

## A short synthesis of ( $\pm$ )-furodisinine and ( $\pm$ )-furodisine

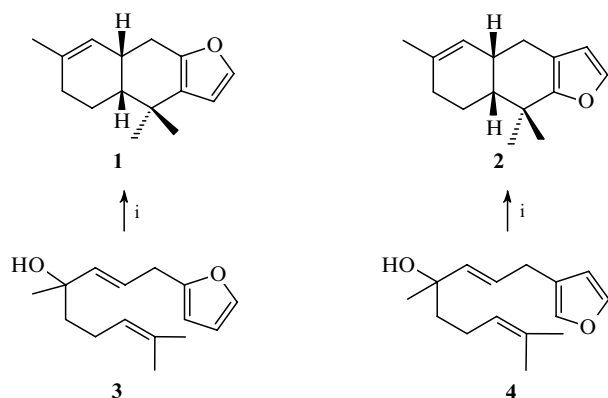
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A simple synthesis of racemic forms of natural furanoterpenoids, furodisinine and furodisine, has been carried out by electrophilic cyclisation of readily accessible  $\alpha$ - and  $\beta$ -furylmethyl derivatives of linalool.

The structures of metabolites of certain types of sea sponges,<sup>1</sup> furodisinin **1** and furodisin **2**, has been confirmed by synthesising their racemic<sup>2</sup> and optically active forms.<sup>3</sup>

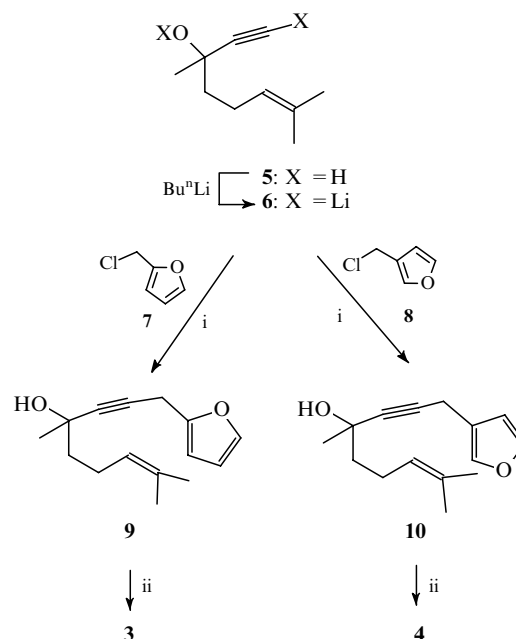


**Scheme 1** Reagents and conditions: i, 0.2 equiv. 85%  $\text{H}_3\text{PO}_4$ , aq., PhMe, 100 °C, 20 min.

We proposed a new strategy for constructing these furanodecalins by cationic cyclisation of readily accessible derivatives of linalool **3** and **4** (Scheme 1). The latter were obtained from ( $\pm$ )-dehydrolinalool **5**, whose dilithium derivative **6** was subjected to CuI-catalysed condensation with chloride **7** (see ref. 4) or **8** (Scheme 2). The resulting alkynes **9** and **10**, respectively, were then reduced into the corresponding dienes **3** and **4** by treatment with Li in  $\text{NH}_3$ .

The subsequent search for conditions of efficient cationic cyclisation of isoprenoids **3**, **4** showed that this reaction should optimally be carried out in the presence of  $\sim 0.2$  mol equiv. 85%  $\text{H}_3\text{PO}_4$  in toluene at 100 °C. The target compounds **1** and **2** were isolated in  $\sim 40\%$  yields from cyclisation products

formed under these conditions by chromatography on  $\text{SiO}_2$ /10%  $\text{AgNO}_3$ . In both cases, the furanodecalins **1** and **2** were accompanied by their hitherto unknown *trans*-fused isomers, **11** and **12** ( $\sim 10\%$ ), and by limonene derivatives, *cis*-/*trans*-**13a,b** ( $< 10\%$ ), respectively (Scheme 3). The latter probably resulted from deprotonation of the corresponding carbo-cationic intermediates **14a** and **14b** formed in the first step of cyclisation of the starting diolefins **3** and **4**.



**Scheme 2** Reagents and conditions: i, CuI, THF,  $-20 \rightarrow 20$  °C,  $> 50\%$ ; ii, Li/ $\text{NH}_3$ /THF,  $-70$  °C,  $\sim 70\%$ .

The spectral characteristics of the (±)-furodisinine **1**, (±)-furodisine **2** and limonene derivatives *cis*-**13a,b** almost coincide with those reported previously.<sup>3</sup> The hitherto unknown compounds **4** and **10–12** were identified by the combination of data from elemental and spectral† analyses.

