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DEBROMINATION OF PHENACYL AND BENZYLIC BROMIDES WITH TERTIARY STIBINE AND THE MECHANISTIC CONSIDERATION

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Tributylstibine is an efficient reagent for debromination of phenacyl and arylmethyl bromides. The mechanistic difference between stibine and phosphine is discussed briefly.

It has long been known that α-haloketones are easily reduced with various reagents, e.g. zinc in acetic acid, NaI, NaI-chlorotrimethylsilane, and sodium hydrogen telluride etc.[1] On the other hand, there is no example for dehalogenation by means of utilizing tertiary stibines inspite of low electronegativity (1.8) of antimony, although the corresponding amine and phosphine were used for such a reaction.[2]

In connection with our studies on hypervalent sulfur chemistry,[3] structural interests as well as expectative unique reactivity of penta-coordinated antimony[4] led us to inquire debromination of several organic bromides with tris-coordinated antimony (Bu_3Sb and Ph_3Sb), during which the former would take part as an intermediate.[5]

The results of debromination are summarized in Table I.[6] Reduction of phenacyl bromide with tributylstibine proceeded quite smoothly to afford the reduced ketone in 67% yield, which was improved by adequate treatment with protic solvents during or after the reaction (entry 1-4).[7] But, reaction of the corresponding chloride gave the ketone in only low yield under the same conditions (entry 5). In the reaction with arylmethyl bromides, the corresponding stibonium salts were precipitated and were refluxed with ethanolic KOH to give the reduced products (entry 6-9).

Notwithstanding, it is noteworthy that the debromination with tributylstibine proved to be very chemo-selective even in the presence of carbonyl or sulfinyl or sulfonyl group (entry 3,8,9).[8] 1,2-Elimination of dibromides with the reagent also occurred to give the corresponding olefin

in high yield (entry 11, 12, 20).

In order to clarify the mechanistic difference between stibine and phosphine in debromination of α-bromoketones, the kinetics of the reaction was examined by using a solution of triphenylstibine (0.039 mmol) and p-bromophenacyl bromide (0.039 mol) in 2 ml of CD_3CN solution (entry 13). In the ^1H NMR spectrum, there were observed characteristic signals [δ, 7.5-7.8 (m, 9H) and 8.0-8.4 (m, 6H)] for triphenylantimony dibromide along with the other signals [δ, 4.60 (s, $COCH_2Br$) and 2.53 (s, $COCH_3$)] assigned to protons for phenacyl derivatives. It should be noted that only a half of the bromide was reduced at the end of the reaction as shown in Figure I. In addition, complete deuterium exchange of α-protons was confirmed during the reaction in CD_3OD (entry 15), while both the starting material and the product were recovered without deuterium exchange under the same conditions.

