*Journal of Organometallic Chemistry*, 366 (1989) 87–93
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands
JOM 09595

# Studies of the use of elemento-organic compounds of the fifteenth and sixteenth groups in organic synthesis

# LXXI *. Reaction of $\alpha$-halogeno carboxylic derivatives with carbonyl compounds promoted by tributylstibine

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(Received February 13th, 1988; in revised form November 4th, 1988)

## Abstract

$\alpha,\beta$-Unsaturated esters and amides were conveniently obtained from the trialkylstibine-promoted reaction of $\alpha$-halogenocarboxylic derivatives with carbonyl compounds. In this reaction, a quaternary stibonium salt is an active intermediate that can be trapped and can undergo further reaction with the substrate.

## Introduction

The use of elemento-organic compounds of Group 15 elements for carbon–carbon bond formation in organic synthesis is of great interest. Compounds such as phosphoranes have long been recognized as effective reagents for the carbon–carbon double bond formation and are known as Wittig reagents [1]. We have found that arsonium ylides bearing an electron-withdrawing substituent in the alkylidene moiety are more reactive than the corresponding phosphonium ylides [2–5]. Some attempts have been made to obtain stibonium ylides and to make them undergo Wittig-like reactions [6], but only triphenylstibonium tetraphenylcyclopentadienylide was found to be successful [7].

In a preliminary communication [8], we reported that tributylstibine can mediate in the olefination of carbonyl compounds with bromoacetic esters. On continuing the study of the organoantimony compounds in organic synthesis [9,10], we have found that trialkylstibines are effective reagents for the formation of a carbon–carbon double bond between $\alpha$-halogenocarboxylic derivatives, including esters and amides, and carbonyl compounds. $\alpha,\beta$-Unsaturated esters and amides

* For paper LXX see ref. 18.

0022-328X/89/$03.50 

were obtained. In the reaction, a quaternary stibonium salt was found to be an active intermediate. This is of interest, because the reaction proceeded by the nucleophilic attack involving the single antimony–carbon bond in the stibonium salt. No similar example has been found in the literature.

## Results and discussion

Treatment of an equimolar mixture of ethyl bromoacetate (**2a**) and benzaldehyde with tri-n-butylstibine (1 equiv.) at 80 °C for 3 h quantitatively gave ethyl cinnamate [8]. Similar treatment of $\alpha$-halogenocarboxylic esters (**2–4**) or amide (**5**) and carbonyl compounds afforded the corresponding $\alpha,\beta$-unsaturated esters (**7–9**) or amide (**10**) in good to excellent yields. The results are summarized in Table 1.

$$\underset{(\mathbf{1})}{R^1R^2C{=}O} + \underset{(\mathbf{2\text{–}5})}{RCH(X)COY} + \underset{(\mathbf{6})}{n\text{-}Bu_3Sb}$$

$$\rightarrow \underset{(\mathbf{7\text{–}10})}{R^1R^2C{=}C(R)COY} + \tfrac{1}{2}\underset{(\mathbf{11})}{n\text{-}Bu_3SbX_2} + \tfrac{1}{2}\underset{(\mathbf{12})}{n\text{-}Bu_3Sb(OH)_2}$$

(**2**,**7**: R = H, Y = OEt; **3**,**8**: R = Me, Y = OEt; **4**,**9**: R = Et, Y = OEt;
**5**,**10**: R = H, Y = $NEt_2$)

In addition to the unsaturated products, dihalogenotri-n-butylstiborane (**11**) and dihydroxytri-n-butylstiborane (**12**) were also produced, as revealed by flash column chromatography.

In the reaction of the ethyl bromoacetate (**2a**) or *N*,*N*-diethyl acetamide (**5**) with aldehydes, the double bonds of all the products formed are *trans*, whereas for **3** and **4**, *E* and *Z* isomers are obtained as shown by $^1$H NMR data [11]. The yields are lower with ketones.

