THE SYNTHESIS OF CHIRAL ALLYLSILANES, SPIROKETALS AND DIOXASPIRO-COMPOUNDS

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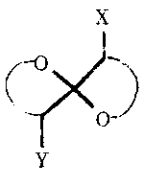
Abstract - A synthesis of allylsilanes from lactones and protected hydroxy esters is reported. These allylsilanes were converted into novel oxygen heterocyclic compounds.

Many spiroketals[1] possess interesting ionophoretic properties and so are of special interest to us, because of our interest in the role of lone pair interactions in the chemistry of saccharide-like molecules.[2] However, current synthetic strategies do not address the preparation of highly oxygenated spiroketals which have chiral, heteroatom-bearing centers flanking the spiro-carbon, as in structure (1). Therefore, we have developed the syntheses of chiral allylsilanes of the type (2) from esters and lactones, and the syntheses of spiroketals and novel dioxaspiro-compounds from these allylsilanes.

Valerolactone (3) reacted with 4 equivalents of (trimethylsilyl)methyl-magnesium chloride (TMSiMMgCl), in ether at room temperature for 18 hours, to give the allylsilane (4) in about 10% yield. Repeating the reaction in the presence of 4 equivalents of trimethylchlorosilane (TMSiCl) also gave a 10% yield of the compound (4), and the compound (5) in 90% yield.

Valerolactone was converted into the ester (6), by allylating the sodium carboxylate salt, followed by t-butyldimethylsilylation of the alcohol. The ester (6) reacted with TMSiMMgCl in the absence of TMSiCl to give a 55% yield of the allylsilane (7). Repeating the reaction, with added TMSiCl, gave the compounds (7) and (8), 5:1 ratio by nmr, in 90% yield.

Chromatography of this mixture on silica gel converted compound (8) into compound (7), so providing the allylsilane (7) in an overall yield of 85%.



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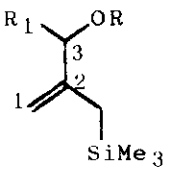

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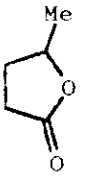

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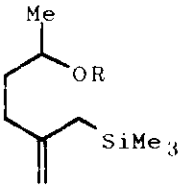
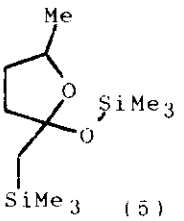


(4) R = H
(7) R = TBDMSi



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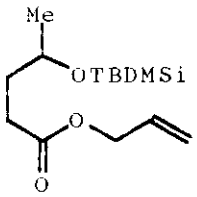

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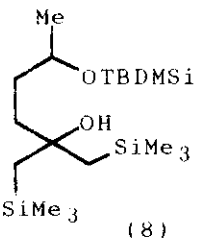

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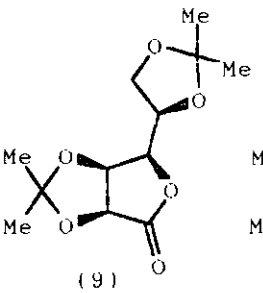

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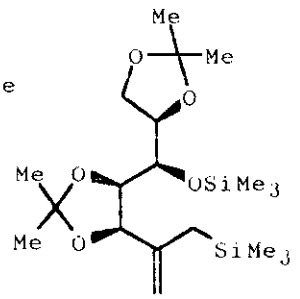

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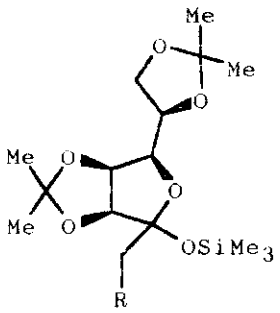
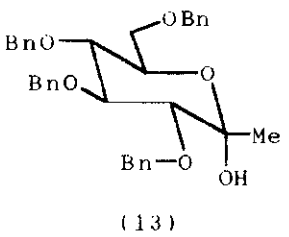


