4796 *Organometallics* **1997,** *16,* 4796−4799

A Novel Copper(II)/Tin(II) Reagent for Aqueous Carbonyl Allylation: In Situ Diagnostics of Reactive Organometallics in Water[†]

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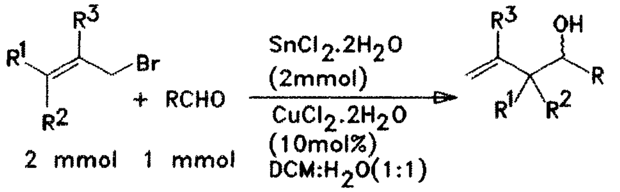
Received May 19, 1997[⊗]

A convenient and synthetically attractive protocol for the allylation of aldehydes using stannous chloride and catalytic cupric chloride in dichloromethane/water is described. In situ probing provides indirect (NMR, CV) and direct (MS) evidence for the copper(I)-catalyzed formation of an allyltrihalostannane intermediate in very high concentration in water.

Introduction

By virtue of its synthetic potential, mechanistic intrigue, and Schlenk-free operational simplicity, the aqueous Barbier reaction has carved out a distinct niche and has importance in organic chemistry.[1] While a broad spectrum of zerovalent metals have been satisfactorily tested under various conditions, aqueous Barbier protocols with metal salts have been slow to emerge.[2] With reference to carbonyl allylation, both preformed[3] as well as in situ generated[4] allylstannanes continue to evoke widespread interest due to their chemo-, regio- and stereoselectivity aspects, which culminated in the recent demonstration of highly efficient catalytic asymmetric allylation by Keck[5] and others.[6] Our continuing interest in the organometallic reactivity of allyl−metal complexes, including allyl−tin reagents[7] and recent interest in catalysis via metal salts[8] prompted us to explore new reagent combinations for aqueous Barbier allylation. Another impetus for this study comes from recent interest among organometallic chemists in the fate of σ-bonded hydrated organometallic species.[9] In this paper we wish to describe a novel Cu(II)/Sn(II)-promoted carbonyl allylation reaction (Scheme 1) as well as in situ NMR and CV evidence which suggests that the present copper-catalyzed reaction is not like that for palladium.[10] In situ MS studies further provide the first direct evidence for the formation of allyltrihalostannanes in water.


Scheme 1

Results and Discussion

The reaction of stannous chloride dihydrate with allyl bromide and 4-chlorobenzaldehyde in the presence of a catalytic amount of cupric chloride dihydrate in dichloromethane−water (1/1 v/v) for 8 h gave rise to the desired homoallylic alcohol in 88% isolated yield. The reaction could also be performed with allyl chloride with increased reaction time (14 h) and gave a slightly lesser yield of alcohol. On the other hand, reactions without cupric chloride or in the absence of water showed $<5\%$ conversion. This highly mild and convenient protocol was employed for the reactions of various aldehydes and substituted allyl bromides, resulting in good to excellent yields of the products (Table 1). It is noteworthy that allyl halides, substituted at the 3-position, showed exclusive γ-regioselectivity and high anti selectivity (entries 4−10).[11] Ferrocenecarboxaldehyde gave exclusively the dehydrated product, albeit in poor yield (Scheme 2).

[†] Presented at the Indo-German Symposium on Organic Synthesis−Growing Interface with Adjacent Sciences, Hyderabad, India, Sept 27−28, 1996. This is IICT Communication No. 3821.

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[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1997.

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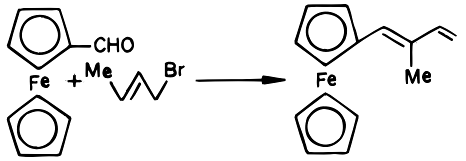
S0276-7333(97)00409-3 CCC: $14.00

Table 1. Allylation of Aldehydes RCHO with Allyl Bromides $R^1R^2C{=}CH(R^3)CH_2Br$

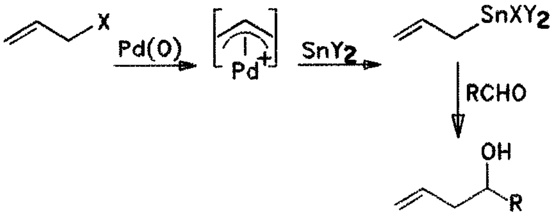
entry no.	R^1	R^2	R^3	R	yield[a] (%)	ratio[b] (syn:anti)
1	H	H	H	4-chlorophenyl	88	
2	H	H	Me	phenyl	61	
3				benzyl	65	
4	Me	H	H	4-chlorophenyl	91	30:70
5				phenyl	85	25:75
6				cinnamyl[c]	48	35:65
7				*n*-hexyl[c]	44	45:55
8				2-furyl[d]	33	34:66
9				piperonyl	71	44:56
10	Ph	H	H	4-chlorophenyl	72	0:100
11	Me	Me	H	4-chlorophenyl	80	

[a] Isolated yields after chromatography based on aldehydes. [b] The ratio was determined by ^{1}H NMR. [c] Reaction was performed at pH 5. [d] Reaction was performed at 0 °C.