Although ethyl chloroacetate (**2b**) reacts with benzaldehyde under mediation by tributylstibine just as well as the bromo-component, ethyl 2-chloropropionate (**3b**) does not react with tributylstibine at 150 °C. Triethylstibine has the same reactivity as n-$Bu_3$Sb. Triphenylstibine, antimony trichloride and tributylphosphine do not promote the reaction under the similar conditions. The $Bu_3$Sb-mediated reaction also proceeds in aprotic solvents such as tetrahydrofuran, acetonitrile, hexane, and benzene, with insignificant solvent effects.

Benzaldehyde does not react with a trialkylstibine at room temperature, but ethyl bromoacetate does react, to afford an oily product, which was identified as a carboethoxymethyl trialkylstibonium bromide (**13**) from its $^1$H NMR, IR and MS data. Anion exchange leads to a corresponding crystalline stibonium tetraphenylborate (**14**), which was characterized by microanalysis. A similar result was obtained with *N*,*N*-diethyl bromoacetamide.

$$\underset{(\mathbf{6})}{R'_3Sb} + \underset{(\mathbf{2,5})}{BrCH_2COY} \xrightarrow{\text{r.t.}} \underset{(\mathbf{13a\text{–}13c})}{\left[R'_3\overset{+}{Sb}CH_2COY\ Br^-\right]} \xrightarrow[\text{EtOH}]{\text{NaBPh}_4} \underset{(\mathbf{14a\text{–}14c})}{R'_3\overset{+}{Sb}CH_2COY\ {}^-BPh_4}$$

(**13**,**14**: **a**, R′ = Et; Y, OEt; **b**, R′ = n-Bu; Y = OEt; **c**, R′ = n-Bu; Y = $NEt_2$)

Heating the stibonium bromide (**13b**) or borate (**14b**) with benzaldehyde gave ethyl cinnamate. The anion did not significantly affect the reactivity.

$$PhCH{=}O + n\text{-}Bu_3\overset{+}{Sb}CH_2CO_2Et\ X^- \longrightarrow PhCH{=}CHCO_2Et$$
$$\begin{array}{l}(\mathbf{13b}\text{: } X = Br,\ 80\,^\circ C/3\ h,\ 100\%)\\(\mathbf{14b}\text{: } X = Ph_4B,\ 90\,^\circ C/3\ h,\ 80\%)\end{array}$$

Thus, the quaternary stibonium bromide is most likely to be an active intermediate in this reaction. In this regard we propose the reaction mechanism as depicted in Scheme 1.

Although tributylstibonium benzoylmethyleneylide is thought to be the intermediate of the reaction of tributylstibine with $\omega$-bromoacetophenone [12], tri-n-butylstibine reacts with an $\alpha$-halogenocarboxylic derivative to afford the corresponding quaternary stibonium bromide (**13**). Pentacovalent stiborane (**15**) can be formed by the coupling of bromide with the antimony cation center of **13** which then dissociates to give zwitterion **16**. The zwitterion **16** adds nucleophilically to a carbonyl substrate. The addition intermediate (**17**) that results fragments on heating. One mode of fragmentation produces hydroxybromotributylstiborane (**18**), which disproportionates to give dibromotributylstiborane (**11**) and dihydroxytributylstiborane (**12**) [13]. The other mode of fragmentation leads to tributylstibine oxide (**19**) and hydrogen bromide, and eventually to **11** and **12** [14].

