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1,2-DIASTEREOSELECTION INDUCED BY CHIRAL SILICON IN THE ADDITION OF GRIGNARD REAGENTS TO ACYLSILANES

Bianca F. Bonini, Stefano Masiero, Germana Mazzanti*, and Paolo Zani Dipartimento di Chimica Organica "A. Mangini", Università di Bologna Viale Risorgimento 4, 40136 Bologna, Italy

Summary. The reaction of acylsilanes 1 with Grignard reagents gives the diastereomeric α -hydroxysilanes 3. The level of asymmetric induction depends on the nature of R¹ and R². Good results were obtained for R¹=t-Bu, R²=Me and R¹= α -Napht, R²=Ph. Subsequent desilylation occurs with predominant inversion of configuration at carbon.

The addition of organometallic reagents to chiral carbonyl compounds is a topic of great interest particularly as a tool in the stereoselective synthesis of natural products.¹

Recently Ohno et al.² reported that acylsilanes bearing an α -chiral carbon show exceptional diastereofacial selectivity in nucleophilic addition of organometallic reagents; the α -hydroxysilanes obtained in these reactions were stereospecifically protiodesilylated giving the alcohols formally derived from the aldehyde chiral at $C\alpha$. These results suggested us to start with acylsilanes chiral at silicon with the potential advantage that, in this case, the chiral inducing group can be easily removed by means of fluoride ion, thus allowing, in principle, an approach towards the asymmetric synthesis of alcohols. The approach based on silicon auxiliaries as equivalents of an "asymmetric" hydrogen has already been exploited by us^{3,4} during the reaction of thioacylsilanes chiral at silicon with 1,3-dienes and with organometallic reagents, which gave good levels of asymmetric induction.

We wish to report here our preliminary results concerning the reaction of acylsilanes chiral at silicon with Grignard reagents as well as the stereochemistry of the desilylation of α -hydroxysilanes obtained. In the majority of cases the inducing potential of chiral silicon was tested with the methyl-phenyl- α -naphthylsilyl group³⁻¹⁰, which gave good results only in very few instances. On this basis we decided to study the effect of the substitution pattern at silicon by replacing the α -naphthyl group with groups exerting a different steric hindrance, like n-butyl and t-butyl. With this aim in mind, we prepared acylsilanes la-f¹¹ using the dithiane route proposed by Brook¹²; the dithiane precursors

6801

2a-f, when racemic, were obtained in a one-pot reaction by treating, at -20°C under argon, a THF solution of dichloromethylphenylsilane firstly with 1 equiv. of the organolithium derivative R^{1} Li and subsequently with 1 equiv. of the lithiodithiane 1^{3} . The homochiral dithiane 2f was prepared from S(-)-methyl- α -naphthyl-phenyl-chlorosilane obtained with the Sommer's method ¹⁴ (Scheme 1).



Scheme 2



Table 1. Reactions of 1 with R³MgBr ¹⁶

Entry	1	R³	3	yield %	d.e. % ¹⁵	diastereoisomer ratio ¹⁵
1	a	Ph	а	97	16	1,4:1
2	b	Ph	ь	60	72	6.1:1
3	c	Ph	с	63	44	2.6:1
4	d	Me	а	98	9	1:1.2
5	e	Me	b	63	19	1:1.5
6	f	Me	c	98	79 ¹⁸	1:8.5

Acylsilanes 1 were then reacted with an excess of Grignard reagent in diethyl ether at a constant temperature of -80° C for both the addition and the quenching steps, resulting in α -hydroxysilanes $3a-c^{15}$ in good to quantitative yields (Scheme 2, Table 1). The data of Table 1 indicate that the diastereoselectivity of the reaction is affected by the substitution pattern at silicon, i.e. replacement of the α -naphthyl by the n-butyl group drastically lowers the chiral induction in the reactions of both acetyl 1a (entry 1) and benzoylsilane 1d (entry 4). Replacement by the t-butyl group increases the chiral induction only in the reaction of acetylsilane 1b with PhMgBr (entry 2), but this decreases it drastically in the cross reaction of 1e with MeMgBr (entry 5). These results that seem contradictory in nature, are difficult to rationalize at this preliminary stage of our work. A more extensive investigation is in progress. By interchange of the substituents R² and R³ at the acylsilane and the Grignard reagent (Table 1, entries 1 and 4, 2 and 5, 3 and 6), there is a reversal in the direction of the asymmetric synthesis, as often observed in cross reactions between carbonyl compounds bearing chiral α -carbon groups and organometallic reagents.¹⁷

In order to verify the general applicability of Ohno's results² on the desilylation of lpha-hydroxysilanes and in conjunction herewith to establish the possibility of asymmetric silicon to act as a chiral auxiliary in the asymmetric synthesis of alcohols, we performed the protiodesilylation of 3c (d.e. = 79%) obtained by addition of MeMgBr on R(+)-lf.¹⁸ The reaction, which was performed with tetrabutylammonium fluoride (TBAF) in either DMF or THF, gave in 85% yield the optically active 1-phenylethanol $[\alpha]_{D} \approx -12.5^{\circ}$ (c 4.7, methanol) with predominant enantiomer having the (S)-configuration (R/S = 36:64).¹⁹ Surprisingly the enantiomeric excess (e.e. = 28%) was found to be much lower than the diastereomeric excess of the starting 3c. Moreover the absolute configuration at carbon of the major enantiomer of 1-phenylethanol is opposite to that of the starting material 3c, which has the configuration SI(R) C(S) for the predominant diastereoisomer 18 (note that retention would have produced the R-phenylethanol). From the results described above it follows that in the present case protiodesilylation is not a highly stereoselective process and that it proceeds with predominant inversion of configuration at the carbon atom bearing the silyl group.¹⁸ Ohno's statement² that the protiodesilylation of α -hydroxysilanes is highly sterespecific is certainly not generally valid but seems to depend on the structure of the substrate.

