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Terminal 1-Halo- and 1-Pseudohalo-1-Alkynes *via* Bis(trimethylsilyl)peroxide (BTMSPO) Promoted *Umpolung* Transfer of Halides and Pseudohalides.

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Abstract: *Reaction of terminal acetylenes with readily available and inexpensive copper and zinc halides and pseudo-halides and BTMSPO has been found to be an effective and general route for obtaining, in the absence of bases and under mild conditions, 1-halo- and 1-pseudohalo-1-alkynes in generally good yields.*

The recent renewed interest[1-3] in the preparation of terminal 1-halo-1-alkynes[4] has not led to the discovery of a general route to these derivatives. A previous report from this laboratory[5], indicated a method for the conversion of alkynes to terminal iodo-derivatives, involving reaction of alkynyl carbanions with bis(trimethylsilyl)peroxide (BTMSPO) and ZnI_2, a methodology which complemented other iodination procedures[1,2] published recently.

Here we report that the BTMSPO/MX_n reagent system envisages a safe method, unique for its generality, for the conversion, in neutral medium and under very mild conditions, of terminal alkynes into the corresponding chlorides, bromides, iodides and nitriles. The procedure, based on the simple treatment of an alkyne with BTMSPO and the appropriate metal salt in THF, is shown in *Scheme 1*.

Scheme 1

$$Me_3SiOOSiMe_3 + \underset{(2)}{MX_n} \xrightarrow[\text{THF}]{\text{R-C}\equiv\text{C-H (1)}} \underset{(3)}{\text{R-C}\equiv\text{C-X}} \qquad \begin{array}{l} M = Cu, Zn;\ \ n = 1, 2; \\ X = Cl, Br, I, CN \end{array}$$

In a typical procedure, to a suspension of (2) (2mmol) in anhydrous THF (6-7 ml) at -15°C under inert atmosfere, the alkyne (1)(2mmol) and then at the same temperature BTMSPO dropwise (2mmol) were added. The reaction mixture was kept at -15°C for 15 min and then allowed to reach room temperature. Usually the reaction mixture was worked up after 2 hrs by diluting with THF (15 ml) and adding saturated NH_4Cl solution, and washing the organic phase twice with brine and drying with $MgSO_4$. Evaporation of the solvent gave a liquid which was analyzed by GC/MS. Isolation of the products was achieved by Kugelrohr distillation or by flash chromatography on silica (n-hexane eluent). The results are summarized in the ***Table***.A survey of the reactivity of R-C≡C-H (1), showed that BTMSPO in the presence of equimolar amounts of metal halides and pseudo-halides (2), led to efficient formation of derivatives (3) according to ***Scheme 1***. Variable amounts of dimeric by-products were also present in the crude reaction mixture.

The title reaction appears to be almost unaffected by the structure of the acetylenic derivative and tolerates (see entries 5,10,11) the presence of other reactive functionalities. On the other hand the role of the metal involved appears to be crucial, with Cu and Zn leading to the best results in terms of reaction yields.

The sequence starting from BTMSPO and (2) and subsequent addition of (1) , outlines a formal transfer of "X^{+}" from MX_n to terminal alkynes in an *umpolung* fashion. A key experiment in which the BTMSPO/CuBr mixture was reacted with cyclohexene in dichloromethane led to 1-siloxy-2-bromo-cyclo-hexane in 60 % yield; the same compound was obtained by treating cyclohexene with an equimolar mixture of Br_2 and Me_3SiONa at -20°C. Mechanistically one can view BTMSPO therefore as providing the oxygenated framework needed for the formation of an intermediate *hypo* species such as Me_3Si-O-X, which accounts for the observed reversal of polarity of the halogenide ions, and is in agreement with the known tendency[15] of cyanates to transfer the CN framework on formal or incipient carbanions with the formation of nitriles.

Table - Functionalized 1-alkynes (3) from BTMSPO, MX_n (2), and (1) in THF.

Entry	R	MX_n	R-C≡C-X[a] (3)	Yield[b] (%)	$(R-C{\equiv}C-)_2$[b] Yield (%)
1	Ph	ZnI_2	Ph-C≡C-I[9]	(90)(85)[c]	(10)
2	n-C_3H_7	ZnI_2	n-C_3H_7-C≡C-I[10]	(45)	(--)
3	Ph	CuI	Ph-C≡C-I[9]	(80)	(15)
4	n-C_3H_7	CuI	n-C_3H_7C≡C-I[10]	(40)	(2)
5	Me_3Si	CuI	Me_3Si-C≡C-I[11]	(90)(80)[c]	(--)
6	n-C_8H_{17}	CuI	n-C_8H_{17}-C≡C-I[12]	(70)	(--)
7	Ph	CuCl	Ph-C≡C-Cl[13]	(50)	(40)
8	Ph	CuBr	Ph-C≡C-Br[14]	(75)(70)[c]	(25)
9	n-C_8H_{17}	CuBr	n-C_8H_{17}-C≡C-Br[15]	(80)	(--)
10	Me_3Si	CuBr	Me_3Si-C≡C-Br[16]	(70)(60)[c]	(--)
11	$(Me_3Si)_2NCH_2$	CuBr	$(Me_3Si)_2NCH_2$-C≡C-Br	(45)	(--)
12	Ph	CuCN	Ph-C≡C-CN[17]	(70)(65)[c,d]	(30)

[a]-All compounds had spectral data and GC/MS analyses in accordance with the proposed structures; [b]-Yields based on alkynes (3) *were determined by GC; [c]-Isolated yields; [d]-2.2 equivalents of CuCN were used.*

Future work will most likely result in an even wider range of application to other pseudohalides and to the fluorination reaction. In this respect, the simplicity, the mild conditions and the high degree of variability of the reagents, is a most valuable asset.

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