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SILVER-ASSISTED REACTIONS OF ORGANOTIN OXIDES. A MILD, NEUTRAL AND ANHYDROUS ONE-STEP CONVERSION OF PRIMARY ORGANIC HALIDES TO ALCOHOLS

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Abstract: *Bis(tributyltin)oxide acts as a mild and neutral oxygen transfer agent in converting primary organic iodides and bromides into alcohols in good to excellent yields. The less reactive chlorides can be converted into alcohols when they are first transformed into bromides or iodides using the Finkelstein reaction. Silver salts are required for this one step conversion.*

Bis(tributyltin)oxide (1) is currently produced in bulk quantity and used as wood preservative, as killer of algae in anti-fouling paint and as general desinfectant.[1] It was first synthesized in 1941[2] and has since been considered as one of the major starting material for making organotin derivatives. In organic chemistry, it has been widely utilized in carbohydrate chemistry in the regioselective activation of hydroxyl groups toward alkylations and acylations.[3] More recently, we found that (1) acts as a general "O^{2-}" transfer agent via the methodology of fluorodestannylation.[4]

We would like to report that bis(tributyltin)oxide (1) reacts smoothly with organic iodides and bromides in the presence of silver salts to give the corresponding alcohols. To the best of our knowledge, this is the first example that an organotin compound is used in tandem with silver salts.

$$Bu_3Sn\text{-}O\text{-}SnBu_3$$

1

Although it has been well known that a tin atom attached to an oxygen atom enhances the nucleophilicity of the latter without increasing its basicity,[3,5] no one tried to use this finding in alkylations of organotin oxides in the presence of silver salts. Indeed, the usual alkylation of organotin oxides by organic halides required extensive heating (often near 200°C) for achieving C-O bond formation.[5] Similar vigorous conditions were required in the alkylation reactions in carbohydrates even with the use of reactive benzyl bromide, allyl bromide or mem-chloride with tetrabutylammonium salts, as catalysts.[6]

In our case, we found that non-activated organic iodides such as 1-iodohexane (1.00 mol) reacted at room temperature with bis(tributyltin)oxide (1) (1.10 mol) in the presence of silver tosylate or silver nitrate (1.10 mol) in DMF, under anhydrous conditions. It gave at least 76% yield of 1-hexanol after 1.5 hr of reaction time, followed by an aqueous work-up (see Eq.1 and Table 1,entry 2). We found later that the organotin oxide and the silver salt should be used in ratio of 2.20 and 2.00 mol for optimal yields. The intermediate tributyltin hexyl oxide is unstable and easily hydrolysed (even in moist atmosphere or on silica gel). In a similar way, 1-bromohexane (1.00 mol) reacted with bis(tributyltin)oxide (1) (2.20 mol) and silver tosylate or silver nitrate (1.10 mol) at 90°C for 20-23 hrs (Eq.1). It afforded 74% yield of 1-hexanol (entry 3). The method seems general for usual primary bromides or iodides. Some starting material could be recovered which accounted for the non-quantitative conversions. Primary chlorides, such as 1-chlorooctane, did not react at all even under forcing conditions (entry 8). However, we found that a primary chloride, first converted to the iodide using the Finkelstein reaction (NaI/acetone), followed by our usual treatments for iodides, provided 1-nonanol in moderate overall yield (entry 9).

A strong coordinating solvent like DMF was crucial in this method. We used indifferently silver tosylate and silver nitrate for non-easily ionizable organic halides. However, we observed some traces of 1-tosylhexane when using silver tosylate with 1-iodohexane (~ 8% yield). It is probably better to use silver nitrate in many cases. When using organic bromides no tosylates were detected.

$$CH_3(CH_2)_5X + (Bu_3Sn)_2O \xrightarrow{Ag(I)} CH_3(CH_2)_5OSnBu_3 \xrightarrow[\text{or work-up} \\ H_2O]{SiO_2} CH_3(CH_2)_5OH \quad (1)$$

$X = Br, I$

Interestingly, the reaction did not give any significant amount of ethers even if the appropriate ratio of 1-iodohexane (2.00 mol) and bis(tributyltin)oxide (1.00 mol) were used (entry 1). The result was a clean conversion of the organotin oxide to form the alcohol (84% yield based on organotin oxide). This clearly demonstrates that the first nucleophilic substitution took place easily but the second alkylation is kinetically less favored.

