A Novel Construction of Polyfunctionalised *trans*-Hydroindanes *via* Sulphur-mediated Intramolecular Double Michael Type Reaction

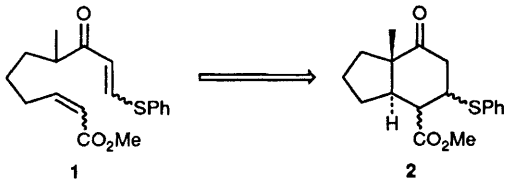
Masataka Ihara,[a] Shuichi Suzuki,[a] Nobuaki Taniguchi,[a] Keiichiro Fukumoto*[a] and Chizuko Kabuto[b]

[a] *Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan*
[b] *Instrumental Analysis Center for Chemistry, Faculty of Science, Tohoku University, Aobayama, Sendai 980, Japan*

trans-Hydroindanes possessing an angular methyl group were stereoselectively synthesised *via* treatment of the four geometrical isomers **1a–1d** of 9-methoxycarbonyl-4-methyl-1-phenylthionona-1,8-dien-3-one with *tert*-butyldimethylsilyl trifluoromethanesulphonate in the presence of triethylamine.

The *trans*-hydroindane structure having a methyl group at the angular position is the partial framework of steroids and various terpenoids. One of the most effective routes to *trans*-hydroindanes is *via* intramolecular Diels–Alder reactions.[1] As an extension of our recent studies using the intramolecular double Michael reaction[2] and sulphenocycloamination,[3] we thought that annulation of the α,β-unsaturated ketone **1** having a sulphide group at the β-position would lead to the construction of the *trans*-hydroindane skeleton **2** (Scheme 1). We now report the stereoselective synthesis of polyfunctionalised *trans*-hydroindanes *via* the sulphur-mediated intramolecular double Michael type reaction.

The four possible geometrical isomers **1a–d** of the α,β-unsaturated ketone **1** were prepared from ε-caprolactone **3**. Treatment of **3** with methyl iodide in the presence of lithium hexamethyldisilazide (LHMDS) and hexamethylphosphoramide (HMPA)[4] afforded the methylated compound **4** in 55% yield. Reduction of **4** with diisobutylaluminium hydride (DIBAH) in a mixture of dichloromethane and dimethoxyethane (1:1 v/v) at −78 °C, followed by treatment of the resulting hydroxy aldehyde with trimethylsilylacetylene in the presence of *n*-butyllithium gave the diol **5** in 64% overall yield. After removal of the trimethylsilyl group of **5** using tetra-n-butylammonium fluoride (95% yield), the diol **6** was oxidised with periodinane[5] to provide the corresponding formyl ketone, which was treated with benzenethiol in the presence of a catalytic amount of triethylamine. The enone **7**, obtained as a mixture of (*E*)- and (*Z*)-isomers in a 1:2 ratio, was treated with methyl triphenylphosphoranylideneacetate without purification to give the unsaturated ester as a mixture of (1*E*,8*E*)-**1a** and (1*Z*,8*E*)-isomers **1b** in a 1:2 ratio in 50% overall yield from **6**. When the mixture of **1a** and **1b** was treated with iodine at ambient temperature for 43 h in carbon tetrachloride, the ratio of **1a** to **1b** changed to 2:1 (Scheme 2). The isomers **1a** and **1b** were separated by HPLC.†