Scheme 2



Scheme 3



Two key questions warranted further investigation in elucidating the mechanism of allylation.

(1) Is there a π-allyl intermediate involved in the catalytic cycle similar to the case in the Pd(0)-mediated carbonyl allylation reaction (Scheme 3)?[10,12]

(2) Are hydrated organometallic cations involved, as suggested[9,13] by Tagliavini and co-workers for carbonyl allylation with preformed allylhalostannanes?

We first carried out in situ ^{1}H NMR observation of the reaction of stannous chloride (1 mmol) and allyl bromide (2 mmol) in D_2O (2 mL, 112 mmol). The mixture attained homogeneity in 24 h; however, only very weak signals due to allyl−tin species could be detected, besides those corresponding to unreacted allyl bromide (spectrum A in Figure 1).

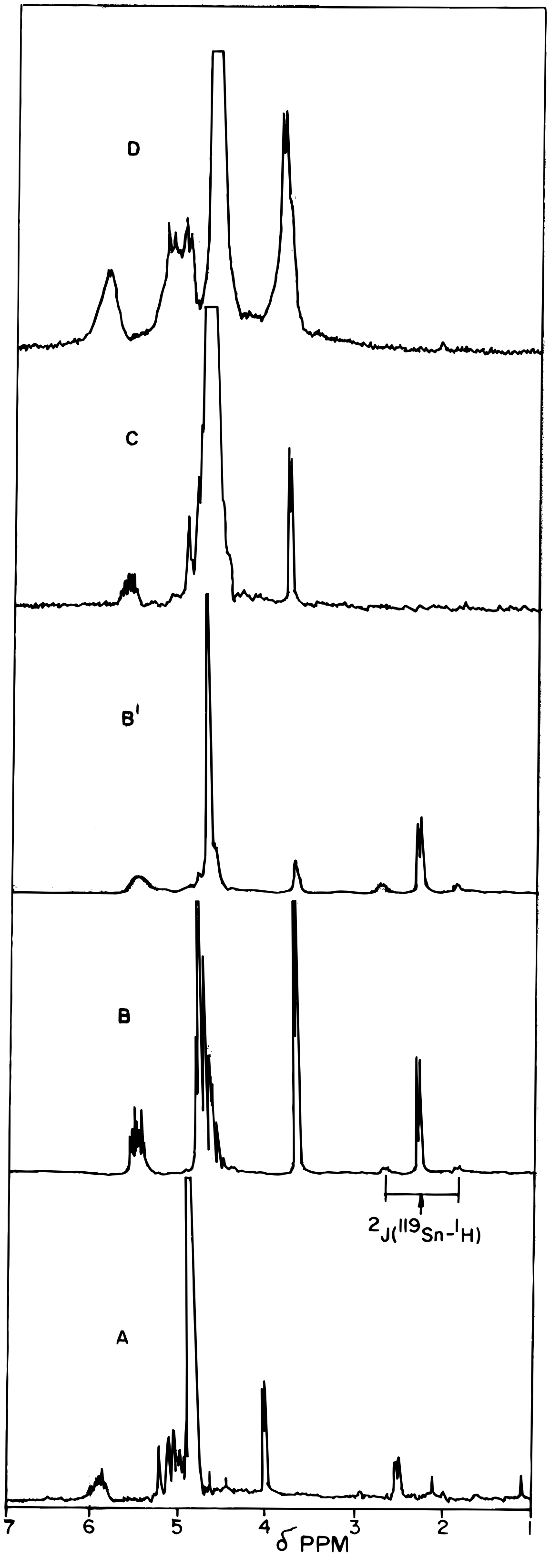


Figure 1. In situ ^{1}H NMR spectra in D_2O of (A) allyl bromide/stannous chloride, (B) allyl bromide/stannous chloride/catalytic cupric chloride after 15 min, (B′) the same solution as in B after 4 h, (C) allyl bromide/cupric chloride/Cu, and (D) allyl bromide. For details see text.