## References

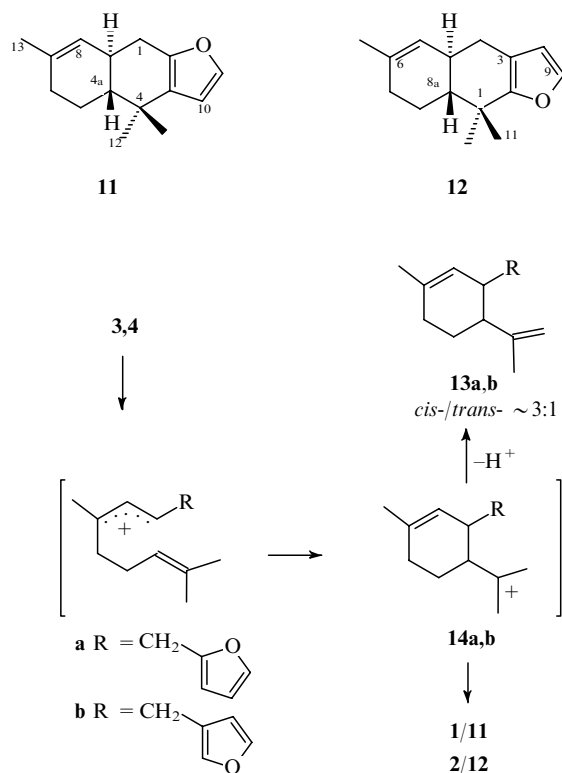
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† **4**: <sup>1</sup>H NMR (200.13 MHz, CDCl<sub>3</sub>) δ 1.28 (s, 3H, 4-Me), 1.56 (m, 2H, 5-H), 1.60 and 1.68 (br. s, 6H, 8-Me), 2.2 (m, 2H, 6-H), 3.18 (br. d, 2H, 1-H, *J* = 6.0), 5.12 (br. t, 1H, 7-H, *J* = 7.1), 5.58 (dt, 1H, 3-H, *J* = 15.5 and 1.1), 5.76 (dt, 1H, 2-H, *J* = 15.5 and 5.9), 6.25 (m, 1H, 4'-H), 7.20 and 7.35 (m, 2H, 2'-H, 5'-H); *m/z*: 234 [M]<sup>+</sup>. Found (%): C, 76.70; H, 9.41. C<sub>15</sub>H<sub>22</sub>O<sub>2</sub>. Calc. (%): C, 76.88; H, 9.46.

**10**: <sup>1</sup>H NMR (200.13 MHz, CDCl<sub>3</sub>) δ 1.50 (s, 3H, 4-Me), 1.62 and 1.70 (br. s, 6H, 8-Me), 1.65 (m, 2H, 5-H), 2.2 (m, 2H, 6-H), 3.38 (br. s, 2H, 1-H), 5.15 (br. t, 1H, 7-H, *J* = 7.0), 6.32 (m, 1H, 4'-H), 7.33 and 7.36 (m, 2H, 2'-H, 5'-H); *m/z*: 232 [M]<sup>+</sup>. Found (%): C, 77.21; H, 8.95. C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>. Calc. (%): C, 77.55; H, 8.68.

**11**: mp 33–37 °C (hexane). <sup>1</sup>H NMR (400.13 MHz, CDCl<sub>3</sub>) δ 1.02 (s, 3H, 11-H), 1.23 (s, 3H, 12-H), 1.30 (m, 1H, 4a-H), 1.37 (m, 1H, 5-H), 1.71 (br. s, 3H, 13-H), 1.90 (m, 1H, 5-H), 2.06 (m, 2H, 6-H), 2.22 (dd, 1H, 1-H, *J* = 15.6 and 11.7), 2.42 (m, 1H, 8a-H), 2.71 (dd, 1H, 1-H, *J* = 15.6 and 5.3), 5.30 (m, 1H, 8-H), 6.30 (br. s, 1H, 10-H), 7.25 (br. s, 1H, 9-H); <sup>13</sup>C NMR (50.32 MHz, CDCl<sub>3</sub>) δ 22.9 (C-5), 23.3 (C-13), 24.4 (C-11), 27.7 (C-12), 30.6 (C-1), 31.4 (C-6), 33.3 (C-4), 34.2 (C-8a), 46.8 (C-4a), 108.2 (C-10), 125.4 (C-8), 127.5 (C-3), 134.2 (C-7), 140.4 (C-9), 148.4 (C-2); HRMS *m/z* 216.15231 [M]<sup>+</sup>, Calc. for C<sub>15</sub>H<sub>20</sub>O 216.15131.

**12**: mp 32–35 °C (hexane). <sup>1</sup>H NMR (400.13 MHz, CDCl<sub>3</sub>) δ 1.10 (s, 3H, 11-H), 1.30 (s, 3H, 12-H), 1.39 (m, 2H, 8-H, 8a-H), 1.70 (br. s, 3H, 13-H), 1.86 (m, 1H, 8-H), 2.04 (m, 2H, 7-H), 2.05 (dd, 1H, 4-H, *J* = 15.3 and 11.6), 2.30 (m, 1H, 4a-H), 2.50 (dd, 1H, 4-H, *J* = 15.3, 5.0) and 5.30 (m, 1H, 5-H), 6.15 (br. s, 1H, 10-H), 7.25 (br. s, 1H, 9-H); <sup>13</sup>C NMR (50.32 MHz, CDCl<sub>3</sub>) δ 22.1 (C-11), 22.6 (C-8), 23.2 (C-13), 25.2 (C-12), 29.7 (C-4), 31.1 (C-7), 34.6 (C-4a), 35.0 (C-1), 47.3 (C-8a), 109.8 (C-10), 114.4 (C-3), 125.6 (C-5), 133.6 (C-6), 140.2 (C-9), 158.0 (C-2); HRMS *m/z* 216.15211 [M]<sup>+</sup>, Calc. for C<sub>15</sub>H<sub>20</sub>O 216.15131.



Scheme 3

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