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REGIO- AND STEREO-CHEMICAL FEATURES OF THE STANNYLCOPPER(I)-INDUCED SUBSTITUTION IN PROPARGYLIC SUBSTRATES

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Summary

Stannylcopper(I) species, R_3SnCu and $[R_3Sn]_2CuLi$, preferentially convert propargylic substrates, $R^1C{\equiv}CCR^2R^3X$ (X = Br, $MeCO_2$, MeS(O)O or $MeSO_3$) into allenes $R_3Sn(R^1)C{=}C{=}CR^2R^3$. Only when the group R^1 causes much greater steric hindrance than with R^2 and R^3 is the acetylenic product $R^1C{\equiv}CCR^2R^3SnR_3$ formed. The stereochemical course of the allene formation has been studied in both the steroid and non-steroid series, and found to be mainly or exclusively *anti*.

Introduction

Stannylcopper(I) species may be used to convert acetylenes into β-stannylvinylcopper(I) compounds [1,2]. This synthetically useful reaction has recently been used to prepare the *cis*-isomer of the presumed sex pheromone of the male dried bean beetle [2]. In another study it was shown that stannylcopper(I) compounds are also capable of inducing substitutions in alkyl halides [3]. Nothing is known, however, about the behaviour of stannylcopper(I) reagents towards propargylic substrates. In principle stannylcopper(I) compounds could induce a S_N2'-like reaction with formation of allenyltin compounds. The latter compounds are useful precursors of, for instance, various allenes and acetylenes [4]. It is rather remarkable that only a few methods are available for preparing tin substituted allenes. One involves the reaction of (triphenylstannyl)lithium with propargylic bromides, which gives allenes in low yields (ca. 30% [5]). Another method involves the reaction of allenylmagnesium halides with organotin halides, but the allenyltin compounds obtained in this way are generally contaminated with substantial amounts of acetylenic products [5]. A third method involves the reaction of allenylsilver(I) compounds with organotin halides, which gives pure allenyltin compounds in high yield [6]. This method does not seem to be appropriate, however, for the preparation of optically active allenyltin compounds. In this paper a new method is described which gives allenyltin

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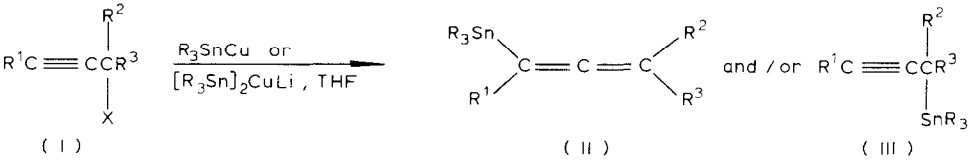
compounds in excellent yields, and which can also be used to prepare optically active allenyltin compounds.

Results and discussion

Conversion of optically inactive propargylic substrates

For our study a number of propargylic substrates, $R^1C{\equiv}CCR^2R^3X$ (I; X = Br, $MeCO_2$, MeS(O)O or $MeSO_3$), were prepared and subjected to reaction with R_3SnCu or $[R_3Sn]_2CuLi$ using tetrahydrofuran (THF) as solvent. The results are listed in Table 1. Table 1 shows that in most cases the reaction proceeds regiospecifically with formation of the allenes $R_3Sn(R^1)C{=}C{=}CR^2R^3$ (II; entries 1–12 in Table 1). The acetylenic product, $R^1C{\equiv}CCR^2R^3SnR_3$ (III), may arise, however, when the group R^1 is not hydrogen. For instance, when R^1 is methyl, R^2 is hydrogen and R^3 is propyl (entry 13), the acetylene formation competes effectively with the allene formation. In entry 14 (R^1 = Me, $R^2 = R^3$ = H) the acetylenic compound is actually exclusively formed. On the other hand, when R^1 is methyl and R^2 and R^3 both are alkyl (entry 12), the S_N2' reaction is again the favoured process. These results indicate that by appropriate choice of the R^1, R^2 and R^3 groups a large number of allenyltin compounds II will be accessible. The total yield of II + III is good ($\geq$ 80%, see Table 1).

