

reflections with $I > \sigma(I)$ were used in the refinement of 302 parameters. The procedure was the same as for **5a**.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102362 and CCDC-102363. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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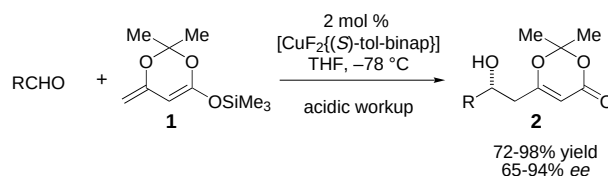
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Mechanistic Insights into Cu-Catalyzed Asymmetric Aldol Reactions: Chemical and Spectroscopic Evidence for a Metalloenolate Intermediate**

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The aldol reaction ranks among the premier methods for carbon–carbon bond formation in chemical synthesis. Advances in both diastereoselective and enantioselective processes have produced remarkable achievements in the synthesis of stereochemically complex structures.^[1] In contrast to the wealth of empirical and theoretical data available for diastereoselective aldol additions of metalloenolates to aldehydes,^[2] mechanistic understanding of catalytic asymmetric processes with enol silanes is less advanced. Insight into the latter would be of considerable assistance in the design of newer, more efficient methods for asymmetric synthesis.^[3]

We recently reported a catalytic aldol addition of the silyl dienolate **1** to a range of aldehydes in the presence of a bisphosphanyl-Cu^I fluoride complex which is generated in situ from (*S*)-Tol-BINAP,^[4] Cu(OTf)₂, and (Bu₄N)Ph₃SiF₂ (Scheme 1).^[5] Aromatic, heteroaromatic, and α,β -unsaturated



Scheme 1. Catalytic aldol addition of **1** to aldehydes.

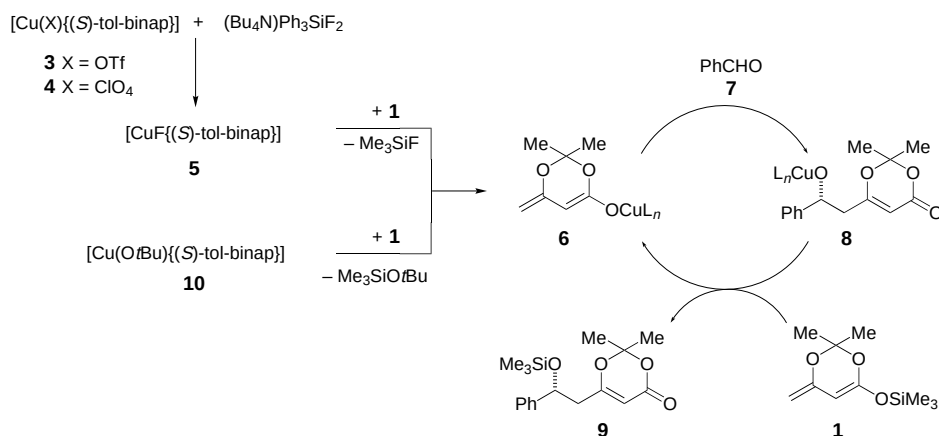
aldehydes furnished aldol adducts with up to 95 % *ee* and in 98 % yield. Importantly, we postulated a metalloenolate as a key intermediate in the catalytic cycle.^[6, 7] This role for a late transition metal catalyst contrasts the more conventional function of such metals as Lewis acids in related processes (Ag^I,^[8] Cu^{II},^[9] Pd^{II},^[6a–c] and Ni^{II}^[10]). Here we report chemical and spectroscopic data that support the postulated catalytic cycle and the involvement of metalloenolate and metal aldolate intermediates.

In mechanistic studies of the Cu-mediated reaction we observed that 5 mol % of the corresponding Cu^IF complex (prepared in situ from (*S*)-Tol-BINAP, [CuOTf·C₆H₆], and (Bu₄N)Ph₃SiF₂) served equally well in the catalytic aldol reaction of **1** and benzaldehyde (**7**; 94 % *ee* and 97 % yield).