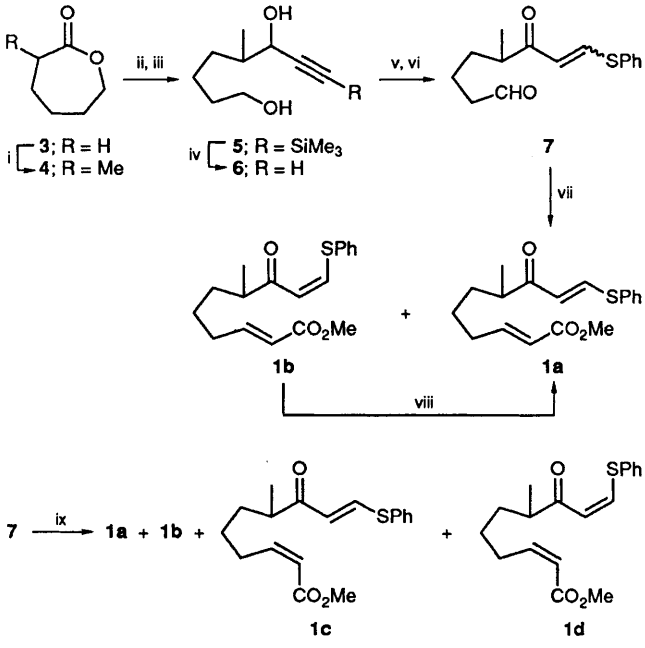


Scheme 1

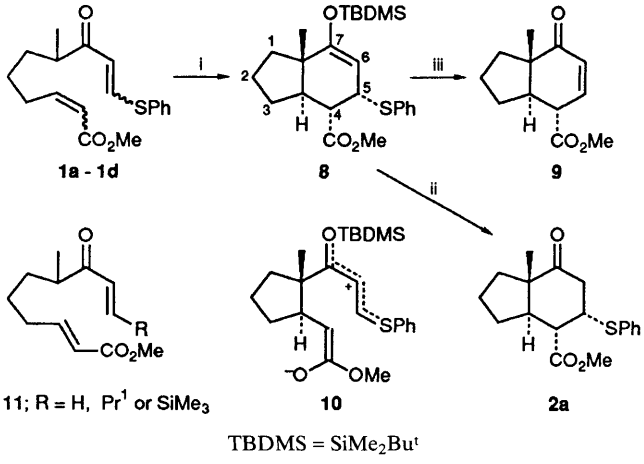
† Selected ^{1}H NMR (500 MHz; $CDCl_3$) data for **1a**: δ 5.81 (dt, 1H, *J* 14.4 and 1.1 Hz), 6.13 (d, 1H, *J* 16.0 Hz), 6.93 (dt, 1H, *J* 14.4 and 7.6 Hz) and 7.80 (d, 1H, *J* 16.0 Hz). For **1b**: δ 5.81 (dt, 1H, *J* 14.4 and 1.1 Hz), 6.40 (d, 1H, *J* 9.8 Hz), 6.93 (dt, 1H, *J* 14.4 and 7.6 Hz) and 7.31 (d, 1H, *J* 9.8 Hz). For **1c**: δ 5.78 (dt, 1H, *J* 11.6 and 1.8 Hz), 6.14 (d, 1H, *J* 14.7 Hz), 6.18 (dt, 1H, *J* 11.6 and 8.0 Hz) and 7.80 (d, 1H, *J* 14.7 Hz). For **1d**: δ 5.79 (dt, 1H, *J* 11.7 and 1.9 Hz), 6.22 (dt, 1H, *J* 11.7 and 7.2 Hz), 6.42 (d, 1H, *J* 9.8 Hz) and 7.30 (d, 1H, *J* 9.8 Hz). For **8**: δ 0.15 (s, 6H), 0.89 (s, 3H), 0.91 (s, 9H), 2.95 (dd, 1H, *J* 11.8 and 5.0 Hz), 3.18 (s, 3H), 4.37 (t, 1H, *J* 5.0 Hz) and 4.68 (d, 1H, *J* 5.0 Hz). For **2a**: δ 1.04 (s, 3H), 2.53 (dd, 1H, *J* 14.8 and 1.9 Hz), 3.02 (dd, 1H, *J* 14.8 and 5.2 Hz), 3.18 (dd, 1H, *J* 11.3 and 4.0 Hz), 3.66 (s, 3H) and 4.07 (ddd, 1H, *J* 5.2, 4.0 and 1.9 Hz). For **9**: δ 0.99 (s, 3H), 3.76 (s, 3H), 5.90 (dd, 1H, *J* 9.8 and 2.9 Hz) and 6.82 (dd, 1H, *J* 9.8 and 1.8 Hz).

Reaction of the aldehyde **7** with bis(2,2,2-trifluoroethyl) methoxycarbonylmethylphosphonate in the presence of potassium hexamethyldisilazide (KHMDS) and 18-crown-6[6] furnished the corresponding (8*Z*)-isomers **1c** and **1d** as major products together with the (8*E*)-isomers **1a** and **1b** in 68% overall yield from **6**. The four isomers **1a, 1b, 1c** and **1d,** obtained in a 1:2:12:24 ratio, were separated by HPLC.

After several trials, the annulation of **1** to **2** was achieved by treatment with *tert*-butyldimethylsilyl trifluoromethanesul-



Scheme 2 *Reagents*: i, LHMDS; MeI, HMPA; ii, DIBAH; iii, $LiC{\equiv}CSiMe_3$; iv, Bu^n_4NF; v, periodinane;[5] vi, PhSH, Et_3N; vii, $Ph_3P{=}CHCO_2Me$; viii, I_2; ix, $(CF_3CH_2O)_2P(=O)CH_2CO_2Me$, KHMDS, 18-crown-6



TBDMS = $SiMe_2Bu^t$

Scheme 3 *Reagents*: i, $TBDMSOSO_2CF_3$, Et_3N; ii, 10% $HClO_4$; iii, Bu^n_4NF

phonate in the presence of triethylamine[7] in dichloromethane at room temperature for 45 min. It was noteworthy that the same product **8**, m.p. 78–80 °C, was produced as a single stereoisomer in *ca.* 63% yield from each of the four isomers. The stereostructure of the product was assigned as the *trans*-isomer **8** possessing an equatorially oriented methoxycarbonyl group and an axially oriented sulphenyl group on the basis of ^{1}H NMR analysis. Thus a 13.7% NOE was observed between the angular methyl group and 4-H. Furthermore, 4-H was coupled with 3a-H and 5-H, with coupling constants J = 11.8 and 5.0 Hz, respectively. The formation of the same product **8** from the four isomers **1a–1d** indicates a stepwise process for the annulation, involving the zwitterion intermediate **10**. Since treatment of the enones **11** (R = H, Pr^i or $SiMe_3$) under the same conditions as above gave none of the desired product, the sulphide group seemingly plays an important role in the cyclisation.

The *tert*-butyldimethylsilyl (TBDMS) group was removed with 10% perchloric acid to afford, in 74% yield, the ketone **2a**, m.p. 79.5–80 °C, whose structure was established by X-ray analysis.‡ On treatment of **8** with tetra-n-butylammonium fluoride, the unsaturated ketone **9** was obtained in 46% yield (Scheme 3). Thus, a novel approach to polyfunctionalised *trans*-hydroindanes was developed through a sulphur-mediated intramolecular double Michael type reaction.

‡ Full details of the crystal structure determination will be published elsewhere.

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