# New Cyclization Reaction of 2-(Trimethylsilylmethyl)pentadienal. Synthesis of Spiro[4.5]decane Ring System

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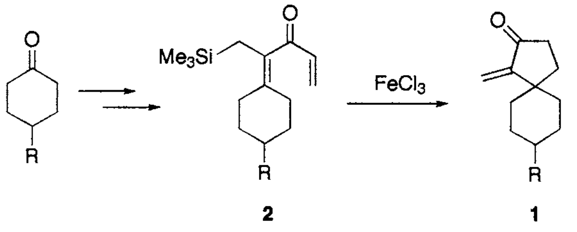
4-Cyclohexylidene-2-(trimethylsilylmethyl)but-2-enal, allylsilane type of linearly conjugated pentadienal, underwent a new self-cyclization reaction to afford 2-methylspiro[4.5]-2-decen-1-one. The reaction of 4-(4-alkylcyclohexylidene)-2-(trimethylsilylmethyl)-2-butenal proceeded stereoselectively.

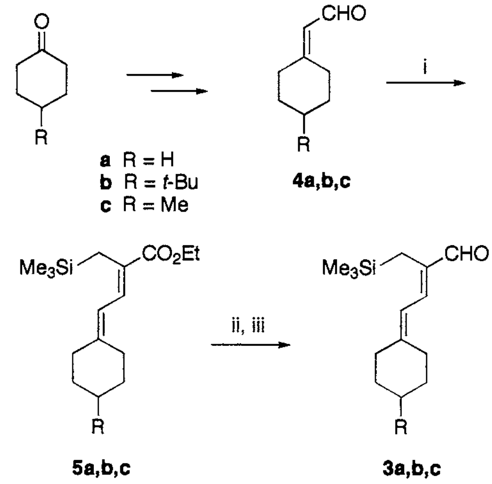
The Nazarov cyclization of a cross-conjugated divinyl ketone is a useful method to synthesize five-memberd carbocycles.[1] We reported the synthesis of spiro[4.5]decanes **1** by Nazarov cyclization of α-(trimethylsilylmethyl)divinyl ketones **2** (Scheme 1),[2] in which the reaction was activated by an allylic trimethylsilyl group.[3,4] In contrast, linearly conjugated dienal is not a suitable substrate for the Nazarov or related type of self-cyclization. We envisioned that this moiety would also be useful if the double bond is activated by silyl group at allylic position, since allylsilanes act as the carbanion equivalent and thus easily react with aldehyde.[5] Here we report a new cyclization reaction of linearly conjugated 2,4-pentadienal substituted by trimethylsilylmethyl group at C(2)-position, by which spiro[4.5]decane ring system,[6] one of the major skeleton in natural sesquiterpenes such as acoranes or vetispiranes,[7,8] was synthesized.



**Scheme 1.**

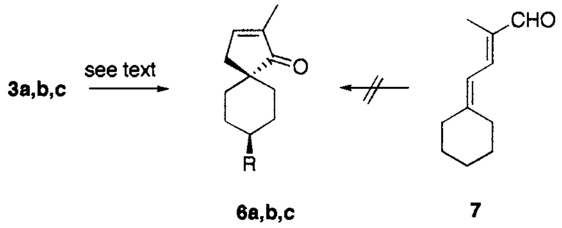
The substrates of the present study are the compounds **3a–c**, which were synthesized by the route illustrated in Scheme 2. Namely, to the aldehyde **4a**, prepared from cyclohexanone, was introduced the β-(ethoxycarbonyl)allylsilane moiety[2] giving **5a** in 51% yield. Compound **5a** was obtained as the only (*Z*)-isomer, and the geometry of which was determined based on the chemical shift of the olefinic proton (δ 7.40; $CH=CCO_2Et$).[9] DIBAL-H reduction of **5a** (92%) followed by $MnO_2$ oxidation afforded aldehyde **3a** (89%). Similarly, **3b** and **3c** were prepared from 4-*tert*-butylcyclohexanone and 4-methylcyclohexanone, respectively.

The cyclization reaction was carried out by the treatment of **3a** with ca. 2 eq of $FeCl_3$[10] in $CH_2Cl_2$ at room temperature[11] giving spiro[4.5]decane compound **6a**[12] in 78% yield (Scheme 3). Some other Lewis acids, such as $AlCl_3$, $Et_2AlCl$ and $BF_3OEt_2$ were also used but without success. The stereochemistry of the cyclization reaction was then studied using **3b** as the substrate, which afforded **6b**[13] as a single diastereomer in 80% yield. The structure of **6b** was determined from NOE signal observed between allylic methylene and axial protons on cyclohexane ring as shown in Figure 1. Compound **3c** afforded **6c**[14] in 70% yield, which was again obtained as a single diastereomer, and its structure was determined independently in the same way (Figure 1). The stereoselectivity of the cyclization reaction can be rationalized by a preferential equatorial attack to the exocyclic double bond.[15]



Reagents and conditions: i) $(EtO)_2P(O)CH(CO_2Et)CH_2SiMe_3$, NaH, DME, reflux (**a**: 51%, **b**: 35%, **c**: 58%); ii) DIBAL-H, $CH_2Cl_2$, -60 °C (**a**: 93%, **b**: 96%, **c**: 91%); iii) $MnO_2$, $CH_2Cl_2$, r.t. (**a**: 89%. **b**: 88%, **c**: 81%).

