First Total Synthesis of Prionoid E, A Bioactive Rearranged Secoabietane Diterpene Quinone from *Salvia prionitis*

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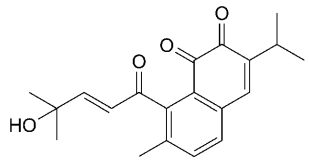
The first total synthesis of prionoid E (**1**), a rearranged secoabietane diterpene quinone isolated from *Salvia prionitis*, was achieved efficiently by means of *Wacker* oxidation (*Scheme 5*) and aldol condensation (*Scheme 7*) as the key steps in the synthetic sequence. Thus **1** was prepared in 15 steps in 3.7% yield starting on one hand from anisole (=methoxybenzene) and methylsuccinic anhydride (=dihydro-3-methylfuran-2,5-dione) *via* **4** (*Scheme 3* and *5*), and on the other hand from 2-hydroxy-2-methylpropanoic acid *via* **5** (*Scheme 6*).

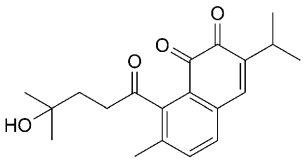
Introduction. – *Salvia prionitis*, a medicinal herb distributed in the southern provinces of the P. R. China, is used in Chinese folk medicine for the treatment of tonsillitis, pharyngitis, pulmonary infection, and bacillary dysentery. More than 50 compounds have been isolated from this plant including a number of abietane diterpenes such as 5,10-friedo-4,5-secoabietanediterpenes. Rearranged 4,5-secoabietane diterpenoids represent a new class of compounds with intensive biological activity [1–7]. Few research work on the bioactivity of this kind of diterpenoids has been reported up to now for their scarcity in nature. To the best of our knowledge, the broad spectrum of biological activity of *Salvia prionitis* is associated with the interesting rearranged secoabietane diterpenoids in the plant. Previously, we have reported the modification of saprorthoquinone and sapriparaquinone, two rearranged 4,5-secoabietane diterpenoids isolated from *Salvia prionitis*, and provided a series of novel analogues with potent antitumor or antioxidation activity [8–10]. Recently, *Chang et al.* reported the isolation of prionoid D (**2**) and prionoid E (**1**) from *Salvia prionitis* [7], which showed significant cytotoxic activity against tumor cell lines *in vitro* (IC_{50} = 0.72 μM against P-388 and IC_{50} = 0.41 μM against A-549, resp.). However, the further investigation of biological activities of these compounds was frustrated by their small amount in the plant.

Many syntheses of the diterpenoids were reported, and the research work mainly concentrated on the construction of the *B*-ring of the diterpenoids [11–19]. However, there were few reports on the synthesis of rearranged 4,5-secoditerpenoids, especially for those molecules with a novel side chain, which is believed to have great influence on the bioactivity of this sort of compounds. Prionoid E (**1**), a rearranged 4,5-secoabietane diterpene quinone, bears a novel side chain characterized as a 4-hydroxy-1-oxopent-2-

en-1-yl chain with (2*E*) configuration. Its unusual structure and potential bioactivity combine to make the compound an attractive synthetic target.



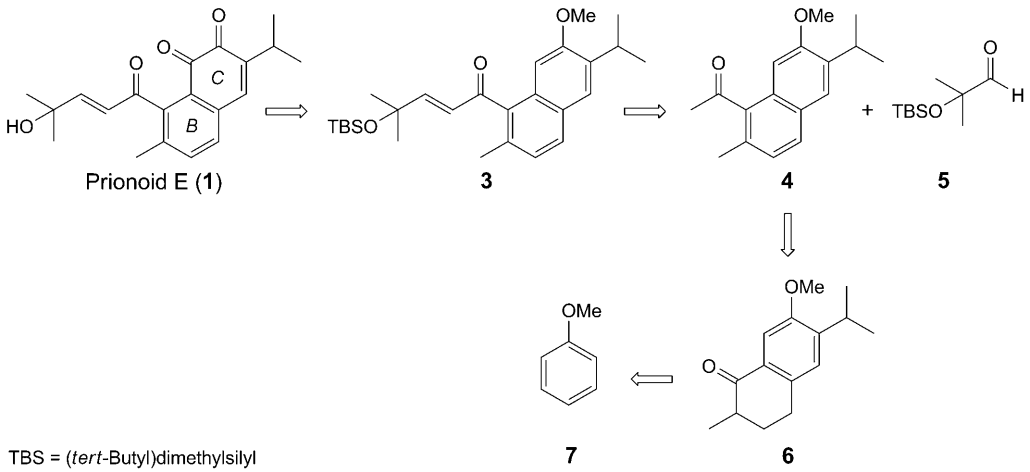
Prionoid E (**1**)



