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# A Convenient Method for the Preparation of Primary Amines by the Use of Bisbenzenesulfenimide and Bis-*p*-chlorophenylsulfenimide

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A convenient method for the preparation of primary amines by the use of bisarylsulfenimide has been established. Primary amines were obtained in good yields under mild reaction conditions by treating *N*-substituted bisarylsulfenimides with hydrochloric acid or mercaptan. The *N*-substituted bisarylsulfenimides were prepared in good yields by the reactions of lithium bisarylsulfenimide with alkyl halides or alkyl *p*-toluenesulfonates or by the addition reactions of bisarylsulfenimide to olefinic compounds.

It is well known that the Gabriel synthesis[1)] is the most general method for the selective preparation of primary amino compounds. However, there is a disadvantage in the method for the preparation of amino compounds with nitrile, ester, amide or carbonyl groups in the same molecule. These functional groups are hydrolyzed to give carboxylic acid or they react with hydrazine at the same time when phthaloyl group is removed from *N*-substituted phthalimide, an intermediate of the Gabriel synthesis.

In the present study, a new route for the convenient preparation of various primary amines from bisarylsulfenimides, such as bisbenzenesulfenimide or bis-*p*-chlorophenylsulfenimide, and alkyl halides or *p*-toluenesulfonates, or olefinic compounds was investigated with the consideration that the sulfur-nitrogen bond of *N*-substituted bisarylsulfenimide is easily cleaved by hydrochloric acid or mercaptan to afford the corresponding primary amine together with sulfenyl chloride or di-

1) a) S. Gabriel, Ber., **20**, 2224 (1887). b) M. S. Gibson and R. W. Bradshaw, *Angew. Chem.*, **80**, 986 (1968).

TABLE 1. YIELDS OF ALKYLAMINES BY THE REACTIONS OF LITHIUM BISBENZENESULFENIMIDE WITH ALKYL *p*-TOLUENESULFONATES OR ALKYL HALIDES

| RX (III) | $RNH_2$(V)[a] $RNHCONHC_6H_5$ | | Formula | Calcd | | | Found | | |
|---|---|---|---|---|---|---|---|---|---|
| | Yield (%) | mp (°C) | | C | H | N | C | H | N |
| *n*-$C_4H_9OTs$ | 78 | 128—129 | $C_{14}H_{16}ON_2$ | 68.72 | 8.39 | 14.57 | 68.74 | 8.19 | 14.85 |
| *n*-$C_8H_{17}OTs$ | 86 | 74— 75 | $C_{15}H_{24}ON_2$ | 72.54 | 9.74 | 11.28 | 72.28 | 9.69 | 11.20 |
| *sec*-$C_4H_9OTs$ | 64 | 145—149 | $C_{14}H_{16}ON_2$ | 68.72 | 8.39 | 14.57 | 68.54 | 8.21 | 14.35 |
| *sec*-$C_8H_{17}OTs$ | 63 | 94— 97 | $C_{15}H_{24}ON_2$ | 72.54 | 9.74 | 11.28 | 72.70 | 9.49 | 11.30 |
| *n*-$C_4H_9Br$ | 60 | 127—128.5 | | | | | | | |
| *n*-$C_8H_{17}Br$ | 62 | 74— 74.5 | | | | | | | |
| *sec*-$C_8H_{17}Br$ | 17 | 94— 96 | | | | | | | |
| $C_6H_5CH_2Br$ | 86 | 169 | $C_{14}H_{14}ON_2$ | 74.31 | 6.24 | 12.38 | 74.21 | 6.25 | 12.48 |
| *p*-$NO_2C_6H_4CH_2Br$ | 67 | — | $C_7H_9N_2O_2Cl$[b] | 44.58 | 4.81 | 14.85 | 44.72 | 4.56 | 15.13 |

a) The yields of amines were determined from the amounts of *N*-alkyl-*N'*-phenylureas.
b) *p*-Nitrobenzylamine was isolated and identified as its hydrochloride.