Scheme 1

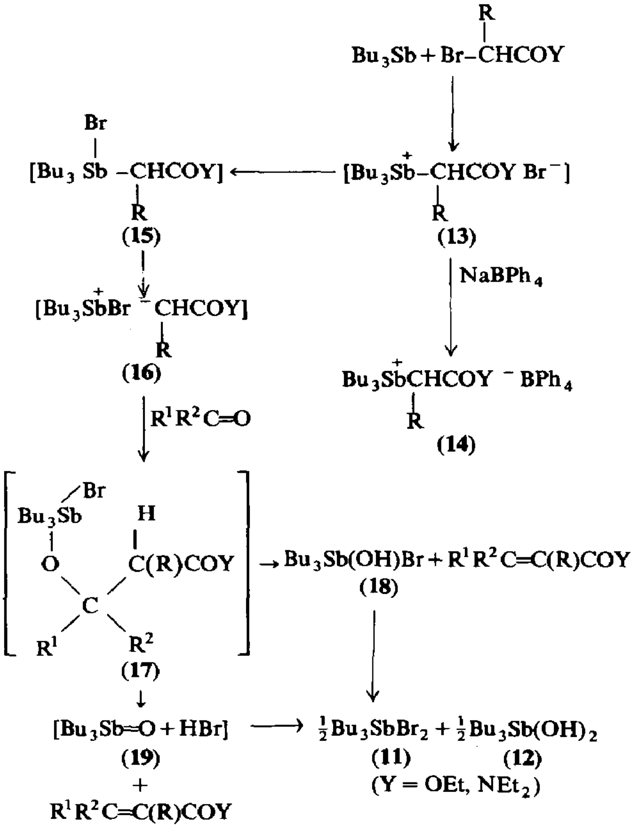

Table 1

$\alpha,\beta$-Unsaturated esters and amides from the n-$Bu_3Sb$-mediated reaction

| | $R^1R^2C{=}O$ (1) | RCH(X)COY | Conditions (°C/h) | Product [a] | Yield [b] (%) | Ratio [c] (E/Z) |
|---|---|---|---|---|---|---|
| **1a** | n-PrCH=O | $BrCH_2CO_2Et$ (**2a**) | 100/3.5 | n-PrCH=$CHCO_2Et$ (**7a**) | 92 | – |
| **1b** | i-BuCH=O | $BrCH_2CONEt_2$ (**5**) | 80/8 | i-BuCH=$CHCONEt_2$ (**10b**) | 64 | – |
| **1c** | n-$C_8H_{17}$CH=O | MeCH(Br)$CO_2Et$ (**3a**) | 120/10 | n-$C_8H_{17}$CH=C(Me)$CO_2Et$ (**8c**) | 84 | 67/33 |
| **1d** | n-$C_{11}H_{23}$CH=O | **2a** | 100/2.5 | n-$C_{11}H_{23}$CH=$CHCO_2Et$ (**7d**) | 88 | – |
| **1e** | $CH_3$CH=CHCH=O | **2a** | 100/4 | $CH_3$CH=CHCH=$CHCO_2Et$ (**7e**) | 84 | – |
| **1f** | n-$C_3H_7$CH=CHCH=O | **3a** | 120/8 | n-$C_3H_7$CH=CHCH=C(Me)$CO_2Et$ (**8f**) | 75 | [d] |
| **1g** | Citral | **2a** | 100/10 | Citryl-CH=$CHCO_2Et$ (**7g**) | 82 [e] | – |
| **1h** | OCH=CHCH=CCH=O | **2a** | 100/2.5 | OCH=CHCH=CCH=$CHCO_2Et$ (**7h**) | 64 | – |
| | | **5** | 90/11 | OCH=CHCH=CCH=$CHCONEt_2$ (**10h**) | 88 | – |
| | | **3a** | 120/7 | OCH=CHCH=CCH=C(Me)$CO_2Et$ (**8h**) | 92 | 60/40 |
| **1i** | SCH=CHCH=CCH=O | **3a** | 120/12 | SCH=CHCH=CCH=C(Me)$CO_2Et$ (**8i**) | 82 | 60/40 |
| **1j** | PhCH=O | **2a** | 80/3 | PhCH=$CHCO_2Et$ (**7j**) | 96 | – |
| | | $ClCH_2CO_2Et$ (**2b**) | 110/6 | **7j** | 71 | – |
| | | $BrCH_2CO_2Me$ (**2c**) | 110/6 | PhCH=$CHCO_2Me$ (**7′j**) | 88 | – |
| | | **3a** | 100/12 | PhCH=C(Me)$CO_2Et$ (**8j**) | 84 | 60/40 |
| | | MeCH(Cl)$CO_2Et$ (**3b**) | 150/6 | **8j** | 0 | |
| | | EtCH(Br)$CO_2Et$ (**4**) | 130/9 | PhCH=C(Et)$CO_2Et$ (**9j**) | 90 | [d] |
| **1k** | p-$ClC_6H_4$CH=O | **5** | 85/20 | p-$ClC_6H_4$CH=$CHCONEt_2$ (**10k**) | 94 | – |
| **1l** | PhCH=CHCH=O | **2a** | 110/3.5 | PhCH=CHCH=$CHCO_2Et$ (**7l**) | 86 | – |
| **1m** | $Me_2C{=}O$ | **2a** | 130/6 | $Me_2C$=$CHCO_2Et$ (**7m**) | 10 [f] | – |
| **1n** | $(CH_2)_4C{=}O$ | **2a** | 120/10 | $(CH_2)_4C$=$CHCO_2Et$ (**7n**) | 40 | – |
| **1o** | $(CH_2)_5C{=}O$ | **2a** | 130/6 | $(CH_2)_5C$=$CHCO_2Et$ (**7o**) | 45 | – |