Prionoid D (**2**)

Results and Discussion. – The *retro*-synthesis of prionoid E (**1**) is shown in *Scheme 1*. Considering the long side chain of the target compound, we chose the stepwise ring-construction method to furnish ring *B* of **1** and thus provide compound **6** as an intermediate to carry out the following side-chain construction. Indeed, the stepwise *B*-ring construction maneuver was widely used in the synthesis of tanshinone and its analogues [19]. However, there were few reports on the synthesis of rearranged 4,5-secoditerpenoids bearing a 5-Me group. Previously, *Duan* and *Cai* reported a synthetic route for the preparation of compound **6** from (4-methoxyphenyl)acetic acid in seven steps [15]. However, the approach was a little tedious. To form the side chain, the strategy of preparing methyl ketone **4** as the key intermediate was chosen, which upon aldol condensation with the corresponding aldehyde **5** should afford compound **3**, the precursor of **1**.

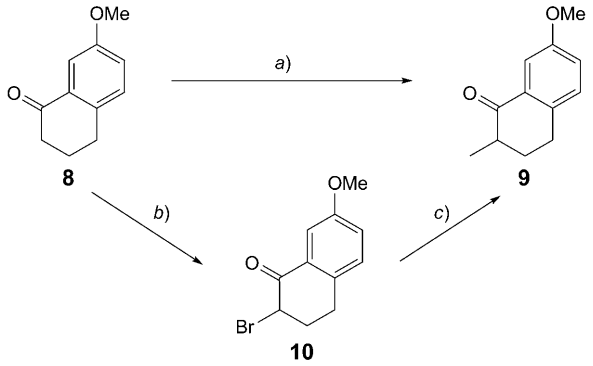
Scheme 1



TBS = (*tert*-Butyl)dimethylsilyl

Compound **8** was easily accessible and was widely used in the synthesis of tanshinones and its analogues [19]. However, in our hands, introducing the Me group to **8** by methylation with MeI/NaH only resulted in quite a low yield of **9**, apparently due to the bimethylation product produced and the difficulty in the isolation of **9** (*Scheme 2*). The two-step transformation *via* **10** also did not afford satisfactory results.

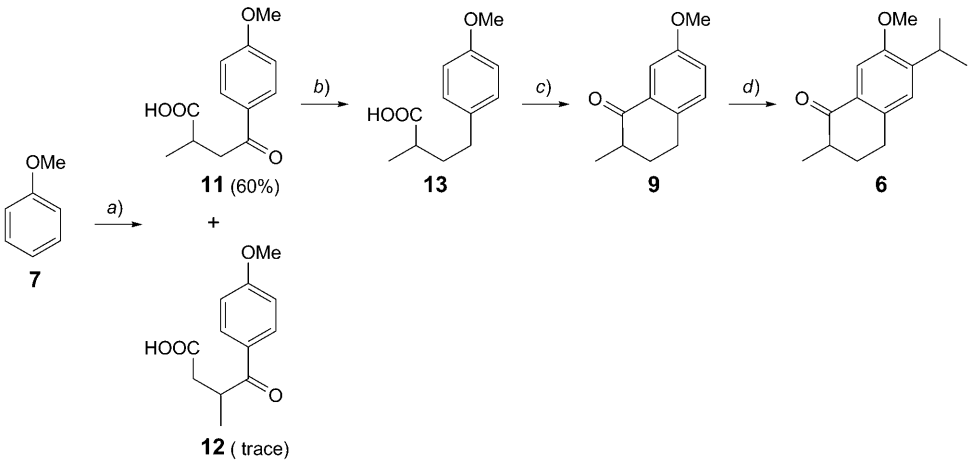
Scheme 2



a) MeI, NaH, benzene, −20°, 1 h; 21%. *b*) $CuBr_2$, AcOEt, reflux, 2 h; 94%. *c*) MeI, DMSO, r.t., 3 h; 30%.

