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DIRECT CONVERSION OF AMINES TO THE CORRESPONDING HALIDES BY DEAMINATION WITH t-BUTYL THIONITRITE OR t-BUTYL THIONITRATE AND COPPER(II) HALIDES

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We reported recently that both t-butyl thionitrite[1)] and t-butyl thionitrate[2)] can be prepared simply by treating t-butyl mercaptan with dinitrogen tetraoxide.

We now have found that various arylamines reacted readily with either t-butyl thionitrite or t-butyl thionitrate and copper(II) halides under mild conditions to afford the corresponding halides in good yields(eq 1).

$$\left.\begin{array}{r}\text{t-Bu-S-N=O}\\ \text{or t-Bu-SNO}_2\end{array}\right] + \text{ArNH}_2 + \underset{\text{X=Cl, Br}}{\text{CuX}_2} \xrightarrow[\text{0-25°C}]{\text{CH}_3\text{CN}} \text{ArX} + \text{N}_2 + (\text{t-Bu-})_2\text{S}_2 + (\text{t-Bu-})_2\text{S}_3 \text{ -----(1)}$$

Both thionitrites and thionitrates are generally known to be unstable, however, t-butyl derivatives,i.e., t-BuSNO and t-BuSNO$_2$, which can be readily synthesized quantitatively by mixing the thiol and N_2O_4, are stable enough to be used for these reactions. Although other nitrosyl compounds such as nitrosyl halide[3)] and alkyl nitrite[4)] have been successfully used for the same reaction, thionitrites or thionitrates are considered to be better reagents for deaminative halogenation of arylamines due both to the relatively weaker S-N bond of t-butyl thionitrite or t-butyl thionitrate than the O-N bond of nitrites and also to the stronger complexation of thio-derivatives with copper salt than the oxygen and chloro analogs. Indeed, this was found to be the case. After a solution of t-BuSNO(0.89g, 7.5 mmol, CH_3CN:20 ml) was added onto well-dried $CuCl_2$(0.85g, 6 mmol) under argon with vigorous stirring, a solid or liquid aromatic amine was slowly added over a period of 15 min. at 25°C and then hydrochloric acid solution (20%, 100 ml) was added. The solution, after saturated with NaCl, was extracted with ether. The extract was washed 3 times with water saturated with NaCl and then concentrated. Purification by TLC or recrystallization gave the pure mono-halogenated product. Other products were t-butyl disulfide(ca. 0.35 mmol) and t-butyl trisulfide(ca. 2.0 mmol)[5)] t-Butyl trisulfide was identified by elemental analysis. Quantitative evolution of N_2 collected during the reaction was identified by mass-spectroscopy.

All the products were identified by comparing their ir and nmr spectra with those of authentic samples. The results are summarized in Table I and Table II.

Treatment of primary amine with t-butyl thionitrite and anhydrous cupric halides probably involves an initial formation of an intermediate diazonium salt (eq 2) like in the case with alkyl nitrites[3)]. t-Butyl trisulfide was formed probably by the attack of t-butyldithio radical formed by homolysis of t-butyl disulfide on t-butyl thionitrite (eq 3)[5)].

