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Additive Effects on Ligand Activated Allylation of Aldehydes by Allyltrichlorosilane

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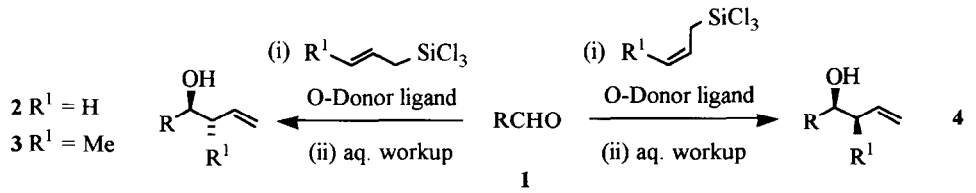
Abstract: The rate of allylation of aldehydes using a combination of allyltrichlorosilane and O-donor ligands can be profoundly accelerated by the addition of a range of simple tetra-*n*-butylammonium salts. Measured $t_{1/2}$ values decrease from over 6 hours under defined conditions to less than 5 minutes in favourable cases. These effects are highly relevant to the development of a catalytic asymmetric variant of this reaction and provide insight into the mechanism. © 1997 Elsevier Science Ltd.

Allylation and crotylation of aldehydes is a deservedly popular method[1] for the synthesis of homoallylic alcohols. Successful asymmetric variants have been developed including a number of stoichiometric chiral reagents. More recently, enantioselective Lewis acid catalysts[2] have been discovered which deliver high asymmetric induction with allyltrialkylsilanes or stannanes. We, and other research groups,[3,4] are interested in developing a series[5] of asymmetric catalytic reactions which rely upon chiral Lewis bases to activate stoichiometric organometallic reagents. Allylation is a known member of this class of reactions. Allylation and crotylation of aldehydes using allyltrichlorosilanes activated by O-donor ligands (Scheme 1) was originally discovered[3] by Kobayashi. Indeed, this reaction can be rendered catalytic in Lewis base[3,4] since in an appropriate solvent, *e.g.* dichloromethane, the background allylation reaction is negligible.



Donor ligand = DMF/$(R'_2N)_3P{=}O$; R = aryl, alkyl

Scheme 1

Asymmetric allylation of aldehydes using chiral phosphoramides[4] is already established. In our investigations using phosphoramides,[6] coincident with the published results of the Denmark group,[4a] chiral diamines based upon *trans*-1,2-diaminocyclohexane gave encouraging levels of asymmetric induction with aromatic aldehydes. However, a feature of concern to us was the attenuation of rate which accompanied the

incorporation of more sterically demanding substituents on the phosphoramide scaffold. Hence, we have been investigating methods to further promote the reactions without compromising the ligand activation effect. We now report that simple ammonium salt additives significantly enhance the reaction rates.

Based on the premise that sequestering of the halide might promote the reactivity, we investigated the reactions[7] of benzaldehyde with allyltrichlorosilane promoted by a stoichiometric quantity of DMF in the presence of silver salts. Under otherwise identical conditions to a control reaction lacking silver ions (Table 1), addition of an equivalent of AgOTs to the reaction mixture caused completion of the reaction after *ca.* 2 hours (88% **2a**) whereas the control required *ca.* 72 hours (66% **2a**). Although AgCl always precipitated, we observed some variation in reactions with different silver salts, *e.g.* TfO^-, ClO_4^-, indicative that the anion is of some importance. Accordingly, tetra-*n*-butylammonium (TBA) salts were screened (entries 3-5) under our standard conditions and, for example, addition of an equivalent of the tosylate salt gave identical results, *i.e.* 88% **2a** after 2 hours, to the silver tosylate. Control reactions with the additives alone reveal that allyl- and crotylations still require the presence of an O-donor ligand, *e.g.* DMF or triphenylphosphine oxide (TPPO).