An excess of (1) is desirable in the case of organic bromides because (1) reacts directly with silver salts at R.T. to produce silver oxide (Ag_2O). It is a parallel and competitive reaction which diverts the reagent (1). This process is amplified when heating. Indeed, a black precipitate took place immediately in CH_3CN or DMF. It is conceivable that Ag_2O is the activating agent in the bromide case since silver tosylate, nitrate, triflate and Ag_2O (entry 4) are equally effective despite their different Lewis acidity. However, we ruled out the possibility of Ag_2O alone acting as the oxygen transfer agent in our method by a control experiment under similar conditions without (1). Silver (I) oxide accounted for less than 12% yield of alcohol as shown in entry 5, proving that (1) is the major oxygen transfer agent.

Although simple, this halide to alcohol conversion had been rare despite its potential usefulness. No practical method exists for converting non-activated organic halides to alcohols in one step in a neutral medium; the existing one often involve basic hydrolysis or silver-assisted hydrolysis of reactive benzyl or allyl halides.[7] Other common procedures involve at least two steps by using the acetate anion as

Table 1: Conversion of Organic Halides to Alcohols

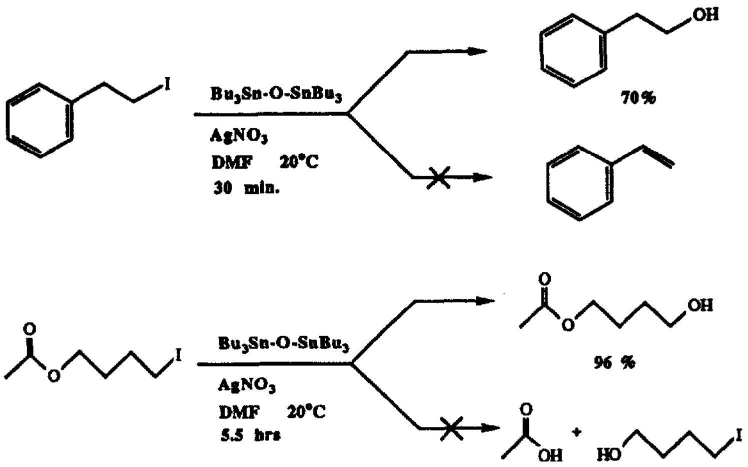
Entry	Halide	Organotin[a]	Solvent	T(°C)	Time(hr)	Ag$^+$	Alcohol	Yield(%)[b]
1	$CH_3(CH_2)_5I$	$(Bu_3Sn)_2O$[c]	DMF	20	2	AgTos	$CH_3(CH_2)_5OH$	84
2	$CH_3(CH_2)_5I$	$(Bu_3Sn)_2O$[d]	DMF	20	2	AgTos	$CH_3(CH_2)_5OH$	76
3	$CH_3(CH_2)_5Br$	$(Bu_3Sn)_2O$	DMF	90	22	AgTos	$CH_3(CH_2)_5OH$	74
4	$CH_3(CH_2)_5Br$	$(Bu_3Sn)_2O$	DMF	90	14	Ag_2O	$CH_3(CH_2)_5OH$	71
5	$CH_3(CH_2)_5Br$	nil	DMF	90	22	Ag_2O	$CH_3(CH_2)_5OH$	12
6	$CH_3(CH_2)_8Br$	$(Bu_3Sn)_2O$	DMF	80	23	AgTos	$CH_3(CH_2)_8OH$	47
7	$CH_3(CH_2)_5Cl$[e]	$(Bu_3Sn)_2O$	DMF	20	2	AgTos	$CH_3(CH_2)_5OH$	74[f]
8	$CH_3(CH_2)_7Cl$	$(Bu_3Sn)_2O$	DMF	125	36	$AgNO_3$	$CH_3(CH_2)_7OH$	nil
9	$CH_3(CH_2)_8Cl$[e]	$(Bu_3Sn)_2O$	DMF	20	3.0	$AgNO_3$	$CH_3(CH_2)_8OH$	50[f]
10	$CH_3COO(CH_2)_4Br$	$(Bu_3Sn)_2O$	DMF	90	24	$AgNO_3$	$CH_3COO(CH_2)_4OH$	28
11	$CH_3COO(CH_2)_4Br$[e]	$(Bu_3Sn)_2O$	DMF	20	5	$AgNO_3$	$CH_3COO(CH_2)_4OH$	91[f]
12	$CH_3COO(CH_2)_4I$	$(Bu_3Sn)_2O$[h]	DMF	20	5.5	AgTos	$CH_3COO(CH_2)_4OH$	96
13	$PhCH_2CH_2I$	$(Bu_3Sn)_2O$[i]	DMF	20	0.5	$AgNO_3$	$PhCH_2CH_2OH$	70
14	$PhCH_2CH_2Br$[e]	$(Bu_3Sn)_2O$	DMF	20	0.5	$AgNO_3$	$PhCH_2CH_2OH$	63[f]
15	$c\text{-}C_6H_{10}CH_3(Br)$[g]	$(Bu_3Sn)_2O$	DMF	20	4	$AgNO_3$	$c\text{-}C_6H_{10}CH_3(OH)$	0-5
16	$c\text{-}C_6H_{11}\text{-}I$	$(Bu_3Sn)_2O$	DMF	75	28	AgTos	$c\text{-}C_6H_{11}\text{-}OH$	0-5