[a] All the products gave satisfactory $^1H$ NMR, IR, MS spectra or microanalysis. [b] Isolated yield. [c] Determined by $^1H$ NMR analysis (ref. 11). [d] Not distinguishable by $^1H$ NMR. [e] The E/Z ratio of the starting material was 3/2. [f] Estimated by $^1H$ NMR analysis.

## Summary

In conclusion, the olefination of carbonyl compounds by α-halogenocarboxylic derivatives can be achieved conveniently under the action of a trialkylstibine in good to excellent yields. The reaction is unusual in that it takes place in absence of base. The reaction mechanism is described.


## Experimental

$^1$H NMR spectra were recorded on Varian-360L instrument in $CCl_4$ solution with $Me_4Si$ as an internal standard and are in δ (ppm). IR spectra were recorded with an Shimadzu IR-440 infrared spectrophotometer and are in $cm^{-1}$ units (neat, unless otherwise stated). Mass spectra were recorded on Finnigan GC-MC 4021 spectrometer. Triethylstibine [15] and tri-n-butylstibine [16] were prepared by published procedures.

*$Bu_3Sb$-mediated reaction of carbonyl compounds with α-halogenocarboxylic derivatives, typical procedure.* To a mixture of ethyl 2-bromopropionate (200 mg, 1.1 mmol) and benzaldehyde (100 mg, 0.94 mmol) in a capped vessel under nitrogen was injected tributylstibine (340 mg, 1.16 mmol). After having been stirred at 100 °C for 12 h, the mixture was chromatographed on an alumina-silica gel (1/1) column, and eluted with ethyl acetate. Redistillation of the crude product gave 150 mg (84%) of ethyl 2-methylcinnamate. The work-up was carried out as follows: the reaction mixture was treated with 2% aqueous sodium hydroxide solution and extracted with ether or benzene. The organic layar separated was washed with water, dried and evaporated to remove the solvent. The residue was chromatographed on silica gel, and eluted with 85/15 petroleum ether/ethyl acetate to give the product.

*Ethyl 2-methylundec-2-enate (**8c**).* B.p. 142 °C/15 Torr; $^1$H NMR: 0.87 (3H,t, *J* 6 Hz, $CH_3$), 1.30 (15H, m, $(CH_2)_6$, $CH_3$), 1.75 (0.9H, s, *Z*-form $CH_3$), 1.76 (2.1H, s, *E*-form $CH_3$), 1.90–2.44 (2H, m, $CH_2$), 4.08 (2H, q, *J* 7 Hz, $OCH_2$), 6.36 (0.3H, t, *J* 7 Hz, *Z*-form, =CH), 6.80 (0.7H, t, *J* 7 Hz, *E*-form $CH_3$); IR: 1718(s), 1658(w); *m/z*: 227 ($M^+ + 1$, 100%), 226($M^+$, 4%); Anal. Found: C, 74.03; H, 11.29. $C_{14}H_{26}O_2$ calcd.: C, 74.29; H, 11.58%.

