.20–2.00 (m, 2 H), 1.90–1.80 (dd, 1 H, *J* = 14.7, 8.8 Hz) 1.19 (s, 3 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 154.2, 144.8, 135.6, 134.3, 130.1 (2), 129.9 (2), 129.3 (2), 120.3 (2), 109.2, 65.0, 64.6, 60.2, 37.5, 32.5, 32.0, 26.1 (3), 24.5, 22.0, 18.6, –4.0.

MS (IE 20 eV): *m*/*z* (%) = 504 (M^+, 15), 286 (39), 221 (89), 87 (100).

Anal. Calcd for $C_{27}H_{40}O_5SSi$: C, 64.25; H, 7.99; S, 6.35. Found: C, 64.65; H, 8.28; S, 6.05.

2-(2-{2-[4-(*tert*-Butyldimethylsilyloxy)phenyl]ethyl}-2-[(4-methylphenyl)sulfonyl]pent-4-enyl)-2-methyl-1,3-dioxolane (6)

A solution of *t*-BuLi (1.4 mL, 1.3 M, 1.8 mmol) in hexane was added dropwise to a cooled (0 °C) solution of **5** (0.90 g, 1.8 mmol) in anhyd THF (40 mL). After 20 min, allyl bromide (0.15 mL, 1.8 mmol) was added and the resulting solution was allowed to reach r.t. After 12 h, the reaction mixture was poured into H_2O and extracted with EtOAc (3 × 50 mL). The combined extracts were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, petroleum ether–EtOAc, 8:2) to afford 0.73 g (75%) of **6** as a colorless oil.

IR (KBr): 1600, 1509, 1288, 1136, 1256, 916, 1638 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.81 (d, 2 H, *J* = 8.2 Hz), 7.36 (d, 2 H, *J* = 8.2 Hz), 7.04 (d, 2 H, *J* = 8.4 Hz), 6.75 (d, 2 H, *J* = 8.4 Hz), 6.20–6.05 (m, 1 H), 5.10–5.00 (m, 2 H), 4.00–3.85 (m, 4 H), 3.05–2.80 (m, 2 H), 2.70–2.60 (dd, 1 H, *J* = 15.5, 6.8 Hz), 2.62–2.55 (d, 1 H, *J* = 15.3 Hz), 2.55–2.50 (dd, 1 H, *J* = 15.5, 6.2 Hz), 2.46 (s, 3 H), 2.39 (d, 1 H, *J* = 15.3 Hz), 2.20–2.00 (m, 1 H), 2.00–1.90 (m, 1 H), 1.39 (s, 3 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 154.2, 144.9, 135.5, 133.2. 130.8 (2), 130.0 (2), 129.8 (2), 120.3 (2), 110.2, 69.9, 64.1, 63.9, 41.6, 39.2, 38.5, 37.2, 36.4, 36.0, 32.2, 30.3, 30.0, 26.6, 26.0 (3), 22.0, 21.9, 18.5, –4.0.

MS (EI 20 eV): *m*/*z* (%) = 326 (21), 221 (19), 87 (100).

Anal. Calcd for $C_{30}H_{44}O_5SSi$: C, 64.14; H, 8.14; S, 5.88. Found: C, 64.40; H, 8.22; S, 5.95.

5-[4-(*tert*-Butyldimethylsilyloxy)phenyl]-3-(2-methyl-1,3-dioxolan-2-ylmethyl)-3-[(4-methylphenyl)sulfonyl]pentanal (7)

Oxygen containing 0.8 mmol of ozone per litre was passed through a cooled (–78 °C) solution of **6** (0.4 g, 0.68 mmol) in CH_2Cl_2 (30 mL) at a rate of 50 L/h during 10 min. After excess of ozone was purged under reduce pressure, the solution was cooled (–78 °C) and AcOH (0.25 mL) and zinc dust (0.1 g, 1.60 mmol) were added. The resulting solution was allowed to reach r.t. and after 2 h was filtered and washed with H_2O (20 mL), $NaHCO_3$ (10%) (20 mL), brine and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford 0.30 g (80%) of **7** as a yellow oil.

