

# Assembly of bicyclo[2.2.1]heptane derivatives by two types of domino reaction

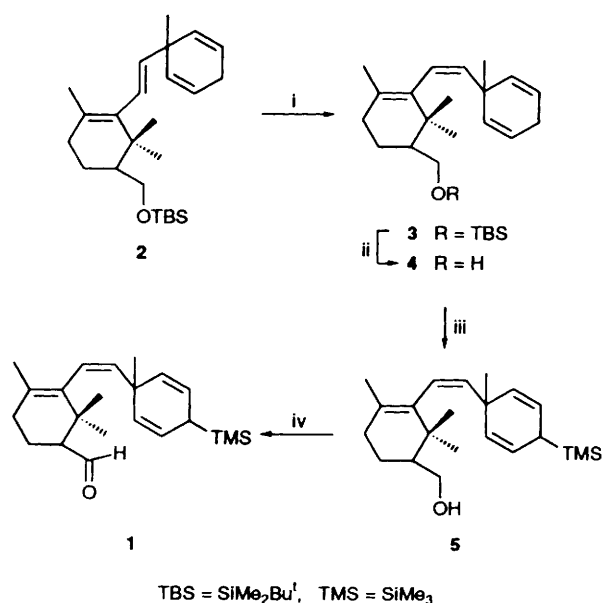
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On treatment with titanium(IV) chloride, the allylsilane **1** readily cyclised by a domino-type process to give a spiro compound **6** as the main product, while the reaction of unsilylated **8** or **9** with tin(IV) chloride provided the aromatic products **7**.

During the course of our synthetic study of taxol<sup>1</sup> and analogues, the Sakurai–Hosomi reaction<sup>2</sup> of the allylsilane **1** was examined in the hope of forming an eight-membered ring. However, treatment of **1** with Lewis acid produced unexpected compounds. We report here two types of domino reaction<sup>3</sup> forming a spiro compound and aromatized compounds.

The allylsilane **1** was prepared as described in Scheme 1.

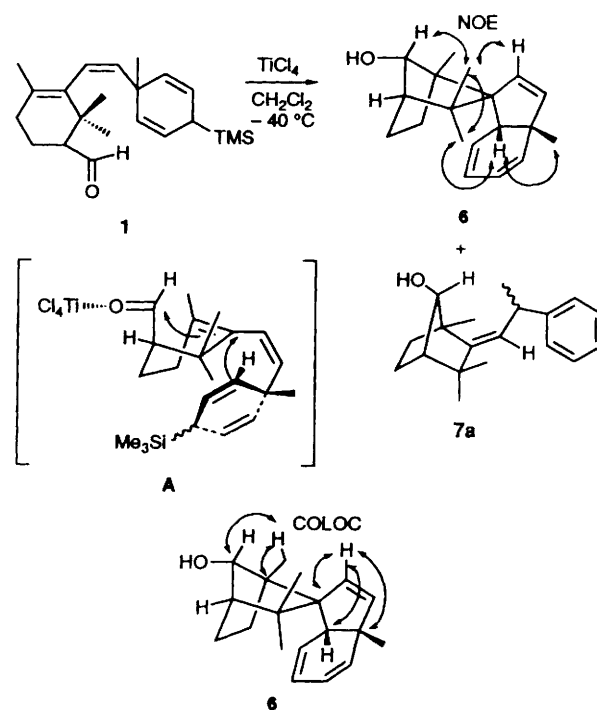


**Scheme 1** Reagents and conditions: i, *hν* (450 W), 2-acetylnaphthalene, benzene; ii, Bu<sub>4</sub>NF, THF; iii, BuLi, TMEDA, THF then TMSCl; iv, 1 mol dm<sup>-3</sup> H<sub>2</sub>SO<sub>4</sub>, THF; v, Pr<sub>4</sub>NRuO<sub>4</sub>, NMO, 4 Å MS, CH<sub>2</sub>Cl<sub>2</sub>

