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Synthesis of Spiro[4.5]decane Ring System through Allylsilane Promoted Spiroannulation

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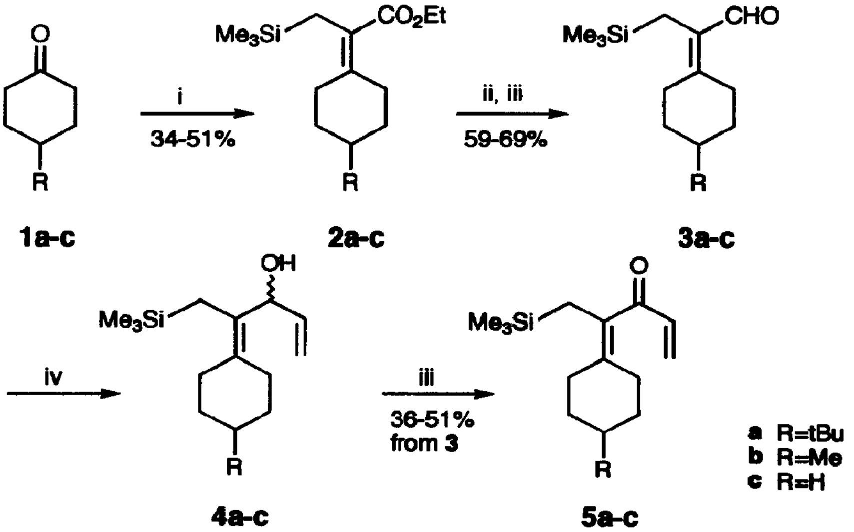
Abstract: Spiro[4.5]decane ring system with methylene ketone on five membered ring was synthesized by Nazarov cyclization of α-(trimethylsilylmethyl)divinyl ketone derivatives.

β-(Ethoxycarbonyl)allylsilane is an interesting organic bifunctional unit which can react with both nucleophiles and electrophiles. We are interested in the application of this unit to the synthesis of terpenoid skeleton, and have reported a synthesis of α-methylene-γ-lactone fused to carbocycles[1] and that of bicyco[4.3.0]nonanes.[2] Here we report a synthesis of the spiro[4.5]decane carbon framework by spiroannulation of cyclohexanone through β-(ethoxycarbonyl)allylsilane. The spiro[4.5]decane ring system is one of the common carbon skeletons in sesquiterpenoids, such as acoranes or vetispiranes.[3,4]

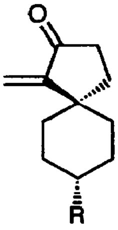
Synthesis of the precursors **5a-c** was carried out from the cyclohexanones **1a-c** as shown in scheme 1. A β-(ethoxycarbonyl)allylsilane moiety was first introduced by Hoffmann's Wittig reaction[1] to give **2**, which



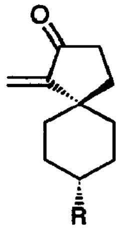
Scheme 1. Reagents and Conditions. i, $(EtO)_2P(O)CH(CO_2Et)CH_2SiMe_3$, NaH, DME, 70 °C. ii, $LiAlH_4$, Et_2O, 0 °C. iii, MnO_2, CH_2Cl_2, r.t. iv, $CH_2{=}CHMgBr$, THF, 0 °C.

was converted to the aldehyde **3** by $LiAlH_4$ reduction and subsequent MnO_2 oxidation. The Grignard reaction of **3** with vinyl magnesium bromide afforded the alcohol **4**, which was found to be an 1:1 diastereomeric mixture on the basis of ^1H NMR spectra. The alcohol **4** was oxidized to yield the ketone **5**, the precursor of cyclization reaction.

The Nazarov cyclization of α'- and/or β'-substituted-α-(trimethylsilylmethyl)divinyl ketone is recently reported by Kang *et al.*.[5,6] However, cyclization of β,β'-disubstituted compound is not studied. When **5a** was treated with $FeCl_3$ according to Kang's procedure with slight modification,[5,7] a diastereomeric mixture of spiro compounds, **6a** and **7a**, was formed in 59% yield (**6a**:**7a** = 5:1).[8] The stereochemistry of the cyclized product was determined from NOE, which was observed between *t*-butyl group and one of exo-methylenic protons for **7a**. Similarly, **5b** produced a mixture of **6b** and **7b** (61% yield, 5:1 ratio),[8] while **5c** gave **6c** (67%). The observed stereoselectivity can be rationalized by the steric congestion caused by trimethylsilylmethyl group. It is interesting that this stereoselectivity of spirocyclization, with respect to the configuration of exo-methylene group, is opposite to carbomercuration method recently reported by Huang and Forsyth.[4b]



6a R=tBu
6b R=Me
6c R=H



7a R=tBu
7b R=Me

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7. $FeCl_3$ was added to a solution of **5a** in CH_2Cl_2 at -60 °C, then the reaction mixture was slowly warmed to room temperature. The reaction of **5a** at -60 °C proceeded very slowly, while the addition of $FeCl_3$ at 0 °C gave unsatisfactory yield.
8. The diastereomeric mixture was not separated and the ratio was determined from the ^1H-NMR spectra. The structure of **6b** and **7b** was determined from chemical shift of olefinic protons compared with **6a** and **7a**; **6a**: δ 5.18 and 5.98; **7a**: δ 5.46 and 6.01; **6b**: δ 5.18 and 5.98; **7b**: δ 5.41 and 6.00 ($CDCl_3$).

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