^{1}H NMR ($CDCl_3$): δ = 9.88 (m, 1 H), 7.78 (d, 2 H, *J* = 8.2 Hz), 7.40 (d, 2 H, *J* = 8.2 Hz), 7.00 (d, 2 H, *J* = 8.4 Hz), 6.75 (d, 2 H, *J* = 8.4 Hz), 4.10–3.80 (m, 4 H), 3.00–2.80 (m, 3 H), 2.72 (d, 1 H, *J* = 15.6 Hz), 2.65 (d, 1 H, *J* = 17.8 Hz), 2.55–2.45 (m, 4 H), 2.10–2.00 (m, 1 H), 2.00–1.85 (m, 1 H), 1.43 (s, 3 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 199.5, 154.3, 145.8, 134.7, 132.0, 131.0 (2), 130.2 (2), 129.5 (2), 120.4 (2), 110.5, 68.3, 64.2, 63.1, 46.8, 37.8, 34.1, 29.7, 26.1, 26.0 (3), 22.0, 18.6, –4.0.

Anal. Calcd for $C_{29}H_{42}O_6SSi$: C, 63.70; H, 7.74; S, 5.86. Found: C, 63.87; H, 7.64; S, 6.00.

6-[4-(*tert*-Butyldimethylsilyloxy)phenyl]-4-(1,3-dithiolan-2-ylmethyl)-4-[(4-methylphenyl)sulfonyl]hexan-2-one (8)

To a cooled (–20 °C) solution of **7** (1.7g, 3.2 mmol) in anhyd CH_2Cl_2 (60 mL) were added 1,2-ethanedithiol (0.3 mL, 3.2 mmol) and $BF_3{\cdot}OEt_2$ (0.15 mL). The reaction mixture was kept at this temperature for 15 h and then washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, petroleum ether–EtOAc, 7:3) to afford 1.02 g (55%) of **8** as a white solid; mp 139.5–140.0 °C.

^{1}H NMR ($CDCl_3$): δ = 7.79 (d, 2 H, *J* = 8.2 Hz), 7.40 (d, 2 H, *J* = 8.2 Hz), 7.00 (d, 2 H, *J* = 8.4 Hz), 6.74 (d, 2 H, *J* = 8.4 Hz), 5.15 (dd, 1 H, *J* = 8.6, 3.9 Hz), 3.44 (d, 1 H, *J* = 18.3 Hz), 3.30–3.05 (m, 5 H), 2.90–2.70 (m, 1 H), 2.60–2.40 (m, 5 H), 2.40–2.30 (m, 1 H), 2.28 (s, 3 H), 2.25–2.10 (m, 1 H), 2.00–1.90 (m, 1 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 204.8, 154.3, 145.8, 134.3, 132.4, 130.8 (2), 130.3 (2), 129.6 (2), 120.4 (2), 69.0, 48.7, 43.1, 40.7, 39.1, 38.6, 36.3, 31.9, 29.8, 26.1 (3), 22.0, 18.6, –4.0.

MS (EI 20 eV): *m*/*z* (%) = 424 (5), 149 (12), 105 (100).

Anal. Calcd for $C_{29}H_{42}O_4S_3Si$: C, 60.17; H, 7.31; S, 16.61. Found: C, 59.76; H, 7.41; S, 16.46.

3-{2-[4-(*tert*-Butyldimethylsilyloxy)phenyl]ethyl}-5-oxo-3-[(4-methylphenyl)sulfonyl]hexanal (9)

To a stirred solution of **8** (50 mg, 0.09 mmol) in MeCN–H_2O (8:2, 40 mL) were added $CaCO_3$ (17 mg, 0.18 mmol), $HgCl_2$ (103 mg, 0.38 mmol) and $AgNO_3$ (130 mg, 0.76 mmol). The reaction mixture was heated at 60 °C for 1 h. Then Et_2O (100 mL) was added, the solution was filtered and washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford 45 mg of **9** quantitatively as a colorless oil.

