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SYNTHESIS OF 4-HALOTETRAHYDROPYRANS FROM ALLYLSILANES AND CARBONYL COMPOUNDS IN THE PRESENCE OF LEWIS ACIDS

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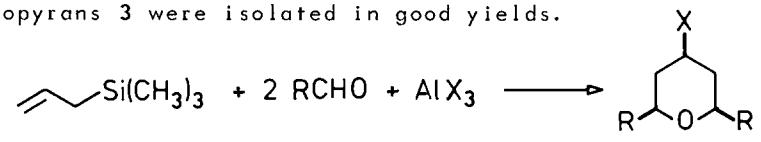
Summary. An unexpected behaviour of the rection of allylsilanes and carbonyl compounds allowed the stereospecific preparation of differently substituted 4-halotetrahydropyrans with an " all cis " configuration.

Allylation of carbonyl compounds with allylsilanes and Lewis acids is a well established procedure for the preparation of homoallyl alcohols[1]. Nevertheless, in the previous papers on this argument, different authors evidenced the presence of by-products and yields lowering on changing the recommended experimental procedure[2].

Engaged in a study of the reaction of C-centred optically active allylsilanes with aldehydes and Lewis acids[3], we noticed that in the presence of $AlCl_3$ high yields of an halogenated product were recovered together with only traces of the expected homoallyl alcohol.

When this reaction was repeated with allyltrimethylsilane **1** and 2 equivalents of different aldehydes **2** in the presence of $AlCl_3$ or $AlBr_3$,(Scheme 1) the halotetrahydropyrans **3** were isolated in good yields.



1 2 3

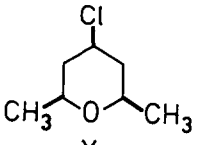
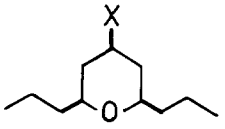
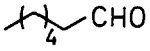
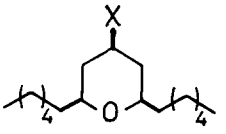
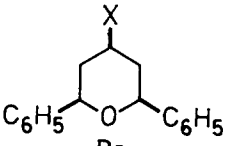
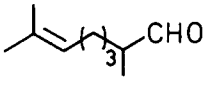
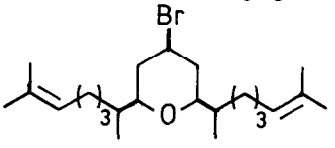
Scheme 1

The reaction was stereospecific giving products **3a-g** (see Table I) as single isomers in an " all cis " conformation as revealed by glc and ^1H and ^{13}C NMR analyses[4].

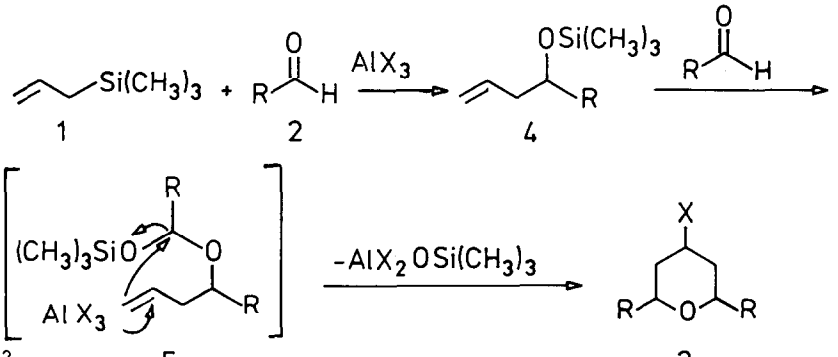
This reactional behaviour has never been evidenced in reactions of allylsilanes[5], although a quite similar reaction between allylhalostannanes and aldehydes in presence of SnX_4 was reported by Tagliavini[6].

Results reported in Scheme 1 can be accounted for by a mechanism implying coupling of the allyl mojety on the carbonyl compound in the first step of the reaction followed by reaction of the alkoxy-intermediate with a second molecule of the carbonyl compound. The so formed acetals **5** undergoes a Prins-type cyclisation[7], mediated by the same Lewis acid used for the coupling (see Scheme 2).