a) For organic bromides or chlorides: ratio $(Bu_3Sn)_2O/Ag^+/$bromide = 2.2/1.1/1.0 (mol). b) Isolated yields, non optimized; products characterized by ^1H NMR (200 MHz), T.L.C.; G.C. and by comparison to authentic material. c) Ratio $(Bu_3Sn)_2O/Ag^+/$iodide = 2.2/2.0/1.0 (mol). d) Ratio $(Bu_3Sn)_2O/Ag^+/$iodide = 1.1/1.1/1.0 (mol) e) 2 steps: prior conversion to the iodide (NaI 3.0 eq./1.0 eq organic bromide or chloride/acetone, reflux) then conditions as described in the table. f) Overall yields. g) 1-bromo-1-methyl cyclohexane. h) Ratio $(Bu_3Sn)_2O/Ag^+/$iodide = 2.0/1.3/1.0 (mol) i) Ratio $(Bu_3Sn)_2O/Ag^+/$iodide = 2.2/2.0/1.0 (mol).

nucleophile which is usually a difficult displacement and often gives rise to some elimination. The acetate formed has to be hydrolyzed (usually under basic conditions) in the second step.[8] An alternative method involves the transformation of halides into hydroperoxides or peroxides with the use of silver triflate and hydrogen peroxide.[9] *Then a reduction of the peroxide or hydroxiperoxide is required.*

An advantage of the present reactions is that elimination reaction which often accompanies subtitution reaction of halides is minimized. As an ultimate proof, the base-sensitive (2-iodoethyl)benzene was readily converted to 2-phenethyl alcohol instead of giving styrene (scheme 1 and entry 13). Furthermore, ester groups remain unchanged in the reaction. Thus, 4-iodobutyl acetate was converted smoothly to the corresponding alcohol in nearly quantitative yield (scheme 1 and entry 12). On the other hand, secondary (iodocyclohexane, entry 16) or tertiary (1-bromo-1-methylcyclohexane, entry 15) halides did not afford significant yield of the corresponding alcohols. Elimination reactions predominated in these cases.

SCHEME 1



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