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Direct Conversion of Arylamines to the Corresponding Halides, Biphenyls, and Sulfides with *t*-Butyl Thionitrate

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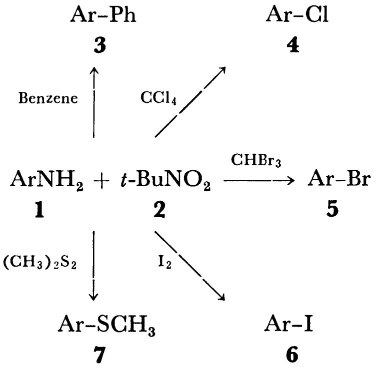
t-Butyl thionitrate have been found to be an excellent diazotizing reagent of arylamines in aprotic nonpolar media, affording eventually such products as aryl chlorides, aryl bromides, aryl iodides, biphenyls, and aryl methyl sulfides in the presence of CCl_4, $CHBr_3$, I_2, benzene, and dimethyl disulfide, respectively, *via* extrusion of N_2.

In the course of our studies on the synthetic applications of thionitrites or thionitrates, we now have found that *t*-butyl thionitrate (**2**)[1) was an excellent diazotizing reagent in neutral, aprotic, and homogeneous media to convert various arylamines (**1**) in the presence of carbon tetrachloride, bromoform, iodine in benzene, benzene alone, and dimethyl disulfide to afford the corresponding aryl chloride (**4**), aryl bromide (**5**), aryl iodide (**6**), biphenyls (**3**), and methyl aryl sulfides (**7**), respectively, in good yields.



Although alkyl nitrites have been used for the same purposes,[2) thionitrites and thionitrates are considered to be better reagents for deamination of arylamines **1** due to the relatively weak S–N bonds of thionitrites and thionitrates. Indeed, the thionitrate **2** was found to be a remarkably effective reagent for deamination. Although *t*-butyl thionitrite is also an effective deaminating reagent which can afford aryl halides in the reaction with arylamines in the presence of copper(II) halides in acetonitrile at room temperature,[3) it is not thermally stable as compared to the thionitrate **2** and decomposes readily in boiling benzene or carbon tetrachloride, and hence it was not used for these uncatalyzed reactions.

Reactions of various arylamines (**1a**—**i**) with **2** in benzene gave the corresponding biphenyls (**3a**—**i**) in good yields (Table 1). The reaction was found to proceed in a short time when *p*-methoxyaniline (**1c**), which possesses an electron-donating methoxyl group, was treated with thionitrate **2**. However, the yield of 4-methoxybiphenyl (**3c**) was relatively low because of the formation of a large amount of dark uncharacterized substance. On the contrary, *p*-nitroaniline (**1d**) was found to react rather slowly but converted to the corresponding 4-nitrobiphenyl (**3d**) in a good yields in several hours.

$$\underset{\mathbf{1}}{\mathrm{ArNH_2}} + \underset{\mathbf{2}}{t\text{-}\mathrm{BuSNO_2}} \xrightarrow[80\,^{\circ}\mathrm{C}]{\text{Benzene}} \underset{\mathbf{3}}{\mathrm{Ar\text{-}Ph}}$$

1a, **3a**: Ar=Ph
1b, **3b**: Ar=*p*-Cl-C_6H_4
1c, **3c**: Ar=*p*-MeO-C_6H_4
1d, **3d**: Ar=*p*-NO_2-C_6H_4
1e, **3e**: Ar=*o*-NO_2-C_6H_4
1f, **3f**: Ar=*p*-Br-C_6H_4
1g, **3g**: Ar=*p*-CH_3-C_6H_4
1h, **3h**: Ar=*m*-CH_3-C_6H_4
1i, **3i**: Ar=*o*-CH_3-C_6H_4

Meanwhile, when isopentyl nitrate (**8**) was treated in a similar way with *p*-chloroaniline (**1b**), no reaction took place due undoubtedly to the relatively strong O–N bond of **8**.

$$\mathbf{1b} + \underset{\mathbf{8}}{\mathrm{(CH_3)_2CH(CH_2)_2ONO_2}} \overset{\text{Benzene}}{\not\longrightarrow} \mathbf{3b}$$

When aniline (**1a**) was treated with **2** in toluene, methylbiphenyl (**3j**) was obtained as a mixture of its positional isomers. GLC and ^{1}H-NMR analyses of this reaction mixture showed that the ortho, meta, and para isomers are formed in the ratio of *ca.* 4:2:1.