Table 1 . Synthesis of symmetrical 2,6-disubstituted-4-halotetrahydropyrans

Carbonyl compound	Lewis acid	Product		Yield[a]
CH_3CHO	$AlCl_3$		**3a**	56%
	$AlCl_3$	 X= Cl	**3b**	86%
	$AlBr_3$	X= Br	**3c**	70%
	$AlCl_3$	 X= Cl	**3d**	51%
	$AlBr_3$	X= Br	**3e**	43%
C_6H_5CHO	$AlCl_3$	 X= Cl	3f	72%
	$AlBr_3$	X= Br	**3g**	49%
	$AlBr_3$		3h	48%

a) Yields of isolated and fully characterized products.



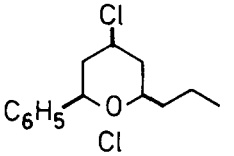
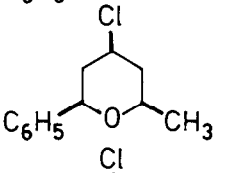
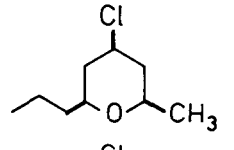
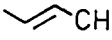
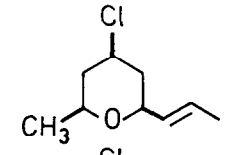
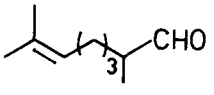
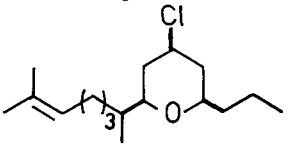
1 2 4 5 3

Scheme 2

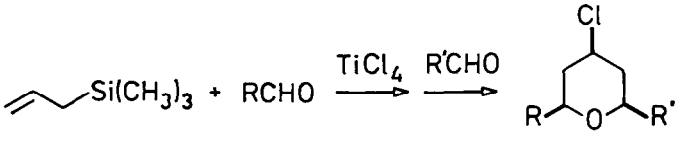
According to this mechanism the above reaction can be use to prepare differently substituted 2,6-tetrahydropyrans, performing consecutive addition of different aldehydes. In fact under the conditions previously described as the best for the preparation of the homoallyl alcohols[2] and quenching the reaction mixture with a different aldehyde, products **6a-e** were prepared as reported in Scheme 3 and Table II.

$TiCl_4$ proved to be the most suitable Lewis acid because its use minimized the

Table II. Synthesis of differently substituted 4-halotetrahydropyrans.

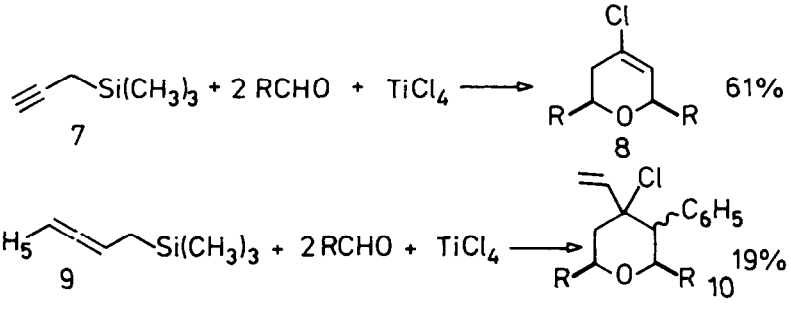
Carbonyl compounds First	Second	Product	Yield[a]
C_6H_5CHO		 6a	62%
	C_6H_5CHO		55%
C_6H_5CHO	CH_3CHO	 6b	56%
	CH_3CHO	 6c	41%
CH_3CHO		 6d	56%
		 6e	60%

a) Yields of isolated and fully characterized products.