(11) R = H
(12) R = $SiMe_3$



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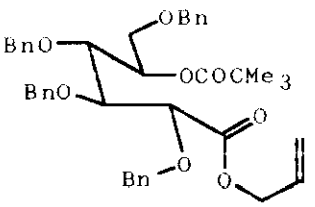
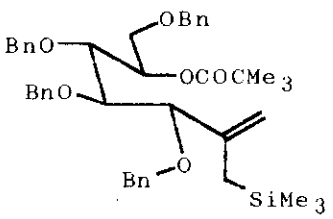


(14)

Mannonolactone (9) reacted with TMSiMMgCl and TMSiCl to give the desired allylsilane (10) in 40% yield, and the compounds (11) and (12) in 35% and 10% yields respectively. The nmr spectrum of the crude reaction mixture had showed only traces of the compound (11), and so compound (11) had been formed from the compound (12) during column chromatography on silica gel, by the elimination of hexamethylsiloxane and hydration of the resulting enol ether. This reaction was repeated, but was quenched with allyl bromide and left to stir for a further period of 18 hours (a non-aqueous work-up). No C-allylated, or any new, materials were produced, showing that no enolates had been formed in these reactions.[3]

The reaction of 2,3,4,6-tetra-O-benzylgluconolactone also gave the compound (13), 85% yield after column chromatography. Thus, the formation of a hemiketal during the reaction of a lactone can be a limiting event and, except for some sterically hindered lactones like 9 , the acyclic ester approach is best for the preparation of these allylsilanes.

We achieved a great improvement in the efficiency of these preparations of allylsilanes if they were performed at -78 °C in tetrahydrofuran (THF) for 3 hours. Cerium(III) salts,[3] or a variety of polyether chelating agents, failed to improve the process further. TMSiCl was important in these reactions. Thus, we converted the compounds (6), (9) and (14) into the allysilanes (7), (10) and (15), in about 90% yield each.



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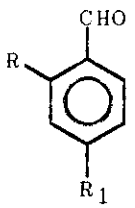
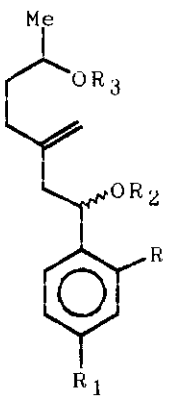


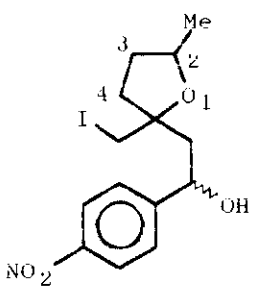
(16) R = R_1 = H
(17) R = H, R_1 = NO_2
(18) R = $OCOCMe_3$, R_1 = H
(19) R = OCOMe, R_1 = H



(20) R = R_1 = R_2 = R_3 = H
(21) R_1 = NO_2, R = R_2 = R_3 = H
(22) R = $OCOCMe_3$, R_1 = R_2 = R_3 = H
(23) R_2 = COMe, R = OH, R_1 = R_3 = H
(24) R = R_1 = H, R_2 = R_3 = COMe
(25) R = H, R_1 = NO_2, R_2 = R_3 = COMe
(26) R = $OCOCMe_3$, R_1 = H, R_2 = R_3 = COMe
(27) R = OCOMe, R_1 = H, R_2 = R_3 = COMe

The boron trifluoride, or titanium tetrachloride, catalyzed[4] reactions of the allysilane (7) in acetonitrile at room temperature, with each of the aldehydes (16), (17), (18) and (19) gave the diols (20), (21), (22) and (23), each in about 90% yield. The nmr spectra of these products showed that the new secondary hydroxyl group had been generated without diastereoselection (in a 1:1 ratio). Note that the formation of compound (23) occurred with the migration of the acetyl group from the phenolic to the

newly formed alcohol, during the reaction. These diols were easily converted into their peracetates (24), (25), (26) and (27).