TABLE 1

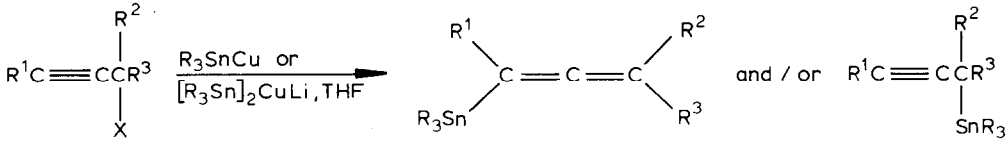


(I) (II) (III)

CONVERSION OF OPTICALLY INACTIVE PROPARGYLIC SUBSTRATES

Entry	Compound I				Copper reagent	Ratio II/III	Yield of II + III
	R^1	R^2	R^3	X			
1	H	H	H	Br	Ph_3SnCu	100/0	90
2	H	H	H	$MeSO_3$	Ph_3SnCu	100/0	90
3	H	H	Me	$MeCO_2$	$[Ph_3Sn]_2CuLi$	100/0	80
4	H	H	Me	$MeSO_3$	$[Ph_3Sn]_2CuLi$	100/0	80
5	H	H	Ph	$MeSO_3$ [a]	Ph_3SnCu	100/0 [b]	90
6	H	Me	Me	$MeSO_3$	Ph_3SnCu	100/0	95
7	H	H	Pr	$MeSO_3$	Me_3SnCu	100/0	90
8	H	$-(CH_2)_4-$		MeS(O)O	Ph_3SnCu	100/0	95
9	H	$-(CH_2)_5-$		$MeSO_3$	Me_3SnCu	100/0	95
10	H	$-(CH_2)_5-$		$MeSO_3$	Ph_3SnCu	100/0	90
11	H	H	t-Bu	$MeSO_3$	Ph_3SnCu	100/0	80
12	Me	Me	Me	$MeSO_3$	Ph_3SnCu	100/0	90
13	Me	H	Pr	$MeSO_3$	Ph_3SnCu	56/44	90
14	Me	H	H	$MeSO_3$	$[Ph_3Sn]_2CuLi$	0/100	90

[a] The optically active ester, viz. compound (*R*)-IV in the paper was also used. [b] The optically active allene, viz. compound (*R*)-(−)-VII in the paper, was also prepared.

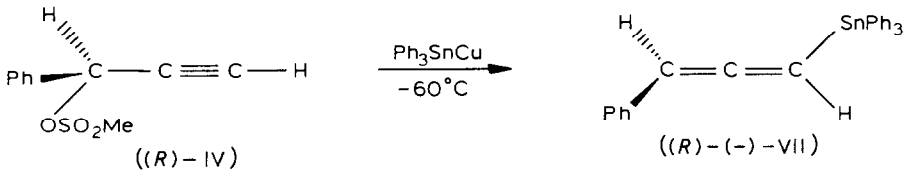


(I : X = Br, $MeCO_2$, MeS(O)O or $MeSO_3$) (II) (III)

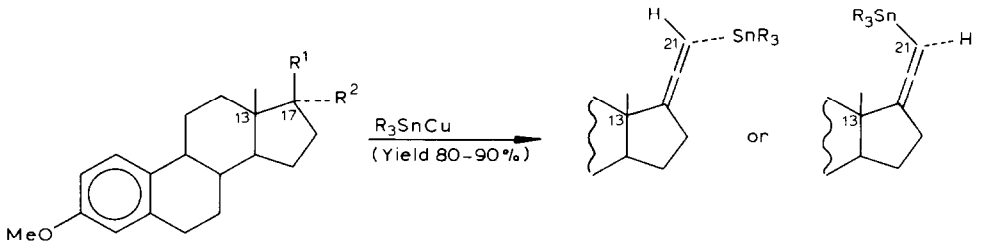
When homocuprates, $[R_3Sn]_2CuLi$, are used, it is possible to transfer both available R_3Sn groups, so that only 0.5 mol equivalent of the cuprate is required. The reactions are also reasonably fast. In the case of experiments 1, 2 and 4–11 the reactions smoothly proceed even at −60°C, while the less reactive acetate of entry 3 and the non-terminal acetylenic substrates of entries 12–14 readily undergo substitution at −30°C.