To avoid the harsh reaction conditions associated with the methylation, we tried to introduce the desired Me group to **8** by using methylsuccinic anhydride (=dihydro-3-methylfuran-2,5-dione) under ambient reaction conditions, which turned out to be a more efficient way (*Scheme 3*). Anisole (**7**) reacted with methylsuccinic anhydride in the presence of $AlCl_3$ in toluene to give the desired product **11** as the major product in 60% yield, and only a trace of by-product **12** was produced, which was easily separated by column chromatography. Compound **11** was treated with Zn powder, $HgCl_2$, and conc. HCl solution to provide reduction product **13** in 92% yield. The latter, upon

Scheme 3

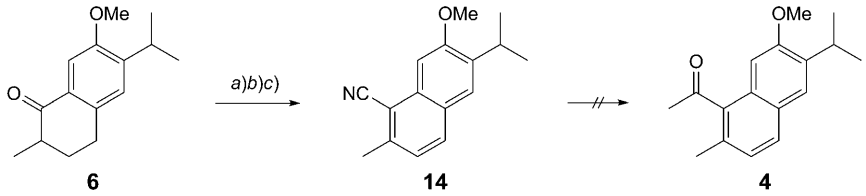


a) Methylsuccinic anhydride, $AlCl_3$, nitrobenzene, r.t., overnight; 60%. *b*) Zn(Hg), conc. HCl soln., toluene, reflux, 24 h; 92%. *c*) PPA (=polyphosphoric acid), 80°, 3 h; 90%. *d*) i-PrOH, PPA, 80°, 3 h; 81%.

treatment with polyphosphoric acid (PPA) at 80°, underwent cyclization to afford compound **9** in 90% yield. Subsequent alkylation with i-PrOH in PPA at 80° afforded regioselectively compound **6** in 81% yield.

With compound **6** in hand, we then constructed the side chain. Considering the cyano group as prone to react with a nucleophilic methylation reagent and considering the product obtained as easily transformable to the corresponding methyl ketone by hydrolysis, a synthetic route to introduce a cyano group at C(1) of **6** for further functional-group transformation was envisaged (*Scheme 4*). Thus, starting from **6**, the aromatic nitrile **14** was synthesized *via* three steps with 76% overall yield [20]. However, the subsequent reaction of **14** with a nucleophilic methylation reagent such as MeMgBr, MeLi, or $MeCeCl_2$ to give the desired compound **4** was unsuccessful, probably due to steric hiderance caused by the *ortho*-Me group. In fact, *Timberlake* and co-workers previously reported the steric hinderance effect of an *ortho*-Me group on the cyano group in cumyl systems [21].

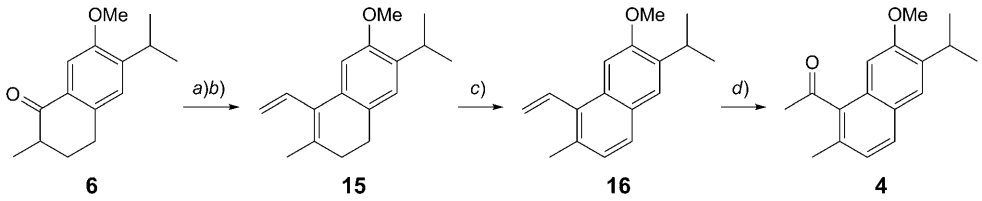
Scheme 4



a) Me_3SiCN, $AlCl_3$, benzene, 70°, 12 h. *b*) TsOH, benzene, reflux, 0.5 h. *c*) DDQ (=4,5-dichloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile), benzene, reflux, 0.5 h; 76% over three steps.

Since the cyano-group transformation failed, we resorted to another strategy to form methyl ketone **4**, *i.e.*, *via Wacker* oxidation of an alkene moiety (*Scheme 5*). Thus compound **6** was treated with CH_2=CHMgBr in THF at 0° to yield the addition product, followed by dehydration with *p*-toluenesulfonic acid (=4-methylbenzenesulfonic acid; TsOH) and $MgSO_4$ in refluxing benzene for 1 h to provide product **15** in 65% yield over two steps. Aromatization of compound **15** with DDQ in refluxing benzene for 0.5 h gave naphthalene **16** in 96% yield. The vinyl group of **16** was converted into methyl ketone **4** by using the *Wacker*-oxidation protocol. Thus, oxidation of **16** with O_2 in the

Scheme 5

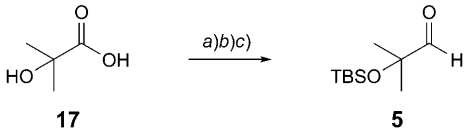


a) CH_2=CHMgBr, THF, 0°, 2 h. *b*) TsOH, benzene, reflux, 0.5 h; 65% over two steps. *c*) DDQ, benzene, reflux, 0.5 h; 96%. *d*) O_2 , CuCl, $PdCl_2$, THF/H_2O, r.t., 12 h; 71%.

presence of CuCl and $PdCl_2$ in THF/H_2O provided the key intermediate **4** in 71% yield [22][23].

