Pergamon

Tetrahedron Letters, Vol. 37, No. 22, pp. 3811-3814, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00710-1

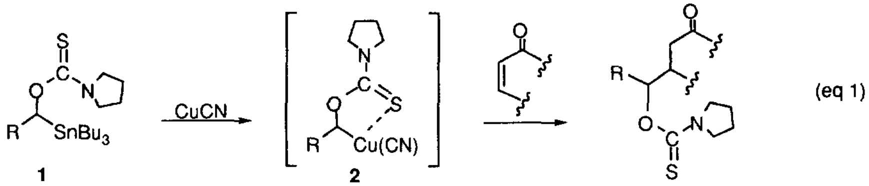
Conjugate Addition of α-Alkoxystannanes via *In Situ* Transmetalation using Catalytic CuCN

Rama K. Bhatt, Jianhua Ye, J.R. Falck*

Departments of Molecular Genetics and Pharmacology
University of Texas Southwestern Medical Center
Dallas, TX 75235 USA

Abstract: Catalytic CuCN mediates the *in situ* transmetalation of α-thionocarbamoyl stannanes and subsequent conjugate addition to α,β-unsaturated carbonyls in the presence of chlorotrimethlysilane at or a little above room temperature. Copyright © 1996 Elsevier Science Ltd

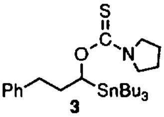
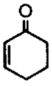
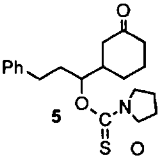
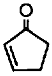
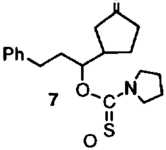
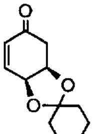
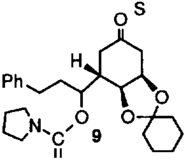
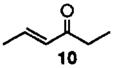
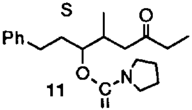
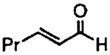
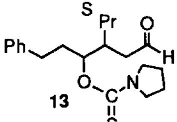
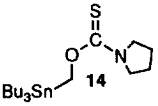
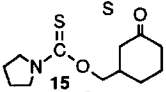
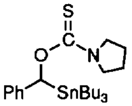
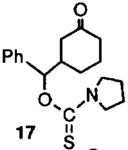
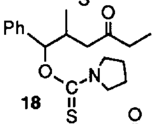
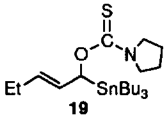
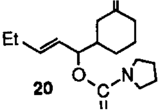
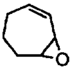
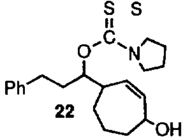
Organocopper reagents have gained wide acceptance due largely to their low basicity as compared with other common anionic species and their unique chemical reactivities.[1] A hallmark of the latter is an unparalleled proclivity towards conjugate or Michael additions. Typically, organocopper reagents are prepared by slow addition of the corresponding, but more reactive, organolithium or Grignard to a suspension of Cu(I) salt at low temperature. We[2] and others,[3] however, have demonstrated a direct and facile transmetalation between copper salts and organostannanes.[4] In the case of α-heteroatom substituted alkyltributylstannanes, the overall process of transmetalation and cross-coupling with organohalides proceeds with retention of configuration.[2] Herein, we report that the coordinatively stabilized, lower order cyanocuprates **2**, generated *in situ* from α-thionocarbamoyl stannanes **1** and CuCN, readily undergo conjugate addition to α,β-unsaturated carbonyls (eq 1).[5,6]



(eq 1)