^{1}H NMR ($CDCl_3$): δ = 9.78 (m, 1 H), 7.77 (d, 2 H *J* = 8.2 Hz), 7.41 (d, 2 H, *J* = 8.2 Hz), 6.99 (d, 2 H, *J* = 8.4 Hz), 6.75 (d, 2 H, *J* = 8.4 Hz), 3.32 (d, 1 H, *J* = 18.0 Hz), 3.22 (d, 1 H, *J* = 18.0 Hz), 3.04 (dd, 1 H, *J* = 16.7, 2.5 Hz), 2.92 (dd, 1 H, *J* = 16.7, 1.5 Hz), 2.86–2.78 (td, 1 H, *J* = 12.5, 5.2 Hz), 2.63–2.55 (td, 1 H, *J* = 12.5, 5.6 Hz), 2.49 (s, 3 H), 2.24 (s, 3 H), 2.24–2.10 (m, 2 H), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 205.0, 198.3, 146.2, 133.7, 132.1, 130.9 (2), 130.4 (2), 129.6 (2), 120.5 (2), 67.8, 45.4, 41.7, 36.4, 32.0, 29.9, 26.1 (3), 22.1, 18.6, –4.0.

MS (EI 20 eV): *m*/*z* (%) = 328 (43), 221 (100), 121 (30).

Anal. Calcd for $C_{27}H_{38}O_5SSi$: C, 64.51; H, 7.62; S, 6.38. Found: C, 64.63; H, 7.48; S, 6.11.

3-[2-(4-*tert*-Butyldimethylsilyloxy)phenyl]ethyl-5-hydroxycyclohex-2-enone (10)

K_2CO_3 (26 mg, 0.18 mmol) was added to a cooled (0 °C) solution of **9** (48 mg, 0.09 mmol) in anhyd MeOH (15 mL). The reaction mixture was stirred at 0 °C for 3 h and then kept overnight in a freezer. The mixture was poured into H_2O and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, petroleum ether–EtOAc, 4:6) to afford 15 mg (45%) of **10** as a colorless oil.

^{1}H NMR ($CDCl_3$): δ = 7.03 (d, 2 H, *J* = 8.2 Hz), 6.77 (d, 2 H, *J* = 8.2 Hz), 5.96 (s, 1 H), 4.30 (m, 1 H), 2.80–2.77 (m, 2 H *J* = 7.7 Hz), 2.68 (dd, 1 H, *J* = 16.1, 4.0 Hz), 2.60 (dd, 1 H, *J* = 17.5, 4.1 Hz) 2.54 (t, 2 H, *J* = 7.7 Hz), 2.46 (dd, 1 H, *J* = 16.1, 8.7 Hz), 2.40 (dd, 1 H, *J* = 17.5, 6.8 Hz), 1.00 (s, 9 H), 0.20 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 197.9, 161.8, 156.2, 133.4, 129.5 (2), 120.52 (2), 126.6, 67.2, 46.8, 40.1, 39.1, 32.9, 26.1 (3), 18.6, –4.0.

MS (EI 20 eV): *m*/*z* (%) = 290 (11), 289 (72), 221 (100).

Anal. Calcd for $C_{20}H_{30}O_3Si$: C, 69.32; H, 8.73. Found: C, 69.65; H, 8.53.

Prelunularin (1)

A solution of TBAF (15mg, 0.06 mmol) in anhyd THF (1 mL) was added dropwise to a cooled (0 °C) solution of **10** (20 mg, 0.06 mmol) in anhyd THF (14 mL). After that, the reaction mixture was poured into H_2O and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel, EtOAc) to afford 10.4 mg (75%) of **1** as a white solid; mp 66.2–66.7 °C.

IR (disposable IR card): 3319, 2910, 2849, 1650, 1617, 1595, 1515, 1448, 1413, 1372, 1247 cm^{-1}.

^{1}H NMR (MeOD): δ = 7.04 (d, 2 H, *J* = 8.8 Hz), 6.72 (d, 2 H, *J* = 8.8 Hz), 5.85 (s, 1 H), 4.19 (m, 1 H), 2.77 (m, 2 H), 2.66 (dd, 1 H, *J* = 17.9, 4.2 Hz), 2.61 (dd, 1 H, *J* = 16.1, 4.2 Hz), 2.55 (m, 2 H), 2.40 (dd, 1 H, *J* = 17.9, 6.6 Hz), 2.39 (dd, 1 H, *J* = 16.1, 8.1 Hz).