A similar reaction mixture, but in the presence of cupric chloride (20 mol %), attained homogeneity (solution 1) in 15 min; the NMR spectrum (spectrum B in Figure 1) showed a distinct (σ-allyl)tin species (δ (ppm) 2.3; $^2J(^{119}Sn-H) = 154$ Hz)[14] along with another species characterized by a methylene doublet at 3.7 ppm. When the latter is compared with methylene signals of allyl bromide in D_2O (spectrum D in Figure 1) and of allyl bromide/cupric chloride/copper metal (spectrum C in Figure 1), the second species in solution 1 is found to be an allyl−copper(I) intermediate having a preferential alkene−metal interaction.[15] The higher intensity of the allyl−copper signal in spectrum B (reaction time 15 min) could be attributed to its faster rate of formation.

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(12) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577.

(13) (a) Furlani, D.; Marton, D.; Tagliavini, G.; Zordan, M. *J. Organomet. Chem.* **1988**, *341*, 345. (b) Marton, D.; Tagliavini, G.; Vanzan, N. *J. Organomet. Chem.* **1989**, *376*, 269.

(14) It is interesting to note that the in situ NMR spectra presented in ref 12 from the reaction of stannous chloride, allyl chloride, and catalytic Pd(0) in THF-d_7 showed similar $^2J(^{119}Sn-^1H)$ coupling.

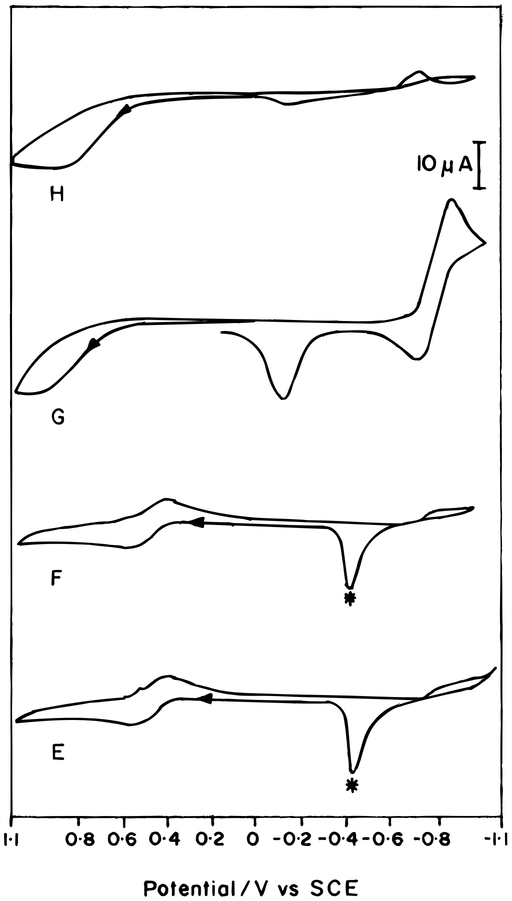


Figure 2. Cyclic voltammograms in MeCN of (E) cupric chloride, (F) cupric chloride/allyl bromide, (G) stannous chloride, and (H) stannous chloride/allyl bromide. For details see text. Asterisks in E and F indicate copper(0) adsorption on the electrode surface.

Assistance of this allyl−copper species in the formation of the allyl−tin species could further be confirmed from spectrum B′, recorded after 4 h of reaction time. Here the intensity of the peak at 3.7 ppm is markedly reduced with a concomitant increase in allyl−tin peak intensity at 2.3 ppm. The above set of experiments tentatively rules out the participation of a π-allyl intermediate in our system.

Further support for the stronger oxidative interaction of allyl bromide with tin(II) as compared to copper(I) comes from CV experiments in water and in acetonitrile (Figure 2).[16] In acetonitrile, the voltammograms of cupric chloride before (E in Figure 2) and after (F in Figure 2) the addition of allyl bromide are nearly alike, the Cu(I)/Cu(II) formal potentials (vs Fc^+/Fc) being 0.43 and 0.44 V, respectively. However, in the case of stannous chloride, the addition of allyl bromide causes a rapid collapse of the reversible peaks (Sn(II)/Sn(0) formal potential 0.772 V vs Fc^+/Fc) and the Sn(II)/Sn(IV) signal (anodic potential at −0.128 V) (see voltammograms G and H in Figure 2). Keeping in mind the profound catalytic effect of copper halide in the present carbonyl allylation and the in situ NMR and CV results, we propose a copper(I)-assisted allylstannation mechanism (Scheme 4).