*Ethyl 2-methylocta-2E,4(E,Z)-dienate (**8f**).* $^1$H NMR: 0.95(3H, t, *J* 6Hz, $CH_3$), 1.40(3H, t, *J* 6.5 Hz, $CH_3$), 1.40–1.69 (2H, m, $CH_2$), 1.90 (3H, s, $CH_3$), 2.15 (2H, dt, *J* 6, 6 Hz, $CH_2$), 4.10 (2H, q, *J* 6.5 Hz, $OCH_2$), 5.96–6.50(2H, m, =CHCH=), 7.01 (1H, dm, *J* 10 Hz, CH=); IR: 1702(s), 1640(m), 1608(m); *m/z*: 183 ($M^+ + 1$, 100%), 182 ($M^+$, 53%); Anal. Found: C, 72.65; H, 10.15. $C_{11}H_{18}O_2$ calcd.: C, 72.49; H, 9.95%.

*N,N-Diethyl-5-methylhex-2E-enamide (**10b**).* Colorless oil, b.p. 95 °C/15 Torr. $^1$H NMR: 0.94 (6H, d, *J* 7 Hz, $CH_3$), 1.15 (6H, t, *J* 6.5 Hz, $CH_3$), 1.35–1.88 (1H, m, CH), 2.05 (2H, dd, *J* 6, 6.5 Hz, $CH_2$), 3.31 (4H, q, *J* 6.5 Hz, $CH_2$), 5.98 (1H, d, *J* 15 Hz, =CH), 6.68 (1H, dt, *J* 15, 6.5 Hz, CH=); IR: 1660(s), 1618(s); *m/z*: 183 ($M^+$, 8%); Anal. Found: C, 72.34; H, 11.65; N, 7.53. $C_{11}H_{21}NO$ calcd.: C, 72.08; H, 11.55; N, 7.64%.

### *Isolation and determination of the antimony products*

Crotonaldehyde (350 mg, 5.0 mmol) was injected into a capped flask containing ethyl bromoacetate (835 mg, 5.0 mmol) and tributylstibine (1240 mg, 4.22 mmol) under nitrogen. The mixture was stirred at 100 °C for 3 h, then poured onto a silica gel column. Elution with 85/15 petroleum ether/ethyl acetate gave 1065 mg of oil, from which 950 mg (98%) of dibromotri-n-butylstiborane was obtained after rechromatography. The residue on silica gel was eluted with methanol and 440mg (61%) of dihydroxytri-n-butylstiborane was obtained by another chromatographic technique.

*Dibromo-tri-n-butylstiborane (11).* Colorless oil [17]; $^1H$ NMR: 0.90 (9H, t, $J$ 6.5 Hz, $CH_3$), 1.04–2.10 (12H, m, $CH_2CH_2$), 2.70 (6H, t, $J$ 6.5 Hz, $CH_2$); IR: 2900(s), 1240(s), 1140(s), 890(m), 720(m); $m/z$: 395 ($M^+$ − Bu, 3%), 373 ($M^+$ − Br, 82%).

*Dihydroxy-tri-n-butylstiborane (12).* Colorless oil; $^1H$ NMR: 0.90 (9H, t, $J$ 6.5 Hz, $CH_3$), 1.06–2.40 (20H, m, $(CH_2)_3$); IR: 3340(s), 2960(s), 1462(m), 680(s); $m/z$: 619($2M^+ - 2H_2O$, 16%), 327 ($M^+$, 3%), 309 ($M^+ - H_2O$, 12%); Anal. Found: C, 43.80; H, 8.80. $C_{12}H_{29}O_2Sb$ calcd.: C, 44.08; H, 8.94%.