The silyloxy-substituted aldehyde **5** was synthesized according to a reported route with some modifications [24]: starting from 2-hydroxy-2-methylpropanoic acid (**17**), the aldehyde was synthesized in three steps with 62% overall yield (*Scheme 6*). Aldol addition of methyl ketone **4** and aldehyde **5** in the presence of lithium bis(trimethylsilyl)amide (LHMDS) in THF at $-78°$ proceeded smoothly to afford the corresponding hydroxy compound **18**, which after dehydration provided compound **3**, the precursor of prionoid E (**1**) (*Scheme 7*). However, elimination of the OH group to form the α,β-unsaturated ketone was problematic due to the presence of the acid-sensitive (*tert*-butyl)dimethylsilyl group which is prone to leave with concomitant dehydration under acidic conditions. After failure with reagents such as TsOH or methanesulfonyl chloride (MsCl)/Et_3N, ultimately **18** was dehydrated to give the α,β-unsaturated ketone **3** by refluxing in benzene in the presence of a catalytic amount of TsOH/pyridine [25]. The product thus obtained was exclusively the (*E*)-isomer. Treatment of **3** with BBr_3 in CH_2Cl_2 at $-78°$ for 12 h only gave a desilylated product. Then, after increasing the

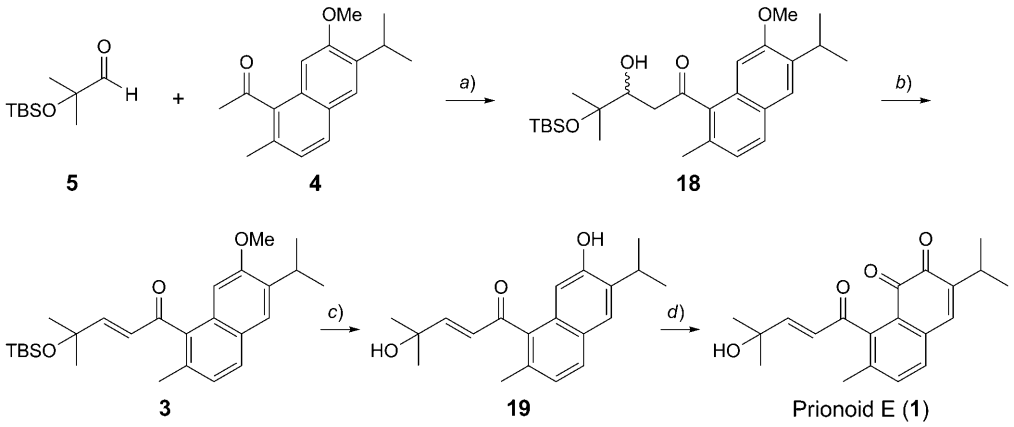
Scheme 6



17 **5**

a) EtOH, H_2SO_4, benzene, reflux, 12 h. *b*) TBSOTf (=^{t}BuMe$_2$SiOSO$_2$CF$_3$), CH_2Cl_2, r.t., 12 h. *c*) DIBALH (=diisobutylaluminium hydride), Et_2O, $-78°$, 1 h; 62% over three steps.

Scheme 7



5 **4** **18** **3** **19**

TBS = (*tert*-Butyl)dimethylsilyl

a) LHMDS, THF, $-78°$, 1 h. *b*) Cat. TsOH/pyridine, benzene, reflux, 24 h; 65% over two steps. *c*) BBr_3, r.t., 5 h; 62%. *d*) *Fremy*'s salt, acetone, H_2O, r.t., 12 h; 52%.

reaction temperature to room temperature and stirring for another 5 h, the desilylation was complete in a one-pot procedure to provide compound **19** in 62% yield. Finally, oxidation of **19** with *Fremy*'s salt in acetone at room temperature for 12 h gave the target molecule prionoid E (**1**). The spectroscopic data of the synthesized product were in excellent agreement with those of the natural product [7].

Conclusion. – We have achieved the first total synthesis of prionoid E (**1**) by an efficient and practical route in 3.7% overall yield, with *Wacker* oxidation and aldol condensation as the key steps. Application of this strategy to obtain prionoid E (**1**) and its analogs for evaluation of their biological activity is under progress and will be reported in due course.

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Experimental Part

General. Solvents and org. reagents were purchased from *Lancaster*, *Acros*, and *Shanghai Chemical Reagent Company*, and were used without further purification. TLC: *HG* F_{254} (150–200 μm thickness; *Yantai Huiyou Company*, P. R. China). Column chromatography (CC): commercial silica gel (SiO_2; 200–300 mesh; *Qingdao Haiyang Chemical Group Co.*). IR Spectra: *Nicolet-Magna-750* spectrophotometer; films or KBr discs; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker-DRX-400* spectrometer; at 400 (^1H) and 100 (^{13}C); δ in ppm rel. to Me_4Si as internal standard, J in Hz. ESI-HR-MS: *Finnigan MAT-95*, *LCQ-DECA*, and *Agilent-1100* LC-MS spectrometer; in m/z.

