Diastereoselective Asymmetric Allylation of Chiral α-Keto-amides with Allyltrimethylsilane. Preparation of Protected Homoallylic Alcohols

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In the presence of Lewis acids, protected homoallylic alcohols of high diastereoisomeric excesses (up to 89%) were obtained by the addition of allyltrimethylsilane to chiral α-keto-amides derived from (S)-proline esters.

Lewis acid-promoted allylation of carbonyl compounds with allyltrimethylsilane (Sakurai reaction) has served as a versatile tool for the preparation of homoallylic alcohols.[1] Asymmetric reactions for carbon–carbon bond formation are of current interest,[2] but only moderate asymmetric induction [23—56% diastereoisomeric excess (d.e.)] is reported in such a reaction using a chiral α-keto-ester derived from (−)-menthol.[3] We recently reported the use of the chiral α-keto-amide (**1a,b**) derived from methyl (*S*)-prolinate in the diastereoselective reduction with sodium borohydride.[4]

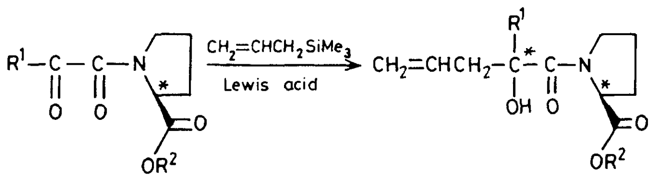
When (**1a**) was treated with allyltrimethylsilane in the presence of tin tetrabromide in CH_2Cl_2 at 0 °C, (**2a**) in 87%

Table 1. Asymmetric addition of allyltrimethylsilane to (**1**) in the presence of a Lewis acid.[a]

(**1**)	Lewis acid	Temp. (°C)	Time (h)	(**2a**—**c**) Yield[b] (%)	(% d.e.)[c]
a	$SnCl_4$	−40	3	40	80
a	$SnCl_4$	−78	4	32	87
a	$SnBr_4$	−40→Room temp.	44	53	81
a	$SnBr_4$	0	24	50	87
a	$SnBr_4$[d]	0→Room temp.	46	17	84
a	$TiCl_4$	0	1	80	7
a	$TiCl_4$	−40	3	65	18
a	$TiCl_4$[d]	−40	3	65	75
a	$TiCl_4$	−78	6	52	47
a	$TiCl_4$[d]	−78	6	17	70
a	$AlCl_3$	−40	3	66	41
b	$TiCl_4$	−78	3	47	56
b	$SnCl_4$	−78	3	67	45
c	$TiCl_4$	−78	5	58	75
c	$SnCl_4$	−78	4.5	46	89

[a] Unless otherwise noted, CH_2Cl_2 was used as solvent. [b] Isolated yield. [c] D.e. = diastereoisomeric excess, determined by g.l.c. analysis. (**2a**); Silicone SE-30, 25 m capillary column, column temp. 170 °C, flame ionisation detector; retention time 37.6 min for the major diastereoisomer and 45.6 min for the minor isomer. (**2b**); Poly(ethylene glycol) (PEG)-20M, 25 m capillary column, column temp. 180 °C, flame ionisation detector; retention time 14.1 min for the minor isomer and 15.1 min for the major isomer. Compound (**2c**) was converted into (**2a**) by titanate-mediated transesterification (D. Seebach, E. Hungerbuhler, R. Naef, P. Schnurrenberger, B. Weidmann, and M. Zuger, *Synthesis*, 1982, 138), and then characterized as described for (**2a**). [d] Mixed solvent was used [CH_2Cl_2 : n-hexane 2 : 1 (v/v)].

d.e. (g.l.c.) was obtained, see Table 1. It should be noted that the enhancement of % d.e. of (**2a**) by recrystallisation was promising. One recrystallisation of (**2a**) in 81% d.e. from n-hexane afforded (**2a**) in 98% d.e. When titanium tetrachloride was used as the Lewis acid, a heterogeneous reaction mixture (mixed solvent of n-hexane and CH_2Cl_2) was found to achieve higher stereoselectivity than a homogeneous reaction mixture (solvent, CH_2Cl_2 only). Compounds (**1b**) and (**1c**) were also converted into (**2b**) and (**2c**) respectively in good to high diastereoisomeric excesses (56—89% d.e.). Chelation of the Lewis acid with oxygen atom(s) of the ester group of (**1**), which does not occur in the conventional method,[3] may reduce the number of possible conformations of (**1**), and hence be one of the reasons for the high diastereoselectivity.



(1) (2)

a; R^1 = Ph, R^2 = Me
b; R^1 = Me, R^2 = Me
c; R^1 = Ph, R^2 = $PhCH_2$

As noted previously,[5] (**2**) is the synthetic equivalent of the product from a crossed-aldol reaction. The present observations compete with the recently reported diastereoselective ene reaction of chiral α-keto-esters.[5]

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