Table I. Dehalogenation of Organic Halides

entry	halide	R_3Sb[a,b]	solvent	reaction conditions	treatment[c]	product	yield,[d] %
1	p-$BrC_6H_4COCH_2Br$	B	CH_3CN	rt, 45 min.	-	p-$BrC_6H_4COCH_3$	60
2	$C_6H_5COCH_2Br$	B	CH_3CN	rt, 30 min.	-	$C_6H_5COCH_3$	67
3	$C_6H_5COCH_2Br$	B	THF	rt, 45 min.	H	$C_6H_5COCH_3$	80
4	$C_6H_5COCH_2Br$	B	50% CH_3CN/MeOH	rt, 1 day	-	$C_6H_5COCH_3$	76
5	$C_6H_5COCH_2Cl$	B	CH_3CN	rt, 3 days	H	$C_6H_5COCH_3$	10
6	$(o\text{-}BrCH_2C_6H_4)_2O$	B	CH_3CN	rt, 1 day	OH	$(o\text{-}CH_3C_6H_4)_2O$	80
7	$(o\text{-}BrCH_2C_6H_4)_2S$	B	CH_3CN	rt, 1 day	OH	$(o\text{-}CH_3C_6H_4)_2S$	68
8	$(o\text{-}BrCH_2C_6H_4)_2SO$	B	CH_3CN	rt, 1 day	OH	$(o\text{-}CH_3C_6H_4)_2SO$	97
9	$(o\text{-}BrCH_2C_6H_4)_2SO_2$	B	CH_3CN	rt, 1 day	OH	$(o\text{-}CH_3C_6H_4)_2SO_2$	60
10	p-$NO_2C_6H_4CH_2Br$	B	CH_3CN	rt, 3 days	-	p-$NO_2C_6H_4CH_3$	33
11	$C_6H_5(CHBr)_2CO_2Et$	B	CH_3CN	rt, 30 min.	-	t-$C_6H_5CH{=}CHCO_2Et$	71
12	$(C_6H_5CHBr)_2$	B	CH_3CN	rt, 4 days	-	t-$C_6H_5CH{=}CHC_6H_5$	89
13	p-$BrC_6H_4COCH_2Br$	P	CD_3CN	35 °C, 16 days	-	p-$BrC_6H_4COCH_3$	59
14	p-$BrC_6H_4COCH_2Br$	P	CD_3CN	35 °C, 10 days	H	p-$BrC_6H_4COCH_3$	73[e]
15	p-$BrC_6H_4COCH_2Br$	P	CD_3OD	35 °C, 10 days	D	p-$BrC_6H_4COCD_3$	89
16	$C_6H_5COCH_2Br$	P	CD_3CN	35 °C, 6 days	H	$C_6H_5COCH_3$	78
17	$C_6H_5COCHMeBr$	P	CD_3CN	70 °C, 3 days	H	$C_6H_5COCH_2Me$	38
18	$C_6H_5COCMe_2Br$	P	CD_3CN	70 °C, 8 days	H	no reaction	
19	p-$BrC_5H_4COCHBr_2$	P	CD_3CN	70 °C, 2 days	H	p-$BrC_6H_4COCH_2Br$	10
						p-$BrC_6H_4COCH_3$	22
20	$C_6H_5(CHBr)_2CO_2Et$	P	CD_3CN	70 °C, 3 days	-	t-$C_6H_5CH{=}CHCO_2Et$	71

[a], B: tri-n-butylstibine. P: triphenylstibine. [b], One equivalent of stibine was used for one halogeno-function in every case. [c], H: addition of methanol after reaction. OH: reflux of the reaction mixture with ethanolic KOH after reaction. D: addition of CD_3OD after reaction. [d], isolated yield by preparative TLC on silica gel. [e], Triphenylantimony dibromide was isolated in 70% yield along with p-bromoacetophenone.

Triphenylphosphine reacted immediately with phenacyl bromide under the same conditions to give a mixture of α-ketophosphonium bromide, the reduced ketone, and enol phosphonium bromide together with the other minor products.[2c]

These results are rationalized by the sequence that the nucleophilic attack of stibine to α-bromoketone gives the stibonium salt (A) which equilibrates with the enolantimony (B). Then, protonolysis of B with A takes place to afford the reduced ketone (in 50% yield), antimony dibromide, and the stibonium ylide (C).[9] The stibonium ylide (C) should be protonated by an additional protic solvent or during work-up and gives an additional amount of the reduced ketone. The mechanism is illustrated in Scheme I. It seems to be the reason why the charactristic signals for α-ketostibonium salt (A) could not be observed in the ^{1}H NMR spectrum burying the ylide proton in aromatic region and a half of the substrate was reduced under anhydrous conditions without any additional protic solvent.

According to the above considerations, the rearrangement of the stibonium salt (A) to the enolantimony (B) and the succeeding disproportionation of the two into the product must be the characteristic features distinct from phosphonium salt.[2c,4,11]

Further synthetic application utilizing such a property of antimony along with the detail mechanistic investigation is now in progress.