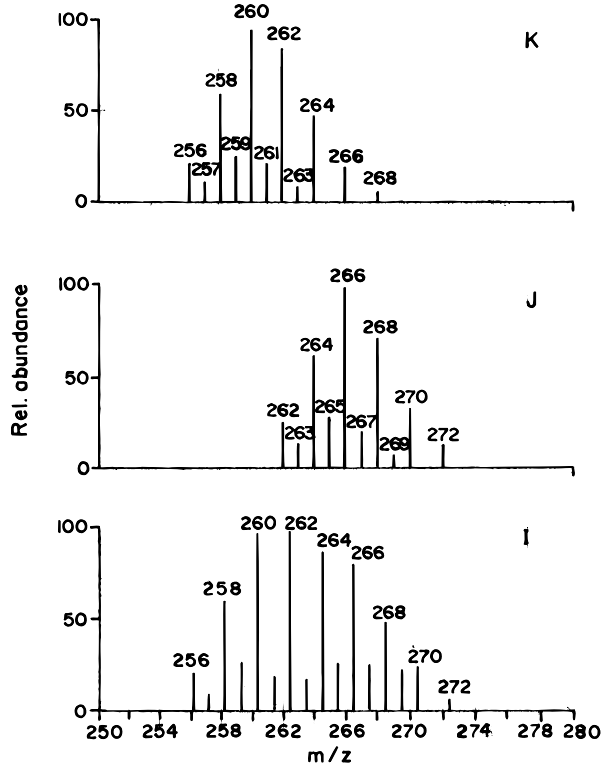
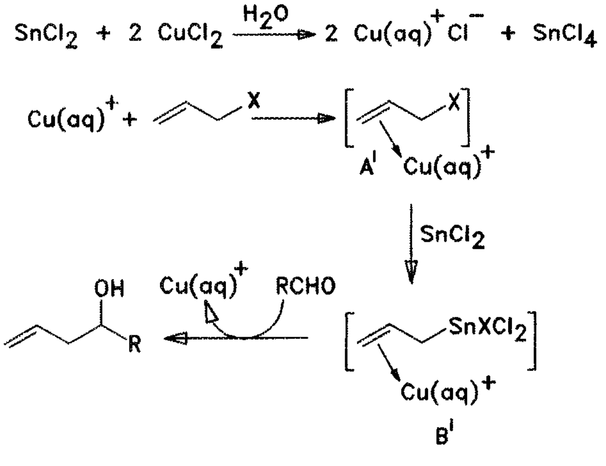


Figure 3. (I) In situ EIMS spectrum of allyl chloride/stannous chloride/catalytic cupric chloride in water, showing a mixture of allytrichlorostannane and stannic chloride in a 40:60 ratio. (J) Simulated spectrum of allyltrichlorostannane. (K) Simulated spectrum of stannic chloride.

Scheme 4



Since the ^1H NMR spectrum in D_2O corresponding to the allyltin species (spectrum B in Figure 1) closely matched with that reported[12,14] by Masuyama et al. in THF-d_7, we were prompted to carry out in situ EIMS studies[17] to ascertain the stability of the proposed allyltrihalostannane intermediate (Scheme 4, B′) in very

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(15) (a) Although the equillibrium constant for Cu(I) disproportionation to Cu(II) and Cu(0) in water is on the order of 10^6 (Jardine, F. H. *Adv. Inorg. Chem. Radiochem.* **1975**, *17*, 115), metastable solutions of aquocopper(I) complexes can be generated in acidic aqueous media by reducing Cu(II) salts with Eu(II), Cr(II), V(II), or Sn(II) halides (Nunes, T. L. *Inorg. Chem.* **1970**, *9*, 1325). (b) For an olefin−copper(I) interaction see: Quinn, H. W.; Tsai, J. H. *Adv. Inorg. Chem. Radiochem.* **1969**, *12*, 327. Munakata, M.; Kitagawa, S.; Kosome, S.; Asahara, A. *Inorg. Chem.* **1986**, *25*, 2622. (c) For a discussion on allyl−copper(I) interaction see: Baruah, J. B.; Samuelson, A. G. *New J. Chem.* **1994**, *18*, 961.

(16) CV in aqueous media did not show reversibility, indicating the instability of the redox species in the absence of coordinative stabilization.