4-(4-Methoxyphenyl)-2-methyl-4-oxobutanoic Acid (=*4-Methoxy-α-methyl-γ-oxobenzenebutanoic Acid*; **11**). To a soln. of methylsuccinic anhydride (5 g, 0.044 mol) and anisole (=methoxybenzene; **7**; 10 ml) in nitrobenzene (40 ml) was slowly added $AlCl_3$ (13.5 g, 0.1 mol) at 0°. The resulting mixture was stirred overnight at r.t. The mixture was then poured into ice-water (50 ml) and extracted with Et_2O (3 × 50 ml). The aq. layer was acidified with 2N HCl and again extracted with AcOEt (3 × 50 ml). The combined org. extract was washed with brine (2 × 100 ml), dried ($MgSO_4$), and concentrated and the residue purified by CC (petroleum ether/AcOEt 10:1): **11** (5.8 g, 60%) and **12** (0.2 g, 2%). Spectra: identical with those published in [26].

4-(4-Methoxyphenyl)-2-methylbutanoic Acid (=*4-Methoxy-α-methylbenzenebutanoic Acid*; **13**). Zn powder (8.9 g, 0.04 mol), $HgCl_2$ (0.9 g, 0.003 mol), conc. HCl soln. (1 ml), and H_2O (10 ml) were mixed under stirring for 10 min. The aq. layer was decanted, and the resulting mixture was washed with H_2O. Compound **11** (3.3 g, 0.015 mol) in toluene (30 ml) was added to the mixture, followed by conc. HCl soln. (12 ml) and H_2O (6 ml). The mixture was heated to reflux for 24 h. After cooling, H_2O (50 ml) was added. The resulting mixture was extracted with AcOEt (3 × 50 ml), the combined org. extract was washed with H_2O (3 × 50 ml), dried ($MgSO_4$), and concentrated, and the crude product purified by CC (petroleum ether/AcOEt 80:1): **13** (2.9 g, 92%). Colorless oil. Spectra: identical with those published in [15].

*3,4-Dihydro-7-methoxy-2-methylnaphthalen-1(2*H*)-one* (**9**). Compound **13** (3.5 g, 0.017 mol) was added to PPA (100 g) at 80°, and the mixture was stirred at 80° for 3 h. Ice-water (50 ml) was added to decompose PPA, and the mixture was extracted with Et_2O (3 × 50 ml). The combined Et_2O extract was washed with 10% aq. K_2CO_3 soln. (2 × 30 ml) and brine (2 × 30 ml), dried ($MgSO_4$), and concentrated and the residue purified by CC (petroleum ether/AcOEt 100:1): **9** (2.9 g, 90%). Colorless oil. Spectra: identical with those published in [15].

*3,4-Dihydro-7-methoxy-2-methyl-6-(1-methylethyl)naphthalen-1(2*H*)-one* (**6**). Compound **9** (2.0 g, 10.5 mmol) and i-PrOH (2.5 ml) were added to PPA (8.0 g) at 80°, and the resulting mixture was stirred at 80° for 3 h. Ice-water (30 ml) was added to decompose PPA, and the mixture was extracted with Et_2O

(3×30 ml). The combined Et_2O extract was washed with 10% aq. K_2CO_3 soln. (2×20 ml) and brine (2×20 ml), and dried ($MgSO_4$), and concentrated: **6** (1.95 g, 81%). Colorless oil. IR (KBr): 2960, 1682, 1608, 1497, 1464, 1414, 1357, 1331, 1250, 1200, 1074, 1053, 1014, 889, 766, 536. ^{1}H-NMR ($CDCl_3$): 7.46 (*s*, 1 H); 7.02 (*s*, 1 H); 3.84 (*s*, 3 H); 3.32 (*sept.*, $J = 6.9$, 1 H); 2.91 – 2.95 (*m*, 2 H); 2.53 – 2.56 (*m*, 1 H); 2.15 – 2.19 (*m*, 1 H); 1.81 – 1.85 (*m*, 1 H); 1.24 (*d*, $J = 6.9$, 3 H); 1.20 (*d*, $J = 6.9$, 6 H). ^{13}C-NMR ($CDCl_3$): 155.6; 143.5; 136.9; 130.7; 126.2; 107.4; 55.4; 42.2; 31.7; 28.0; 26.9; 22.3; 15.5. HR-MS: 232.1461 (M^+, $C_{15}H_{20}O_2^+$; calc. 232.1463).

