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# Asymmetric allylation of aldehydes with allyltrichlorosilane promoted by chiral sulfoxides

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**Abstract**—Allylation of aldehydes with allyltrichlorosilane in the presence of sulfoxides is reported. The use of excess of (*R*)-methyl-*p*-tolylsulfoxide resulted in the formation of the corresponding homoallylic alcohols in good yields and moderate enantiomeric excesses.
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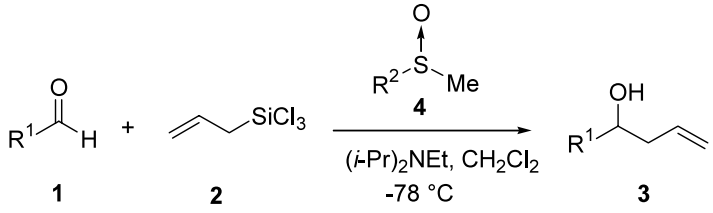
Allylation of aldehydes is an important preparative reaction in organic synthesis for C–C bond formation and, in recent years, allylboranes,[1] allylstannanes[2] and allylsilanes[3] have proven to be very efficient reagents to achieve this goal.

In view of a rather poor reactivity of allylsilanes, a typical approach involves activation of the carbonyl group by Lewis acids.[3] Conversely, activation of the nucleophilic allyltrichlorosilanes by means of a Lewis base, such as *N*,*N*-dimethylformamide (DMF),[4,5] hexamethylphosphoramide (HMPA),[4,5] and pyridine *N*-oxide[6] also proved viable.

The high level of diastereoselectivity observed when using (*E*)- and/or (*Z*)-crotyltrichlorosilanes was rationalized by assuming the formation of a hypervalent silicate intermediate and the involvement of a six-membered cyclic transition state.[7] As a logical consequence of this finding, chiral phosphoramides,[5,8a,9] formamides,[8b] and pyridine-*N*-oxides[6,10] have been conveniently used in new procedures for asymmetric allylation reactions.

Unlike the N–O and P–O type Lewis bases, which proved to be excellent activators of allyltrichlorosilane, sulfoxides (e.g. $Me_2SO$) have been regarded inefficient,[4b,5,11] in spite of their very good coordination ability.[12] Herein, we report that, by choosing the right experimental conditions, the formation of homoallylic alcohols 3 can be obtained in satisfactory yields and with moderate enantioselectivity in the presence of chiral sulfoxides (Scheme 1 and Table 1).

In a set of model experiments, benzaldehyde (**1a**) was treated with allyltrichlorosilane **2** in the presence of the cheap and readily available methyl *p*-tolylsulfoxide as a Lewis base. The results, summarized in Table 1, demonstrate that the amount of the Lewis base and the temperature are the critical factors for attaining satisfactory efficiency. Furthermore, employing diisopropyl ethyl amine appears to be the key pre-requisite to avoid




**Scheme 1.**

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**Table 1.** Allylation of benzaldehyde (**1a**) with allyltrichlorosilane (**2**) using racemic methyl sulfoxides (**4**)

| Entry | **4**: $R^2$ | (±)-**4** (equiv.) | Temp. (°C) | Time (h) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1[b] | **4a**: *p*-tolyl | 0.4 | −78 | 7 | 33 |
| 2[c,d] | **4a**: *p*-tolyl | 0.4 | −78 | 7 | 0[e] |
| 3[f] | **4a**: *p*-tolyl | 0.4 | −30 | 24 | 16 |
| 4[b] | **4a**: *p*-tolyl | 1.5 | −78 | 7 | 44 |
| 5[b] | **4b**: *p*-$MeOC_6H_4$ | 1.5 | −78 | 7 | 44 |
| 6[b] | **4c**: $CH_2C_6H_5$ | 1.5 | −78 | 7 | 39 |
| 7[b] | **4d**: *p*-$NO_2C_6H_4$ | 1.5 | −78 | 7 | 0[e] |
| 8[b] | **4a**: *p*-tolyl | 1.5 | −78 | 65 | 63 |
| 9[g] | **4a**: *p*-tolyl | 2.0 | −78 | 7 | 50 |
| 10[g] | **4a**: *p*-tolyl | 3.0 | −78 | 7 | 61 |

[a] Yields refer to isolated, chromatographically pure compounds, whose structures were confirmed by spectroscopic data ($^1H$ and $^{13}C$ NMR).
[b] The sulfoxide was recovered in 85% yield.
[c] The reaction was carried out in the absence of $(i\text{-Pr})_2NEt$.
[d] The sulfoxide disappeared in the course of the reaction.
[e] No reaction.
[f] The sulfoxide was recovered in 22% yield.
[g] The sulfoxide was recovered in 95% yield.

a rapid decomposition of the sulfoxide (entry 2) and the consequent inhibition of the allylation reaction.

As expected, increasing the amount of the sulfoxide resulted in acceleration of the reaction (entries 4–10). It is noteworthy that when larger amounts of the additive were used (entries 9 and 10), it could be recovered from the reaction mixture almost completely.