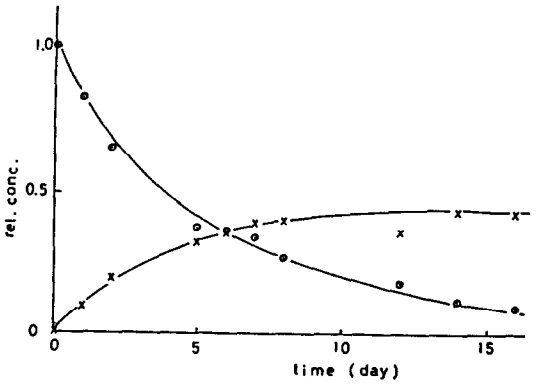
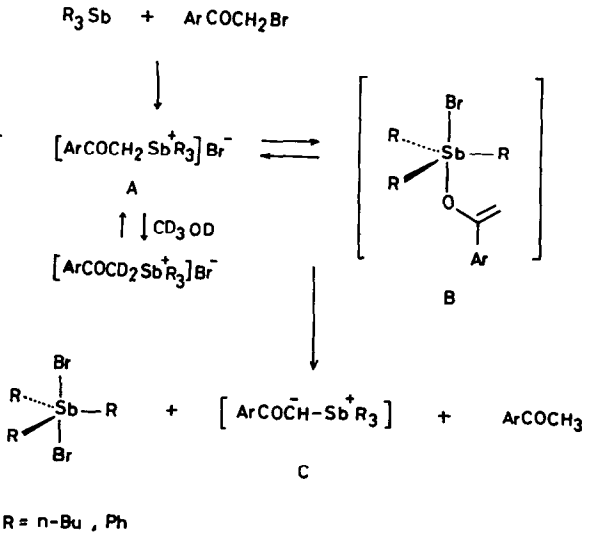


Figure I. Rate of disappearence of p-bromophenacyl bromide (-⊙-) and appearence of p-bromoacetophenone (-×-) in CD_3CN at 35 ° C.[10]

Scheme I



References and Notes

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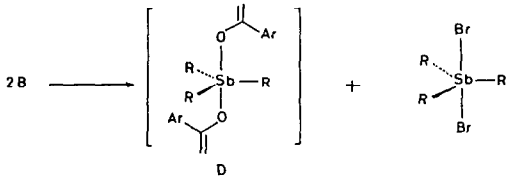
5) Preparation of tertiary stibine: For n-Bu_3Sb, J. Seifter, J. Am. Chem. Soc., 61, 530 (1939). For Ph_3Sb, G. S. Hiers, "Org. Synth.", Coll. Vol. I, p-550 (1941).

6) All new compounds gave correct elemental analyses and spectral data in accord with the assigned structures.

7) Typical procedure: Procedure (H); A mixture of 147 mg (0.74 mmol) of phenacyl bromide and tri-n-butylstibine (212 mg, 0.72 mmol) in 2 ml of THF was allowed to stand at room temperature for 45 min. After addition of methanol to the reaction mixture and evaporation of solvent, TLC separation on silica gel gave 118 mg of acetophenone in 80% yield. Procedure (OH); a sample of di(o-bromomethylphenyl)sulfoxide (130 mg, 0.34 mmol) was reacted with tri-n-butylstibine (267 mg, 0.91 mmol) at room temperature for 1 day in 2 ml of acetonitrile. After the reaction mixture was heated with 10% ethanolic KOH at reflux temperature for 5 h, TLC separation on silica gel furnished 76 mg (97%) of di(o-tolyl)sulfoxide.

8) Sulfinyl group was reduced to give sulfide by triphenylphosphine under mild conditions. a) J. P. A. Castrillon and H. H. Szmant, J. Org. Chem., 30, 1338 (1965). b) H. H. Szmant and O. Cox, ibid., 31, 1596 (1966).

9) Triphenylantimony dibromide can be isolated and recrystallized from ethanol. Another explanation is also possible: enolantimony (B) disproportionates to the symmetric antimony (V), i.e., bisenolantimony (D) and antimony dibromide, followed by protonolysis of D with A. It is established that hypervalent bond is electron-rich and polarizable [J. I. Musher, Angew. Chem. Intern. Ed., 8, 54 (1969)].



10) The relative concentrations were evaluated from integral values of characteristic signals by comparison with that of CD_2HCN (0.5%) in CD_3CN.

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