Stereochemistry

To investigate the stereochemical course of the allene formation we prepared, in situ, the three optically active methanesulfonates IV–VI (see below) by reaction of methanesulfonyl chloride with the lithium alcoholates of (*R*)-(−)-1-phenyl-2-propyn-1-ol, mestranol and epimestranol, respectively. Reaction of ester IV with Ph_3SnCu, at −60°C, during 3 min, gave the levorotatory allene VII ($[\alpha]_D^{20}$ −570°, in EtOH) *. The specific rotation of the optically pure allene is not known and so the optical purity of allene VII cannot yet be determined. Nevertheless, by application of the Lowe-Brewster rules [7] it can be deduced that the reaction mainly proceeds *anti*, since levorotatory 1,3-disubstituted allenes in which the two substituents are more polarisable than hydrogen possess the *R*-configuration.



((*R*)-IV) ((*R*)-(-)-VII)



(V : R^1 = $MeSO_3$, R^2 = HC≡C ; VI : R^1 = HC≡C, R^2 = $MeSO_3$) (VIII ; R = Me or Ph) (IX ; R = Me or Ph)

The steroidal esters V and VI also smoothly undergo the S_N2' reaction, to give the epimeric allenes, viz. VIII and IX. It is easy to distinguish VIII from IX by the positions of their 13-Me signals in the ^1H NMR spectra (see Experimental section).

* This $[\alpha]_D^{20}$ corresponds to reaction of optically pure (*R*)-(−)-1-phenyl-2-propyn-1-ol.

It appears that the substitutions in V and VI proceed with 100% inversion (V → VIII; VI → IX). *anti*-Stereospecificity has also been observed for the reaction of V and VI with methylcopper [8,9] * and other organocopper compounds [10].

Conclusion

Stannylcopper(I) species are synthetically useful reagents for conversion of propargylic substrates into allenyltin compounds. An important feature of the reaction is its high stereoselectivity or even stereospecificity. The method is therefore highly attractive for preparation of optically active allenyltin compounds.

Experimental

All operations with organometallic reagents were performed under dry nitrogen. The products were analysed by NMR (Varian EM-390 and CFT-20 spectrometers) and IR spectroscopy.

Ph_3SnLi and Me_3SnLi were prepared by known procedures [11]. The substrates I were prepared as described in [9]. Copper(I) bromide was prepared as described by Keller and Wycoff [12]. Epimestranol was prepared from mestranol as described in [13]. The methanesulfonate of mestranol was obtained as described in ref. [13]. (*R*)-(−)-1-Phenyl-2-propyn-1-ol was prepared by the procedure described in ref. [14].

1 General procedure for the preparation of R_3SnCu

To a stirred suspension of CuBr (0.010 mol) in THF (25 ml) is added a solution of lithium bromide (0.010 mol) in THF (5 ml). The homogeneous solution is cooled to −60°C and a solution of R_3SnLi (0.010 mol) in THF (10 ml) is added dropwise. The resulting mixture is stirred for 30 min at −60°C and then used directly.

2 General procedure for the preparation of $[R_3Sn]_2CuLi$

The stannylcuprates $[R_3Sn]_2CuLi$ (0.010 mol) are prepared from CuBr (0.010 mol), lithium bromide (0.010 mol) and R_3SnLi (0.020 mol) in THF (35 ml) by the procedure given under 1. The solutions of the cuprates are used directly.

