Intramolecular Cyclizations of Allyl- and Prop-2-ynyl-silanes with the Terminal Group governing the Regiochemical Outcome of the Cyclization

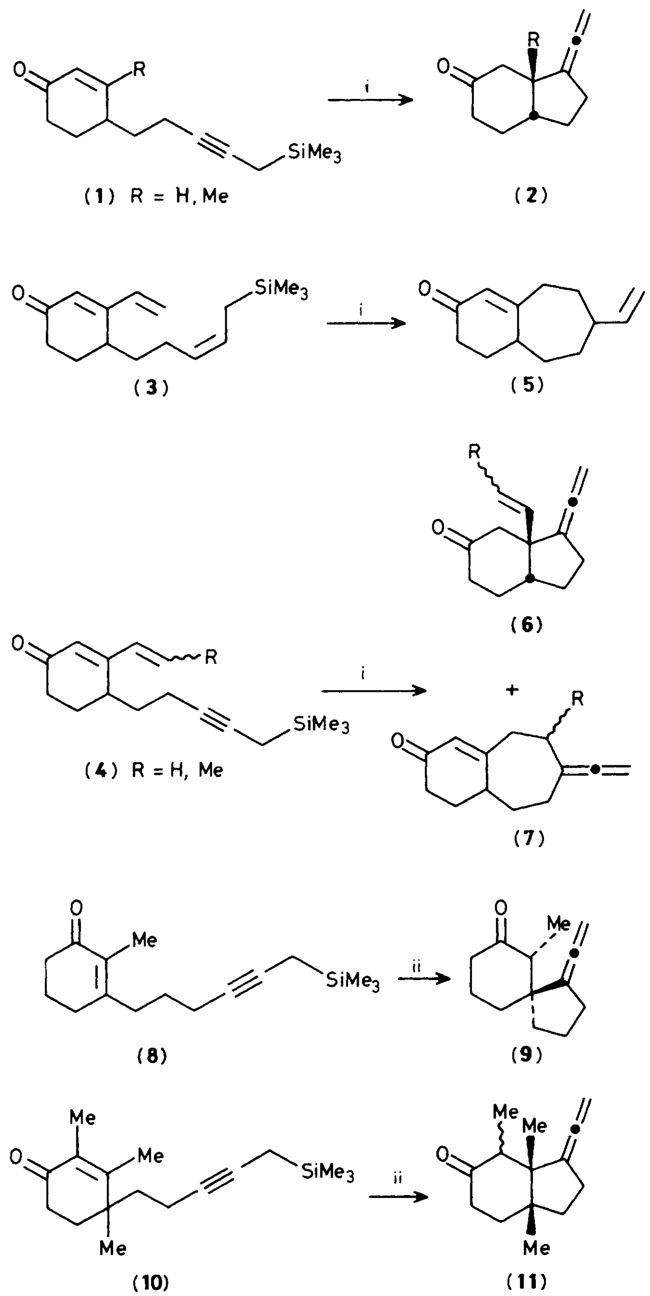
Dieter Schinzer,* Jürgen Steffen, and Sándor Sólyom

Institut für Organische Chemie, Universität Hannover, Schneiderberg 1 B, D-3000 Hannover 1, Federal Republic of Germany

The intramolecular additions of allyl- and prop-2-ynyl-silanes to enones and dienones are described; cyclizations carried out using 1.1 equiv. of either $EtAlCl_2$ in toluene or $TiCl_4$ in methylene chloride at low temperature have shown that the terminal group governs the regiochemical outcome of the cyclization, with allylsilane leading to 1,6 addition and prop-2-ynylsilane to 1,4 addition.

As part of a general study of Lewis-acid promoted intramolecular reactions of allyl- and prop-2-ynyl-silanes we have recently introduced $EtAlCl_2$ as a useful catalyst for intramolecular Sakurai reactions that lead stereoselectively to spiro-[4.5]decanones[1,2] and to fused [4.3.0]nonanones.[3] The products obtained are potentially useful precursors for a number of natural products.[3] We now describe further syntheses and additions of allyl- and prop-2-ynyl-silanes to enones and conjugated dienones. Related work by Majetich and co-workers[4] has recently been published.

Following Stork's[5] early studies, 3-ethoxycyclohex-2-enone was used to construct the desired starting materials. Alkylation of 3-ethoxycyclohex-2-enone with 5-trimethylsilyl-pent-3-enyl or -pent-3-ynyl iodide[6] yielded the alkylation products.



Reagents and conditions: i, $EtAlCl_2$, toluene, −78 °C; ii, $TiCl_4$, CH_2Cl_2, −78 °C.

These were then used in reactions with *e.g.*, di-isobutylaluminium hydride (DIBAH), MeLi, vinyl Grignard reagents, and 6-trimethylsilylhex-4-ynylmagnesium bromide[3] to afford the starting materials (**1**), (**3**), (**4**), (**8**), and (**10**). The cyclizations were carried out in toluene at −78 °C with 1.1 equiv. of $EtAlCl_2$ or in CH_2Cl_2 with 1.1 equiv. of $TiCl_4$ as Lewis acid catalysts. From (**1**) we obtained single isomers of the expected *cis* fused products (**2**) in 50% (R = H) and 87% (R = Me) yields.†

The intramolecular addition of allyl- and prop-2-ynyl-silanes (**3**) and (**4**) to conjugated dienones showed an interesting behaviour. Compound (**3**) cyclized only in 1,6 fashion leading to the bicyclo[4.5.0]undecenones (**5**). The reaction proceeded diastereoselectively at −78 °C forming a single diastereoisomer (60% yield).†‡ In contrast with (**3**), the prop-2-ynylsilanes (**4**) *reversed* the regioselectivity to afford the 1,4 addition products, bicyclo[4.3.0]nonanones (**6**) with an angular vinyl group as the major products, with only a minor amount of the 1,6 addition products (**7**) [ratio (**6**) : (**7**) = 10 : 1; yields R = H: (**6**) 80%, (**7**) 8%; R = Me: (**6**) 68%, (**7**) 6%].†

The preference for 1,4 addition is probably influenced by the low nucleophilicity of the prop-2-ynylsilane terminal group. Therefore, the formation of the five-membered ring reflects a reaction at the centre with the highest charge density. The 1,6 addition of the allylsilane could be a result of higher nucleophilicity; steric interactions become more important and the molecule reacts at the less hindered site forming a seven-membered ring.

Treatment of compounds (**8**) and (**10**) with $EtAlCl_2$ as the Lewis acid catalyst did not afford the cyclization products. However, the reactions proceeded smoothly with $TiCl_4$ at −78 °C. The spirocyclic product (**9**) is diastereoisomerically pure and was obtained in 46% yield.†§ Finally we have examined the cyclization of the sterically hindered compound (**10**). Again, reaction proceeded with $TiCl_4$ at −78 °C forming a highly functionalized hydrindanone (**11**) with two quaternary centres in 62% yield.

These results demonstrate an interesting change in ring-size selectivity between allyl- and prop-2-ynyl-silanes, governed by the terminal group, and provide a route to controlled annulation.

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† All new compounds have been fully characterized.

‡ Compound (**5**) shows only one set of lines in the ^{13}C n.m.r. spectrum, (100.61 MHz $CDCl_3$): δ 199(s), 171(s), 143.4(d), 127.6(d), 112.6(t), 44.9(d), 39.5(d), 37.3(t), 35.5(t), 34.7(t), 33.0(t), 30.56(t), 30.0(t).

§ Assignment of the configurations of the product followed from nuclear Overhauser effect (n.O.e.) experiments.