7-Methoxy-2-methyl-6-(1-methylethyl)naphthalene-1-carbonitrile (**14**). To a soln. of **6** (250 mg, 1.08 mmol) in benzene (10 ml) was added Me_3SiCN (122 mg, 1.23 mmol) and a cat. amount of $AlCl_3$, and the mixture was stirred at 70° for 12 h. Then, TsOH (2 mg) was added to the mixture, which was heated to reflux for an additional 0.5 h, and after addition of DDQ (320 mg, 1.41 mmol), heating was continued for another 0.5 h. The mixture was cooled to r.t., and the precipitate was filtrated off through *Celite*. The solvent was evaporated and the residue purified by CC (petroleum ether): **14** (197 mg, 76%). Colorless oil. IR (KBr): 2962, 2871, 2213,1627, 1498, 1460, 1407, 1228, 1168, 1020, 845, 765, 447. ^{1}H-NMR ($CDCl_3$): 7.81 (*d*, $J = 8.6$, 1 H); 7.60 (*s*, 1 H); 7.39 (*s*, 1 H); 7.20 (*d*, $J = 8.7$, 1 H); 4.01 (*s*, 3 H); 3.40 (*sept.*, $J = 6.9$, 1 H); 2.70 (*s*, 3 H); 1.28 (*d*, $J = 6.8$, 6 H). ^{13}C-NMR ($CDCl_3$): 158.5; 142.3; 139.7; 133.2; 132.1; 126.7; 125.3; 125.2; 117.8; 107.3; 102.2; 55.5; 26.9; 22.4; 21.1. HR-MS: 239.1312 (M^+, $C_{16}H_{17}NO^+$; calc. 239.1310).

1-Ethenyl-3,4-dihydro-7-methoxy-2-methyl-6-(1-methylethyl)naphthalene (**15**). To a soln. of **6** (200 mg, 0.86 mmol) in anh. THF (10 ml) was slowly added 1.0M CH_2=CHMgBr in THF (1.72 ml, 1.72 mmol) at 0°, and the mixture was stirred at 0° for 2 h. The reaction was quenched with sat. NH_4Cl soln. (10 ml), the aq. layer extracted with Et_2O (3×20 ml), the Et_2O extract was washed with sat. $NaHCO_3$ soln. (10 ml) and brine (10 ml), dried (Na_2SO_4), and concentrated, and the residue dissolved in dry benzene (20 ml). $MgSO_4$ (1 g, 8.3 mmol) and TsOH (2 mg) were added to the soln. The mixture was refluxed for 0.5 h. After cooling to r.t., the $MgSO_4$ was filtered off, the filtrate washed with sat. $NaHCO_3$ soln. (10 ml) and brine (10 ml), dried ($MgSO_4$), and evaporated, and the residue purified by CC (petroleum ether): **15** (135 mg, 65%). Colorless oil. IR (KBr): 3081, 2958, 2929, 2831, 1627, 1610, 1562, 1500, 1463, 1407, 1317, 1203, 1062, 887, 763. ^{1}H-NMR ($CDCl_3$): 6.98 (*s*, 1 H); 6.85 (*s*, 1 H); 6.55 (*dd*, $J =$ 17.5, 11.4, 1 H); 5.46 (*dd*, $J = 11.4$, 2.4, 1 H); 5.30 (*dd*, $J = 17.6$, 2.4, 1 H); 3.79 (*s*, 3 H); 3.27 (*sept.*, $J = 6.9$, 1 H); 2.64 (*t*, $J = 7.7$, 2 H); 2.24 (*t*, $J = 7.6$, 2 H); 1.98 (*s*, 3 H); 1.20 (*d*, $J = 6.8$, 6 H). ^{13}C-NMR ($CDCl_3$): 154.9; 134.3; 134.1; 133.7; 133.4; 130.2; 127.6; 124.9; 118.5; 107.7; 55.6; 31.2; 27.5; 26.4; 22.8; 21.0. HR-MS: 265.1562 ($[M + Na]^+$, $C_{17}H_{22}NaO^+$; calc. 265.1568).