3 In situ preparation of the methanesulfonates IV and VI

The methanesulfonate esters IV ** and VI are prepared by adding, at −60°C, n-butyllithium (0.010 mol, 1.4 *M* solution in n-hexane) to a stirred solution of the alcohol (0.010 mol) (and LiBr for VI (0.010 mol)) in THF (25 ml) followed, after 30 min by methanesulfonyl chloride (0.010 mol). The mixture is stirred during 3 min at −60°C (IV) or 30 min, at −60°C (VI). The methanesulfonate esters are used as such.

4 General procedure for the preparation of II, III, VIII and IX

To the stannylcopper(I) reagents R_3SnCu (0.010 mol) or $[R_3Sn]_2CuLi$ (0.010

* The configurational assignment is based upon a comparison of the sign of rotation observed for VIII and IX with those reported for the 21-Me isomers of VIII and IX (see refs. [8 and 9]; As shown in ref. [8], the wrong configuration was assigned to the steroid allene in ref. [9]). The Lowe-Brewster rules are not reliable for predicting absolute configurations in the steroid series (see ref. [8]).

** The optically inactive ester given in entry 5 of Table 1 was prepared by the same procedure and was used as the THF solution.

mol) is added at −60°C, compound I (see Table 1); 0.010 mol when R_3SnCu is used; 0.020 mol when $[R_3Sn]_2CuLi$ is used. In the case of the steroids R_3SnCu is used.

The resulting mixture is stirred for 1 h, at either −60°C (Table 1, entries 1, 2 and 4–11, V and VI) or −30°C (Table 1, entries 3, 12–14). (*R*)-IV is stirred during 3 min, at −60°C. The mixture is then poured into a saturated solution of ammonium chloride in water (200 ml) containing NaCN (1 g). The product is extracted with ether/pentane (v/v 50/50; 3 × 100 ml). The combined extracts are washed with water (3 × 150 ml) and dried with $MgSO_4$. The solvent is evaporated in vacuo and the residue purified by column chromatography (Al_2O_3-5% H_2O/n-hexane) or crystallized from methanol.

Physical constants and characteristic spectroscopic data for compounds II, III, VIII and IX are as follows:

(Triphenylstannyl)propadiene. M.p. 52–54°C. IR (NaCl): 1930 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 4.28 (d, 2 H, CH_2=), 5.31 (t, 1 H, =C*H*–Sn) ppm.^{13}C NMR ($CDCl_3$): δ 212.4 ppm (=C=). Mass spectrum, *m/z* 388 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-1,2-butadiene. M.p. 35–36°C. IR (NaCl): 1933 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 4.68 (dq, 1 H, MeC*H*=), 5.33 (dq, 1 H, =C*H*–Sn) ppm. ^{13}C NMR ($CDCl_3$): δ 211.6 ppm (=C=). Mass spectrum, *m/z* 402 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-3-phenyl-1,2-propadiene. n_D^{20} 1.6411. IR (NaCl): 1920 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 5.78 and 5.82 ppm (2 × d, 2 × 1 H, PhC*H*= and =C*H*–Sn). ^{13}C NMR ($CDCl_3$): δ 209.9 ppm (=C=). Mass spectrum, *m/z* 464 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-3-methyl-1,2-butadiene. M.p. 46–48°C. IR (NaCl) 1942 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 5.27 ppm (m, 1 H, =C*H*–Sn). ^{13}C NMR ($CDCl_3$): δ 210.5 ppm (=C=). Mass spectrum, *m/z* 416 (M^+ for ^{118}Sn).

1-(Trimethylstannyl)-1,2-hexadiene. n_D^{20} 1.5068. IR (NaCl): 1934 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 4.58 (dt, 1 H, =C*H*–C_3), 4.96 (dt, 1 H, =C*H*–Sn) ppm. ^{13}C NMR ($CDCl_3$) δ 208.0 ppm (=C=). Mass spectrum *m/z* 244 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-3,3-tetramethylenepropadiene. n_D^{20} 1.6045. IR (NaCl): 1937 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 5.35 ppm (tt, 1 H, =C*H*–Sn). ^{13}C NMR ($CDCl_3$): δ 206.0 ppm (=C=). Mass spectrum, *m/z* 456 (M^+ for ^{118}Sn).