**Scheme 2.**



**Scheme 3.**

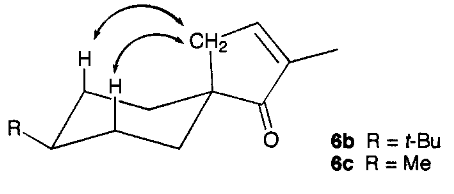
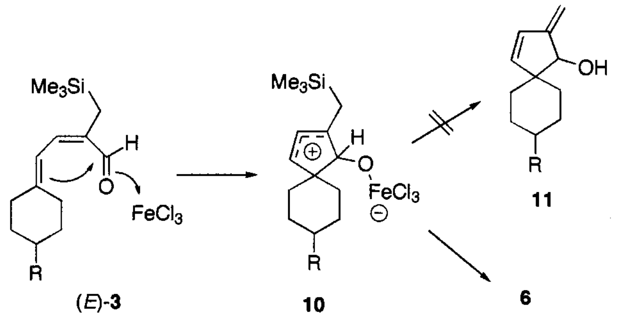


**Figure 1.**

In order to clarify the role of the trimethylsilyl group, the cyclization reaction of desilylated substrate **7**, prepared in the same way, was also examined. However, as expected, compound **7** did not afford any cyclization product after treatment under the same reaction conditions (Scheme 3). This indicates that the cyclization of **3** proceeds through silicon-stabilized carbocation **10** (Scheme 4).[5] It is interesting that the product was not the expected alcohol **11** but enone **6**. The reaction mechanism is not clear as yet, however isomerization from **11** to **6** is a plausible pathway. The double-bond isomerization from (*Z*)-**3** to (*E*)-**3** should occur prior to the cyclization, as observed previously,[9] since the cyclization must be proceeded from (*E*)-**3**.

Another interesting aspect of the present cyclization is the reaction mode, which is illustrated in Figure 2. We previously reported[9] that 2-(trimethylsilylmethyl)pentadienoic acid or its ester reacts with proton to afford lactone, where the reaction proceeded through mode A (E = $R^3$ = H, $R^4$ = OH or OEt) but not mode B. In contrast, the present reaction apparently proceeded via mode B (E = $FeCl_3$, $R^1$ = $R^4$ = H).



**Scheme 4.**

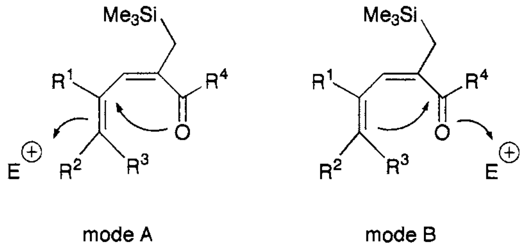


**Figure 2.**

In conclusion, a new self-cyclization reaction of linearly conjugated pentadienal assisted by allylic trimethylsilyl group was established. Since the carbonyl position in the product is different from that of the Nazarov cyclization, it is possible to obtain both spiro[4.5]decan-1-one (**6**) and -2-one (**1**) derivatives from cyclohexanone by two different types of spiroannulation reaction, the present dienal cyclization and the Nazarov cyclization.

## References and Notes

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10 Anhydrous $FeCl_3$ was used without careful handling.

11 $FeCl_3$ was added to a solution of **3** at –60 °C, and the reaction mixture was slowly warmed to room temperature; See Ref. 2a.

**12** **6a**: IR (neat) 1702 and 1640 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.20–1.40 (6H, m) 1.52–1.77 (4H, m), 1.77 (3H, dt, $J$ = 1.3, 2.3 Hz), 2.42 (2H, quint, $J$ = 2.3 Hz), and 7.23 (1H, tq, $J$ = 2.3, 1.3 Hz).

**13** **6b**: IR (neat) 1706 and 1637 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.85 (9H, s), 1.00–1.11 (3H, m), 1.24–1.35 (2H, m), 1.53–1.66 (2H, m), 1.73–1.80 (2H, m), 1.77 (3H, dt, $J$ = 1.4, 2.2 Hz), 2.39 (2H, quint, $J$ = 2.2 Hz), and 7.23 (1H, tq, $J$ = 2.2, 1.4 Hz).

**14** **6c**: IR (neat) 1703 and 1641 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.90 (3H, d, $J$ = 6.5 Hz), 0.93–1.05 (2H, m), 1.21–1.28 (2H, m), 1.36–1.49 (1H, m), 1.61 (2H, br dt, $J$ = 3.5, 13 Hz), 1.66–1.72 (2H, m), 1.77 (3H, dt, $J$ = 1.4, 2.3 Hz), 2.39 (2H, quint, $J$ = 2.3 Hz), and 7.23 (1H, tq, $J$ = 2.3, 1.4 Hz).

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