Pergamon

Tetrahedron Letters 43 (2002) 7541–7543

TETRAHEDRON
LETTERS

Efficient solvent-free in situ tin-mediated homoallylation reactions

Philip C. Andrews,[a,]* Anna C. Peatt[a] and Colin L. Raston[b]

[a]*Centre for Green Chemistry/School of Chemistry, Monash University, Clayton, Victoria 3800, Australia*
[b]*Department of Chemistry, University of Leeds, Leeds LS2 9JT, UK*

Received 4 July 2002; accepted 23 August 2002

Abstract—Various carbonyl compounds were converted to their corresponding homoallylic alcohols under ultrasonic irradiation and solvent free conditions, in the presence of metallic Sn and excess allyl bromide. Diallyltin(IV) dibromide was identified as the reactive species, with several allyl tin(II/IV) species being detected in the organic extracts of the reactions. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

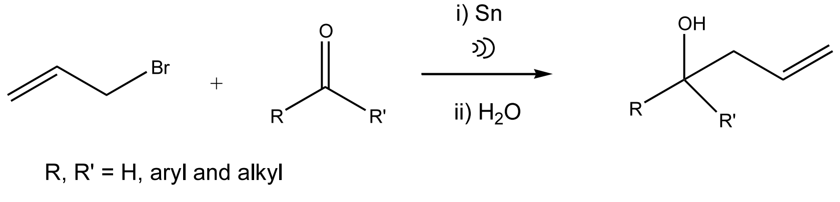
Recently we reported the successful solvent-free, metal-mediated, synthesis of homoallylic alcohols via Barbier–Grignard type reactions utilising elemental In, Bi and Zn.[1] In broadening our investigations we have turned our attention to Sn since in recent years it has proved to be an effective mediator in the production of homoallylic alcohols in environmentally benign solvents, namely ionic liquids[2] and H_2O.[3,4] There are several obvious reasons why Sn and its organic derivatives could be attractive reagents; in comparison with the more commonly used Li and Mg reagents, Sn compounds do not require rigorously dry conditions and an inert atmosphere, and in comparison with most metals it is relatively inexpensive and readily available.[4]

We were particularly interested to know whether the high yields for the allylation reactions obtained with Sn in water could be replicated under solvent-free conditions. This could be particularly important since many compounds with double bonds, such as imines, are hydrolytically unstable.[5] Furthermore, the toxicity of low molecular weight alkyl and allyl Sn compounds can significantly hinder their practical use in pharmaceutical development if any of the Sn compound(s) are carried through into the target products.[6] Thus, we have also investigated the nature of the reactive allyl tin species and whether these compounds were present in the organic extracts of these reactions.

Herein, we report the conversion of several representative carbonyl compounds to their corresponding homoallylic alcohols, utilising Sn as the mediator under solvent free conditions (Scheme 1).

2. Experimental

A typical experiment involved the addition of the carbonyl compound (5 mmol) to a suspension of allyl bromide (20 mmol) and commercially available Sn powder (5 mmol) in a stoppered, 50 ml, round-bottomed flask. This suspension was then allowed to react under sonication for 12 h before being quenched with



Scheme 1.

---

* Corresponding author. Tel.: +6-3990-54514; fax: +61-39905-4597; e-mail: philip.andrews@sci.monash.edu.au

0040-4039/02/$ - see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(02)01811-7

water (ca. 0.5 ml) and extracted with Et_2O (3×15 ml). The products were analysed by ^1H NMR and GC–MS.

Good yields were obtained for both aromatic and aliphatic aldehydes (80–100%) (Table 1) comparable to those produced in equivalent reactions performed in H_2O and ionic liquids.[2–4] The reaction with *trans*-cinnamaldehyde produced consistently only the 1,2-addition product while the reactions involving ketones, such as acetophenone and benzophenone, failed to react, most likely as a result of the reduced reactivity of the carbonyl group.

