C-CENTRED OPTICALLY ACTIVE ORGANOSILANES, 2 . APPLICATION TO ENANTIOSELECTIVE ALLYLATION OF CARBONYL COMPOUNDS.

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Summary. C-Centred optically active allylsilanes react with carbonyl compounds in presence of Lewis acids to give the corresponding homoallyl alcohols with ee varying from 21 to 56 %. The role of the Lewis acid is crucial for a correct development of the reaction; different procedures are tested and the results compared.

Enantioselective synthesis of homoallyl alcohols from carbonyl compounds has recently received a great deal of attention la-f. From β -allyldiisopinocamphenylborane le to organotin(II) derivatives lc, lf, different organometallic reagents have been developed for this purpose.

We report now the enantioselective allylation of different carbonyl compounds using the C-centred optically active allylsilane **2** prepared from the chloride² **1** and allylmagnesium bromide (Scheme I).



Scheme I

Compound 2 was treated with aldehydes or ketones and Lewis acids and the results are summarized in Table II .

A noteworthy feature of this reaction was the relative complexity of the crude reaction mixture after hydrolysis, shown by glc/mass analysis.

In fact as reported in Scheme II relatively to the reaction of 2 with butanal (3a) and TiCl₄, the predominant product was the silvl ether 5 accompanied by silanol **6a** and by small amounts of the homoallyl alcohol **4a**. By-product **7a** could also be formed⁴ in sizeable yields (see Table I).



Scheme II

The composition of the reaction mixture varies on changing the sequence of the reagents addition or with the temperature and is dramatically affected by the nature of the Lewis acid.

Using the reaction with butanal for the search of the reaction conditions for optimizing enantiomeric and chemical yields, we compared the use of different Lewis acids and the results are reported in Table I.

Lewis acid	starting material	4a	5α	6 a	7α	eea
TiCla b	0	4	65	20	11	46%
TiCl ₄ c	17	7	39	18	19	40%
TiCl ₄ d	0	6	29	39	26	5%
BF3 Et20	0	12	0	88 ^e	0	
AICI3	0	0	53	36	41	-
Et ₂ AICI	87	4	0	9	0	-
Zn I ₂	74	0	14	12	0	(59%) ^f
BBr ₃	0	39	33	0	269	(31%) ^f
Cp ₂ TiCl ₂	85	0	3	12	0	-
Thermi c ^h	86	0	14	0	0	(48%) ^f

a) ee determined by polarimetric analysis and comparison with literature data⁵. b)Procedure described above. c) Sequence: $TiCl_4$ and butanal at -78°C followed by allylsilane. d) Sequence: $TiCl_4$ and allylsilane at -78°C followed by butanal. e) Figure relative to R^*Me_2SiF . f) Calculated from the glc ratio of diastereoisomeric mixture of **5a**. g) Figure relative to 2,6-dipropyl-4-bromotetrahydropyran. h) Neat, 120°C for 12 h.

Table 1. Composition (%) of the crude in the reaction of **2** and butanal(**3**a).

The best experimental procedure is the following :

To a solution of 2 (0.68 g 2.6 mmol) and butanal 3a (0.185 g 2.6 mmol) in dry CH_2Cl_2 cooled at -78°C, TiCl_4 (0.49 g 2.6 mmol) was added slowly with a syringe. After stirring 4 h at that temperature, a buffer solution at pH 7.5 (5 ml) was added followed by Et_2O (20 ml). The mixture was warmed to room temperature and the organic layer separated. After washing with a NaHCO₃ sat. aqueous solution, water and brine and drying on anhydrous Na₂SO₄, the solvent was evaporated to give 0.8 g ca. of a crude analysed by glc/mass. An accurate glc analysis (capillary column) allowed the separation of the two diasteroisomers of 5a showing a glc ratio of 78 to 22 (ee 56%).

The crude was dissolved in dry $\text{Et}_2O(20 \text{ ml})$ and dry HCl bubbled through the solution for 6 h. The solution was then dried on anhydrous $\text{Na}_2CO_3(0.8 \text{ g})$, decanted and the solvent evaporated. The alcohol **4a** was isolated by bulb to bulb distillation from which also the chloroderivative **1** can be recovered (0.34 g.).



The alcohol **4a** (172 mg, 58% yield) was further purified by PTLC and the polarimetric analysis showed an ee of 46% and a predominant R configuration⁶.

Table II. Enantioselective allylation of carbonyl compounds .



a) Yields of isolated products. b) ee determined by polarimetric data and NMR analysis (Mosher's method) and comparison with the literature⁷.

A preliminary conclusion which can be drawn from these results is that the

allylsilane 2, built with the new chiral auxiliary, reacts with aldehydes and ketones with low enantioselectivity. Up to now, the ambiguity of the absolute configuration of 2 doesn't allow, however, a stereochemical definition of the mechanism.

References and notes.

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2) See previous letter.

3) To a solution of allylmagnesiumbromide (10 ml of a 0.9 M solution in THF, 9 mmol), the chlorosilane 1 (1.8 g, 7 mmol) in THF (15 ml) was added dropwise at 0°C. The mixture was refluxed 1h. After the hydrolytic work up and evaporation of the solvent, product 2 was isolated by fractional distillation under vacuum; obtained 1.5 g, 80% yield. ¹H NMR (CCl₄/TMS) 0.24 (s, 6H, (CH₃)₂Si), 0.54 (m, 1H, CHSi), 1.0 (m, 1H, CHSi), 1.24 (s, 3H, CH₃), 1.40 (s, 3H, CH₃), 1.7 (m, 1H, CHSi), 2.2 (m, 7H, CH and CH₂), 3.17 (d+d, 1H, J_a=9Hz, J_b=3Hz, CHO), 3.37 (s, 3H, OCH₃), 3.50 (d+d, J_a=9Hz, J_b=6Hz, CHO), 5.00 (m, 2H, CH₂=), 5.66 (m, 1H, CH=). ¹³C NMR (C₆D₆/TMS) -7.40, -7.00, 14.63, 19.82, 21.02, 26.39, 26.71, 30.40, 37.45, 40.26, 41.62, 57.24, 76.72, 112.77, 135.61. Mass spectrum (m/e) 266 (M⁺), 225, 99, 89 (base).

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6) The difference with the glc data can be ascribed to the 4% of alcohol already present in the mixture and to a possible enantioselectivity in the formation of the silylated intermediate.

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