TABLE 1. REACTIONS OF ARYLAMINES **1a**—**i** WITH THIONITRATE **2** IN BENZENE

Compound	$\frac{[2]}{[1]}$[a)	Reaction temp/°C[b)	Reaction time/h	Product	Yield/% c)	Yield/% d)	Mp/°C or Bp/°C/mmHg of the product
1a	1.4	80	2	**3a**	62	47	69—70 (lit,[2b) 68)
1b	1.4	80	6	**3b**	67	60	75—76 (lit,[2b) 76)
1c	1.4	80	0.2	**3c**	28	26	88—90 (lit,[2b) 90)
1d	1.4	80	19	**3d**	75	67	113—115 (lit,[2a) 111—113)
1e	1.4	80	14	**3e**	39	33	142—147/2[e) (lit,[2a) 180—82/20)
1f	1.4	80	7	**3f**	76	58	85—87 (lit,[5) 89.5—90)
1g	1.4	80	8	**3g**	39	38	46—47 (lit,[2a) 49—50)
1h	1.4	80	6	**3h**		35	110—115/2[e) (lit,[2a) 265—269/714)
1i	1.4	80	6	**3i**		27	114—120/2[e) (lit,[2a) 250—253/716)

a) Mol ratio. b) Refluxed in benzene. c) GLC yield. d) Isolated yield. e) Bath temperature.

TABLE 2. REACTIONS OF ARYLAMINES **1** WITH THIONITRATE **2** IN SEVERAL AROMATIC SOLVENTS

Compound	Solvent	$\frac{[\mathbf{2}]^{a)}}{[\mathbf{1}]}$	Reaction temp/°C	Reaction time/h	Product	Isolated yield/%$^{b)}$
1a	Toluene	1.4	110$^{c)}$	2	**3j**	30
1d	Toluene	1.4	110$^{c)}$	2	**3k**	47
1d	Chlorobenzene	1.4	110$^{c)}$	1	**3l**	58
1e	Toluene	1.4	110$^{c)}$	2	**3m**	45
1g	Nitrobenzene	1.4	100	1	**3n**	42

a) Mol ratio. b) Mixture of isomers. c) Refluxed in solvents.

TABLE 3. REACTIONS OF ARYLAMINES **1** WITH THIONITRATE **2** IN HALIDES

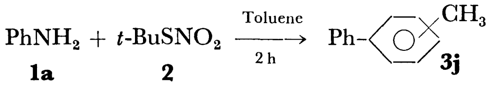
Compound	Solvent	$\frac{[\mathbf{2}]^{a)}}{[\mathbf{1}]}$	Reaction temp/°C	Reaction time/min	Product	Yield/%	
						c)	d)
1b	CCl_4	1.4	76$^{b)}$	60	**4a**	46	40
1c	CCl_4	1.4	76$^{b)}$	60	**4b**	37	28
1c	$CHBr_3$	1.4	25	5	**5a**	48	34
1d	$CHBr_3$	1.4	120	40	**5b**	80	75
1e	$CHBr_3$	1.4	76$^{b)}$	30	**4c**	38	25
1f	$CHBr_3$	1.4	100	20	**5d**	65	60

a) Mol ratio. b) Refluxed in CCl_4. c) GLC yield. d) Isolated yield.

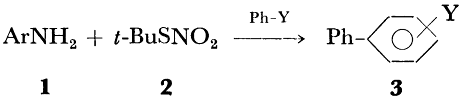
TABLE 4. REACTIONS OF ARYLAMINES **1** WITH THIONITRATE **2** IN THE PRESENCE OF IODINE

Compound	$\frac{[\mathbf{2}]^{a)}}{[\mathbf{1}]}$	Reaction temp/°C	Reaction time/h	Product	Yield/%	
					c)	d)
1b	1.0	80$^{b)}$	0.7	**6a**	35	32
1c	1.0	25	0.2	**6b**	51	48
1d	1.0	80$^{b)}$	15	**6c**	80	71
1e	1.0	80$^{b)}$	16	**6d**	64	53
1f	1.0	80$^{b)}$	1.5	**6e**	79	64
1g	1.0	80$^{b)}$	0.3	**6f**	79	74

a) Mol ratio. b) Refluxed in benzene. c) GLC yield. d) Isolated yield.



Steric hindrace of methyl group seems to have little effect in this reaction. Similar treatment of *p*-nitroaniline (**1d**), *o*-nitroaniline (**1e**), and *p*-toluidine (**1g**) in several solvents such as toluene, nitrobenzene, and chlorobenzene gave corresponding biphenyls (**3j**—**n**) as the mixture of ortho, meta, and para isomers. The results are listed in Table 2.