TABLE 2. YIELDS OF ALKYLAMINES BY THE REACTIONS OF LITHIUM BIS-*p*-CHLOROPHENYLSULFENIMIDE WITH ALKYL *p*-TOLUENESULFONATES OR ALKYL HALIDES

| RX [III] | $(p\text{-}ClC_6H_4S)_2NR$ [IV] | | RNH [V] Yield (%) |
|---|---|---|---|
| | Yield (%) | mp (°C) | |
| $C_6H_5CH_2Br$ | 79 | 89—90 | 100 |
| *p*-$NO_2C_6H_4CH_2Br$ | 86 | 131 | 91 |
| $C_2H_5O_2CCH_2CH_2OTs$ | 57[b] | 45—46 | |
| *n*-$C_4H_9OTs$ | — | | 80 |
| *n*-$C_8H_{17}OTs$ | — | | 85 |
| *n*-$C_4H_9Br$ | — | | 61 |
| *n*-$C_8H_{17}Br$ | — | | 54 |

a) These compounds were isolated as their hydrochlorides or picrates to give satisfactory purity.
b) In this case, bis-*p*-chlorophenylsulfenimide was isolated in 8% yield.

sulfide.

It was shown that primary amines are obtained in good yields under mild reaction conditions by treating *N*-substituted bisbenzenesulfenimide with hydrochloric acid or mercaptan.[2] The *N*-substituted bisbenzenesulfenimides are successfully derived from lithium bisbenzenesulfenimide and alkyl halides or alkyl *p*-toluenesulfonates. As an example, benzylamine was obtained in 86% yield by treating *N*-benzyl bisbenzenesulfenimide formed by the reaction of bisbenzenesulfenimide with *n*-butyllithium in tetrahydrofuran at −20°C for 5 min, and the subsequent reaction with benzyl bromide in tetrahydrofuran for 5 hr with 3 N hydrochloric acid at room temperature for 3 hr. The yield of the amine was determined from the amount of *N*-benzyl-*N'*-phenylurea obtained by the subsequent reaction with phenyl isocyanate.

$$\underset{[I]}{(ArS)_2NH} + n\text{-BuLi} \longrightarrow \underset{[II]}{(ArS)_2NLi}$$

$$[II] + RX \longrightarrow \underset{[III]}{} \underset{[IV]}{(ArS)_2NR} \xrightarrow{HCl} \underset{[V]}{RNH_2} + 2ArSCl$$

$$Ar = C_6H_5,\ p\text{-}ClC_6H_4$$

Similarly, various primary amines were prepared from alkyl halides or alkyl *p*-toluenesulfonates and lithium bisbenzenesulfenimide or lithium bis-*p*-chlorophenylsulfenimide. (see Tables 1 and 2).

*N*-Substituted bisbenzenesulfenimides could not be isolated as pure substances because the imides decomposed on distillation or on silica gel column chromatography. On the other hand, some *N*-substituted bis-*p*-chlorophenylsulfenimide was obtained as crystalline; for example, *N*-benzyl bis-*p*-chlorophenylsulfenimide was obtained in 79% yield as a white crystalline, mp 90°C, by treating lithium bis-*p*-chlorophenylsulfenimide formed by the reaction of bis-*p*-chlorophenylsulfenimide with *n*-butyllithium at −50°C in tetrahydrofuran, with benzyl bromide at room temperature in tetrahydrofuran for 5 hr. Treatment of *N*-benzyl bis-*p*-chlorophenylsulfenimide with dry hydrogen chloride in dry ether gave benzylamine and *p*-chlorophenylsulfenyl chloride in quantitative yields.

Bisbenzenesulfenimide was obtained instead of the corresponding condensation product when lithium bisbenzenesulfenimide was allowed to react with β-carbethoxyethyl *p*-toluenesulfonate. Formation of bisbenzenesulfenimide and acrylonitrile in the above reaction may be explained by considering the abstraction of an acidic hydrogen atom on the α-carbon atom of β-carbethoxyethyl *p*-toluenesulfonate by lithium bisbenzenesulfenimide. On the other hand, lithium bis-*p*-chlorophenylsulfenimide, the acidity of which is higher than that of bisbenzenesulfenimide, reacted with the *p*-toluenesulfonate to give *N*-β-carbethoxyethyl bis-*p*-chlorophenylsulfenimide in 57% yield.

$$(ArS)_2NLi + C_2H_5O_2CCH_2CH_2OTs \longrightarrow \begin{cases} (ArS)_2NH + CH_2{=}CHCO_2C_2H_5 \\ (ArS)_2NCH_2CH_2CO_2C_2H_5 \end{cases}$$