1-(Trimethylstannyl-3,3-pentamethylenepropadiene. n_D^{20} 1.5351 IR (NaCl) 1941 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 4.90 ppm (tt, 1 H, =C*H*–Sn). ^{13}C NMR ($CDCl_3$): δ 204.2 ppm (=C=). Mass spectrum, *m/z* 270 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-3,3-pentamethylenepropadiene. n_D^{20} 1.6281. IR (NaCl): 1942 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 5.25 ppm (tt, 1 H, =C*H*–Sn). ^{13}C NMR ($CDCl_3$): δ 207.3 ppm (=C=). Mass spectrum, *m/z* 470 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-4,4-dimethyl-1,2-pentadiene. M.p. 92–93°C. IR (NaCl): 1930 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ 5.45 (d, 1 H, =C*H*–Sn), 4.73 (d, 1 H, =C*H*-t-Bu) ppm. ^{13}C NMR ($CDCl_3$): δ 208.5 (=C=) ppm. Mass spectrum *m/z* 349 (M^+ for 118 Sn).

2-(Triphenylstannyl)-4-methyl-2,3-pentadiene. M.p. 41–42°C. IR (NaCl): 1942 (C=C=C) cm^{-1}. ^1H NMR (CCl_4, TMS): δ1.92 (s, 3 H, CH_3C(Sn)=), 1.53 (s, 6 H, =C(CH_3)$_2$) ppm. ^{13}C NMR ($CDCl_3$): δ 204.8 (=C=) ppm. Mass spectrum, *m/z* 430 (M^+ for ^{118}Sn).

1-(Triphenylstannyl)-2-butyne. M.p. 73–74°C. IR (NaCl): 2208 (C≡C) cm^{-1}. ^1H

NMR (CCl_4, TMS): δ 2.00 (s, 3 H, CH_3–C≡C), 1.66 (s, 2 H, ≡C–CH_2–Sn) ppm. Mass spectrum, m/z 402 (M^+ for ^{118}Sn).

3-Methoxy-21-α-(trimethylstannyl)-19-nor-1,3,5,(10), 17(20), 20-pregnapentaene (Yield: 90%). M.p. 78–79°C. ^{1}H NMR (CCl_4, TMS): δ 5.11 (t, 1 H, =C*H*–Sn), 0.91 (s, 3 H, 13-CH_3), 0.15 (s, 9 H), Sn–CH_3) ppm. $[\alpha]_D^{20}$ −133.9° (CH_2Cl_2).

3-Methoxy-21-β-(trimethylstannyl)-19-nor-1,3,5(10), 17(20), 20-pregnapentaene. (Yield: 80%) M.p. 88–89°C. ^{1}H NMR (CCl_4, TMS): δ 5.13 (t, 1 H =C*H*–Sn), 0.87 (s, 3 H, 13-CH_3), 0.15 (s, 9 H, Sn–CH_3) ppm. $[\alpha]_D^{20}$ +147.1° (CH_2Cl_2).

3-Methoxy-21-α-(triphenylstannyl)-19-nor-1,3,5(10), 17(20), 20-pregnapentaene. (Yield: 90%). M.p. 65–66°C. ^{1}H NMR (CCl_4, TMS): δ 5.42 (t, 1 H, =C*H*–Sn), 0.84 (s, 3 H, 13-CH_3) ppm. $[\alpha]_D^{20}$ −127.9° (CH_2Cl_2).

3-Methoxy-21-β-(triphenylstannyl)-19-nor-1,3,5(10), 17(20), 20-pregnapentaene. (Yield: 80%). M.p. 85–86°C. ^{1}H NMR (CCl_4, TMS): δ 5.47 (t, 1 H, =C*H*–Sn), 0.46 (s, 3 H, 13-CH_3) ppm. $[\alpha]_D^{20}$ +121.3 (CH_2Cl_2).

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