1-Ethenyl-7-methoxy-2-methyl-6-(1-methylethyl)naphthalene (**16**). The mixture of **15** (500 mg, 2.0 mmol) and DDQ (750 mg, 3.0 mmol) in benzene (20 ml) was refluxed for 0.5 h. The mixture was cooled to r.t., the precipitate filtrated off through *Celite*, the filtrate concentrated, and the residue purified by CC (petroleum ether): **16** (496 mg, 96%). Colorless oil. IR (KBr): 2958, 1629, 1496, 1461, 1398, 1228, 1169, 1070, 1027, 889, 802, 769. ^{1}H-NMR ($CDCl_3$): 7.58 (overlapping, 2 H); 7.37 (*s*, 1 H); 7.18 (*d*, $J = 8.3$, 1 H); 7.00 (*dd*, $J = 18.0$, 11.3, 1 H); 5.75 (*dd*, $J = 11.4$, 2.3, 1 H); 5.45 (*dd*, $J = 18.0$, 2.2, 1 H); 3.93 (*s*, 3 H); 3.38 (*sept.*, $J = 6.9$, 1 H); 2.44 (*s*, 3 H); 1.28 (*d*, $J = 7.0$, 6 H). ^{13}C-NMR ($CDCl_3$): 156.1; 137.3; 134.7; 132.9; 132.1; 131.1; 127.5; 126.3; 126.2; 124.7; 120.4; 102.6; 55.1; 27.0; 22.7; 20.8. HR-MS: 240.3405 (M^+, $C_{17}H_{20}O^+$; calc. 240.3401).

1-[7-Methoxy-2-methyl-6-(1-methylethyl)naphthalen-1-yl]ethanone (**4**). To a soln. of **16** (200 mg, 0.83 mmol) in THF (20 ml) and H_2O (2 ml), $PdCl_2$ (7.4 mg, 0.042 mmol) and CuCl (82 mg, 0.83 mmol) were added. The mixture was stirred at 70° for 2 h. After cooling to r.t., the mixture was stirred vigorously under a balloon of O_2 for 12 h. The mixture was extracted with Et_2O (3×20 ml), the combined org. phase washed with brine (10 ml), dried ($MgSO_4$), and concentrated, and the residue purified by CC (petroleum ether/AcOEt 60 : 1): **4** (153 mg, 71%). Colorless oil. IR (KBr): 3442, 2956, 2929, 2856, 1728, 1701, 1631, 1464, 1363, 1253, 1168, 1055, 835, 773, 689. ^{1}H-NMR ($CDCl_3$): 7.66 (*d*, $J = 8.2$, 1 H); 7.59 (*s*, 1 H); 7.16 (*d*, $J = 8.3$, 1 H); 6.80 (*s*, 1 H); 3.89 (*s*, 3 H); 3.37 (*sept.*, $J = 6.9$, 1 H); 2.62 (*s*, 3 H); 2.40 (*s*, 3 H); 1.28 (*d*, $J = 6.9$, 6 H). ^{13}C-NMR ($CDCl_3$): 208.8; 156.8; 138.3; 137.2; 129.5; 128.2; 128.1; 127.2; 126.0; 124.9; 101.1; 55.2; 32.6; 27.0; 22.6; 19.5. HR-MS: 256.1461 (M^+, $C_{17}H_{20}O_2^+$; calc. 256.1463).

4-{[(1,1-Dimethylethyl)dimethylsilyl]oxy}-1-[7-methoxy-2-methyl-6-(1-methylethyl)naphthalen-1-yl]-4-methylpent-2-en-1-one (**3**). To a soln. of **4** (104 mg, 0.41 mmol) in dry THF (2 ml) was added 1.0M

LHMDS in THF (0.5 ml, 0.5 mmol) at $-78°$, and the resulting mixture was stirred at $-78°$ for 0.5 h. To the mixture was slowly added a soln. of **5** (240 mg, 1.19 mmol) in dry THF (0.5 ml) at $-78°$, and the mixture was stirred at $-78°$ for an additional hour. The reaction was quenched by the addition of sat. NH_4Cl soln. (10 ml), and the resulting mixture was extracted with CH_2Cl_2 (2×20 ml). The combined org. phase was washed with 5% $NaHCO_3$ soln. (10 ml) and brine (10 ml), dried ($MgSO_4$), and concentrated: **18** as pale yellow solid which was used without further purification.