Table I. $RNH_2 + t\text{-}BuSNO + CuX_2 \longrightarrow RX$

Amines	Halides X=Cl or Br	Reaction Temp. (°C)	Reaction Time (hr)	RNH_2: t-BuSNO: CuX_2	Yields (%)	
					RCl	RBr
$p\text{-}NO_2\text{-}C_6H_4NH_2$	$p\text{-}NO_2\text{-}C_6H_4X$	25	2	10:15:12	98[a,d]	78[a]
$p\text{-}NO_2\text{-}C_6H_4NH_2$	$p\text{-}NO_2\text{-}C_6H_4X$	0	1	10:15:12	85[a]	
$p\text{-}NO_2\text{-}C_6H_4NH_2$	$p\text{-}NO_2\text{-}C_6H_4X$	50	0.5	10:15:12	61[a]	
$p\text{-}NO_2\text{-}C_6H_4NH_2$	$p\text{-}NO_2\text{-}C_6H_4X$	25	1	10:10:12	51[b]	
$p\text{-}HO_2C\text{-}C_6H_4NH_2$	$p\text{-}HO_2C\text{-}C_6H_4X$	25	2	10:15:12	97[a]	78[a]
$p\text{-}Cl\text{-}C_6H_4NH_2$	$p\text{-}Cl\text{-}C_6H_4X$	25	2	10:15:12	78[b]	71[b]
$C_6H_5NH_2$	C_6H_5X	25	2	10:15:12	86[b]	58[b]
$p\text{-}MeO\text{-}C_6H_4NH_2$	$p\text{-}MeO\text{-}C_6H_4X$	25	2	10:15:12	61[b]	36[b]
$p\text{-}HO\text{-}C_6H_4NH_2$	$p\text{-}HO\text{-}C_6H_4X$	25	2	10:15:12	57[a]	40[a]
$C_6H_5CH_2NH_2$	$C_6H_5CH_2X$	25	2	10:15:12	18[a,c]	

a: Isolated yield. b: GC yield. c: Benzaldehyde(13%) and benzyl alcohol(26%) was isolated.
d: Other side products were $(t\text{-}Bu)_2S_2$(0.32 mmol) and $(t\text{-}Bu)_2S_3$(2.2 mmol), which were obtained in nearly the same yields in all the runs.

Table II. $RNH_2 + t\text{-}BuSNO_2 + CuX_2 \longrightarrow RX$

Amines	Halides X=Cl or Br	Reaction Temp. (°C)	Reaction Time (hr)	RNH_2: t-$BuSNO_2$: CuX_2	Yields (%)		
					RCl	RBr	Other
p-NO_2-$C_6H_4NH_2$	p-NO_2-C_6H_4X	25	2	10:15:12	$98^{a,e}$	74^{a}	
p-NO_2-$C_6H_4NH_2$	p-NO_2-C_6H_4X	0	1.5	10:10:10	87^{b}		
p-HO_2C-$C_6H_4NH_2$	p-HO_2C-C_6H_4X	25	1.5	10:15:12	86^{a}		
p-HO_2C-$C_6H_4NH_2$	p-HO_2C-C_6H_4X	25	1	10:15:12		75^{a}	
p-Cl-$C_6H_4NH_2$	p-Cl-C_6H_4X	25	2	10:15:12	71^{b}	55^{b}	
$C_6H_5NH_2$	C_6H_5X	25	2	10:15:12	82^{b}	83^{b}	
p-MeO-$C_6H_4NH_2$	p-MeO-C_6H_4X	25	1.5	10:15:12	63^{b}	57^{b}	
p-HO-$C_6H_4NH_2$	p-HO-C_6H_4X	25	1	10:15:12	0		23^{c}
p-HO-$C_6H_4NH_2$	——— [f]	25	1.5	10:20:0	0		56^{f}
$C_6H_5CH_2NH_2$	$C_6H_5CH_2X$	25	2	10:15:12	$18^{a,d}$		

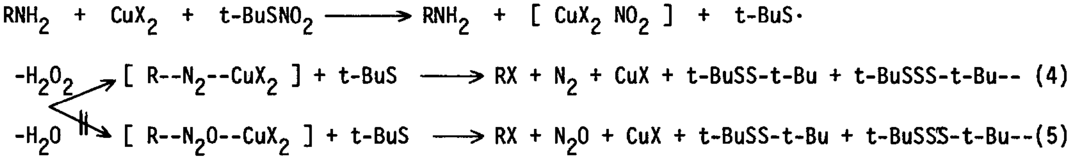
a: Isolated yield. b: GC yield. c: N-S-C(CH_3)$_3$ was isolated in 23% yield. Elemental analysis and spectral data support this structure. d: Benzaldehyde(32%) and benzyl alcohol(16%) were isolated. e: Other products were $(t\text{-}Bu)_2S_2$(0.31 mmol) and $(t\text{-}Bu)_2S_3$(2.1 mmol), and about same yield of trisulfide and disulfide were confirmed in most of cases. f: From the reaction of p-aminophenol and t-$BuSNO_2$ without using CuX_2, N-S-C(CH_3)$_3$ was obtained in 56% of GC yield based on the amount of p-HO-$C_6H_4NH_2$.

