Iron(III)-induced tandem Nazarov cyclization–rearrangement of α-(trimethylsilylmethyl)divinyl ketone. Synthesis of the bicyclo[4.3.0]nonane ring system *via* spiro[4.4]nonane

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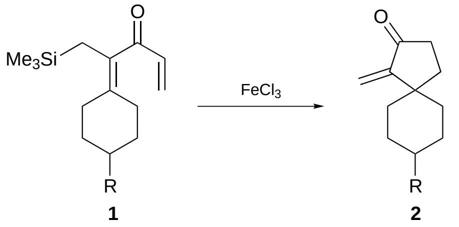
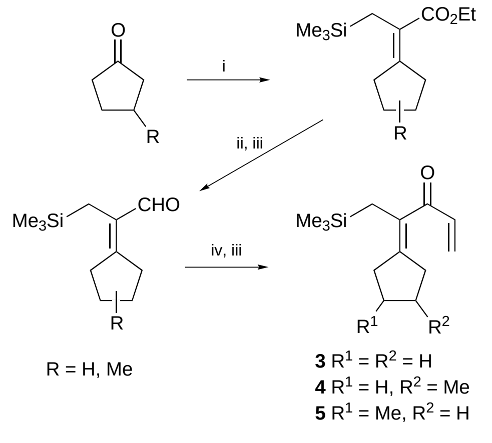
6-Methylbicyclo[4.3.0]non-8-en-7-one was synthesized by $FeCl_3$-induced tandem Nazarov cyclization–rearrangement of 4-cyclopentylidene-5-trimethylsilylpent-1-en-3-one, *via* 7-methyl-1-methylenespiro[4.4]nonan-2-one as intermediate.

Construction of various carbocyclic ring systems is fundamental chemistry in the synthesis of terpenoids and related compounds.[1] Allylsilanes have been developed as useful intermediates for this purpose.[2] We are studying the synthesis of carbocycles[3] and lactones,[4] basic structures of terpenoids,[5] utilizing intramolecular cyclization of β-(ethoxycarbonyl)-allylsilane. Recently we reported that Nazarov cyclization of α-(trimethylsilylmethyl)divinyl ketone derivatives **1**, derived from β-(ethoxycarbonyl)allylsilane attached to a six-membered ring, gives spiro[4.5]decanes **2** (Scheme 1).[6,7] Here we report that the α-(trimethylsilylmethyl)divinyl ketone attached to a five-membered ring undergoes tandem Nazarov cyclization–skeletal rearrangement to yield the bicyclo[4.3.0]nonane ring.[8]



Scheme 1

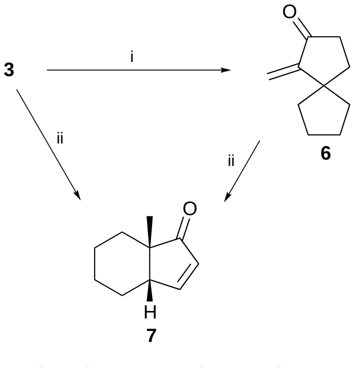
Synthesis of the cyclization precursors, α-(trimethylsilylmethyl)divinyl ketone **3**, was executed from cyclopentanone in five steps according to Scheme 2.[6] Similarly, **4** and **5** were prepared from 3-methylcyclopentanone and were separated by column chromatography.



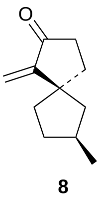
Scheme 2 *Reagents and conditions*: i, $(EtO)_2POCH(CO_2Et)CH_2SiMe_3$, NaH, DME, room temp.; ii, $LiAlH_4$, Et_2O, 0 °C; iii, MnO_2, CH_2Cl_2, room temp.; iv, $CH_2{=}CHMgBr$, THF, 0 °C

The Nazarov cyclization of **3** was carried out by treatment with $FeCl_3$ (2.5 equiv.) in CH_2Cl_2 at 0 °C† for 4 h, giving spiro[4.4]nonane **6**‡ in 56% yield. However, when **3** was subjected to the same treatment at room temperature§ for 24 h, compound **7**[9]¶ was obtained as the sole product in 62% yield. Treatment of **6** under the same reaction conditions (room temp., 24 h)§ gave **7** in 60% yield. From this result, along with the observation of behaviour on TLC, it was suggested that **7** was formed from **3** *via* **6** as intermediate (Scheme 3).

A further study of the stereochemistry of this Nazarov cyclization and subsequent skeletal rearrangement was made using methyl derivatives **4** and **5** as substrates. First, **4** and **5** were treated with $FeCl_3$ at 0 °C,† giving two isomers of spiro[4.4]nonanes¶ **8** and **9** as inseparable mixtures. The ratios of the two isomers were **8** : **9** = 4 : 1 from **4**, and 1 : 1 from **5**. The tandem Nazarov cyclization–rearrangement reaction was next examined and the results are summarized in Table 1. The rearranged product **10** consisted of five isomers **10a–e** as inseparable mixtures. Although the exact structures of each isomer could not be determined, the major isomer **10a** was shown to have the illustrated structure by ^1H NMR spectroscopy. It was confirmed here again that the bicyclo-[4.3.0]nonene is formed *via* spiro[4.4]nonane. Thus both direct treatment of **4** (entry 1) and treatment of spiro compounds obtained from **4** (entry 3) afforded **10** in similar ratios. Compound **5** showed parallel results (entries 2 and 4). Different ratios of the isomers were obtained when the reaction