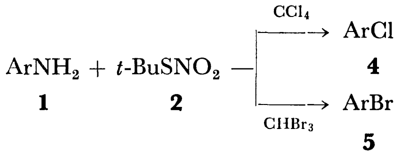


3j: Ar=Ph, Y=CH_3
3k: Ar=*p*-NO_2-C_6H_4, Y=CH_3
3l: Ar=*p*-NO_2-C_6H_4, Y=Cl
3m: Ar=*o*-NO_2-C_6H_4, Y=CH_3
3n: Ar=*p*-CH_3-C_6H_4, Y=NO_2

Reaction of *p*-bromoaniline (**1f**) with **2** in pyridine did not give any deaminated product, since **2** rapidly decomposed in pyridine to give *S*-*t*-butyl 2-methyl-2-propanethiosulfonate (**9**).

$$\underset{\mathbf{1f}}{p\text{-Br-}C_6H_4NH_2} + \mathbf{2} \xrightarrow{\text{Pyridine}} \underset{\mathbf{9}}{t\text{-BuSO}_2\text{S-Bu-}t} + \mathbf{1f}$$

Various aryl chlorides **4** and aryl bromides **5** were also obtained by treating the corresponding arylamines **1** with **2** in carbon tetrachloride and bromoform, respectively. The results are listed in Table 3.



4a: Ar=*p*-Cl-C_6H_4
4b, **5a**: Ar=*p*-CH_3O-C_6H_4
5b: Ar=*p*-NO_2-C_6H_4
4c, **5d**: Ar=*p*-Br-C_6H_4
5c: Ar=*o*-NO_2-C_6H_4

The thionitrate **2** was found to be far better than alkyl nitrite in the syntheses of iodides **6** from the arylamines **1**. Upon treatment of **1** with **2** in the presence of iodine (half mol of amine) in refluxing benzene, the corresponding aryl iodides **6** were obtained in good yields as shown in Table 4. *p*-Toluidine (**1g**) was found to be converted to *p*-iodotoluene with isopentyl nitrite in the presence of iodine after a long reaction time (4 h) in a lower yield (40%).[2d] In

Table 5. Reactions of arylamines **1** with thionitrate **2** in dimethyl disulfide

Compound	$\frac{[\mathbf{2}]^{a)}}{[\mathbf{1}]}$	Reaction temp/°C	Reaction time/min	Product	Isolated yield/%	Mp/°C or Bp/°C/mmHg of the product
1c	1.5	110	10	**7a**	47	90—95/2[b)] (lit,[6)] 104—106/7.1)
1d	1.5	110	10	**7b**	79	65—67 (lit,[4)] 67)
1e	1.7	110	10	**7c**	77	58—60 (lit,[7)] 60)
1f	1.1	110	10	**7d**	88	35—36 (lit,[8)] 38—39)
1g	1.5	110	10	**7e**	62	90—93/53[b)] (lit,[9)] 94/31)

a) Mol ratio. b) Bath temperature.

the reaction of **1** and **2** in benzene, the yields of the corresponding biphenyls **3** were found to be very low due mainly to the superior reactivity of iodine over benzene to result in the rapid formation of **6**.

$$\underset{\mathbf{1}}{ArNH_2} + \underset{\mathbf{2}}{t\text{-}BuSNO_2} + I_2 \xrightarrow{\text{Benzene}} \underset{\mathbf{6}}{Ar\text{-}I}$$

6a: Ar=*p*-Cl-C_6H_4 **6d**: Ar=*o*-NO_2-C_6H_4
6b: Ar=*p*-MeO-C_6H_4 **6e**: Ar=*p*-Br-C_6H_4
6c: Ar=*p*-NO_2-C_6H_4 **6f**: Ar=*p*-CH_3-C_6H_4

Reactions of various arylamines **1** and **2** in dimethyl disulfide gave the corresponding aryl methyl sulfide (**7**) in good yields in a short reaction time and the results are listed in Table 5. Heating the solution prior to the addition of **2** is essential for the reaction. When the reaction was carried out at room temperature, deamination of arylamines **1** was slow and **2** was consumed by the reaction with dimethyl disulfide and the yields of the aryl methyl sulfides were low.

$$\underset{\mathbf{1}}{ArNH_2} + \underset{\mathbf{2}}{t\text{-}BuSNO_2} \xrightarrow{(CH_3)_2S_2} \underset{\mathbf{7}}{ArSCH_3}$$

7a: Ar=*p*-MeO-C_6H_4 **7d**: Ar=*p*-Br-C_6H_4
7b: Ar=*p*-NO_2-C_6H_4 **7e**: Ar=*p*-CH_3-C_6H_4
7c: Ar=*o*-NO_2-C_6H_4