$$RNH_2 + \underset{X=Cl,\ Br}{CuX_2} + t\text{-}Bu\text{-}S\text{-}N{=}O \longrightarrow RNH_2 + [CuX_2 \cdot NO] + t\text{-}BuS\cdot \xrightarrow{-H_2O}$$

$$[\ RN_2\text{--}Cu\text{--}X_2\ ] + [\ t\text{-}BuS\cdot\ ] \longrightarrow RX + N_2 + CuX + (t\text{-}Bu\text{-})_2S_2 + (t\text{-}Bu\text{-})_2S_3 \text{ ---(2)}$$

$$t\text{-}Bu\text{-}SS\text{-}t\text{-}Bu \longrightarrow [\ t\text{-}Bu\text{-}SS\cdot\ ] \xrightarrow{t\text{-}BuSNO} t\text{-}Bu\text{-}SSS\text{-}t\text{-}Bu\text{-------}(3)^{5)}$$

When t-butyl thionitrate was used instead of t-butyl thionitrite, nearly the same results were obtained (Table II). If the reaction proceed via a similar path as in the case of the thionitrite, either H_2O_2 (instead of H_2O) or N_2O (instead of N_2) should be formed according to the equation (4 or 5). However, gc mass spectrum of gas trapped during the reaction showed only N_2 but not $N_2O$$^{6)}$. Though H_2O_2 could not be confirmed$^{7)}$, the reaction is presumed to proceed via a diazonium salt intermediate as shown by equation (4).$^{8)}$



$$RNH_2 + CuX_2 + t\text{-}BuSNO_2 \longrightarrow RNH_2 + [\ CuX_2\ NO_2\ ] + t\text{-}BuS\cdot$$

$$-H_2O_2 \rightarrow [\ R\text{--}N_2\text{--}CuX_2\ ] + t\text{-}BuS \longrightarrow RX + N_2 + CuX + t\text{-}BuSS\text{-}t\text{-}Bu + t\text{-}BuSSS\text{-}t\text{-}Bu\text{--}\ (4)$$

$$-H_2O \nrightarrow [\ R\text{--}N_2O\text{--}CuX_2\ ] + t\text{-}BuS \longrightarrow RX + N_2O + CuX + t\text{-}BuSS\text{-}t\text{-}Bu + t\text{-}BuSSS\text{-}t\text{-}Bu\text{--}(5)$$

It is noteworthy that t-butyl trisulfide is formed as the major product along with a minor product i.e., t-butyl disulfide. This interesting reaction will be reported shortly.

References and Notes

1). S. Oae, D. Fukushima and Y. H. Kim, J. Chem. Soc., Chem. Commun., 407 (1977).

2). Y. H. Kim, K. Shinhama, D. Fukushima and S. Oae, Tetrahedron Letters, 1211 (1978).

3). M. P. Doyle, B. Siegfried and J. J. Hammond, J. Am. Chem. Soc., 98, 1627 (1976).

4). a) M. P. Doyle and B. Siegfried, J. Chem. Soc., Chem. Commun., 433 (1976).

b) M. P. Doyle, B. Siegfried and J. F. Dellaria, Jr., J. Org. Chem., 42, 2426 (1977).

5). The reaction of t-butyl disulfide with $CuCl_2$ under the same condition afforded both the trisulfide and the tetrasulfide. Probably, in the presence of t-BuSNO or t-$BuSNO_2$, the radical intermediate, t-BuSS· reacts with the thionitrite or thionitrate to give the t-butyl trisulfide.

6). A possibility of decomposition of N_2O to NO and N_2 in mass process was ruled out by control mass spectroscopic analysis of the authentic sample of N_2O which showed a strong molecular peak (M^+, 44) of N_2O.

7). Thiane and diphenyl sulfide in acetic acid was added for trapping H_2O_2 to the reaction mixture both at the begining and after the complete reaction. However, the sulfide was recoverd quantitatively and no sulfoxide was detected. H_2O_2 formed in the reaction may be readily consumed for the oxidation of copper complex.

8). Investigation on the mechanism is now in progress in this laboratory.

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