

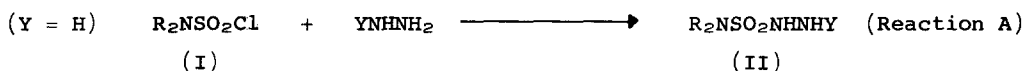
FREE RADICAL REACTIONS BETWEEN SUBSTITUTED
HYDRAZINES AND SULPHAMYL HALIDES

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The reaction of dimethyl (and diethyl) sulphamyl chlorides with hydrazine (1) yields, as expected, the corresponding sulphamyl hydrazides thus :



We have found that this reaction is not general and that depending upon the nature of Y, any of three different reactions can take place.

With benzhydrazide (Y = C₆H₅CO) and 2-hydrazinopyridine (Y = 2-pyridyl) reaction of type (A) was indeed realized. A typical run involved maintaining a mixture of 2-hydrazinopyridine, dimethyl sulphamyl chloride and triethylamine (all present in equimolar quantities) in benzene solution for 24 hours at ambient temperatures, followed by maintaining the mixture at 50° for one hour. Workup yielded 1-(2'-pyridyl)-4,4-dimethylsulphamyl hydrazide, ((II), Y = 2-pyridyl, R = CH₃) in 94% yield. The other successful reactions in this category are summarized in Table I.

These reactions of type (A) represent normal nucleophilic displacements at sulphamyl sulphur. The other two reactions encountered appear to be homolytic. The first of these was realised when the hydrazine component used was p-chlorophenylhydrazine, methylhydrazine or 1,1-dimethylhydrazine. The reaction conditions involved refluxing a benzene solution of two equivalents of the substituted hydrazine with one equivalent of the substituted sulphamyl chloride for 4 hours, when the only identifiable materials isolated, in varying yields, were the corresponding tetrasubstituted sulphamides. Table (II) summarizes the data obtained. The reaction concerned may be summarized thus:



and we outline our proposed mechanism for it in Figure 1.

We felt that the high efficiency with 1,1-dimethylhydrazine present might

TABLE I
FORMATION OF SULPHAMYL HYDRAZIDES

<u>Sulphamyl Halide</u>	<u>Hydrazine</u>	<u>Product</u> ^a	<u>M.P.</u>
<u>I, R =</u> (CH ₃) ₂ N ^b	C ₆ H ₅ CONHNH ₂	C ₆ H ₅ CONHNHSO ₂ N(CH ₃) ₂	-87-188°
(C ₂ H ₅) ₂ N ^b	C ₆ H ₅ CONHNH ₂	C ₆ H ₅ CONHNHSO ₂ N(C ₂ H ₅) ₂	^c 154-155°
C ₄ H ₈ NO ^{b, d}	C ₆ H ₅ CONHNH ₂	C ₆ H ₅ CONHNHSO ₂ C ₄ H ₈ NO ^d	^e 139°
(C ₂ H ₅) ₂ N ^f	C ₅ H ₄ N ^g -NHNH ₂	C ₅ H ₄ N ^g -NHNHSO ₂ N(C ₂ H ₅) ₂	^c 153-155°
C ₄ H ₈ NO ^{f, d}	C ₅ H ₄ N ^g -NHNH ₂	C ₅ H ₄ N ^g -NHNHSO ₂ C ₄ H ₈ NO ^d	^e 139°

^a Yields were essentially quantitative, (i.e. between 93 and 95%). ^b Reaction conditions : mixture in chloroform solution, refluxed at 92° for 4 hrs. . A hydrazine : halide ratio of 1 : 1 was used. ^{c, e} The similarity in M.Ps. is coincidental, both samples depress in M.P. when mixed. ^d C₄H₈NO represents N-morpholinyl. ^f Reaction conditions : mixture in benzene solution, 1 equivalent of triethylamine present, 24 hrs. at room temp., 1 hr. at 50°. ^g C₅H₄N represents 2-pyridyl.

TABLE II
Tetrasubstituted Sulphamide Formation

<u>Halide</u>	<u>Hydrazine</u>	<u>Product</u>	<u>M.P.</u>	<u>Yield %</u>
(CH ₃) ₂ NSO ₂ Cl	p-ClC ₆ H ₄ NHNH ₂	(CH ₃) ₂ NSO ₂ N(CH ₃) ₂	75-77°	26
C ₄ H ₈ NO-SO ₂ Cl ^a	p-ClC ₆ H ₄ NHNH ₂	C ₄ H ₈ NO-SO ₂ -C ₄ H ₈ NO ^a	140-141°	10
(CH ₃) ₂ NSO ₂ Cl	CH ₃ NHNH ₂	(CH ₃) ₂ NSO ₂ N(CH ₃) ₂	75-77°	55
(CH ₃) ₂ NSO ₂ Cl	(CH ₃) ₂ N-NH ₂	(CH ₃) ₂ NSO ₂ N(CH ₃) ₂	75-77°	95

^a C₄H₈NO represents N-morpholinyl.

perhaps be due to the intervention of another reaction, that is oxidation of the hydrazine component was occurring together with homolysis of the halide and incorporation of hydrazine-derived radicals into the product, (a scheme described in Figure 2). We verified this using 1-phenyl-1-methyl hydrazine as the hydrazine component when the following process occurred (via the formation of C₆H₅-N-CH₃ radical) with the formation of the

1-(C₆H₅)-1,3,3-trimethylsulphamide in 51% yield.

