Stereoselective Allylsilane Additions to α-Diketone Diketals

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Titanium tetrachloride mediated addition of allyltrimethylsilane to α-diketone diketals (*cis*-1,6-dialkyl-2,5,7,10-tetraoxabicyclo[4.4.0]decanes) leads to 2,3-diallyl-2,3-dialkyl-1,4-dioxanes with very high diastereoselectivity involving an invertive (S_N2-like) substitution.

There have been many recent reports concerning the mechanism and diastereoselectivity of nucleophilic additions to cyclic acetals. As for the reaction of acetals with allyltrimethylsilane, the diastereoselectivity is dependent upon the structure of the cyclic acetal and the Lewis acid employed. Mechanistic hypotheses involving either synchronous (S_N2-like) or dissociative (S_N1-like) substitution processes have been proposed, as well as the involvement of equilibrating ion pairs.[1]

It is known that the acetalisation of butane-2,3-dione (biacetyl) with ethane-1,2-diol gives only a single product, *cis*-1,6-dimethyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane **1a** (quantitative yield).[2] Compound **1a** was treated with allyltrimethylsilane in the presence of $TiCl_4$ (3 equiv.) at −85 °C. The desired allylation proceeded smoothly to give *meso*-2,3-diallyl-2,3-dimethyl-1,4-dioxane **2a** along with small amounts of (DL)-2,3-diallyl-2,3-dimethyl-1,4-dioxane **3a** (**2a**:**3a**, 85:15) (78% of overall yield).† Both products result from a double addition of the allylic moiety, which takes place exclusively on a vicinal position rather than on a geminal one, Scheme 1.

The structure of allylation adduct **2a** was established by a series of 1D, NOESY, NOE and decoupling experiments. However, the relative stereochemistry of the two methyl groups remains uncertain. In order to confirm the *meso* configuration, diketone **4** [$Pd(OAc)_2$, benzoquinone, $HClO_4$, quantitative yield][3] was synthesized and then converted into **5** (KOBu^t, Bu^tOH, 30% yield).[4] The spectroscopic data of **5** are consistent with the rings having a *cis*-junction. Particularly, in the NOESY experiment, we observed that only one methyl group (Me) gives cross peaks with one axial hydrogen (H^a) of the 1,4-dioxane moiety.‡

The stereochemical results can be rationalized in terms of a synchronous (S_N2-like) substitution process. Ketal **1a** presents a high degree of symmetry, the only two possible ketal–Lewis acid complexes are enantiomers and therefore the addition process leads to only one product, regardless of which carbon atom the attack occurs (use of a large excess of $TiCl_4$ excludes formation of chelated complexes). Allylation of ketal–Lewis acid complex **A** according to a synchronous mechanism leads to a monocyclic derivative. Then, the second inverted allylation probably occurs on ketal–Lewis acid complex **B**. Transition states of both successive substitutions are stabilized through an anomeric effect.[5]

A similar trend was observed for the allylation reaction of pentane-2,3-dione diketal (*cis*-1-ethyl-6-methyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane) **1b**, since a mixture of **2b** and **3b** (**2b**:**3b**, 9:1) was formed in a combined yield of 74%.

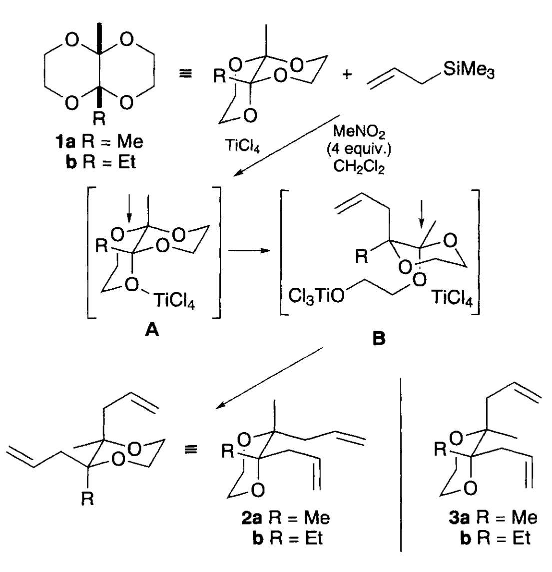
When dioxane **2a** was treated with 2 equiv. $TiCl_4$ at −50 °C, two rearranged ketones **6a** and **7** were isolated by chromatography in moderate yield (34%; **6a**:**7**, 53:47). Cleavage of dioxane **2a** giving ketone **6a** involves the migration of one allylic group (*cf.* transition state **C**), while the formation of **7** comes from the migration of one methyl group (*cf.* transition state **D**). In either case, the O–C and C–C bonds involved have the antiperiplanar relationship appropriate for 1,2-migration, Scheme 2.[6]