Unlike the analogous reactions with elemental In, Zn and Bi, the Sn mediated reactions required ultrasonic activation of the metal powder and longer reaction times (ca. 12 h). Also, to achieve high yielding reactions the use of 4 equiv. of allyl bromide was necessary. In reactions where only 2 equiv. was added, significantly lower yields were obtained. However, in contrast with more traditional synthetic methods for the production of allylstannanes, normally involving a combination of a catalyst (e.g. $HgCl_2$ or HBr) and heat, the solvent-free approach is significantly less cumbersome.[7]

The need for induction can be understood by considering the relative kinetic stability of the metallic Sn surface, which results from the stable octet configuration of the outer electrons. While the longer reaction times can also be traced to the relatively high kinetic stability of the C–Sn bond in comparison with those of other main group metals.[8] To investigate whether ultrasound was required for both the formation of the allyltin bromide intermediate and the subsequent allylation reaction allyl bromide and tin powder were allowed to react under ultrasonic irradiation for 12 h. Benzaldehyde was then added to the preformed allyltin bromide species and the reaction mixture simply stirred for 4 h. On quenching, the allylic alcohol was obtained in relatively high yield (ca. 68%). The comparative reaction with no ultrasound gave no allylic alcohol. Thus, ultrasonic irradiation is necessary to accelerate the reaction of the metal, presumably initially activating the metal surface, but also contributes slightly to the formation of the Sn alkoxide intermediate.

Recently the toxicological effects of low molecular weight alkyl derivatives of Sn have received a lot of attention due to an influx of these compounds into the environment, resulting from their wide and varied use in industry and as marine anti-fouling agents.[9,10] Toxicologically, the tetra-substituted and tri-substituted tin organyls are more harmful than the mono- and di-substituted analogues.[6] For example there is a significant increase in acute oral toxicity values observed in rats, when moving from butyltin tetrachloride at LD_{50} 2140 mg/kg to tributyltin chloride LD_{50} 129 mg/kg.[6]

Table 1. % Yields for allylation reactions of various carbonyl compounds in the presence of Sn

Carbonyl compound	Allyl bromide:aldehyde/ketone:Sn	Yield[a]
PhCHO	4:1:1	98
2-HOC_6H_4CHO	4:1:1	96
PhCH=CHCHO	4:1:1	87
3,4-$(MeO)C_6H_3CHO$	4:1:1	82
Ph_2C=O	4:1:1	0
Ph(Me)C=O	4:1:1	0

[a] Estimated by GC–MS.

It would clearly be of concern and contrary to our aim of developing benign synthetic protocols if these compounds persisted to any degree in the reaction products.

From GC–MS studies the presence of both allyltin, and allyltin bromide species were detected in the organic extracts of the reactions. Such species have also been observed in reactions performed in ionic liquids using $(CH_2{=}CHCH_2)_4Sn$.[2] The presence of highly toxic allyltin compounds contrasts with the results of our study on In, Bi and Zn, where no intermediate allyl metal species were detected in the products extracted into ether, in any of the reactions.

From an analysis of the final reaction mixtures the most reactive Sn species appears to be $(CH_2{=}CHCH_2)_2SnBr_2$. The reactions which led only to a complete recovery of starting compound (i.e ketones) showed a large amount of $(CH_2{=}CHCH_2)_2SnBr_2$ in the ether extract with relatively small amounts of $(CH_2{=}CHCH_2)_4Sn$, $(CH_2{=}CHCH_2)_3SnBr$ and $(CH_2{=}CHCH_2)_2Sn$. Corresponding reactions which produced homoallylic alcohols in high yields showed no trace of $(CH_2{=}CHCH_2)_2SnBr_2$, only $(CH_2{=}CHCH_2)SnBr_3$, $(CH_2{=}CHCH_2)_3SnBr$ and $(CH_2{=}CHCH_2)_2Sn$, suggesting that $(CH_2{=}CHCH_2)_2SnBr_2$ is the reactive Sn species.

To prove this hypothesis we followed the established reaction protocol without the addition of any carbonyl compound. On analysis of the ether extract by GC/MS it was observed that the predominant allyltin species was in fact $(CH_2{=}CHCH_2)_2SnBr_2$ (*m*/*z* 359), with no observations of allyltin derivatives of type R_3SnBr, $RSnBr_3$ or R_2Sn ($R = CH_3{=}CHCH_2$). Thus, $(CH_2{=}CHCH_2)_2SnBr_2$ is both the most stable Sn intermediate formed and the one most responsible for allylation of the aldehyde. Surprisingly an additional peak at *m*/*z* 439 was also observed which was attributed to $[(CH_2{=}CHCH_2)_2SnBr_3]^-$ (Fig. 1). Formation of such negatively charged species is a known phenomena for tin complexes of the type R_3SnX (R = Ph and X = Cl or Br), in negative ion electrospray mass spectrometry and also in ^1H and ^{119}Sn NMR, which are conducted in halogen rich environments.[11]

From this, theoretically only two equivalents of allyl bromide would be required to produce $(CH_2{=}CHCH_2)_2SnBr_2$ and efficient synthesis of the homoallylic alcohols. However, in reactions where only 2 equiv. were added significantly reduced reaction yields were obtained and 4 equiv. of allyl bromide were necessary to obtain high yields. The reason is physical rather than chemical and stems from the volatility of