To a soln. of crude **18** in benzene (10 ml) was added TsOH (2 mg) and pyridine (5 µl), and the mixture was refluxed for 24 h. The mixture was washed with brine (5 ml), dried ($MgSO_4$), and concentrated and the residue purified by CC (petroleum ether/AcOEt 80:1): **3** (118 mg, 65% from **4**). Colorless oil . IR (KBr): 2956, 1660, 1629, 1496, 1463, 1413, 1361, 1319, 1232, 1169, 1041, 891, 837, 775, 696, 611. ^{1}H-NMR ($CDCl_3$): 7.67 (*d*, *J* = 8.5, 1 H); 7.57 (*s*, 1 H); 7.15 (*d*, *J* = 8.6, 1 H); 6.79 (*s*, 1 H); 6.59 (*d*, *J* = 15.7, 1 H); 6.48 (*d*, *J* = 15.7, 1 H); 3.83 (*s*, 3 H); 3.37 (*sept.*, *J* = 6.9, 1 H); 2.33 (*s*, 3 H); 1.28 (overlapping, 12 H); 0.83 (*s*, 9 H); 0.01 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$): 201.8; 159.4; 156.6; 138.1; 134.8; 131.3; 129.9; 128.2; 128.0; 127.2; 125.9; 124.6; 102.1; 72.9; 55.2; 29.7; 27.1; 25.7; 22.6; 19.8; 18.0; −2.2. HR-MS: 440.2749 (M^+, $C_{27}H_{40}O_3Si^+$; calc. 440.2747).

4-Hydroxy-1-[7-hydroxy-2-methyl-6-(1-methylethyl)naphthalen-1-yl]-4-methylpent-2-en-1-one (**19**). To a soln. of **3** (200 mg, 0.45 mmol) in dry CH_2Cl_2 (5 ml) was slowly added 1.0M BBr_3 in CH_2Cl_2 (0.5 ml, 0.5 mmol) at $-78°$. The mixture was slowly warmed to r.t. and stirred at r.t. for 5 h. The reaction was quenched by the addition of 10% $NaHCO_3$ soln. (10 ml), and the resulting mixture was extracted with CH_2Cl_2 (2×20 ml). The combined org. phase was washed with brine (10 ml), dried ($MgSO_4$), and concentrated and the residue purified by CC (CH_2Cl_2): **19** (88 mg, 62%). Colorless oil. IR (KBr): 3425, 2923, 2854, 1705, 1658, 1629, 1461, 1419, 1259, 1232, 1172, 1099, 804. ^{1}H-NMR ($CDCl_3$): 7.68 (*d*, *J* = 8.6, 1 H); 7.60 (*s*, 1 H); 7.15 (*d*, *J* = 8.5, 1 H); 6.92 (*s*, 1 H); 6.74 (*d*, *J* = 16.0, 1 H); 6.44 (*d*, *J* = 16.0, 1 H); 5.49 (br. *s*, 1 H); 3.32 (*sept.*, *J* = 6.9, 1 H); 2.42 (*s*, 3 H); 1.38 (*d*, *J* = 6.9, 6 H); 1.34 (*s*, 3 H); 1.32 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 201.6; 154.9; 153.2; 136.8; 133.2; 131.9; 129.8; 128.9; 127.5; 127.1; 125.9; 125.4; 106.6; 59.9; 32.4; 27.4; 19.8; 18.1. HR-MS: 312.1721 (M^+, $C_{20}H_{24}O_3^+$; calc. 312.1725).

Prionoid E (= *8-[(2*E*)-4-Hydroxy-4-methyl-1-oxopent-2-en-1-yl]-7-methyl-3-(1-methylethyl)naphthalene-1,2-dione*; **1**). To a soln. of **19** (162 mg, 0.52 mmol) in acetone (5 ml) was added a soln. of 0.06M aq. *Fremy*'s salt soln. (30 ml) and 0.6M aq. KH_2PO_4 soln. (20 ml). The mixture was stirred in the dark at r.t. for 12 h and then extracted with Et_2O (2×50 ml). The combined org. phase was washed with brine (2×20 ml), dried ($MgSO_4$), and concentrated, and the residue purified by CC (CH_2Cl_2): **1** (84 mg, 52%). Red powder. IR (KBr): 3407, 2968, 2873, 1677, 1662, 1628, 1467, 1419, 1375, 1282, 1196, 1163, 1068, 943, 847, 601. ^{1}H-NMR ($CDCl_3$): 7.46 (*d*, *J* = 7.8, 1 H); 7.26 (*d*, *J* = 7.8, 1 H); 7.14 (*s*, 1 H); 6.52 (*d*, *J* = 16.2, 1 H); 6.49 (*d*, *J* = 16.2, 1 H); 3.03 (*sept.*, *J* = 6.9, 1 H); 2.21 (*s*, 3 H); 1.36 (*s*, 3 H); 1.31 (*s*, 3 H); 1.18 (*d*, *J* = 6.8, 6 H). ^{13}C-NMR ($CDCl_3$): 197.8; 179.7; 178.8; 154.1; 146.0; 143.7; 138.5; 137.5; 137.0; 133.7; 129.8; 127.4; 126.8; 70.6; 29.0; 28.8; 27.0; 21.4; 18.7. HR-MS: 326.1515 (M^+, $C_{20}H_{24}O_3^+$; calc. 326.1518).

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