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Synthesis of Tricyclic Furans by a Novel Tandem Reaction: Intramolecular [3 + 2]-Hetero-Annulation of Allylsilanes with Cyclic 1,3-Diketones[1]

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Silicon-containing compounds have found widespread application in natural product synthesis.[2] In this paper, we wish to report a novel tandem reaction utilizing a silicon-terminated cyclization of allylsilanes with cyclic 1,3-diketones.[3] A tricyclic furan system is formed in a stereoselective way probably via an intramolecular [3 + 2]-hetero-annulation reaction.[4] Compounds of type **3** are useful precursors for D−E−F subunits of the complex triterpenes of the hopane type (Scheme 1).[5]

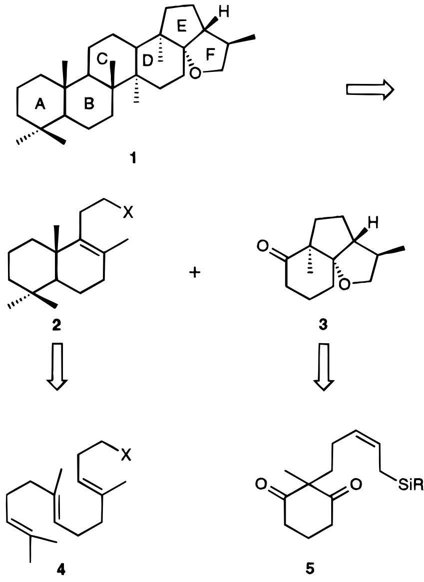
Triterpenoid **1** of the hopane type has been isolated from leaflets of *Cyathea spinulosa* ("hego" in Japanese), a tall evergreen tree fern (more than 4 m high) with large leaves (2 m long), distributed in the subtropical and tropical areas of Japan, Taiwan, the Philippines, China, Burma, India, and Nepal.[6]

As part of an ongoing program dealing with diastereoselective cyclizations using allyl- and propargylsilanes, we are interested in developing a new annulation strategy for heterocycles.[7−9] 1,3-Diketones of types **10**, **11**, **12**, and **14** can be synthesized by simple alkylation reactions of **6** and the requisite silanes **7**, **8**, and **9** in DMF as solvent and with NaH as base (Scheme 2).[10]

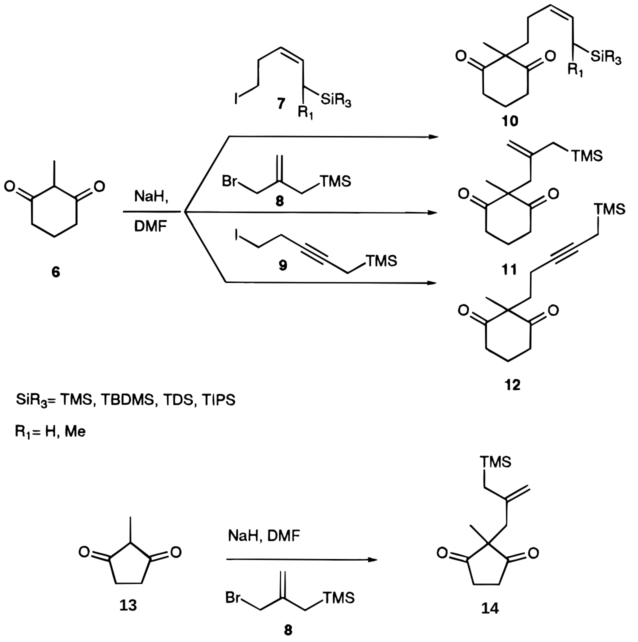
1,3-Diketones of type **10**, **11**, **12**, and **14** are useful precursors for cyclization studies since they are prochiral, which can be used for asymmetric cyclizations.[11]

The following cyclizations were carried out using Et$_2$AlCl as the Lewis acid catalyst. As shown in Scheme 3,[12] compound **10** (SiR$_3$ = TMS, R$_1$ = H) gave hydrindanones **15** (R$_1$ = H, R$_2$ = H) and **16** (R$_1$ = H, R$_2$ = H) in a ratio of 3:1 (47% yield). Compound **11** generated **17** in 57% yield. In addition, compound **18** was obtained in 12% yield and subsequently transformed into **17** by the use of TBAF. Finally, compounds **12** and **14** cyclized to form **19** and **20** in 71% and 74% yield.

