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A CONVENIENT METHOD FOR THE PREPARATION OF PRIMARY ALKYLAMINES BY THE USE OF BISBENZENESULFENIMIDE

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The Gabriel Synthesis[1)] is the most general method for the selective preparation of primary amino compounds, however, this method has a disadvantage in the preparation of amino compounds which have nitrile, ester, or amide group in the same molecule. In these cases, the latter groups are hydrolyzed to give carboxylic acid at the same time when the 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 primary alkylamines from bisbenzenesulfenimide[2)] and alkyl halides or alkyl p-toluenesulfonate was investigated with the consideration that the sulfur-nitrogen bond of N-alkylsubstituted bisbenzenesulfenimide is easily cleaved by hydrochloric acid or mercaptans to afford the corresponding primary amine together with benzenesulfenylchloride or disulfide.

It was found that various primary alkylamines were obtained in good yields by treating N-alkyl bisbenzenesulfenimide with 3N hydrochloric acid ; for example, n-octylamine was produced in 86% yield by treating N-n-octyl bisbenzenesulfenimide, formed by the reaction of bisbenzenesulfenimide with n-butyllithium in tetrahydrofuran at -20°C for 5 minutes and the subsequent reaction with n-octyl p-toluenesulfonate in tetrahydrofuran for 5 hours, with 3N hydrochloric acid at room temperature for 3 hours. The yield of the amine was determined from the amount of N-n-octyl-N'-phenylurea obtained by the subsequent reaction with phenyl isocyanate.

$$(C_6H_5S)_2NH + n\text{-}C_4H_9Li \longrightarrow [(C_6H_5S)_2NLi] \xrightarrow{n\text{-}C_8H_{17}OTs} [(C_6H_5S)_2NC_8H_{17}\text{-}n]$$

$$\xrightarrow{HCl} n\text{-}C_8H_{17}NH_2HCl \quad + \quad 2[C_6H_5SCl]$$

$$Ts = SO_2C_6H_4CH_3\text{-}p$$

Similarly, various aliphatic primary amines were prepared from alkyl p-toluenesulfonates or alkyl bromides and lithium bisbenzenesulfenimide (see Table I).

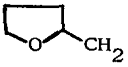
Table I

The Yields of Alkylamines by the Reactions of Lithium Bisbenzenesulfenimide with Alkyl Bromides or Alkyl p-Toluenesulfonates

R-Br	RNH_2 Yield %	ROTs	RNH_2 Yield %
n-C_4H_9	60	n-C_4H_9	78
n-C_8H_{17}	62	n-C_8H_{17}	86
$C_6H_5CH_2$	86	sec-C_4H_9	64
sec-C_4H_9	19	sec-C_8H_{17}	63
sec-C_8H_{17}	17	$CH_3OCH_2CH_2$	42

Further, it was found that amines, which are very soluble in water, were also successfully obtained along with diphenyl disulfide, when N-substituted bisbenzenesulfenimide is treated with benzenethiol ; for example, β-methoxyethylamine is obtained in 74% yield as its picrate by the reaction of lithium bisbenzenesulfenimide with β-methoxyethyl p-toluenesulfonate in tetrahydrofuran at -20°C for 5 hours and the subsequent addition of 2 molar equivalents of benzenethiol in ether at room temperature.

$$(C_6H_5S)_2NR + 2\ C_6H_5SH \longrightarrow RNH_2 + 2\ C_6H_5SSC_6H_5$$

R	RNH_2	mp °C	Analysis					
	Yield %	RNH_2Picrate	C	H	N	C	H	N
$CH_3OCH_2CH_2$	74	144.5-145.5	35.78	3.71	18.50	35.53	3.98	18.42
	46	133-134.5	40.34	4.35	17.00	40.00	4.27	16.97

The results of the condensation reaction of lithium bisbenzenesulfenimide with alkyl p-toluenesulfonate in various solvents showed that tetrahydrofuran and dimethoxyethane are suitable for this reaction. On the other hand, when diethyl ether or anisole was used as the solvent, the decomposition of lithium bisbenzenesulfenimide took place faster than the above mentioned condensation reaction, which causes the diminution in the yield of amine and conversely the increase in the yield of unsymmetrical sulfide.