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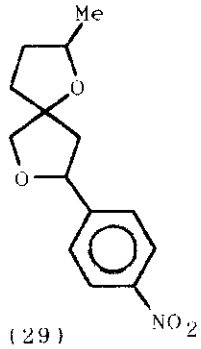

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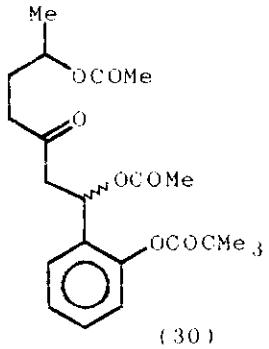

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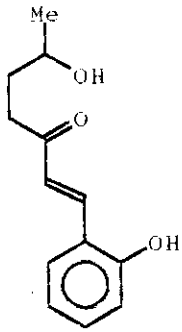


(31)

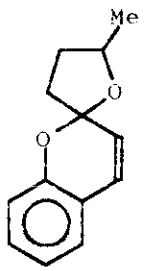
Compound (21) reacted with iodine at room temperature in THF containing suspended sodium bicarbonate to give the compound (28) in 100% yield. The nmr spectrum of compound (28) showed that the new chiral center had been generated in a 3:1 diastereoisomeric ratio. Thus, this cyclization had been influenced by the geometry at the C2. We were unable to separate these isomers and so have not ascertained their stereochemical identities. Compound (28) was converted into the 1,7-dioxaspiro[4,4]nonane (29) in 100% yield by its reaction with silver nitrate in dimethylformamide at room temperature.

The compound (26) reacted with osmium tetroxide/sodium periodate[5] in t-butanol to give the ketone (30) in 90% yield, which was converted by sodium carbonate in methanol at room temperature into the unsaturated ketone (31) in 85% yield. The ketone (31) was converted by p-toluenesulfonic acid in THF into a 1:1 mixture of the novel unstable spiroketal (32) and diene (33), in 80% yield.

The diol (23) reacted with osmium tetroxide/sodium periodate in t-butanol to give the spiroketal (34) in 90% yield. The migration of the acetyl group had thus selectively deblocked the phenolic hydroxyl group and prepared this molecule for spirocyclization.

The chiral allylsilanes (10) and (15) reacted with 4-nitrobenzaldehyde to

produce the compounds (35) and (36), each in 90% yield. The nmr spectra of these compounds showed that the new secondary hydroxyl groups were formed with marked stereoselectivity, 9:1 for the compound (35) and 7:1 for the compound (36), thus confirming that the chiral centers at C3 of the allylsilanes did influence the paths of the reactions.



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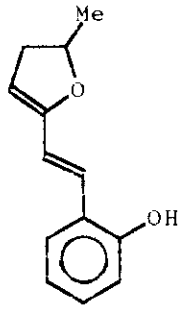

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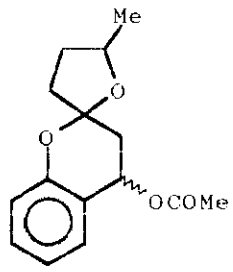

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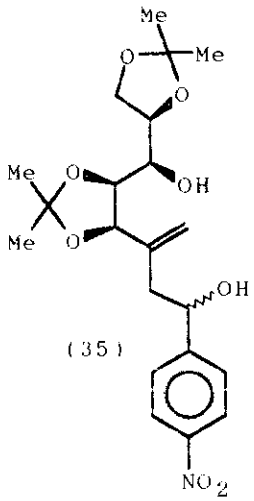

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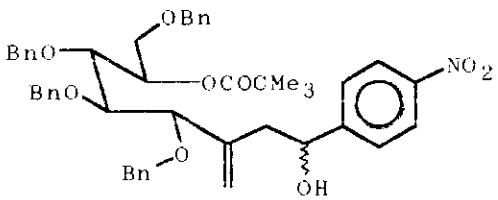

(36)

All the new compounds reported above gave satisfactory spectroscopic data, consistent with their assigned structures.

REFERENCES

1. K. Albizati and F. Perron, Chem. Rev., 1989, 89, 1617.
2. V. G. S. Box, Heterocycles, 1990, 31, 1157 and references cited therein.
3. T. V. Lee, J. A. Channon, C. Cregg, J. R. Porter, F. S. Roden, and H. T.-L. Yeoh, Tetrahedron, 1989, 45, 5886 and references cited therein.
4. G. Majetich, J. Defauw, and C. Ringold, J. Org. Chem., 1988, 53, 50.
5. S. H. Graham and A. J. S. Williams, J. Chem. Soc. C, 1966, 655.

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