Allylsilanes in Organic Synthesis: a Synthesis of Prostaglandins

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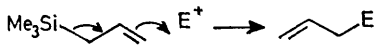
Summary The allylsilane (**2**) reacts with a variety of electrophiles in the sense shown in Scheme 1; one electrophile, methoxymethyl chloride in the presence of stannic chloride, gives an intermediate (**7**), which can be converted into prostaglandins.

IN an earlier communication,[1] we drew attention to some uses of allylsilanes in synthesis, based largely on reactivity of the type illustrated in Scheme 1. In this and the following paper we report some reactions of another allylsilane, namely, the adduct (**2**) of dichloroketen and trimethylsilylcyclopentadiene (**1**), extending our earlier claim and leading to syntheses of both prostaglandins and loganin.

Trimethylsilylcyclopentadiene is known[2] to be largely the 5-substituted isomer (**1**), with the 1- and 2-substituted isomers making up, at equilibrium at 30 °C, only 7% and 3% of the mixture, respectively. We find that dichloroketen is reactive enough at 0—5 °C to give the crystalline

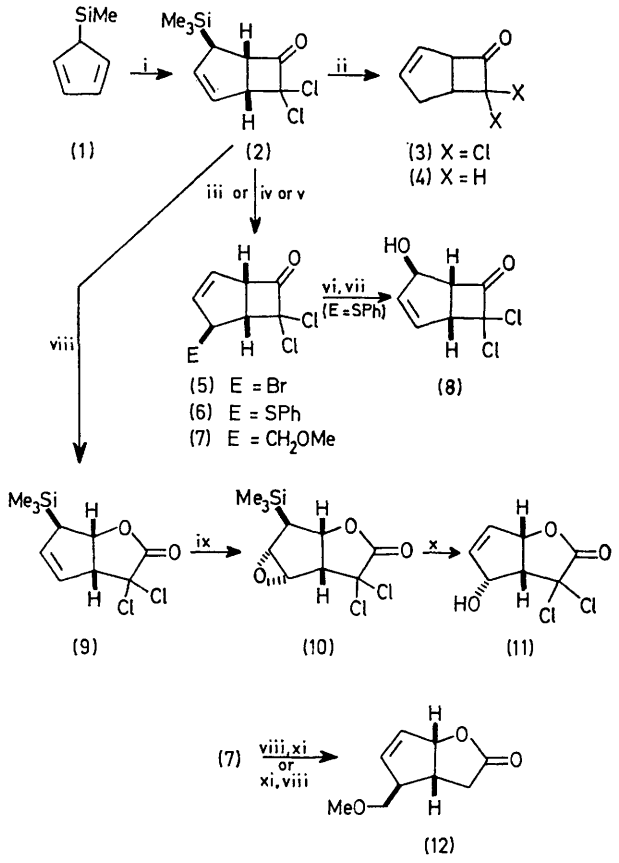
adduct (**2**) in 70% yield. Less reactive ketens, such as 2-carbonyl-1,3-dithian[3] (like less reactive dienophiles[2]) react instead with the minor, but evidently more reactive isomers, to give adducts which are vinyl- and not allyl-silanes.



SCHEME 1

The allylsilane (**2**) reacts with a variety of electrophiles (Scheme 2) in the sense shown in Scheme 1. The product (**3**) (69%) from the reaction with acid is the regioisomer of the cycloadduct of cyclopentadiene and dichloroketen.[4] It can easily be dechlorinated to give a ketone (**4**), hitherto got, with more trouble, by photoisomerising norbornenone.[5] The product (**5**) (63%) with bromine is the minor product obtained[6] when the adduct of cyclopentadiene and dichloroketen is treated with *N*-bromosuccinimide. Phenylsulphenyl chloride reacts with (**2**) to give an adduct (80%), which gives the allyl sulphide (**6**) (93%) on treatment with sodium fluoride. The allyl sulphide can then be converted into the allyl alcohol (**8**) (45%), using Evans' procedure.[7] We had difficulties in the reaction of the allylsilane (**2**) with peracids, partly, but not entirely, stemming from Baeyer–Villiger reactions leading to the lactone (**9**). However, this lactone (82%) gave the very unstable but isolable epoxide (**10**) (28%), which, on treatment with acid, gave the allylic alcohol (**11**). If the intermediate epoxide is not isolated, the overall yield of (**9**) → (**11**) is 73%. *endo*-Epoxidation is not surprising in view of Corey's observations[8] on the corresponding lactone lacking the silicon group and the chlorine atoms.

Most significantly, the allylsilane (**2**) reacts with methoxymethyl chloride and stannic chloride to give the ether (**7**) (78%). Treatment of this compound with hydrogen peroxide in acetic acid followed by dechlorination gave the crystalline racemic lactone (**12**) (62%), identical with an authentic sample.[9,10] Since (**12**) has been converted into the prostaglandins of the A and F series,[10] this constitutes an interesting variation on existing prostaglandin syntheses. Corey's route[11] and Ranganathan's[10] both involve highly reactive intermediates, which would pose problems in large scale use. By contrast, the silylated cyclopentadiene (**1**) does not dimerise appreciably and can be kept, for example, for at least six months at room temperature without serious deterioration. One disadvantage of our route is that the electrophilic substitution of the cyclopentadiene takes place in two stages: first the introduction of the trimethylsilyl group and then its replacement by the methoxymethyl.



SCHEME 2. i, $Cl_2CHCOCl$–Et_3N; ii, H_2SO_4–MeOH; iii, Br_2–hexane; iv, PhSCl, NaF–MeOH–H_2O; v, $MeOCH_2Cl$–$SnCl_4$; vi, $NaIO_4$; vii, $(MeO)_3P$; viii, H_2O_2–AcOH; ix, *m*-$ClC_6H_4CO_3H$–CH_2Cl_2–$NaHCO_3$; x, H_2SO_4–H_2O; xi, Zn–AcOH–H_2O.

The extra step (with other factors) makes the overall yield in our route lower, but our route does have the advantage that it can be held up at any stage, and each of the intermediates kept, if need be, for prolonged periods.

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