Very similar yields were observed by carrying out the reaction in the presence of methyl *p*-methoxyphenylsulfoxide **4b** and methyl benzylsulfoxide **4c** as Lewis bases since the corresponding alcohol **3a** was obtained in 44 and 39% yield, respectively (entry 5 and 6). On the other hand, methyl *p*-nitrophenylsulfoxide **4d** proved to be incompatible with **2** (entry 7); in fact, very fast formation of a precipitate was observed after the addition of allyltrichlorosilane to the solution containing the sulfoxide, and no homoallylic alcohol could be detected in the reaction mixture after a prolonged reaction time.

The enantiopure (*R*)-methyl-*p*-tolylsulfoxide **4a** was employed under the optimized reaction conditions (shown in Table 1, entries 8 or 10) to evaluate the enantioselectivity of the reaction. Good yields and moderate enantioselectivities were observed with aromatic and α,β-unsaturated aldehydes **1** (Table 2).

It is noteworthy that, owing to the mild conditions of this procedure, the chiral sulfoxide could be recovered with only a very slightly reduced e.e. (97%) and in almost quantitative yields (>95%).

In conclusion, racemic and/or enantioenriched homoallylic alcohols can be obtained in satisfactory yields by allylation of aldehydes with allyltrichlorosilane in the presence of sulfoxides, as racemic and/or chiral Lewis bases. The catalysts are easily available both in racemic and chiral forms and can be almost quantitatively recovered and recycled. Further studies will be devoted to the investigation of the influence of different chiral non racemic sulfoxides on the efficiency and enantioselectivity of the reaction.

*Typical experimental procedure*: Diisopropylethylamine (0.44 mL, 2.5 mmol) and allyltrichlorosilane **2** (150 μL, 0.93 mmol) were successively added to a solution of the sulfoxide **4** (1.50 mmol) in dry $CH_2Cl_2$ (4.5 mL) at −78°C under argon and the mixture was stirred for 5 min. Aldehyde **1** (0.50 mmol) was then added and the reaction mixture was stirred at −78°C for 7 h. The mixture was then poured into an ice-cooled mixture of

**Table 2.** Allylation of aldehydes **1** using enantiopure (*R*)-methyl-*p*-tolylsulfoxide **4a**

| Entry | **1** ($R^1$) | **4a** (equiv.) | Time (h) | Yield (%)[a] | % ee of (*S*)-**3**[b] |
|---|---|---|---|---|---|
| 1[c] | **1a** (Ph) | 1.5 | 65 | 70 | 51[d] |
| 2[e] | **1a** (Ph) | 3.0 | 7 | 62 | 55[d] |
| 3[e] | **1b** (2-furyl) | 1.5 | 65 | 88 | 42[f] |
| 4[e] | **1c** (PhCH=CH) | 1.5 | 65 | 79 | 46[d] |

[a] See note 'a' in Table 1.
[b] The absolute configuration of **3** was found to be (*S*) according to the optical rotation reported in the Refs. 5 and 6.
[c] The sulfoxide was recovered in 85% yield and 85% e.e.
[d] Determined by HPLC analysis employing a Daicel Chiralcel OB column.
[e] The sulfoxide was recovered in >95% yield and 97% e.e.
[f] Determined by HPLC analysis of the corresponding 3,5-dinitrobenzoate (Daicel Chiralcel AD column).

$CH_2Cl_2$ (40 mL) and saturated aqueous $NaHCO_3$ (20 mL), the organic layer was separated and the aqueous phase was extracted with $CH_2Cl_2$ (2×40 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated at reduced pressure. The residue was purified by flash chromatography on silica gel with a petroleum ether–$Et_2O$ mixture (from 98:2 to 90:10) to afford pure **3**, followed by AcOEt to recover the pure sulfoxide **4**.

## References


1. Kramer, G. W.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 2292.
2. Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 1527.
3. Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, *16*, 1295.
4. (a) Kobayashi, S.; Nishio, K. *Tetrahedron Lett.* **1993**, *34*, 3453; (b) Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620.
5. Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161.
6. Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S. *J. Am. Chem. Soc.* **1998**, *120*, 6419.
7. Sakurai, H. *Synlett* **1989**, 1.
8. (a) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron* **1997**, *53*, 3513; (b) Iseki, K.; Mizumo, S.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron Lett.* **1998**, *39*, 2767.
9. Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001**, *123*, 9488.
10. (a) Malkov, A. V.; Orsini, M.; Pernazza, D.; Muir, K. W.; Langer, V.; Meghani, P.; Kocovský, P. *Org. Lett.* **2002**, *4*, 1047; (b) Malkov, A. V.; Bell, M.; Vassieu, M.; Bugatti, V.; Kocovský, P. *J. Mol. Catal. A* **2003**, *196*, 179.
11. During the preparation of this manuscript, a new procedure for allylation of *N*-acylhydrazones with the system of $Cl_3SiCH_2CH{=}CH_2$ and chiral sulfoxides as activators has been reported (3 equivalents were required): Kobayashi, S.; Ogana, C.; Konishi, H.; Sugiura, M. *J. Am. Chem. Soc.* **2003**, *125*, 6610.
12. DMSO, DMF, HMPA belong to the class of polar aprotic solvents. Szwarc, M. *Ions and Ions Pairs in Organic Reactions*; John Wiley & Sons: New York, 1972.