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This result, along with the known reduction of Cu^{II} to Cu^{I} by ketone-derived enol silanes,^[11] suggested that a Cu^{I} complex functions as the catalytically relevant species. In the postulated catalytic cycle (Scheme 2), Cu^{I} complex **5** reacts with **1**



Scheme 2. Catalytic cycle with the metalloenolate **6** as central intermediate. OTf = trifluoromethanesulfonate.

to generate metalloidienolate **6**,^[12] which undergoes aldol addition to form the copper alkoxide **8**. Silylation by **1** converts **8** into the silylated adduct **9** with concomitant regeneration of metalloenolate **6**. This mechanistic pathway suggests that direct entry into the catalytic cycle may be possible with a Cu^{I} alkoxide. Accordingly, when the aldol reaction was conducted with 5 mol % of $[\text{Cu}(\text{OTf})\{(\text{S})\text{-tol-binap}\}]$ (**10**) (from $(\text{S})\text{-Tol-BINAP} + \text{Cu}(\text{OTf})$ ^[13]), aldol adducts were obtained for a range of aldehydes in yields and enantioselectivities identical to those that were obtained with the corresponding Cu^{I} or Cu^{II} fluoride complexes. These observations are not only consistent with the intermediacy of a Cu^{I} alkoxide species, but also underscore the ability of a metal alkoxide to participate in the catalytic cycle. For further in-depth spectroscopic studies, this more direct approach to the catalytic cycle was employed since it avoids salt formation and redox processes.

The progress of the reaction of trimethylsilyl dienolate **1**, **7**, and 5 mol % of **10** at -78°C in THF was monitored under an inert atmosphere by IR spectroscopy (ReactIR, Figure 1).^[14] The IR spectrum of the starting dienolate **1** in THF displays a

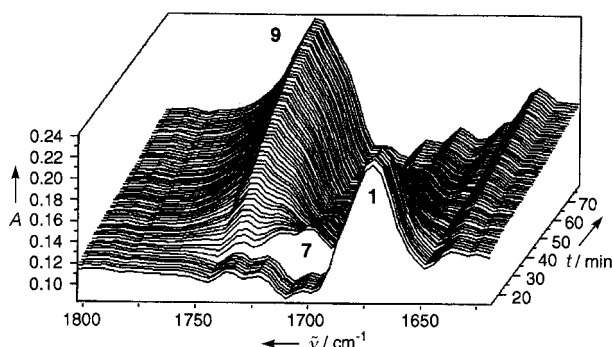


Figure 1. ReactIR of the reaction of **1**, **7**, and 5 mol % of **10**.

characteristic resonance at 1671 cm^{-1} , which was monitored throughout the progress of the reaction. When **7** (1710 cm^{-1}) and **10** were added, a time-dependent diminution in the intensity of the bands was observed for each reactant, with the

emergence of a new absorption signal at 1729 cm^{-1} , which we assigned to the aldol adduct **9**.^[15]

Additional insight into the process was obtained by examination of the reaction with stoichiometric amounts of complex **10**. Thus, treatment of **1** with one equivalent of **10** resulted in rapid disappearance of the dienolate signal at 1671 cm^{-1} and the emergence of two bands at 1690 and 1550 cm^{-1} ,

which we assigned to the copper enolate **6**. This species was stable at -78°C , but subsequent addition of **7** resulted in replacement of the two bands by a new resonance at 1729 cm^{-1} for adduct **8**.^[15]

Metalation experiments provided supporting evidence for assignment of the resonances at 1690 and 1550 cm^{-1} to an intermediate metalloenolate (Figure 2, Scheme 3). Reaction of **1** with $(\text{Bu}_4\text{N})\text{Ph}_3\text{SiF}_2$ produced a new species (1625 cm^{-1}), which we assigned as the naked enolate **11**.^[16] Addition of one equivalent of $[\text{Cu}(\text{ClO}_4)\{(\text{S})\text{-tol-binap}\}]$ ^[17] resulted in the

