Novel Asymmetric Cyclopropanation Utilizing Sulfinyl Chirality: Application to Construction of a Spiro[4.5]decane System

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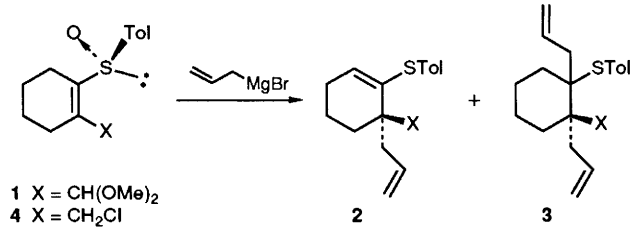
An optically active vinylic sulfoxide is stereoselectively transformed into a chiral cyclopropane by means of a Michael addition reaction with an allyl Grignard reagent, and using this novel cyclopropanation, asymmetric construction of a spiro[4.5]decane is achieved.

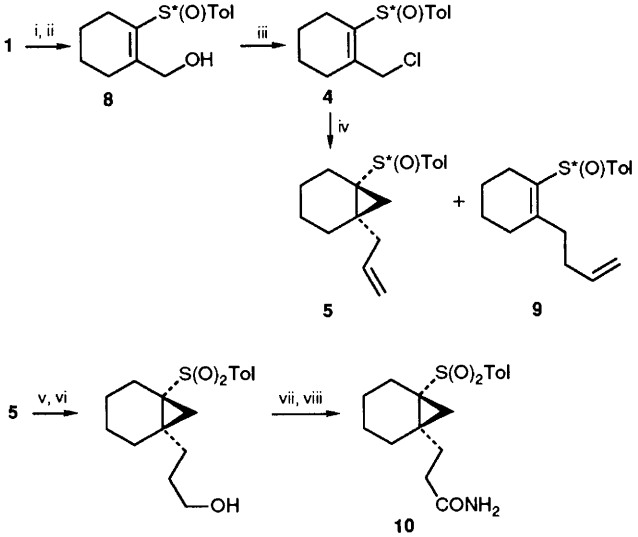
In the course of our studies on novel methods for asymmetric construction of quarternary carbon centres using a chiral sulfinyl auxiliary,[1] we recently described (Scheme 1) that reaction of a vinylic sulfoxide **1** with allylmagnesium bromide afforded the monoallylated product **2** with almost 100% enantiomeric excess, along with the diallylated compound **3**.[2] On the other hand, the same treatment on **4** was found to lead to a quite different mode of reaction. In this communication we describe the stereoselective preparation of the chiral cyclopropane **5** and its derivation into a spiro[4.5]decane **6** *via* a ring-opened product **7**.

The vinylic sulfoxide **4**, prepared from the acetal **1** *via* **8** as outlined in Scheme 2, was treated with 3 equiv. of allylmagnesium bromide in tetrahydrofuran (THF) at −78 °C to give the cyclopropane compound **5** (66%) as a single diastereoisomer along with the coupling product **9** (16%). The absolute configuration of **5** was confirmed by an X-ray crystallographic study of a derivative **10** (obtained from **5** by a four-step sequence). The highly diastereoselective cyclopropanation can be explained as follows. The magnesium centre of Grignard reagent, which can coordinate both to the oxygen atom of the sulfinyl group and to the chloride atom at the γ-position, is believed to approach exclusively from the α-face through the more energetically favourable transition state **A** (Fig. 1) rather than *via* the opposite face (transition state **B**).[3]

Although many synthetic methods for cleavage of cyclopropane rings have been explored,[4] few ring-opening reactions of cyclopropanes derivatized with sulfur have been reported in comparison with that of siloxycyclopropanes.[5] Such a regioselective ring-opening of **5** was attempted by use of a variety of electrophilic reactions on the electron-rich cyclopropyl sulfide **11**, derived from **5** by the following sequence: (i) reduction of sulfoxide to sulfide; (ii) hydroboration–oxidation; (iii) Swern oxidation; (iv) Horner–Emmons reac-



Scheme 1 Tol = C_6H_4Me



Scheme 2 *Reagents and conditions*: i, *p*-$MeC_6H_4SO_3H$, acetone, H_2O (97%); ii, $NaBH_4$, THF (90%); iii, $MeSO_2Cl$, LiCl, 2,4,6-collidine, DMF, Bu_4NCl, 0 °C (94%); iv, (allyl)MgBr, THF, −78 °C (82%); v, H_2O_2, AcOH (93%); vi, BH_3·Me_2S, THF, 0 °C; 3 mol dm^{-3} NaOH, 30% H_2O_2, room temp. (84%); vii, Jones oxidation (91%); viii, $ClCO_2Et$, Et_3N; NH_3(g) (86%)

