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β-TRIBUTYLSTANNYLACRYLATES. STEREOSPECIFIC SYNTHESIS <u>VIA</u> CONJUGATE ADDITON OF TRIBUTYLSTANNYLCOPPER

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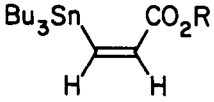
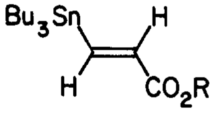
Abstract. The synthesis of cis- and trans-β-tributylstannylacrylates from conjugate addition of tributylstannylcopper to various β-substituted acrylates is shown to be a highly stereospecific reaction. Of four tributylstannylmetal reagents examined for this conversion, optimum results were obtained with tributylstannylcopper.

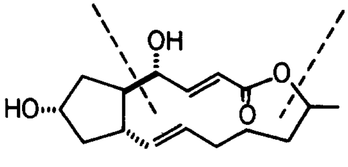
The ability of tin, suitably positioned in an organic molecule, to undergo a variety of useful transformations (e.g. electrophilic destannylation,[1] transmetalation,[2] oxidative destannylation[3]) has occasioned considerable interest in the development of highly stereo- and regiospecific methods for assembling functionalized organostannanes. For example, investigations in this laboratory on an electrophile-induced demetalation approach to the synthesis of the γ-oxygenated α,β-unsaturated lactone moiety common to a number of biologically active macrocyclic structures, such as brefeldin-A,[4] require cis- and trans-β-tributylstannylacrylates (**1** a,b) as intermediates.



1a



1b



brefeldin-A

Although hydrostannation of alkyne derivatives is often a convenient method for securing vinylstannanes,[5] preparation of **1** via additon of trialkyltin hydrides to esters of propiolic acid yields a mixture of compounds whose resolution is attended with difficulty.[6] Trialkylstannylmetal reagents undergo smooth Michael-type addition to a variety of α,β-unsaturated ketones, esters and nitriles to provide the corresponding saturated organostannanes, however, relatively few examples of this technique are recorded for the preparation of unsaturated organostannanes. Piers has described the syntheses of cyclic β-trimethylstannyl enones and (E)- and (Z)-β-trimethylstannyl α,β unsaturated esters from reaction of the corresponding β-iodo enones and acetylenic esters respectively with phenylthio(trimethylstannyl)cuprate.[7,8]

We report that the desired *cis*- and *trans*-β-tributylstannylacrylates are available by the highly stereospecific addition of tributylstannyllithium (**2**)[9] to a variety of β-substituted acrylates in the presence of one equivalent of copper(I) iodide (Table). Of the four tributylstannylmetal reagents examined for this conversion, tributylstannyllithium (**2**), lithium di(tributylstannyl)-cuprate (**3**), lithium tributylstannyl(phenylthio)cuprate (**4**) and tributylstannylcopper (**5**),[10] optimum conditions were obtained with the latter. The cuprate

Bu_3SnLi	$(Bu_3Sn)_2CuLi$	$Bu_3Sn(PhS)CuLi$	Bu_3SnCu
2	**3**	**4**	**5**

reagents **3** and **4** afforded diminished yields of product relative to **5** while the lithium reagent **2** appeared to give a saturated 2·1 adduct, methyl 3,3-bis(tributylstannyl)propanoate, a result similar to that noted earlier by Piers.[7] At -78°C, the reaction of the haloacrylates proceeded with complete stereospecificity. The tosyloxy and phenylthio derivatives, however, were unreactive under these conditions and required a more elevated temperature. The isomerization observed for the *trans*-phenylthioacrylate apparently is a result of competing equilibration of the copper intermediate in the absence of a suitable proton donor as suggested by Piers.[8]

The application of these β-tributylstannylacrylates to carbon-carbon bond formation and synthesis *via* electrophilic destannylation is currently under investigation.[11]