Formation of nitrogen gas was clearly observed by mass spectrum, divulging the reaction to proceed *via* the $ArN_2^+OH^-$ that rapidly decomposes forming an aryl radical (**10**) which then reacts with the solvent or I_2 to afford the corresponding substitution product. Thiosulfonic *S*-ester **9** was also isolated in this reaction.

$$\underset{\mathbf{2}}{t\text{-}BuSNO_2} \rightleftarrows t\text{-}BuSONO \xrightarrow{\overset{Ar}{:NH_2}\ \mathbf{1}}$$

$$t\text{-}BuSO^- + ArN^+H_2NO \rightarrow t\text{-}BuSOH + ArN_2^+OH^- \rightarrow$$

$$\underset{\mathbf{10}}{Ar\cdot} + N_2 + H_2O + \underset{\mathbf{9}}{1/2\ t\text{-}BuSO_2S\text{-}Bu\text{-}t}$$

When octylamine **11** was treated with **2** under similar conditions, no formation of deaminated product was observed, but *N*-(*t*-butylthio)octylamine (**12**) was obtained in a good yield.

$$\underset{\mathbf{11}}{n\text{-}C_8H_{17}NH_2} + \underset{\mathbf{2}}{t\text{-}BuSNO} \xrightarrow[81\%]{} \underset{\mathbf{12}}{n\text{-}C_8H_{17}NHS\text{-}Bu\text{-}t}$$

Experimental

All the melting points and boiling points were uncorrected. Elemental analyses were carried out by the Chemical Analysis Center at our University. Analytical determinations by GLC were performed on a Hitachi 163 gas chromatograph fitted with the following column (3 mm o.d.× 3 m): 10% SE-30 on Chromosorb W. ^1H-NMR spectra were taken at 60 MHz on a Hitachi R-24 A apparatus. IR spectra were recorded with a Hitachi 215 spectrometer. Mass spectra were recorded with a Hitachi RMU-6M spectrometer. The starting arylamines are all commercial products. Thionitrate **2** was prepared from the corresponding thiol with dinitrogen tetroxide.[1)] Purely isolated deaminated products were used for GLC analyses.

Reactions of Arylamines (1) with Thionitrate (2) in Aromatic Compounds. The following is a typical procedure. *p*-Chloroaniline (**1b**) (637 mg, 5 mmol) and **2** (875 mg, 7 mmol) were refluxed in dry benzene (20 ml) for 6 h. The reaction mixture was concentrated by removing benzene *in vacuo*, and purified by TLC (silica gel, hexane:ether=10:1), affording 569 mg (60%) of 4-chlorobiphenyl (**3b**): mp 75—76 °C (recrystallized from ethanol), (lit,[2b)] 76 °C).

Structures of **3a**—**n** were identified by IR, NMR, and mass spectroscopic data. Melting or boiling points of **3a**—**i** were identical with those of literatures as shown in Table 1. Physical and elemental analytical data of **3j**—**n** are listed in Table 6.

Reaction of Arylamines (1) with Thionitrate (2) in CCl_4 or $CHBr_3$. The following is a typical procedure. The thionitrate **2** (845 mg, 7 mmol) was added for a few minutes to a stirred solution of *p*-nitroaniline (**1d**) (690 mg, 5 mmol) in bromoform (10 ml) at 120 °C. After several minutes, vigorous evolution of nitrogen gas was observed. The solution was further stirred for 40 min at 120 °C. The solution was cooled and the solvent was evaporated *in vacuo*. TLC (silica gel, hexane:ether=10:1) gave 752 mg (75%) of pure *p*-bromonitrobenzene (**5b**).

IR spectra of all the halides in Table 3 were identical with those of commercial authentic samples.

Reactions of Arylamines (1) with Thionitrate (2) in the Presence of Iodine. The following is a typical procedure. *p*-Toluidine (**1g**) (535 mg, 5 mmol) and **2** (675 mg, 5 mmol) were added to a stirred solution of iodine (635 mg, 5 mmol) in dry benzene (20 ml). The solution was refluxed for 17 min. After the solution was cooled, diethyl ether was added to the solution and washed with aq sodium thiosulfate solution to remove iodine. The solution was dried ($MgSO_4$), concentrated, and purified by TLC (silica gel, hexane:ether=10:1) to give 812 mg (74%) of pure *p*-iodotoluene (**6f**).

IR spectra of all the iodides in Table 4 were identical with those of commercial authentic samples.