(17) For organostannanes, EIMS is a more effective probe than FABMS: Harrison, P. G. *Chemistry of Tin*; Blackie: London, 1989; p 105.

high concentration in water. Following the reaction of stannous chloride (1 mmol), allyl chloride (2 mmol), and a catalytic amount of cupric chloride (0.1 mmol) in water (2 mL, 111 mmol) for 1 h, excess halide was removed under vacuum and the aqueous solution was directly injected into the mass spectrometer probe. To our delight, we could detect peaks due to allyltrichlorostannane (spectrum I in Figure 3). This and all other major fragmentation peaks in the spectrum were fully characterized with the help of simulated MS data. No organometallic species having an Sn−OH moiety could be detected as opposed to earlier proposals.[12,13b] Rather surprisingly, a similar experiment with allyl bromide showed the formation of allyltribromostannane as the only organometallic species, for which we do not have an explanation as yet. Attempts are underway to quantitate the species distribution in water.

Summary

In this paper we have described a mild and efficient protocol for carbonyl allylation in aqueous media using readily available reagents. Further examination of the reactive organometallics was carried out using in situ NMR, CV, and EIMS probes, which suggested the intermediacy of aquocopper(I) species. More interestingly, the existence of an allyltrihalostannane intermediate in very high concentration in water could be established, perhaps for the first time.[18]

Experimental Section

All reactions were performed under an inert atmosphere of IOLAR grade nitrogen. ^{1}H NMR spectra were taken on a Varian 200 spectrometer in $CDCl_3$ or D_2O. Chemical shifts are reported in δ (ppm) relative to TMS as internal standard. Cyclic voltammetric experiments were carried out using a glassy-carbon electrode under a nitrogen purge on a Electrochemistry System Model 370 instrument. The supporting electrolyte used was tetrabutylammonium chloride (0.1 M). The system was calibrated against the ferrocene/ferrocenyl couple before and after each experiment. EIMS (20 and 70 eV) spectra were taken using VG MicroMass 70 70H and VG Autospec M mass spectrometers. Stannous chloride dihydrate (Ranbaxy) and cupric chloride dihydrate (S. D. Fine Chemicals) were used as received.

Typical Procedure for the Allylation of Aldehydes. A mixture of 4-chlorobenzaldehyde (140 mg, 1 mmol) and 1-bromobut-2-ene (270 mg, 2 mmol) in dichloromethane (3 mL) was slowly added to a stirred solution containing $SnCl_2{\cdot}2H_2O$ (451 mg, 2 mmol) and $CuCl_2{\cdot}2H_2O$ (17 mg, 0.1 mmol) in water (3 mL) and under nitrogen. The solution was stirred at room temperature for 8 h (TLC monitoring on silica gel; eluent ethyl acetate−hexane, 1/4 v/v) and then extracted with diethyl ether (3 × 15 mL). The organic layer was washed with 5% aqueous sodium bicarbonate (10 mL), water (2 × 5 mL), and brine (2 × 10 mL), dried over magnesium sulfate, and concentrated under reduced pressure. Column chromatography (silica gel 60−120 mesh, Acme-India; eluent acetone−hexane, 3/97 v/v) afforded pure 1-(4-chlorophenyl)-2-methylbut-3-en-1-ol as a light yellow oil (176 mg, 91% with respect to aldehyde; syn: anti = 30:70 (see the NMR spectrum)).

Details of in Situ NMR Experiments. In a typical procedure, stannous chloride dihydrate (225 mg, 1 mmol) and cupric chloride dihydrate (34 mg, 0.2 mmol) were taken up in D_2O (2 mL) under a nitrogen atmosphere. After the mixture was stirred for 10 min, allyl bromide (242 mg, 2 mmol) was added to the resulting milky white solution, which became clear after 15 min. The clear solution was briefly evacuated, purged with nitrogen, and transferred via cannula to the NMR tube.

Acknowledgment. Financial support from the UGC (fellowship to A.K.) and the CSIR (to S.P.) is gratefully acknowledged. We thank Prof. Bhaskar G. Maiya, Central University, Hyderabad, India, for generous assistance in conducting CV experiments and Dr. A. C. Kunwar for help with in situ NMR spectral recording.

Supporting Information Available: Listings of NMR and MS spectral data of homoallylic alcohols, along with figures giving in situ NMR spectra, cyclic voltammograms in water, and in situ EIMS and simulated mass spectra (38 pages). Ordering information is given on any current masthead page.

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(18) The exclusive formation of tribenzyltin chloride from the reaction of benzyl chloride and tin metal in water was reported earlier: Sisido, K.; Takeda, Y.; Kinugawa, Z. *J. Am. Chem. Soc.* **1961**, *83*, 538.