Irradiation<sup>4</sup> of the *trans*-olefin **2**, which was obtained by our improved Julia olefination using samarium(II) iodide and hexamethylphosphoramide,<sup>5</sup> resulted in formation of the *cis*-isomer **3** in 67% yield (98% yield based on the recovered **2**). In the <sup>1</sup>H NMR spectra of **3** at ambient temperature, two conformational isomers were detected as in the case of *cis*-β-ionol derivatives.<sup>6</sup> After deprotection of the silyl group (95% yield), the dianion which was derived from **4** with butyllithium (2.1 equiv.) in the presence of tetramethylethylenediamine (TMEDA), was subjected to silylation, followed by hydrolysis, to give **5** in 94% overall yield as a mixture of two diastereoisomers. Oxidation of **5** using Ley's method<sup>7</sup> afforded **1** quantitatively.

After its successful synthesis, we examined the cyclization of **1** under various conditions. When **1** was treated with titanium(IV) chloride (1.2 equiv.) in dichloromethane at –40 °C, the spiro compound **6** was obtained in 28% yield as a single stereoisomer along with **7a** in 5% yield as a mixture of two isomers. The total

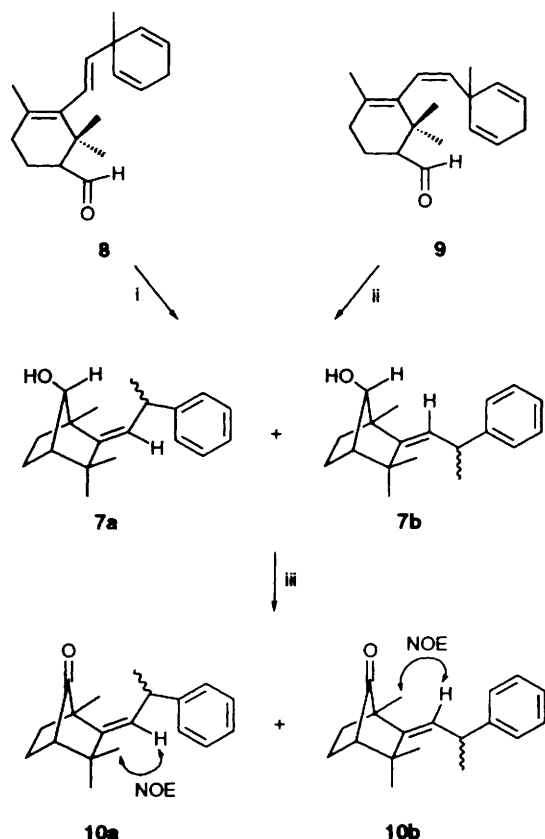
planar structure of **6** was suggested by long-range couplings observed in the COLOC spectrum. Furthermore, the relative stereochemistry was determined on the basis of a NOESY experiment. The exclusive formation of **6** indicates the concerted nature of the cyclization *via* the transition state **A** as shown in Scheme 2. To our knowledge, the production of spiro



**Scheme 2**

compounds by allylsilane terminated domino reactions has not been previously reported. The structural assignment of the aromatized product **7a** was deduced from spectroscopic and chemical evidence (*vide infra*).

Next, the two olefinic aldehydes **8** and **9** carrying no silyl group were synthesized from **2** and **4**, respectively, and then treated with a variety of Lewis acids. Treatment of **8** with tin(IV) chloride in dichloromethane provided the aromatized products **7a** and **7b** in 90% yield as a 1:1:6:6 mixture of four isomers, while similar treatment of **9** gave **7a** and **7b** in 50% yield as a 1:1:7.5:7.5 mixture of the four isomers. The minor two isomers were identical with the **7a** obtained from **1**. The mixture of four isomers **7a** and **7b** was oxidized by Ley's procedure<sup>7</sup> to give quantitatively a mixture of the two stereoisomers **10a** and **10b**. Geometries about the double bond of **10a** and **10b** were established, respectively, by <sup>1</sup>H NMR spectroscopy including



**Scheme 3** Reagents and conditions: i,  $\text{SnCl}_4$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-30^\circ\text{C}$ ; ii,  $\text{SnCl}_4$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-30 \rightarrow -10^\circ\text{C}$ ; iii,  $\text{Pr}_4\text{NRuO}_4$ , NMO, 4 Å MS,  $\text{CH}_2\text{Cl}_2$ .