Reactions of Arylamines (1) with Thionitrate (2) in Dimethyl Disulfide. The following is a typical procedure. The solution of *p*-nitroaniline (**1d**) (690 mg, 5 mmol) in dimethyl disulfide (5 ml) was heated (*ca.* 100 °C) in advance. Then, **2** (1.01 g, 7.5 mmol) was added to the stirred solution

Table 6. Physical and analytical data of compounds **3j**—**n**[a]

Compound	Physical and analytical data
3j	IR (neat): 1472, 842, 750, and 687 cm^{-1}. NMR (CCl$_4$): δ 2.23 (s, 1.5H, C$\underline{H}_3$-),[b] 2.40 (br, s, 1.5H, C$\underline{H}_3$-),[c] and 7.00—7.60 (m, 9H, ring protons). Found: C, 92.55; H, 7.12%. Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19%.
3k	IR (neat): 1590, 1510, 1340, 848, 740, and 693 cm^{-1}. NMR (CCl$_4$): δ 2.23 (s, 1.7H, C$\underline{H}_3$-), 2.40 (s, 1.3H, C$\underline{H}_3$-), 7.00—7.73 (m, 6H, ring protons), and 7.73—8.20 (m, 2H, ring protons). Found: C, 72.93; H, 5.17; N, 6.75%. Calcd for $C_{13}H_{11}O_2N$: C, 73.23; H, 5.20; N, 6.57%.
3l	IR (neat): 1512, 1348, 1103, 850, 745, and 690 cm^{-1}. NMR (CCl$_4$): δ 7.14—7.70 (m, 6H), and 7.70—8.17 (m, 2H). Found: C, 61.42; H, 3.80; N, 5.95%. Calcd for $C_{12}H_8ClO_2N$: C, 61.69, H, 3.45, N, 5.99%.
3m	IR (neat): 1510, 1350, 843, 780, 743, and 700 cm^{-1}. NMR (CCl$_4$): δ 2.03 (s, 1.6H, C$\underline{H}_3$-), 2.28 (s, 1.4H, C$\underline{H}_3$-), and 7.4—8.0 (m, 8H, ring protons). Found: C, 72.85; H, 5.22; N, 6.82%. Calcd for $C_{13}H_{11}O_2N$: C, 73.23; H, 5.20; N, 6.57%.
3n	IR (neat): 1508, 1345, 812, 742, 700 cm^{-1}. NMR (CCl$_4$): δ 2.30 (s, 3H, C$\underline{H}_3$-), and 6.45—8.10 (m, 8H, ring protons). Found: C, 72.99; H, 5.25; N, 6.90%. Calcd for $C_{13}H_{11}O_2N$: C, 73.23; H, 5.20; N, 6.57%.

a) A mixture of its positional isomers. b) Ortho isomer. c) Meta and para isomers.

in a few minutes. The solution was stirred further for 10 min, then cooled and the solvent was evapolated *in vacuo*. Purification by TLC (silica gel, hexane:ether=20:1) gave 664 mg (79%) of methyl *p*-nitrophenyl sulfide (**7b**): mp 65—67 °C (recrystallized from ethanol), (lit,[4] 67 °C).

Structures of **7a**—**e** were identified by IR, NMR and mass spectroscopic data. Melting or boiling points of **7a**—**e** were identical with those of literatures as shown in Table 5.

N-*(*t-*Butylthio)octylamine (**12**).* Thionitrate **2** (875 mg, 7 mmol) was added in a few minutes to a stirred solution of amine **11** (648 mg, 5 mmol) in benzene (10 ml). The solution was refluxed for 10 min, cooled, and then concentrated *in vacuo*. The mixture was purified by TLC (silica gel, hexane), to give 885 mg (81%) of **12** as a colorless oil, bp (bath temp) 85—95 °C/533 Pa. IR (neat): 1460, 1135, and 910 cm^{-1}. NMR (CCl$_4$): δ=0.6—2.0 (m, 15H, C$\underline{H}_3$-(C$\underline{H}_2$)$_6$-), 1.17 (s, 9H, *t*-Bu), 2.36 (br, 1H, N$\underline{H}$), and 2.86 (br, 2H, -C$\underline{H}_2$-NH). MS (70 eV), *m/e* (rel intensity), 217 (36, M$^+$), 160 (39, *n*-$C_8H_{17}NHS^+$), 128 (16, *n*-$C_8H_{17}NH^+$), and 57 (100, *t*-Bu$^+$).

Found: C, 65.95, H, 12.41; N, 6.32%. Calcd for $C_{12}H_{17}NS$: C, 66.29; H, 12.52; N, 6.44%.

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