^{13}C NMR (MeOD): δ = 200.1, 164.7, 155.8, 131.9, 129.3 (2), 126.6, 115.2 (2), 66.4, 45.8, 40.2, 38.4, 32.5.

MS (IE 20 eV): *m*/*z* (%) = 232 (M^+, 5), 107 (100).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.22, H, 7.02.

5-Oxo-3-phenethyl-3-[(4-methylphenyl)sulfonyl]hexanal (11)

IR (KBr): 1717, 1597, 1497, 1287, 1138 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 9.78 (dd, 1 H, *J* = 2.5, 1.7 Hz, CHO), 7.78 (d, 2 H, *J* = 8.2 Hz, $ArSO_2$), 7.40 (d, 2 H, *J* = 8.2 Hz, $ArSO_2$), 7.27 (m, 2 H, ArH), 7.18 (m, 3 H, ArH), 3.33 (d, 1 H, *J* = 18.0 Hz, C*H*$_2$COCH$_3$), 3.22 (d, 1 H, *J* = 18.0 Hz, C*H*$_2$COCH$_3$), 3.05 (dd, 1 H, *J* = 16.7, 2.6 Hz, C*H*$_2$CHO), 2.93 (dd, 1 H, *J* = 16.7, 1.7 Hz, C*H*$_2$CHO), 2.93–2.88 (m, 1 H, PhCH$_2$C*H*$_2$), 2.72–2.62 (m, 1 H, PhCH$_2$C*H*$_2$), 2.48 (s, 3 H, C*H*$_3$Ph), 2.25 (s, 3 H, CH$_3$C=O), 2.30–2.10 (m, 2 H, PhC*H*$_2$CH$_2$).

^{13}C NMR ($CDCl_3$): δ = 205.1, 198.3, 146.2, 141.1, 132.0, 130.9 (2), 130.8 (2), 129.0 (2), 128.9 (2), 126.7, 67.8, 45.4, 41.7, 36.4, 32.0, 30.1, 22.1.

MS (EI 20 eV): *m*/*z* (%) = 205 (9), 143 (12), 86 (100).

5-Hydroxy-3-phenethylcyclohex-2-enone (13)

^{1}H NMR ($CDCl_3$): δ = 7.31–7.38 (m, 5 H, ArH), 5.97 (s, 1 H, C=CH), 4.31 (m, 1 H, C*H*OH), 2.85 (t, 2 H, *J* = 7.8 Hz, PhC*H*$_2$), 2.70 (dd, 1 H, *J* = 16.3, 3.7 Hz, CH$_2$C=O), 2.64–2.52 (m, 3 H, PhCH$_2$C*H*$_2$ and CH$_2$C=C), 2.50–2.38 (m, 2 H, CH$_2$C=O and CH$_2$C=C).

^{13}C NMR ($CDCl_3$): δ = 198.2, 161.9, 140.8, 129.0 (2), 128.6 (2), 126.8, 126.6, 67.1, 46.7, 39.9, 39.1, 33.6.

MS (EI 70 eV): *m*/*z* (%) = 216 (M^+, 3), 198 ($M^+ – H_2O$, 7%), 91 (100).

5-Oxo-3-phenethylhex-3-enal (14) (1:2 Mixture of *Z*/*E* Isomers)

^{1}H NMR ($CDCl_3$): δ = 9.82 (d, 2 H, *J* = 6.1 Hz, CHO, alkene *E*), 9.77 (d, 1 H, *J* = 7.7 Hz, CHO, alkene *Z*), 7.40–7.10 (m, 15 H, ArH, alkene *E* and *Z*), 6.14 (d, 2 H, *J* = 6.1 Hz, C*H*CHO, alkene *E*), 5.90 (d, 1 H, *J* = 7.7 Hz, C*H*CHO, alkene *Z*), 3.73 (s, 4 H, C*H*$_2$COCH$_3$, alkene *E*), 3.32 (s, 2 H, C*H*$_2$COCH$_3$, alkene *Z*), 3.00–2.40 [m, 12 H, Ph(C*H*$_2$)$_2$, alkene *Z* and *E*], 2.25 (s, 3 H, CH$_2$COC*H*$_3$, alkene *E*), 2.20 (s, 3 H, CH$_2$COC*H*$_3$, alkene *Z*).

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