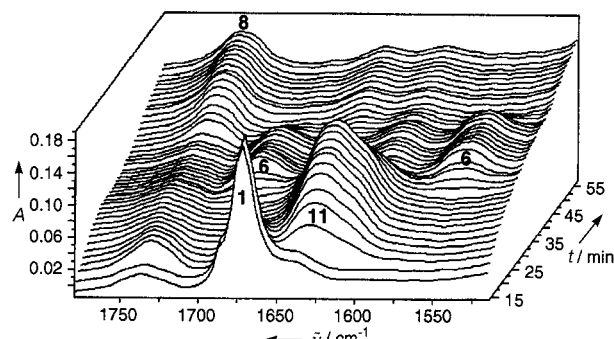
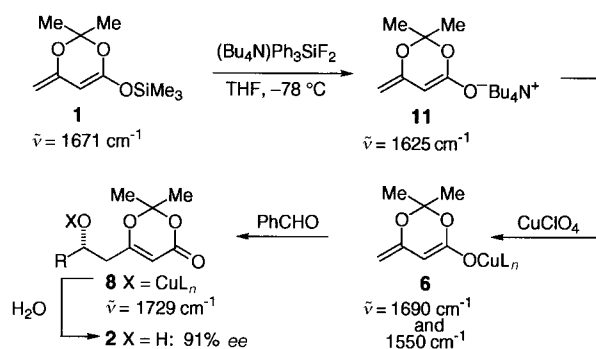


Figure 2. Metalation experiment depicted in Scheme 2 monitored by ReactIR.



Scheme 3. IR absorption maxima of the participating species.

generation of the same two peaks (1690 and 1550 cm^{-1}) that were observed by direct metalation of **10** with **1**. These were also replaced by the signal corresponding to adduct **8** after the addition of **7**.^[15]

In summary we have shown that tol-binap–copper(I) complexes are active catalysts for the asymmetric addition of dienolate **1** to aldehydes. Utilization of CuOrBu for the preparation of the catalyst permits a more direct entry into the catalytic cycle, avoids the introduction of spectator salts, and circumvents redox chemistry. Successful initiation of the reaction by CuOrBu suggests that a copper(I) alkoxide is recursively generated throughout the reaction process. Additionally, we document spectroscopic and chemical evidence for the existence of a copper enolate as a reactive species. Such a process provides a conceptual and practical alternative to the well-established Lewis acid promoted stereoselective aldol reactions. The development of asymmetric, catalytic carbonyl additions that proceed through metalloenolates offers considerable opportunities for the design of new catalysts in asymmetric organic synthesis.

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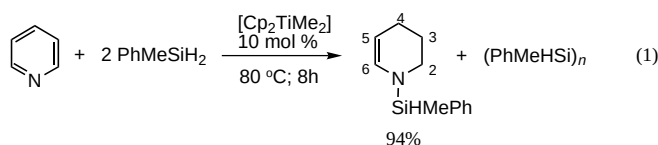
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Homogeneous Catalytic Hydrosilylation of Pyridines**

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Titanocene complexes are versatile catalysts for a large number of reactions.^[1–11] The reaction of Me₃SiH with pyridine catalyzed by *heterogeneous* platinum-group catalysts was reported many years ago.^[12] We now report the first examples of the hydrosilylation of pyridines with *homogeneous*, titanocene-based catalysts, and the first example of homogeneously catalyzed hydrosilylation of an aromatic substrate.

Typically, the reaction was carried out without solvent with a 2:1 molar ratio of silane to pyridine and 10 mol % of [Cp₂TiMe₂] (based on pyridine) at 80°C [Eq. (1)], but an inert



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