We have carried out a similar reaction with dioxane **2b**. We obtained only ketones **6b** (50% yield) and **8** (11% yield) resulting from an allylic group migration as shown in transition state **C** and **E**.

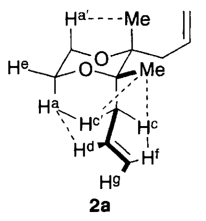
When 1-phenylpropane-1,2-dione diketal (*cis*-1-phenyl-6-methyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane) **9** was allylated under the same conditions as those applied to diketal **1**, we obtained the expected dioxane **10** in 16% yield (as a single diastereoisomer) as well as diol **11** (one diastereoisomer, 62% yield), Scheme 3.

Unexpectedly, diketal **1a** can be isomerized into diethyleneketal **12** by treatment at −50 °C with $TiCl_4$ (2 equiv.; 45% yield). But **12** was completely inert under the allylation conditions used for **1**, Scheme 4.

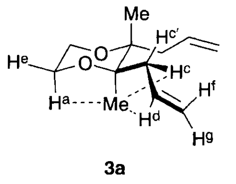
In contrast, the bis(ethyleneketal) of the cyclohexane-1,2-dione **13**, prepared according to a previously described procedure,[7] undergoes a diallylation reaction and gives rise to diol **14** (two isomers; 45% yield), Scheme 5.