Table 1. Ligand Activated Allylation of Aldehydes by Allyltrichlorosilane[a]

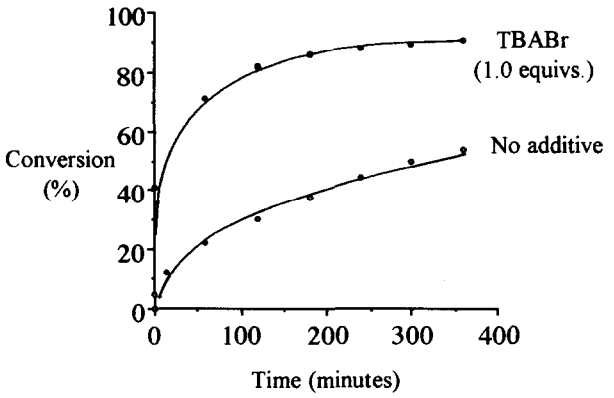
Entry	RCHO	R	R^1	Ligand/ equiv.	Time/h	Additive/equiv.	% Yield
1	**1a**	Ph-	H	TPPO/0.5	72	None	66[b] **2a**
2	**1a**	Ph-	H	TPPO/0.5	2[c]	AgOTs/1.2	81 **2a**
3	**1a**	Ph-	H	TPPO/0.5	2	Bu_4NOTs/1.2	81 **2a**
4	**1a**	Ph-	H	TPPO/0.5	2	Bu_4NI/1.2[d]	84 **2a**
5	**1a**	Ph-	H	DMF/1.0	2	Bu_4NOTf/1.2	86 **2a**
6	**1b**	PhCH=CH-	H	DMF/1.0	2	Bu_4NOTf/1.2	82 **2b**
7	**1c**	$Me(CH_2)_3$-	H	DMF/1.0	2	Bu_4NOTf/1.2	70 **2c**
8	**1d**	CH_2=C(Me)-	H	DMF/1.0	2	Bu_4NOTf/1.2	62 **2d**
9	**1a**	Ph-	Me[e]	TPPO/0.5	3	Bu_4NI/1.2	67[f] **3a**
10	**1a**	Ph-	Me[e]	DMF/1.0	2	Bu_4NOTf/1.2	86[f] **3a**

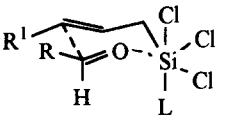
a) Reactions run at 1.0 M in CH_2Cl_2 (reference 7); b) Balance of material is unreacted aldehyde; c) Reaction times not optimised; d) Reaction using 0.6 equivs. TBAI was equally effective; e) (*E*):(*Z*) 86:14; f) **3a**:**4a** 86:14.

To quantify the results, we have investigated a range of TBA salts by studying the rate of conversion over time by GC analysis. By taking timed aliquots from the reaction mixtures we have arrived at a series of $t_{1/2}$ values, *i.e.* the time taken to reach 50% completion at a given concentration, with DMF as the ligand. These results reveal that the TfO^-, TsO^-, and HSO_4^- salts are the most effective additives (PhCHO; $t_{1/2} < 5$ mins.), while I^- is still good (PhCHO; $t_{1/2} \approx 5$ mins.), but Br^- far less so (PhCHO; $t_{1/2} \approx 0.5$ h). However, even the bromide gives significant rate enhancements over the additive free reactions (Figure 1). Interestingly TBACl, which provides the degenerate halide ion, also increases the rates.

The reactions of other representative aldehydes (Table 1; entries 6-8) appear to be enhanced, with the triflate salt giving the best yields. For example, valeraldehyde (entry 7) undergoes complete allylation in 2 hours in the presence of TBA salts compared to *ca.* 72 hours in their absence. Substoichiometric quantities (0.6 equivs.) of additive can also be used to similar effect. Hindered and α-branched aldehydes, *e.g.* isobutyraldehyde, are poor substrates[3] under "catalytic" conditions and require an excess of the O-donor

ligand to be used as solvent. The rate of crotylation using (*E*)-crotyltrichlorosilane is also enhanced to a similar degree to the allylation reactions and significantly, the intrinsic diastereoselectivity[3] of the reactions is unaffected by the presence of the additive, *i.e.* (*E*)-crotyltrichlorosilane affords clean *anti* homoallylic alcohols **3** in good yields, *e.g.* entries 9-10. Qualitatively, these additive effects are also observed with phosphoramide ligands, although we have yet to quantify the magnitudes of the rate accelerations.