Scheme 3 *Reagents and conditions*: i, $FeCl_3$, CH_2Cl_2, −30 to 0 °C, 4 h; ii, $FeCl_3$, CH_2Cl_2, −30 °C to room temp., 24 h



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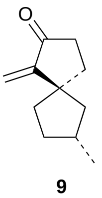

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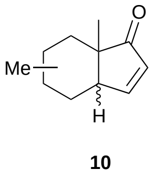

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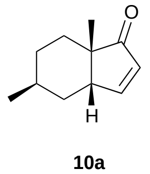
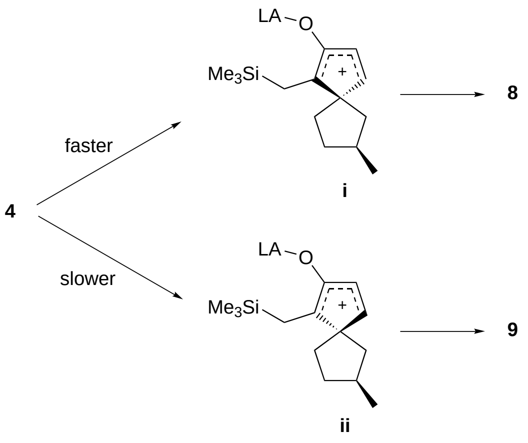


10a

Table 1 Nazarov cyclization–rearrangement of **4** and **5**[a]

Entry	Substrate	Temp.	t/h	Yield (%)	Ratio of isomers[b] **10a : 10b : 10c : 10d : 10e**
1	**4**	room temp.[e]	25	64	72 : 12 : 5 : 3 : 8
2	**5**	room temp.[e]	26	65	46 : 32 : 10 : 6 : 6
3	**8** + **9** (4 : 1)[c]	room temp.[e]	49	67	69 : 13 : 5 : 4 : 9
4	**8** + **9** (1 : 1)[d]	room temp.[e]	53	63	42 : 25 : 10 : 11 : 12
5	**5**	room temp.[f]	25	67	13 : 13 : 9 : 26 : 39

[a] The reactions were carried out in CH_2Cl_2 with $FeCl_3$ (2.5 equiv.). [b] **10a**: δ 5.90 (dd, J 2.5, 6 Hz) and 6.70 (dd, J 2, 6 Hz); **10b**: δ 5.88 (dd, J 2.5, 6 Hz) and 6.65 (dd, J 2, 6 Hz); **10c**: δ 5.84 (dd, J 1.5, 6 Hz) and 6.85 (dd, J 3, 6 Hz); **10d**: δ 5.81 (br d, J 5.5 Hz) and 6.96 (br d, J 5.5 Hz); **10e**: δ 5.80 (br d, J 5.5 Hz) and 6.95 (br d, J 5.5 Hz) (in C_6D_6). [c] Obtained from **4**; see text. [d] Obtained from **5**; see text. [e] The reagents were added at −30 °C and then the mixture was slowly warmed to room temp. over period of 7 h, which is included in the reaction time. [f] The reagents were added at −30 °C and the cooling bath was immediately removed.



Scheme 4

temperature was raised immediately after addition of the reagent (entry 5).

In contrast, this type of skeletal rearrangement did not proceed when analogous spiro[4.5]decanes **2** (R = H, Me, and Bu^t)[6] were subjected to the same treatment. Accordingly, the rearrangement is considered to be limited to the strained spiro five-five membered ring system.

The stereochemistry of the Nazarov cyclization of **4** and **5** can be explained by steric interaction between the methyl group and the vinyl group, but not the trimethylsilylmethyl group (Scheme 4). Thus intermediate **i** derived from **4** is favoured over **ii**, in which the methyl group and the vinyl group are on the same side of the cyclopentane ring, while the distance between these two groups gives non-stereoselectivity for **5**.

Although the reaction mechanism of the rearrangement (*e.g.* **6** to **7**) is not clear, it can be deduced that **10a** is produced from **8** with *ca.* 90% selectivity. Similarly, **10b** must be the major product from **9**.

In conclusion, a new entry to bicyclo[4.3.0]nonane carbon framework was established *via* a tandem Nazarov cyclization–skeletal rearrangement of α-(trimethylsilylmethyl)divinyl ketone. Synthesis of the bicyclo[4.3.0]nonane ring system from a compound having a five-membered ring is one of the classical methods.[1] However, this new entry from cyclopentanone is different, since (i) the newly-formed ring is still five-membered, and (ii) the original five-membered ring becomes a six-membered ring.[10] We have previously reported a synthesis of the bicyclo[4.3.0]nonane ring system using β-(ethoxycarbonyl)allylsilane.[3] Thus the same carbon framework can be synthesized from β-(ethoxycarbonyl)allylsilane by two independent strategies.

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Footnotes

† The reagents were added at −30 °C and the reaction mixture was slowly warmed to 0 °C.

‡ Compound **6**: UV (pentane) 223 nm; IR (neat) 1730, 1645 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.31 (2 H, t, J 8 Hz), 2.04 (2 H, t, J 8 Hz), 4.84 (1 H, d, J 1 Hz), 6.08 (1 H, d, J 1 Hz); m/z 150 (M$^+$).

§ See footnote (*e*) of Table 1.

¶ The stereochemistry was determined from NOE measurements.

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