These results set a limit to the use of asymmetric silicon as chiral auxiliary.

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References and notes

- 1. P.A. Bartlett, Tetrahedron 1980, 36, 3.
- 2. M. Nakada, Y. Urano, S. Kobayashi, M. Ohno, J.Am.Chem.Soc., 1988, 110, 4826.
- 3. B.F. Bonini, G. Mazzanti, P. Zani and G. Maccagnani, J.Chem.Soc., Chem.Commun., 1988, 365.
- B.F. Bonini, G. Maccagnani, S. Masiero, G. Mazzanti and P. Zani, Tetrahedron Lett., 4. 1989, 30, 2677.
- 5. R.G. Daniels and L.A. Paquette, Organometallics, 1982, 1, 1449.
- 6. S.J. Hathaway and L.A. Paquette, J.Org.Chem., 1983, 48, 3351.
- 7. J.L. Fry and M.G. Adlington, J.Am.Chem.Soc., 1978, 100, 7641.
- 8. J.L. Fry and M.A. McAdam, Tetrahedron Lett., 1984, 5859.
- 9. G.L. Larson and E. Torres, J.Organomet.Chem., 1985, 293, 19.
- 10. G.L. Larson, V. Cruz de Maldonado, L.M. Fuentes, L.E. Torres, J.Org.Chem., 1988, 53. 633.
- 11. 1a: δ (CDCl₃) 0.47 (s, 3H, S1Me), 0.63-1.63 (m, 9H, n-Bu), 2.23 (s, 3H, COMe), 7.23-7.77 (m, 5H, Ph) ppm; m/e 220 (M⁺); ψ_{aax} (CCl₄) 1640 cm⁻¹ (CO). 1b: δ (CDCl₃) 0.57 (s, 3H, S1Me), 1.00 (s, 9H, t-Bu), 2.30 (s, 3H, COMe), 7.30-7.93 (m, 5H, Ph) ppm; m/e 220 (M⁺); ν_{max} (neat) 1640 cm⁻¹(CD). lc: δ(CDC1₃) 0.87 (s, 3H, SiMe), 2.27 (s, 3H, 220 (M); ν_{max} (neat) 1640 cm⁻¹(c0). It: ρ (cbcl₃) 0.07 (s, 5m, 5me), 2.27 (s, 5m, C0Me), 7.07–8.07 (m, 12 H, arom) ppm; m/e 290 (M⁺); ν_{max} (neat) 1635 cm⁻¹ (CO). It: δ (CDCl₃) 0.62 (s, 3H, SiMe), 0.85 and 1.10–1.43 (t, m, 9H, n–Bu), 7.30–7.80 (m, 10H, arom) ppm; m/e 282 (M⁺); ν_{max} (neat) 1610 cm⁻¹ (CO). It: δ (CDCl₃) 0.60 (s, 3H, SiMe), 1.03 (s, 9H, t–Bu), 7.13–7.77 (m, 10H, arom) ppm; m/e 282 (M⁺); ν_{max} (neat) 1610 cm⁻¹ (CO). 1f: see ref. 12
- 12. A.G. Brook, J.M. Duff, P.F. Jones and N.R. Davis, J.Am.Chem.Soc., 1967, 89, 431.
- 13. D. Seebach, E.J. Corey, J.Org.Chem., 1975, 40, 231.
- 14. L.H. Sommer, C.L. Frye, G.A. Parker and K.W. Michael, J.Am.Chem.Soc., 1964, 86, 3271.
- 15. Compounds 3a-c were characterized as a mixture of the two diastereoisomers whose ratio was determined by ¹H NMR analysis at 200 MHz (Si-Me proton signals resonating at lower field vs. those resonating at higher field). 3a: $\delta(\text{CCl}_4)$ 0.17 and 0.23 (2s, 3H, SiMe), 0.51-1.47 (m, 9H, n-Bu), 1.53 (s, 3H, Me), 2.0 (s, 1H, 0H), 6.8-7.6 (m, 10H, arom) ppm; m/e 298 (M⁺); ν_{max} (CC1₄) 3550 cm⁻¹ (OH). 3b: δ (C₆D₆) 0.24 and 0.27 (2s, 3H, SiMe), 0.94 and 1.05 (2s, 9H, t-Bu), 1.36 and 1.49 (2s, 3H, Me), 2.08 (s, 1H, 0H), 6.9-7.3 (m, 10H, arom.) ppm; m/e 298 (M⁺); ν_{max} (CC1₄) 3550 cm⁻¹ (OH). 3c: δ (CDC1₃) 0.65 and 0.72 (2s, 3H, SiMe), 1.65 (s, 1H, 0H), 1.78 and 1.83 (2s, 3H, Me), 7.0-8.0 (m, 17 H, arom) ppm; m/e 368 (M^+); ν_{max} (CC1₄) 3550 cm⁻¹ (OH). 16. All reactions were performed on racemic 1, except the one reported in entry 6, Table
- 1, and were repeated at least twice.
- 17. J.D. Morrison, H.S. Mosher, Asymmetric Organic Reactions, Ed. Am.Chem.Soc., Washington D.C., 1976.
- 18. This reaction was also performed by A.G. Brook (Acc.Chem.Res. 1974, 7, 77) to establish the stereochemistry of the base promoted silylcarbinol to silylether rearrangement where inversion of configuration at carbon was found. The absolute configuration of the major diastereoisomer was determined to be Si(R)C(S).
- 19. The reaction was repeated three times in both solvents. The e.e. was determined on the basis of the $[\alpha]_{D}$ value of R(+)-l-phenylethanol (+45°; c 5, methanol).

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