Scheme 3

formation of symmetrical halotetrahydropyrans during the first step of the reaction, still allowing the cyclisation during the subsequent step[8].
Symmetrical by-products were formed in yields ranging from 5 to 15% and were removed by MPCC (Medium Pressure Column Chromatography).
Starting from propargyltrimethylsilane **7** and 1-trimethylsilyl-2,3-butadiene **9**



Scheme 4

the expected pyrans **8** and **10** were formed again but in somewhat lower yields. (see Scheme 4). The above results point out the interest and the synthetic potential of this previously unexplored extension of the already popular allylsilane chemistry. Due to the importance of tetrahydropyrans in natural product chemistry a more careful and comprehensive study of this reaction is currently underway in our laboratory.

References and notes.

1) E.W.Colvin, "Silicon in Organic Synthesis" Butterwoths, London 1980, p.97.
2) A.Hosomi, H.Sakurai, Tetrahedron Lett. **16** , 1295 (1976) ; G.Delerris, J.Dunogues, R.Calas, J.Organomet.Chem. **93** , 43 (1975) ; A.Hosomi, H.Sakurai, Tetrahedron Lett. **18**, 2589 (1978) ; I.Ojima, M.Kumagai, Chem.Lett. 575 (1978).
3) L.Coppi, A.Mordini, M.Taddei, Tetrahedron Lett. under pubblication.
4) To $AlCl_3$ (1.16 g , 8.8 mmol) disperded in dry CH_2Cl_2 (15 ml), a solution of allyltrimethylsilane (1 g , 8.8 mmol) and butanal (1.26 g , 17.6 mmol) in CH_2Cl_2 (5 ml), was added slowly with a syringe at room temperature. An exothermic reaction took place immediately and, after 2 h at room temperature, a buffer solution at pH 7.5 (15 ml) was added followed by Et_2O (50 ml). The ethereal layer was separated and washed with water and brine. After drying and evaporation of the solvent, MPCC gave **3a** as a pale yellow oil. ^1H NMR 0.8 (m, 6H, CH_3), 1.2-1.9 (bs, 12H, CH_2), 2.9 (m, 2H, CHO), 3.6 (m, 1H, CHCl). ^{13}C NMR 13.07(CH_3), 17.86(CH_2), 37.21(CH_2), 41.99(C_3), 55.27(C_4), 75.17(C_2).Mass spectrum (m/e) 204(M^+), 161, 81, 55(base).
5) Russian authors reported the preparation of 4-cholorotetrahydropyran in reaction of allylsilane and $(ClCH_2)_2O$ in presence of $ZnCl_2$ A.S.Arakelion, A.A.Gevorkyan, Arm.Khim.Zh. **37** 663 (1984), C.A. **102** 220697x.
6) A.Boaretto, D.Furlani, D.Marton, G.Tagliavini, A.Gambaro, J.Organo met.Chem, **299**, 157 (1986).
7) W.H.Bunelle, D.W.Seamon, D.L.Mohler, T.F.Ball, D.W.Thompson, Tetrahedron Lett. **24** 2653 (1984).
8) To a solution of acetaldehyde (0.48 g , 10 mmol) in CH_2Cl_2 (10 ml), $TiCl_4$ (1.89 g , 10mmol) was added slowly with a syringe.After 4 min. of stirring at room temperature, allyltrimethylsilane 1 (1.14 g , 10 mmol) was added with a syringe. After 1 min. at room temperature, benzaldehyde (1.06 g , 10 mmol) in CH_2Cl_2 (10 ml) was added so slowly to maintain the solution under a gentle reflux. After 4 h. at room temperature a buffer solution at ph 7.5 was added. followed by Et_2O. After the usual work up, MPCC gave product **6b** as a pale yellow oil (1.13 g , 62%). ^1H NMR 1.35 (d, 3H, CH_3), 1.6 (m, 1H, CH), 1.8 (m, 1H, CH), 2.1 (m, 1H, CH), 2.3 (m, 1H, CH), 3.6 (m, 1H, MeCHO), 4.1 (m, 1H, CHCl), 4.4 (m, 1H, PhCHO), 7.4 (m, 5H, Arom.). ^{13}C NMR 21.37(CH_3), 43.66(C_3 or C_5), 43.84(C_5 or C_3), 55.44(C_4), 72.90(C_2), 78.38(C_6), 126.67, 127.47, 128.20, 141.23(Arom.).Mass spectrum m/e 210(M^+), 121, 91(base).

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