It was found that amines with nitrile group in the same molecule, olefinic amines or highly water-soluble amines were also successfully prepared along with disulfide when the corresponding *N*-substituted bisarylsulfenimide are treated with mercaptan. As an example, β-cyanoethylamine was obtained in 64%

$$\underset{[II]}{(ArS)_2NLi} + \underset{[III]}{RX} \longrightarrow \underset{[IV]}{(ArS)_2NR}$$

$$\underset{[IV]}{(ArS)_2NR} + 2\underset{[VI]}{R'SH} \longrightarrow \underset{[V]}{RNH_2} + 2RSSR'$$

2) T. Mukaiyama and T. Taguchi, *Tetrahedron Lett.*, **1970**, 3411.

Table 3. Reactions of *N*-substituted bisarylsulfenimides with thiols

| $(ArS)_2NH$ [I] | RX [III] | R'SH [VI] | Reaction Conditions | $RNH_2$ [V] Yield (%) | $RNH_2$ [V] Picrate mp (°C) |
|---|---|---|---|---|---|
| $(C_6H_5S)_2NH$ | $CNCH_2CH_2OTs$ | $C_2H_5SH$ | E.[a] r.temp. 30 min | 64 | 176 —180 |
| | $CH_2=CHCH_2I$ | $C_2H_5SH$ | E. r.temp. 10 hr | 73 | 141 —142 |
| | $CH_3OCH_2CH_2OTs$ | $C_6H_5SH$ | E. r.temp. 1 hr | 74 | 144.5—145.5 |
| |  | $C_6H_5SH$ | E. r.temp. 1 hr | 46 | 133 —134.5 |
| $(p\text{-}ClC_6H_4S)_2NH$ | $CNCH_2CH_2OTs$ | $C_6H_5SH$ cat. $ZnCl_2$[d] | THF[b] r.temp. 3 hr | 88[e] | 178 —178.5 |
| | $CH_2=CHCH_2I$ | $C_6H_5SH$ cat. $ZnCl_2$ | THF r.temp. 3 hr | 76 | 138 —141 |
| | $C_6H_5CH=CHCH_2Br$ | $C_6H_5SH$ cat. $ZnCl_2$ | THF–MeOH–AcOH[c] r.temp. 10 hr | 66[e] | 182.5—183 |

a) E: ether b) THF: tetrahydrofuran c) THF: MeOH:AcOH (10:10:1 v/v) d) $ZnCl_2$ was used 5% mol/mol of the imide. e) The yields of amines were determined from *N*-substituted bis-*p*-chlorophenylsulfenimide.

yield as its picrate by the reaction of lithium bisbenzenesulfenimide with β-cyanoethyl *p*-toluenesulfonate in tetrahydrofuran at room temperature for 10 hr and the subsequent treatment with 2 molar equivalents of ethanethiol in ether at room temperature for 1 hr.

Similarly, β-cyanoethylamine was obtained in 88% yield when *N*-β-cyanoethyl bis-*p*-chlorophenylsulfenimide was allowed to react with 2 molar equivalents of benzenethiol in the presence of a catalytic amount of zinc chloride at room temperature in tetrahydrofuran for 3 hr.

On the other hand, *N*-β-cyanoethyl bis-*p*-chlorophenylsulfenimide did not react with benzenethiol even after they were refluxed in tetrahydrofuran for 2 hr.

In a similar way, allylamine, cinnamylamine, β-methoxyethylamine and tetrahydrofurfurylamine were prepared in good yields by the reactions of *N*-substituted bisarylsulfenimides formed from lithium bisarylsulfenimide and alkyl halides or alkyl *p*-toluenesulfonates with mercaptan (see Table 3).

The effects of the solvents on the condensation reactions of lithium bisbenzenesulfenimide with alkyl *p*-toluenesulfonates were studied. It was found that tetrahydrofuran and dimethoxyethane are suitable for this reaction. When diethyl ether or anisole was used as the solvent, diminution in the yield of amine and increase in the yield of unsymmetrical sulfide were observed. This may be due to the rapid decomposition of lithium bisbenzenesulfenimide in comparison with the above mentioned condensation reaction (see Table 4).