Scheme 1



Scheme 2



Another noteworthy aspect is the use of branched allylsilane side chains (R$_1$= Me). To our surprise, in addition to the expected bicyclic cyclization product **16** (47%, R$_1$ = Me, R$_2$ = H), a second tricyclic reaction product **21** (SiR$_3$ = TMS, R$_1$ = Me) was isolated in 18% yield using Et$_2$AlCl as the Lewis acid promoter. Both compounds were isolated as single diastereomers.[12] The product ratio was dependent on the Lewis acid catalyst and the reaction conditions used. By employment of Me$_3$Al the product ratio was changed, and 35% of **21** (SiR$_3$ = TMS, R$_1$ = Me) and 34% of **15** (R$_1$ = Me, R$_2$ = TMS) and **16** (R$_1$ = Me, R$_2$= TMS)[13] as a ratio of 1:4 were isolated (Scheme 4).

In order to improve the yield of tricyclic compounds **21**, the size of the silyl group should be increased.[14] Accordingly, we decided to synthesize several bulky

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(1) Dedicated to Clayton H. Heathcock on the occasion of his 60th birthday.

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(12) All new compounds gave spectral and analytical spectrometric data consistent with the assigned structures. Compounds **19** and **22** have also been synthesized by an independent route by Mori: Kinoshita, A.; Mori, M. *Chem. Lett.* **1994**, *8*, 1475.

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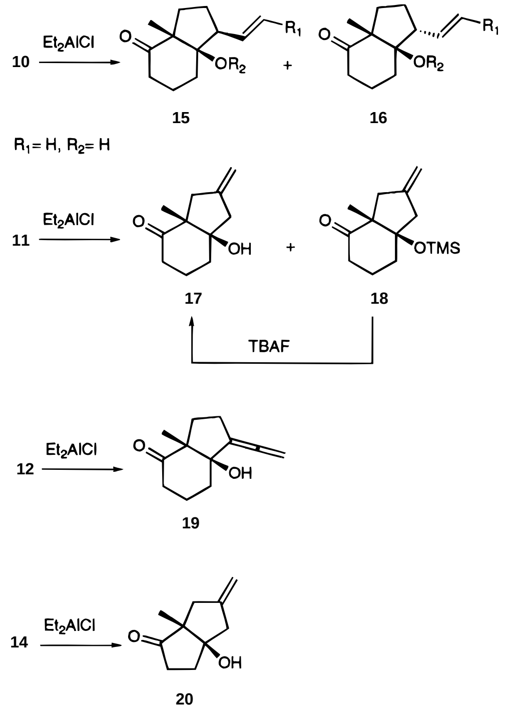
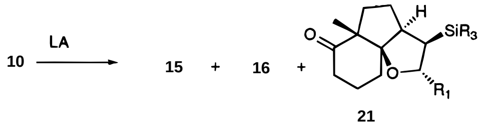
Scheme 3