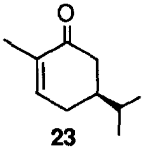
The reaction parameters for conjugate addition were initially explored using equimolar amounts of stannane **3** and 2-cyclohexen-1-one (**4**) as a model system. Acceptable yields of **5**[7] (Table 1), isolated as a ~2:1 diastereomeric mixture after hydrolytic work-up, were only achieved when the addition was conducted in the presence of chlorotrimethylsilane.[6,8] The use of CuCN was also critical, although only a catalytic amount (8 mole %) was needed. Other copper salts, e.g., CuCl, CuBr, $CuBr_2$, or $[ICuPBu_3]_4$, failed or led to low yields. Generally, THF and DME were satisfactory solvents whereas Et_2O, benzene, DMSO and HMPA gave poor results. Cyclopentenone **6** likewise smoothly accepted **3** furnishing **7**. Substituted enone **8** inserted **3** exclusively from the less hindered α-face giving rise to **9** in fair yield. In contrast, (S)-carvone (**23**) was recovered unchanged from the identical reaction conditions. Couplings with acyclic ketone **10** and aldehyde **12** were uneventful and afforded adducts **11** and **13**, respectively. Notably, the best yield of **11** (75%) was obtained in THF/acetone; in acetone or THF alone, this dropped to 66% and 57%, respectively.

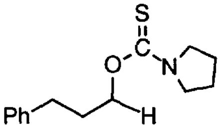
Table 1. Conjugate Addition Using Catalytic CuCN

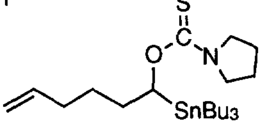
Stannane	Acceptor	Solvent	Time (h) / Temp (°C)	Adduct	Yield^a (%)
 **3**	 **4**	DME	8/45	 **5**	78
3	 **6**	THF	6/50	 **7**	67
3	 **8**	THF	9/45	 **9**	50
3	 **10**	THF/acetone (10:1)	3.5/50	 **11**	75
3	 **12**	THF	9/50	 **13**	54
 **14**	**4**	THF	8/45	 **15**	86
 **16**	**4**	THF/acetone (5:1)	0.7/23	 **17**	43
16	**10**	THF/acetone (5:1)	0.7/23	 **18**	41
 **19**	**4**	THF	2/23	 **20**	65
3	 **21**	THF	6/45	 **22**	30

^{a}Isolated as an ca. 1:1.2-2.4 mixture of diastereomers as determined by NMR analysis after hydrolytic work-up to remove any silyl ethers.

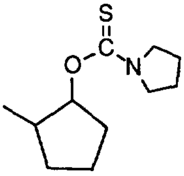
In all of the above examples, destannylation of **3** to thiocarbamate **24** accounted for virtually all of this precursor's remaining material balance. Dimers[9] and/or β-hydride elimination products were not observed. To gain a better insight into the destannylation process, **3** was added to either perdeuterated **4** in THF or to **4** in THF-d_8. Only the latter showed in any significant deuterium incorporation (28%) into **24**. This is consistent with a radical intermediate, most likely from homolytic cleavage of the carbon-tin bond in **3** or derived cuprate, that abstracts a hydrogen atom from solvent to form **24**. Partial validation of this hypothesis was found in the CuCN mediated addition of **25** to **4** (THF,45°C, 8h) which afforded a mixture of 1,4-adduct (51%), destannylated thiocarbamate (20%), and intramolecular cyclization[10] product **26** (12%). Not unexpectedly, the level of substitution at the stannyl carbon[11] also had an influence on the competition between conjugate addition and destannylation. Addition of primary (unsubstituted) stannane **14** to **4** afforded **15** in good yield and was accompanied by ≤ 5% of the destannylation by-product.


23


24



25


26

Following the usual order of reactivity,[2] coupling of benzyl stannane **16** was the most facile and transfer of the benzylic moiety to **4** or **10** could be done at room temperature. Unfortunately, destannylation proved competitve resulting in modest yields of **17** and **18**, respectively. Allylic stannane **19** displayed intermediate reactivity, but still gave a synthetically useful yield of **20**.

General Procedure: A solution of freshly purified chlorotrimethylsilane (2 mmol) and Michael acceptor (0.8 mmol) in the solvent (1.5 mL) specified in Table 1 was added to a suspension of thiocarbamoyl stannane (0.8 mmol) and CuCN (8 mole %) in the same solvent (8 mL) at room temperature under an argon atmosphere. The reaction mixture was maintained at the temperature and for the time indicated in Table 1, then diluted with Et_2O (60 mL), washed with 1 N HCl (25 mL), H_2O (75 mL), and dried over Na_2SO_4. Concentration *in vacuo* and chromatographic purification of the residue over SiO_2 afforded the conjugate.