The reaction of bisbenzenesulfenimide with *n*-butyllithium in tetrahydrofuran at room temperature for 7 hr, followed by the addition of isoamyl bromide in tetrahydrofuran at room temperature for 5 hr, resulted in the formation of isoamyl phenyl sulfide and diphenyl disulfide in 71% and 67% yields, respectively. This may be explained by considering the decomposition of lithium bisbenzenesulfenimide into lithium thiophenolate and phenylthionitrene. The lithium thiophenolate thus formed reacts with isoamyl bromide to give isoamyl phenyl sulfide and the phenylthionitrene further decomposes to nitrogen and diphenyl disulfide as shown below.

$$(C_6H_5S)_2NH + n\text{-BuLi} \longrightarrow [(C_6H_5S)_2NLi]$$

$$\downarrow$$

$$C_6H_5SLi + [:NSC_6H_5]$$

$$\downarrow i\text{-}C_5H_{11}Br \qquad \downarrow$$

$$i\text{-}C_5H_{11}SC_6H_5 \quad C_6H_5SSC_6H_5 + N_2$$

Table 4. Solvent effect

| Solvent | ROTs | $RNH_2$ Yield (%) | $RSC_6H_5$ Yield (%) |
|---|---|---|---|
| Tetrahydrofuran | $n\text{-}C_8H_{17}OTs$ | 86 | — |
| Dimethoxyethane | $n\text{-}C_8H_{17}OTs$ | 73 | — |
| Ether | $n\text{-}C_4H_9OTs$ | 15 | 64 |
| Anisole | $n\text{-}C_4H_9OTs$ | 19 | 74 |

It was also established that primary amines are successfully prepared from bisarylsulfenimide and olefinic compounds. The addition reaction of bisbenzenesulfenimide to acrylonitrile proceeded smoothly in tetrahydrofuran at room temperature in the presence of a catalytic amount of trimethylbenzylammonium hydroxide (Triton B), and β-aminopropionitrile was obtained in 91% yield by treating the adduct with 2 molar equivalents of ethanethiol in ether at room temperature for 1 hr.

$$(C_6H_5S)_2NH + CH_2=CHX \longrightarrow (C_6H_5S)_2NCH_2CH_2X$$
$$\text{[VII]} \qquad\qquad \text{[VIII]}$$

$$\text{[VIII]} + 2RSH \longrightarrow NH_2CH_2CH_2X + 2C_6H_5SSR$$

Similarly, ethyl β-aminopropionate, β-aminoethyl methyl ketone and β-aminopropionamide were obtained

Table 5. Yields of amines from bisbenzenesulfenimide and olefinic compounds

| Olefinic Compounds [VII] | Amines [V] Yield (%) | Amines [V] Picrate mp (°C) |
|---|---|---|
| $CH_2=CHCN$ | 91 | 179 |
| $CH_2=CHCO_2C_2H_5$ | 74 | 76—77 |
| $CH_2=CHCOCH_3$ | 38 | 127.5—129 |
| $CH_2=CHCONH_2$ | 8 | 149 —150 |

from bisbenzenesulfenimide and the corresponding olefinic compounds (see Table 5).[3]

## Experimental

*Synthesis of Bis-*p*-chlorophenylsulfenimide.* Into 1000 m*l* of ether solution saturated with dry ammonia, *p*-chlorophenylsulfenyl chloride (51.0 g, in 150 m*l* of ether) was added dropwise under stirring at a temperature below −5°. The reaction mixture was stirred for 2 hr at −5—0°C. After the resulting precipitate, ammonium chloride, was filtered and washed with 100 m*l* of tetrahydrofuran, the filtrate was evaporated under reduced pressure and a crystalline precipitate was obtained. Recrystallization from benzene gave bis-*p*-chlorophenylsulfenimide, 27.5 g (66%), mp 137—140°C (decomp.).

Found: C, 47.76; H, 3.29; N, 4.76; S, 21.42%. Calcd for $C_{12}H_9NS_2Cl_2$: C, 47.70; H, 3.00; N, 4.64; S, 21.18%.