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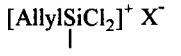

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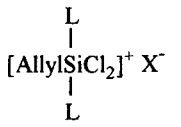

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Figure 1: Additive Effect on Allylation[7] of PhCHO using DMF (1 equiv.)

These simple additive effects have two important ramifications. Firstly, they may allow more scope for the asymmetric variant of this reaction with chiral Lewis bases. A full assessment of the additive effects on enantioselectivity will be reported[6] in due course. Secondly, these effects are significant because they suggest that the mechanism[8] of this process is more involved than we might otherwise assume. Activation could result from nucleophilic substitution at silicon by the anion,[8b] but since non-nucleophilic anions, *e.g.* TfO^-, give high rate enhancements, we believe this explanation to be unlikely. These results and the observation that addition of chloride ions also enhances the rate somewhat, imply an ionic effect is operative. We assume that the most reactive complex in solution (not necessarily the only reactive species) is ionic and that dissociation of a chloride ion is advantageous for reactivity, *i.e.* a modification of TS assembly **5** proposed[3] by Kobayashi. While it is premature to speculate on the exact nature of the ionic complex, we have some evidence[9] of charged complexes in solution, *e.g.* **6**, **7** (X = Cl; L = DMF or TPPO), even *in the absence* of ionic additives. The conductivity of allyltrichlorosilane in dichloromethane (0.38×10^{-5} ohm^{-1}; 0.1M; 21°C), a solvent which alone does not promote allylation, is 1000-times less than the same concentration of allyltrichlorosilane in DMF (0.87×10^{-2} ohm^{-1}; 21°C), an O-donor solvent which promotes allylation rapidly. Furthermore, a linear increase in the conductivity of the dichloromethane solutions was observed with increasing concentrations of TPPO implying a similar ionic complex is formed.

These results suggest that ion paired complexes play a role in the ligand activated allyl- and crotylation of aldehydes and provide considerable impetus for further experimentation. We are actively investigating the mechanism of this reaction[6] and are looking for asymmetric variants including the use of chiral ammonium salts. Finally, we note that other reaction types[5,8] involving group transfer from hypervalent silicon may also benefit from the presence of ammonium salt additives.

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7. **General procedure**: The TBA salt (1.2 mmol), ligand (0.5 mmol), and allyltrichlorosilane (1.2 mmol) were dissolved in dry dichloromethane (1 ml) and cooled to 0°C under an inert atmosphere. After 10 minutes, the aldehyde (1.0 mmol) was added at ambient temperature and the mixture stirred for 2 hrs. The solution was diluted with dichloromethane and washed with KF solution (1.0 M), water, and brine. The products were isolated by column chromatography and fully characterised (300 MHz ^{1}H n.m.r./^{13}C/MS). For GC analyses, the reactions (Figure 1) were run under high dilution (0.025 M RCHO in CH_2Cl_2) with an internal standard, the crude mixtures were silylated with BSTMA and analysed on a SE-54 column.
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9. Preliminary ^{29}Si n.m.r. (40 MHz) measurements are consistent with hypervalent silicon complexes (see reference 3). A 5% solution of allyltrichlorosilane:Bu_4NOTf (1:1 mol:mol) in d_7-DMF gives peaks at -180.5 ppm, -187.0 ppm, and a transient peak at -167.0 ppm which diminishes after 0.5 h. Samples containing ammonium salts visibly decompose (< 0.5 hours) at ambient temperature. For leading references to silylium cations see: Arshadi, M., Johnels, D.,Edlund, U., Ottosson, C-H., Cremer, D., *J. Am. Chem. Soc.*, **1996**, 118, 5120-5131.

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