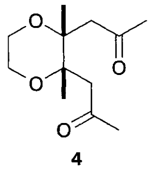
Scheme 1



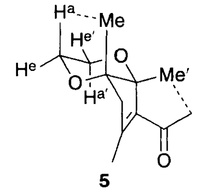
2a



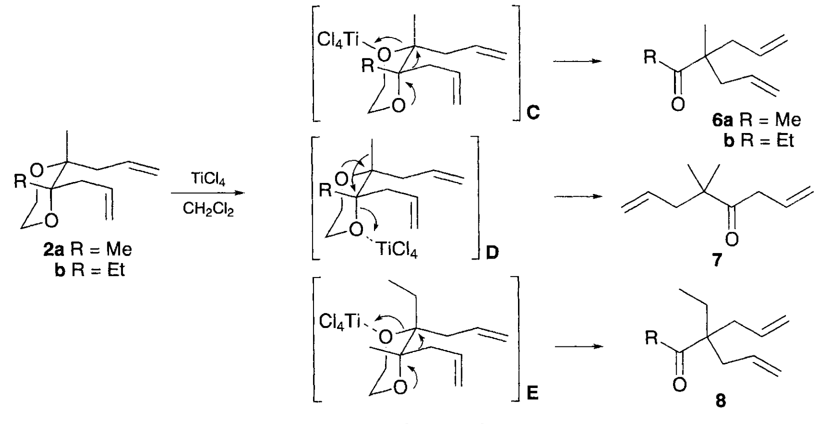
3a



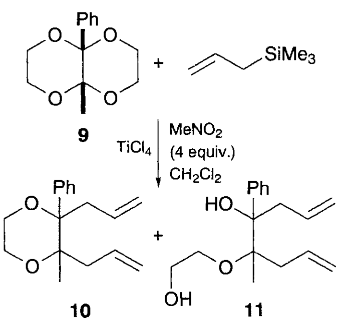
4



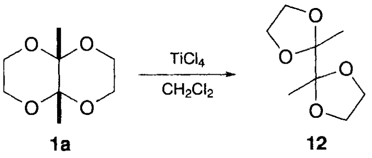
5



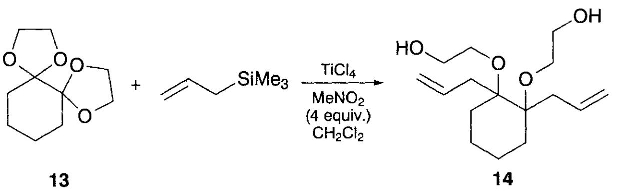
Scheme 2



Scheme 3



Scheme 4



Scheme 5

Now we are in a position to extend the allylation of 1,2-diketone diketals with allylsilanes other than allyltrimethylsilane.

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Footnotes

† **1a** or **1b** (1 equiv.) was allowed to react with allyltrimethylsilane (3 equiv.) in CH_2Cl_2 solution in the presence of $TiCl_4$ (3 equiv.) and nitromethane (4 equiv.) at −85 °C for 2 h. [The influence of the nitro group during the reaction of allylsilanes with various electrophilic compounds has been discussed previously (*cf.* ref. 8)].

‡ *Selected NMR data*: for **2a** ^{1}H NMR (400 MHz, $CDCl_3$; J in Hz) δ 5.82 (H^d, dddd, J_{df} 16.7, J_{dg} 10.6, J_{dc} 8.0, $J_{dc'}$ 6.1), 5.11 (H^g, m), 5.10 (H^h, m), 3.74 (H^a, d, J_{ae} 8.0), 3.54 (H^e, d, J_{ea} 8.0), 2.92 ($H^{c'}$, v br d, J 10.1, w 29.4 Hz), 2.0 (H^c, ddt, $J_{cc'}$ 14.58, J_{cd} 8.0, 1.01), 1.08 (Me, s) [in dioxane derivatives, the resonances of the axial protons appear downfield of the equatorial protons (*cf.* ref. 2)]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.9 (d), 117.9 (t), 76.8 (s), 59.9 (t), 37.0 (br, t), 19.9 (q). NOEs observed [irradiated proton, NOE (%)]: H^a, H^d (1.3), $H^{c'}$ (1.4); H^e, $H^{c'}$ (2.3), Me (1.1); $H^{c'}$, H^d (1.7), H^a (1.9), H^c (10.3), Me (2.9). For **3a** ^{1}H NMR (400 MHz, $CDCl_3$; J in Hz; in part) δ 3.64 (H^a and H^e, s), 2.71 ($H^{c'}$, v br, w 30 Hz), 1.98 (H^c, ddt, $J_{cc'}$ 14.3, J_{cd} 7.4, 1.0), 1.15 (Me, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.0 (d), 117.7 (t), 76.9 (s), 59.9 (t), 38.3 (br, t), 19.6 (q). NOEs observed [irradiated proton, NOE (%)]: Me, H^c (3.2), H^a and H^e (2.8), H^d (2.9); H^a and H^e, Me (3.7). For **5** ^{1}H NMR (400 MHz, $CDCl_3$; J in Hz) δ 3.76 (H^a, ddd, J_{ae} 11.6, $J_{aa'}$ 10.4, $J_{ae'}$ 3.2), 3.56 ($H^{a'}$, ddd, $J_{a'e'}$ 11.6, $J_{a'a}$ 10.4, $J_{a'e}$ 2.5), 3.50 ($H^{e'}$, ddd, $J_{e'a'}$ 11.6, $J_{e'a}$ 3.2, $J_{e'e}$ 1.4), 3.38 (H^e, ddd, J_{ea} 11.6, $J_{ea'}$ 2.5, $J_{ee'}$ 1.4), 2.31 (CH_2, 1/2 AB, J 17.5), 2.25 (CH_2, 1/2 AB J 17.5), 2.31 (acetyl, s), 2.04 (3H, s), 1.31 (Me, s), 1.24 (Me′, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1 (s), 153.3 (s), 118.2 (s), 85.6 (s), 79.3 (s), 61.7 (t), 60.0 (t), 50.2 (t), 30.1 (q), 23.0 (q), 17.9 (q), 16.3 (q).

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