*The stibonium salt from ethyl bromoacetate or N,N-diethyl bromoacetamide and trialkylstibine*

*Carbethoxymethyl triethylstibonium bromide (13a) and tetraphenylborate (14a):* Triethylstibine (460 mg, 2.2 mmol) and ethyl bromoacetate (380 mg, 2.27 mmol) were placed in a capped vessel, which was then flushed with nitrogen. The mixture was stirred with a magnetic stirrer bar at room temperature for 8 h. The resulting oil was identified as **13a**: $^1H$ NMR: 1.30 (t, $J$ 7 Hz, $CH_3$), 1.56 (t, $J$ 7 Hz, $CH_3$), 2.65 (q, $J$ 7 Hz, $CH_2$), 2.76 (s, $CH_2$), 4.09 (q, $J$ 7 Hz, $OCH_2$); IR: 1705(vs), 720(s); $m/z$: 374 ($M^+$, 5%), 345 ($M^+$ − Et, 12%), 329 ($M^+$ − EtO, 6%), 295 ($M^+$ − Br, 7%), 287 ($Et_3SbBr$, 23%), 208 ($Et_3Sb$, 88%), 151 (100%). To the resulting slurry was added 0.5 ml of ethanol with stirring at room temperature. After becoming homogeneous, the mixture was added dropwise to a solution of sodium tetraphenylborate (800 mg, 2.34 mmol) in ethanol (1.5 ml), and a white solid separated. Recrystallization of the solid from ethanol gave 960 mg (71%) of the desired product (**14a**): M.p. 108–111 °C; $^1H$ NMR ($CDCl_3$): 0.93 (9H, t, $J$ 8 Hz, $CH_3$), 1.30 (6H, q, $J$ 8 Hz, $CH_2$), 1.36 (3H, t, $J$ 7 Hz, $CH_3$), 1.96 (2H, s, $CH_2$), 4.06 (2H, q, $J$ 7 Hz, $OCH_2$), 6.95 (12H, m, Ph), 7.48 (8H, m, Ph); IR (KCl): 1705(s); Anal. Found: C, 66.58; H, 6.89. $C_{34}H_{42}BO_2Sb$ calcd.: C, 66.37; H, 6.88%.

*Carbethoxymethyltri-n-butylstibonium tetraphenylborate (14b).* Work-up as described above on the 1.0 mmol scale gave the product (47%). M.p. 144–146 °C; $^1H$ NMR ($CDCl_3$): 0.79 (9H, t, $J$ 5.5 Hz, $CH_3$), 1.04–1.87 (21H, m, $(CH_2)_2$, $CH_3$), 2.10 (2H, s, $CH_2$), 4.08 (2H, q, $J$ 7.5 Hz, $OCH_2$), 6.93 (12H, m, Ph), 7.44 (8H, m, Ph); IR (KCl); 1700(s); Anal. Found: C, 68.09; H, 7.67. $C_{40}H_{54}BO_2Sb$ calcd.: C, 68.69; H, 7.78%.

*N,N-Diethylaminocarbonylmethyltri-n-butylstibonium tetraphenylborate (14c).* Work-up as above in ether gave the product in 61% yield. M.p. 87–88 °C; $^1H$ NMR ($CDCl_3$): 0.63–1.56 (27H,m, n-Pr, $CH_3$), 1.76(6H, m, $CH_2$), 2.76 (2H, s, $CH_2$), 2.82 (2H, q, $J$ 7 Hz, $CH_2$), 3.14 (2H, q, $J$ 7 Hz, $CH_2$), 6.82 (12H, m, Ph), 7.27 (8H, m, Ph); IR (KCl): 1686(s); Anal. Found: C, 70.23: H, 8.49; N, 2.04. $C_{42}H_{59}BNOSb$ calcd.: C, 69.44; H, 8.19; N, 1.93%.

**Acknowledgement**

We thank the National Natural Science Foundation of China and the Academia Sinica for financial support.

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