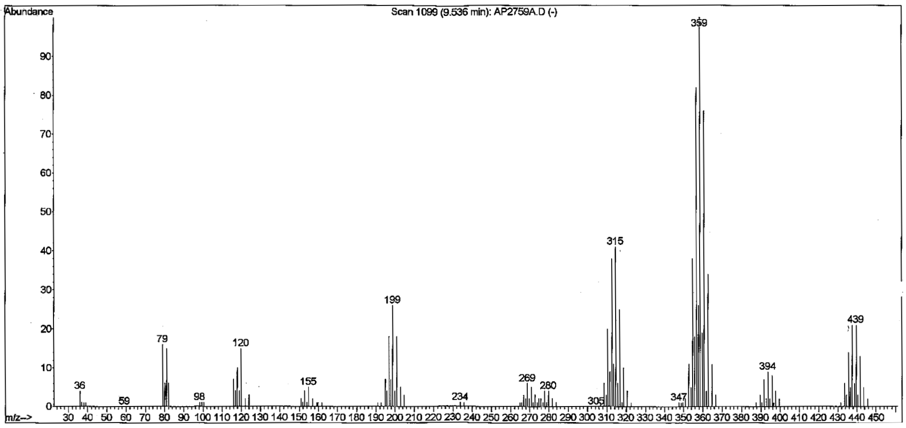


Figure 1. Negative-ion mass spectrum of $(CH_2{=}CHCH_2)_2SnBr_2$ showing $[(CH_2{=}CHCH_2)_2SnBr_3]^-$ at *m/z* 439.

allyl bromide under prolonged ultrasound irradiation. This leads to reflux in the closed system and inefficient production of $(CH_2{=}CHCH_2)_2SnBr_2$. However, this could clearly be overcome on larger scales.

3. Conclusion

The solvent-free Sn-mediated synthesis of homoallylic alcohols can be successfully achieved with aldehydes under ultrasonic irradiation. We have established that the allyltin compounds unfortunately persist in the final products and that the most reactive species is $(CH_2{=}CHCH_2)_2SnBr_2$. Due to the relatively toxic nature of allylstannanes, especially those which are highly substituted, it seems unlikely, from this feasibility study, that these reactions could be applied in downstream fine chemical and pharmaceutical applications without some highly efficient method of removal.

4. General

GC–MS data were obtained on the Aligent 6890 Series GC Systems and the Algent 5973 Network Mass Selective Detector. 1 μL aliquots of the samples were injected, with inlets having a split ratio of 25:1. Helium gas was employed with its pressure set at 7.16 psi and flow rate 26.6 ml/min. The installed column was the HP-5MS 5% phenyl methyl siloxane with the capillary size being 30.0 m×250 μm×0.25 μm. The oven setpoint was 60°C (held for 3 min) increasing at a rate of 10°C/min. to the endpoint of 280°C. ^{1}H NMR spectra of some compounds were recorded in $CDCl_3$ on the Varian Mercury 300 at 400 MHz.

Acknowledgements

We thank the Centre for Green Chemistry at Monash University, the Australian Research Council and the University of Leeds for financial support. Furthermore, we thank Victor F. De Guzman for his assistance in acquiring GC–MS material.

References

1. Andrews, P. C.; Peatt, A. C.; Raston, C. L. *Green Chem.* **2001**, *3*, 313–315.
2. Gordon, C. M.; McCluskey, A. *Chem. Commun.* **1999**, 1431–1432.
3. Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191–193.
4. Chan, T. H.; Yang, Y.; Li, C. J. *J. Org. Chem.* **1999**, *64*, 4452–4455.
5. Chan, T. H.; Wenshuo, L. *Tetrahedron Lett.* **1998**, *39*, 8605–8608.
6. Environmental Health Criteria 15, Tin and Organonotin Compounds; A Preliminary Review, World Health Organisation, Finland, 1980.
7. Sisido, K.; Takeda, Y. *J. Org. Chem.* **1961**, *26*, 2301.
8. Elschenbroich, C.; Salzer, A. *Organometallics*: *A Concise Introduction*; VCH: Weinheim, 1992.
9. Noda, T. J. *Health Sci.* **2001**, *47*, 544–555.
10. Boyer, I. J. *Toxicology* **1989**, *55*, 253–298.
11. Henderson, W.; Taylor, M. J. *Polyhedron* **1996**, *15*, 1957–1964.