The above methodology offers several distinct advantages, *viz.*, (a) operational simplicity, (b) use of catalytic amounts of copper, (c) transfer of a stereogenic center, and (d) complete utilization of the organic ligand versus homocuprates in which only one-half of the organic ligands is usually transferred. Initial results, e.g., conversion of **21** to **22**, suggest extensions of the procedure may be applicable to other classes of Michael acceptor.[12] Progress toward this objective as well as intramolecular versions will be reported elsewhere.

Acknowledgment: Supported financially by the Robert A. Welch Foundation (I-782) and NIH (GM31278).

References and Notes

1. Review: Lipshutz, B.H.; Sengupta, S. *Org. Reactions* **1992**, *41*, 135-631.
2. Falck, J.R.; Bhatt, R.K.; Ye, J. *J. Am. Chem. Soc.* **1995**, *117*, 5973-5982. Also see, Ye, J.; Bhatt, R.K.; Falck, J. *J. Am. Chem. Soc.* **1994**, *116*, 1-5.
3. Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L.S. *J. Org. Chem.* **1994**, *59*, 5905-5911 and cited references.
4. For an example of transmetalation between vinylstannanes and higher order cyanocuprates see, Behling, J.R.; Babiak, K.A.; Ng, J.S.; Campbell, A.L.; Moretti, R.; Koerner, M.; Lipshutz, B.H. *J. Am. Chem. Soc.* **1988**, *110*, 2641-2643.
5. The CuCl-mediated conjugate addition of vinyltrimethylstannanes to α,β-unsaturated carbonyls has been reported: Piers, E.; McEachern, E.J.; Burns, P.A. *J. Org. Chem.* **1995**, *60*, 2322-2323. Tanaka, H.; Kameyama, J.; Sumida, S.-i.; Torii, S. *Tetrahedron Lett*, **1992**, *33*, 7029-7030.
6. α-Alkoxyorganocuprates generated by conventional methodology undergo conjugate additions: Linderman, R.J.; Godfrey, A. *Tetrahedron Lett.* **1986**, *27*, 4553-4556. Linderman, R.J.; Godfrey, A.; Horne, K. *ibid.* **1987**, *28*, 3911-3914. Hutchinson, D.K.; Fuchs, P.L. *J. Am. Chem. Soc.* **1987**, *109*, 4930-4939. Linderman, R.J.; Godfrey, A. *ibid.* **1988**, *110*, 6249-6251. Linderman, R.J.; Godfrey, A.; Horne, K. *Tetrahedron* **1989**, *45*, 495-506. Knochel, P.; Chou, H.G.C.; Yeh, M.C.P.; Rozema, M.J. *J. Org. Chem.* **1989**, *54*, 5202-5204. Knochel, P.; Chou, T.-S. *J. Org. Chem.* **1990**, *55*, 4791. Linderman, R.J.; Griedel, B.D. *ibid.* **1990**, *55*, 5428-5432. Linderman, R.J.; Griedel, B.D. *ibid.* **1991**, *56*, 5491-5493.
7. Satisfactory spectral data ($^1H/^{13}C$, MS) were obtained for all new compounds.
8. Other trapping agents, e.g., N-phenyltrifluoromethane sulfonimide, TMS-triflate, TMS-CN, $^tBuMe_2SiCl$, and AcCl, gave little or no adduct.
9. Piers, E.; McEachern, E.J.; Romero, M.A. *Tetrahedron Lett.* **1996**, *37*, 1173-1176.
10. Clive, D.L.J.; Cheshire, D.R.; Set, L. *J. Chem. Soc., Chem. Comm.* **1987**, 353-355.
11. While quaternary α-hydroxystannanes are readily available from addition of lithium stannyl anions to ketones, the adducts can not be converted to α-thionocarbamoyl stannanes in preparative useful yields.
12. Conjugate addition to allylic epoxides by organocopper reagents is well known: Anderson, R.J. *J. Am. Chem. Soc.* **1970**, *92*, 4978-4979.

(*Received in USA* 4 *March* 1996; *accepted* 8 *April* 1996)