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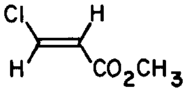
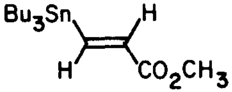
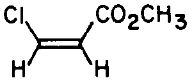
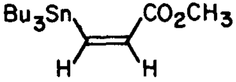
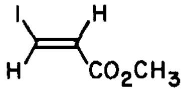
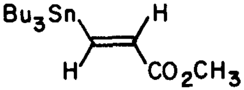
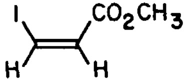
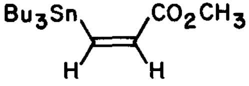
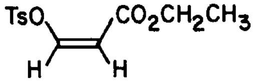
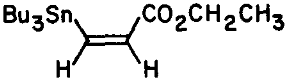
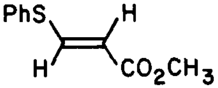
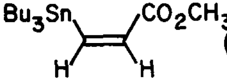
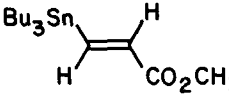
TABLE

Substrate[a]	Equivalents Bu_3SnCu (*5*)	Temp (°C)/Time	Product[a]	Yield[b] (%)
	2.0	−78°/40 min		58
	1.3	−78°/2.5 hr		62
	2.0	−78°/40 min		62
	1.5	−78°/3 hr		47
	1.5	−78°/1 hr, 0°/4 hr, 25°/1 hr		59
	1.9	−78°/1 hr, 0°/4 hr, 25°/1 hr	 (*4*)[c] +  (*1*)[c]	50

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a. all compounds exhibited spectral data in full accord with assigned structures and gave satisfactory combustion analyses.

b. all yields refer to isolated purified products.

c. product ratio was determined from NMR spectrum.

References and Notes

1. For a review, see: M. Pereyre and J.-C. Pommier, J. Organomet. Chem. Libr., 1, 161 (1976). For recent examples, see: D.E. Seitz, G.L. Tonnesen, S. Hellman, R.N. Hanson and S.J. Adelstein, J. Organomet. Chem., 186, C33 (1980); D.E. Seitz, R.A. Milius and H. El-Wakil, Synthetic Commun., 11, 281 (1981); G.L. Tonnesen, R.N. Hanson and D.E. Seitz, Int. J. Appl. Radiat. Isotopes, 32, 171 (1981).

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3. W.C. Still, J. Am. Chem. Soc., 99, 4836 (1977).

4. For examples, see: K.C. Nicolaou, Tetrahedron, 33, 683 (1977); T.G. Back, Tetrahedron, 33, 3041 (1977).

5 For reviews, see: W.P. Neumann, "The Organic Chemistry of Tin," John Wiley and Sons, New York, 1970, pp. 96-99; E-i. Negishi, "Organometallics in Organic Synthesis," John Wiley and Sons, New York, 1980, pp. 410-412.

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7. E. Piers and H.E. Morton, J. Chem. Soc., Chem. Commun., 1033 (1978).

8. E. Piers and H.E. Morton, J. Org. Chem., 45, 4263 (1980).

9. W.C. Still, J. Am. Chem Soc., 100, 1481 (1978).

10. The cuprate (or copper) reagents were prepared by adding a tetrahydrofuran solution of tributylstannyllithium, prepared from reaction of tributyltin hydride and lithium diisopropylamide,[9] to the required amount of cuprous iodide or phenylthiocopper at -78°C and stirring for ten minutes. The coupling constants observed for the vinyl protons in the *cis*- and *trans*-β-tributylstannylacrylates, 13.0 and 19.5 Hz, agree with those reported earlier for a series of related compounds (ref. 6b). The haloacrylates employed in this study were synthesized according to J. Biougne and F. Théron, C.R. Acad. Sci., 272, 858 (1971). Spectral data were in full agreement with those reported. The phenylthioacrylate was secured from reaction of the *trans*-iodoacrylate with thiophenoxide at -78°C and exhibited a vinyl proton coupling constant of 15.2 Hz. The preparation of the tosyloxyacrylate was modeled after S. Danishefsky, T. Harayama and R.K. Singh, J. Am Chem. Soc., 101, 7008 (1979). This derivative exhibited a vinyl proton coupling constant of 7.0 Hz. The geometrical purity of starting materials and products was deduced from analysis of the 60 MHz proton NMR spectra.

11. For a detailed discussion of the addition of various trimethylstannylmetal reagents to alkynoates, see: E. Piers, J.M. Chong and H.E. Morton, accompanying communication.

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