NOE measurements between olefinic hydrogen and methyl groups.

Although the desired cyclization failed, we found two types of novel domino reaction.

### Experimental

#### Treatment of 2,2,4-trimethyl-3-[2-(1-methyl-4-trimethylsilylcyclohexa-2,5-dienyl)vinyl]cyclohex-3-ene-1-carbaldehyde **1** with titanium(IV) chloride

To a stirred solution of **1** (32 mg, 0.093 mmol) in anhyd. dichloromethane ( $1.7\text{ cm}^3$ ) was slowly added a solution of titanium(IV) chloride ( $12\text{ mm}^3$ , 0.11 mmol) in anhyd. dichloromethane ( $0.1\text{ cm}^3$ ) at  $-40^\circ\text{C}$ , and the mixture was stirred for 2 h at the same temperature. It was then quenched with saturated aq. ammonium chloride, after which the aqueous layer was separated and extracted with diethyl ether. The combined

organic layers were washed with water and brine, dried ( $\text{MgSO}_4$ ) and evaporated to give a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (10:1, v/v) afforded a mixture of **6** and **7a**. Separation of the mixture was achieved by HPLC with hexane-ethyl acetate (15:1, v/v) as eluent to give 1,3,3-trimethyl-2-(2-methyl-2-phenylethylidene)bicyclo[2.2.1]heptan-7-ol **7a** (1.2 mg, 5%);  $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$  3380;  $\delta_{\text{H}}(500\text{ MHz, CDCl}_3)$  1.01–1.06 (6 H, m), 1.23–1.38 (6 H, m), 3.84–3.92 (1 H, m), 3.96–4.04 (1 H, m), 5.12 (1 H, d,  $J$  9.8) and 7.13–7.31 (5 H, m);  $m/z$  270 ( $\text{M}^+$ ).

Further elution yielded 1,3,3,3a'-tetramethylspiro[bicyclo[2.2.1]heptane-2,1'-(*cis*-3a',7a'-dihydroinden)]-7-ol **6** (7.0 mg, 28%);  $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$  3420;  $\delta_{\text{H}}(400\text{ MHz, CDCl}_3)$  0.77 (3 H, s), 0.87 (3 H, s), 1.03 (3 H, s), 1.10 (3 H, s), 1.12–1.18 (1 H, m), 1.65–1.78 (3 H, m), 2.27–2.36 (1 H, m), 2.51 (1 H, dd,  $J$  5.9 and 1.3), 4.00 (1 H, br s), 5.48 (1 H, br d,  $J$  9.3), 5.52 (1 H, d,  $J$  6.1), 5.59 (1 H, d,  $J$  6.1), 5.68–5.73 (1 H, m), 5.81–5.87 (1 H, m) and 5.93–5.99 (1 H, m);  $\delta_{\text{C}}(100\text{ MHz, CDCl}_3)$  16.0, 22.2, 25.3, 26.7, 28.3, 28.4, 39.8, 46.8, 48.9, 53.4, 53.8, 70.7, 79.4, 119.2, 122.0, 129.1, 132.8, 135.4 and 137.1;  $m/z$  270 ( $\text{M}^+$ ).

### Acknowledgements

We thank Mr K. Sasaki and Mr T. Kondoh of Instrument Analysis for Chemistry, Faculty of Science, Tohoku University for NMR measurements. This work was, in part, supported by JSPS Research Fellowships for Young Scientists.

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Paper 5/05960G

Received 8th September 1995

Accepted 19th September 1995