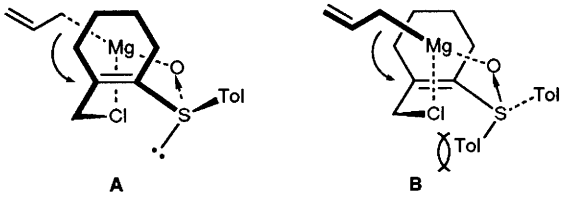
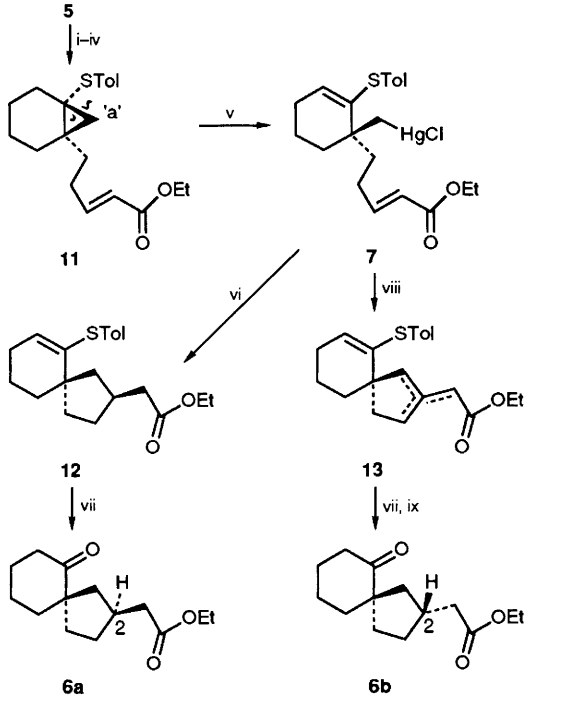
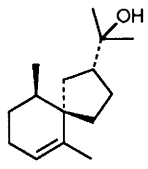


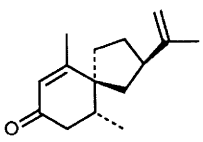
Fig. 1



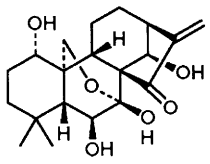
Scheme 3 *Reagents and conditions*: i, $(CF_3CO)_2O$, NaI acetone, 0 °C (100%); ii, BH_3·Me_2S, THF 0 °C; 3 mol dm^{-3} NaOH, 30% H_2O_2, room temp. (84%); iii, $(COCl)_2$, dimethyl sulfoxide (DMSO), CH_2Cl_2, −50 °C; Et_3N, room temp. (87%); iv, $(EtO)_2POCH_2CO_2Et$, NaH, THF room temp. (82%); v, $Hg(OCOCF_3)_2$, NaOAc, CH_2Cl_2, room temp. saturated NaCl, CH_2Cl_2, room temp. (89%); vi, Bu_3SnH, CH_2Cl_2, −40 °C → room temp. (86%); vii, 10% HCl, MeCN, 60 °C (84% for **12** and **13**); viii, Li_2PdCl_4, DMF, THF, reflux (91%); ix, H_2, 10% Pd–C, EtOH, room temp. (100%)



Hinesol **14**



Solavetivone **15**



Oridonin **16**

tion with diethyl phosphonoacetic acid ethyl ester and sodium hydride. Synthetic elaboration for **11** (Scheme 3) revealed that reaction with mercury(II) trifluoroacetate† in methylene chloride in the presence of sodium acetate at room temperature gave rise to the desired α,β-unsaturated γ-sulfenyl alkylmercury chloride **7** in a highly regioselective manner. Cyclization of **7** by a radical reaction with n-butyltin hydride initiated by 2,2′-azoisobutyronitrile (AIBN)[6] proceeded smoothly and gave the spiro[4.5]decane derivative **12** in 86% yield. This was subsequently hydrolysed to give ketone **6a** as the major product (**6a**:**6b** = 89:11, 84%).‡ On the other hand, palladium(II)-assisted cyclization [Li_2PdCl_4, dimethylformamide (DMF)–THF, reflux][7] of **7** afforded a mixture of unsaturated spiro[4.5]decane derivatives **13**, which were converted into ketoesters **6a** and **b** with the latter as the major product (**6a**:**6b** = 17:83, 84%)‡ in two steps [(i) hydrolysis with 10%HCl–MeCN; (ii) catalytic hydrogenation with 10% palladium on charcoal].

† Using mercury(II) acetate in place of $Hg(OCOCF_3)_2$ led to a decrease of reaction rate whilst reaction with mercury(II) perchlorate gave only a complex mixture: Ring-opening reactions of cyclopropane derivatives with mercury(II) salts have been previously demonstrated: R. G. Salomon and R. D. Gleim, *J. Org. Chem.*, 1976, **41**, 1529; D. B. Collum, F. Mohamadi and J. S. Hallock, *J. Am. Chem. Soc.*, 1983, **105**, 6882; J. M. Coxon, P. J. Steel and B. I. Whittington, *J. Am. Chem. Soc.*, 1988, **110** 2988.

‡ The ratios of **6a** to **b** were determined by HPLC (Sumipax OA-2000A, AcOEt–hexane 1:10). The following sequence for lactonization was employed to confirm the stereochemistry at C-2 of **6b**: (*i*) reduction of **6b** with $NaBH_4$ in MeOH; (*ii*) hydrolysis with 3 mol dm^{-3} NaOH in MeOH; (iii) lactonization (di-2-pyridyl disulfide, PPh_3, benzene, room temp. → reflux; $AgOCOCF_3$, NaOAc, benzene, reflux). The same sequence of reactions were applied to **6a** for which no lactone was formed.

In conclusion, we have performed diastereoselective cyclopropanation of a vinylic sulfoxide with allylmagnesium bromide utilizing sulfinyl chirality (**4** → **5**) and demonstrated the first sulfur-assisted chemo- and regio-selective ring-opening of cyclopropanes (**11** → **7**). Furthermore, these ring-opened products are useful intermediates for the synthesis of natural products and we have illustrated this in the asymmetric synthesis of spiro[4.5]decane derivatives **6a** and **b** which should be capable of further elaboration into important natural products; *e.g.* hinesol **14** (from **6a**), and spirovetivane-type sesquiterpene **15** and kaurane-type diterpene **16** (from **6b**), respectively.

We thank Dr S. Fujii in Osaka University for generous help with the X-ray crystallography.

Received, 21st October 1991; Com. 1/05339F

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