Table II

Solvent Effect*

Solvent	ROTs	RNH_2 Yield %	RSC_6H_5 Yield %
tetrahydrofuran	$n\text{-}C_8H_{17}$	86	—
dimethoxyethane	$n\text{-}C_8H_{17}$	73	—
ether	$n\text{-}C_4H_9$	15	64
anisole	$n\text{-}C_4H_9$	19	74

*The reaction conditions are the same with that described when tetrahydrofuran was used as solvent.

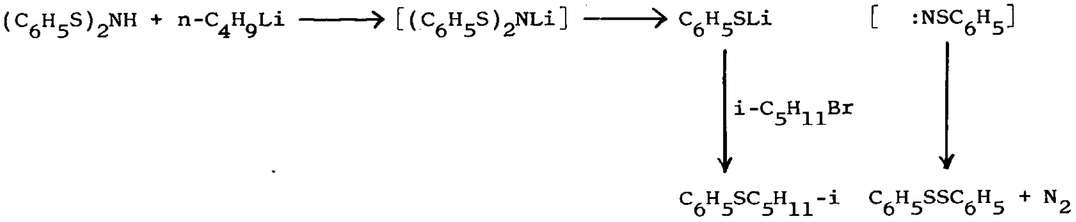
Further, it was found that the addition reaction of bisbenzenesulfenimide to acrylonitrile proceeded in tetrahydrofuran at room temperature smoothly in the presence of a catalytic amount of trimethylbenzylammonium hydroxide (Triton B) and β-aminopropionitrile[3)] was obtained in 91% yield by treating the adduct with 2 molar equivalents of ethanethiol in ether at room temperature for 1 hour. Similarly, ethyl β-aminopropionate was obtained in 74% yield from bisbenzenesulfenimide and ethyl acrylate.

$$(C_6H_5S)_2NH + CH_2{=}CH\text{-}X \xrightarrow{\text{Triton B}} [(C_6H_5S)_2NCH_2CH_2\text{-}X]$$

$$[(C_6H_5S)_2NCH_2CH_2\text{-}X] + 2\ C_2H_5SH \longrightarrow NH_2CH_2CH_2\text{-}X + 2\ C_6H_5SSC_2H_5$$

$$X{=}CN\ ,\ CO_2C_2H_5$$

It is also noted that the reaction of bisbenzenesulfenimide with n-butyllithium in tetrahydrofuran at room temperature for 7 hours, followed by the addition of isoamyl bromide in tetrahydrofuran at room temperature for 5 hours afforded isoamylphenyl sulfide and diphenyl disulfide in 71% and 67% yield, respectively. This results may be explained by considering the decomposition of the intermediate, lithium bisbenzenesulfenimide, into lithium thiophenolate and phenylthionitrene(4). The lithium thiophenolate thus formed reacts with isoamyl bromide to give isoamylphenyl sulfide and the phenylthionitrene further decomposes to nitrogen and diphenyl disulfide as sketched below.



$$\begin{tikzcd}(C_6H_5S)_2NH + n\text{-}C_4H_9Li \arrow[r] & {[(C_6H_5S)_2NLi]} \arrow[r] & C_6H_5SLi \arrow[d, "i\text{-}C_5H_{11}Br"] & {[\ :NSC_6H_5]} \arrow[d] \\ & & C_6H_5SC_5H_{11}\text{-}i & C_6H_5SSC_6H_5 + N_2\end{tikzcd}$$

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The sulfenimide was recrystallized from benzene-petroleumether, 129-130°C (dec.), yield 60%. Anal. Calcd. for $C_{12}H_{11}NS_2$: C, 61.80; H, 4.75; N, 6.01; S, 27.44. Found : C, 62.10; H, 5.05; N, 6.30; S, 27.72.

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