Scheme 4



SiR_3= TMS, TBDMS, TDS, TIPS, R_1= H, Me, R_2= H, TMS, TBDMS
LA= Et_2AlCl, $AlMe_3$

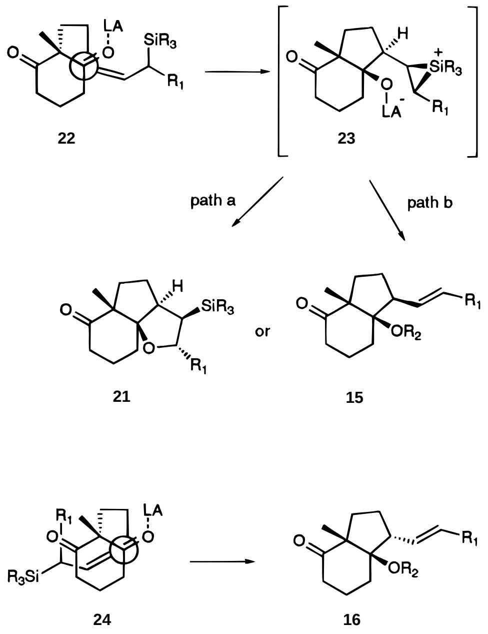
derivatives of **10** (R_1 = H) using SiR_3 = TBDMS, TDS, and the TIPS group (see Scheme 2).

Subsequently, we have tested Me_3Al, $EtAlCl_2$, and Et_2AlCl, but the latter gave the best results in the formation of the tricyclic products **21**. The TBDMS group yielded only 14% of **21** (SiR_3 = TBDMS, R_1 = H) and 31% of **15** (R_1 = H, R_2 = TBDMS) and **16** (R_1 = H, R_2 = TBDMS) as a ratio of diastereomers (7:1), whereas the TDS group produced **21** (SiR_3 = TDS, R_1 = H) in 49% yield. Finally, the TIPS group generated **21** (SiR_3 = TIPS, R_1 = H) in 61% isolated yield. In all reaction runs only one diastereomer of **21** was obtained following the proposed *synclinal* transition state as shown in Scheme 5.[12] The stereochemistry of the substituent groups was established by NOE experiments and single crystal diffractometry on compound **21** (SiR_3 = TMS, R_1 = Me).[13]

The mechanism of the formation of the tricyclic furans **21** has not been unambiguously established but can be explained by a mechanism similar to that proposed recently by Knölker et al. for their novel [3 + 2]-annulation reaction of enones with allylic silanes.[14] Similar observations with allenylsilanes have been observed by Danheiser et al.[15] The use of chiral allylsilanes has been studied by Panek et al.[16]

The formation of compound **21** can be explained by a *synclinal* transition state of type **22**. The intermediate siliranium ion **23** has two options for further reactions.

Scheme 5



SiR_3= TMS, TBDMS, TDS, TIPS
R_1= H, Me, R_2= H, TMS, TBDMS

Path a takes place via an 5-*exo-tet*-cyclization and forms the tricyclic furan **21**. This path is favored with bulky silyl groups (SiR_3 = TDS, TIPS) or branched allylsilanes (R_1 = Me) because the hindered environment in **23** prevents fast desilylation. Proceeding from the pentacoordinated silyl cation **23**, subsequent sila-Wagner Meerwein silyl shift,[14] assisted by the alkoxide formed in the inital cyclization, gives the tricyclic compound **21** in a stereoselective way.

On the other hand, with smaller silyl groups (SiR_3 = TMS, TBDMS, R_1 = H) intermediate **23** collapses either by an intra- or intermolecular attack at the silicon atom to form hydrindanone **15** (R_1 = H, R_2 = H, TBDMS) as the major product (path b). In addition, an *anti-periplanar* transition state **24** can be discussed. **24** precludes the formation of the tricyclic furan **21** but explains the formation of hydrindanone **16** (R_1 = H, Me, R_2 = H, TMS, TBDMS).

In summary, Et_2AlCl promotes the intramolecular cyclization of allyl- and propargylsilanes with 1,3 diketones to form hydrindanones of types **15**−**17**, and **19** and bicyclooctanes of type **20**. The use of branched allylsilanes and bulky silyl groups shifts the reaction path to the formation of tricyclic furans of type **21** via a *synclinal* transition state. The overall convenience of the method, and the complexity of the products obtained, suggests its further application in the synthesis of complex polycyclic natural products, such as hopanes. Work along these lines is in progress and will be reported in due course.

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Supporting Information Available: Procedures and characterization data (29 pages).

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