*Preparation of Alkylamines from Lithium Bisarylsulfenimide (IIa and IIb) and Alkyl Halides or Alkyl* p-*Toluenesulfonates. General Procedure*: *Method A*: A solution of alkyl halide or alkyl *p*-toluenesulfonate (0.005 mol) in tetrahydrofuran was added into a solution of lithium bisarylsulfenimide formed from bisarylsulfenimide (0.005 mol) and *n*-butyllithium (0.005 mol) in tetrahydrofuran at −20—−50°C under stirring. The reaction mixture was stirred at −20—0°C for 2 hr and at room temperature for additional 2—8 hr. After removal of the solvent, the residue was stirred in a mixture of ether (20 m*l*) and 3N hydrochloric acid (10 m*l*) for 10 min—3 hr at room temperature.[4] The aqueous solution extracted from the reaction mixture was concentrated to dryness. The residue was dissolved in an aqueous solution of 20% sodium hydroxide (30 m*l*) and extracted with 50 m*l* of ether four times. The ether extract was dried over anhydrous sodium sulfate.

*Method A-1*: Into the ether extract phenyl isocyanate (0.60 g, 0.005 mol) was added and stirring was continued for 30 min. After removal of ether, a crystalline precipitate was obtained and washed with petroleum ether. Recrystallization from ethanol gave *N*-alkyl-*N'*-phenylurea.

*Method A-2*: Into the ether extract picric acid (1.15 g, 0.005 mol) was added and ether was removed by evaporation. The picrate of the corresponding alkyl amine was obtained by recrystallization from ethanol or a mixture of ethanol and benzene. By means of either *Method A-1* or *Method A-2*, *n*-butylamine, *n*-octylamine, *sec*-butylamine, *sec*-octylamine benzylamine and *p*-nitrobenzylamine were prepared. The results are summarized in Tables 1 and 2.

*Method B*: A solution of alkyl halide or alkyl *p*-toluenesulfonate (0.005 mol) in tetrahydrofuran was added under stirring into a solution of lithium bisarylsulfenimide, formed from bisarylsulfenimide (0.005 mol) and *n*-butyllithium (0.005 mol) in tetrahydrofuran at −20—−50°C. The reaction mixture was stirred at −20—0°C for 2 hr and at room temperature for additional 2—8 hr. After removal of the solvent, the residue was poured into 30 m*l* of water and the mixture was extracted with ether.[4] The extract was dried over anhydrous sodium sulfate and into the solution excess mercaptan (0.015 mol) was added under stirring. After stirring at room temperature for 30 min—3 hr, a yellowish precipitate was obtained by the addition of picric acid (1.15 g, 0.005 mol), followed by evaporation of the solvent. Recrystallization from ethanol gave the corresponding alkylamine as its picrate. By means of *Method B*, β-cyanoethylamine, β-methoxyethylamine, tetrahydrofurfurylamine, allylamine and cinnamylamine were obtained as their picrates. The results are summarized in Table 3.

*Preparation of β-Cyanoethylamine from Bisbenzenesulfenimide and Acrylonitrile.* Into a mixture of bisbenzenesulfenimide (1.17 g, 0.005 mol) and acrylonitrile (0.27 g, 0.005 mol) in tetrahydrofuran, a catalytic amount of trimethylbenzylammonium hydroxide (Triton B) was added under stirring. After stirring at room temperature for 30 min, ethanethiol (0.93 g, 0.015 mol) was added and the mixture was stirred at 0°C for 1 hr. After removal of the solvent, a yellowish precipitate was obtained by the addition of picric acid (1.15 g, 0.005 mol) to the residue. Recrystallization from ethanol gave the picrate of β-cyanoethylamine, 1.32 g, (91%), mp 179°C.

Found: C, 36.13; H, 3.03; N, 23.41%. Calcd for $C_9H_9O_7N_5$: C, 36.62; H, 2.98; N, 23.47%.

Similarly, ethyl β-aminopropionate, β-aminoethyl methyl ketone and β-aminoacrylamide were obtained by the reactions of bisbenzenesulfenimide with ethyl acrylate, methyl vinyl ketone and acrylamide, respectively. The results are listed in Table 5.

3) When bis-*p*-chlorophenylsulfenimide was treated with acrylonitrile in tetrahydrofuran at room temperature for 20 hr in the presence of a catalytic amount of Triton B, *N*-β-cyanoethyl bis-*p*-chlorophenylsulfenimide was obtained only in 18% yield.

4) When alkyl *p*-toluenesulfonate was used in place of alkyl halides, lithium *p*-toluenesulfonate precipitated by the addition of ether was removed by filtration and washed with ether.