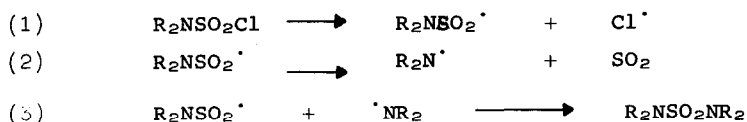
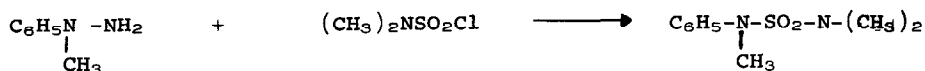


Figure 1.

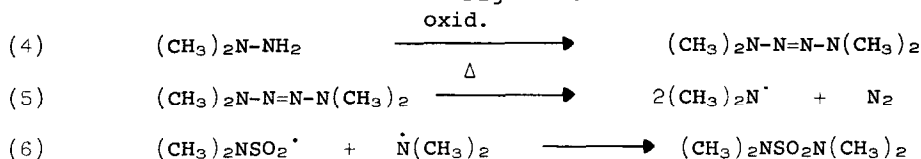


Figure 2.

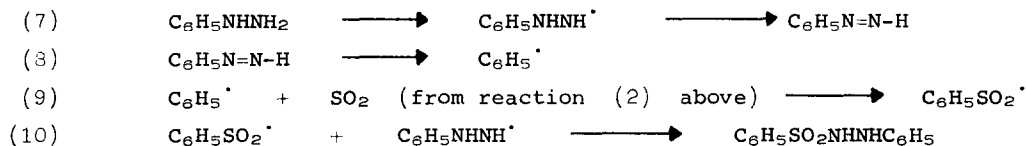
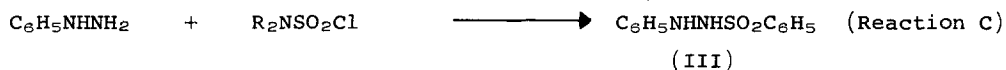


Figure 3.

The third and most surprising reaction was realised when phenylhydrazine itself was used as reagent, the reaction observed being written thus :



A typical experimental run involved maintaining a solution of three equivalents of phenylhydrazine and one equivalent of dimethylsulphamyl chloride in dry benzene solution for 24 hours at room temperature, followed by 1 hour at 50°. Filtering off a 98% yield of phenylhydrazine hydrochloride and evaporation of the solution yielded a 90% yield of N-phenyl-2-benzene-sulphonylhydrazide (III) m.p. 154°, reported m.p. 155° (2). We also prepared this unambiguously from phenylhydrazine and benzenesulphonyl chloride (2). Table III describes some of the other runs performed on this reaction.

The mechanism of the reaction (reaction C) we have outlined in Figure

3, (for steps 7 and 8 in this sequence compare Hardie and Thomson (3)). We have examined the mechanism of this reaction C further using tracer techniques. A sample of radiolabelled phenylhydrazine hydrochloride ($\mu\text{-C}^{14}$) with specific activity 4.138×10^5 cpm/m.mole (4) was prepared from radiolabelled aniline. A solution of 0.04 moles (4.5 g.) of this phenylhydrazine (as its free base) in 30 ml. of dry benzene was treated with 0.013 moles (2 g.) of dimethyl sulphamyl chloride and worked up as described above. From the solution was obtained $\text{C}_6\text{H}_5\text{SO}_2\text{-NHNHC}_6\text{H}_5$ in 69% yield with specific activity 8.167×10^5 cpm/m.mole. This confirms that both phenyl rings in the hydrazide were derived from the phenylhydrazine. This hydrazide (480 mg.) was cleaved by being refluxed in cyclohexylamine at 100° for four hours, when the following reaction occurred :

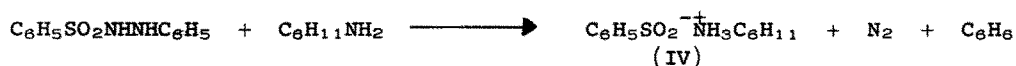


TABLE III
Formation of n-Phenyl-benzenesulphonyl Hydrazide (III)

Sulphamyl Halide (I) R =	Solvent	Yield of III ^a
$(\text{CH}_3)_2\text{N}^b$	CHCl_3	90%
$(\text{C}_2\text{H}_5)_2\text{N}^c$	C_6H_6	92%
$\text{C}_4\text{H}_8\text{NO}^c, d$	C_6H_6	93%
$(\text{CH}_3)_2\text{N}^c$	$\text{C}_6\text{H}_5\text{CH}_3$	88%
$(\text{CH}_3)_2\text{N}^c$	$\text{C}_6\text{H}_5\text{Cl}$	91%

^a Recovery of phenylhydrazine hydrochloride was essentially quantitative in all cases. ^b Reaction conditions : exothermic reaction on mixing

chloroform solutions of halide and phenylhydrazine followed by 1 hour refluxing at 62° : ratio of phenylhydrazine to halide was 2 : 1.

^c Reaction conditions : 24 hours stirring at ambient temp., followed by 1 hour at 50° : ratio of phenylhydrazine to halide was 3 : 1. ^d $\text{C}_4\text{H}_8\text{NO}$ represents N-morpholinyl.

Cyclohexylammonium benzene sulfinate (IV) m.p. $204\text{-}206^\circ$ was isolated

in quantitative yield and it had a specific activity of 4.087×10^5 cpm/m.mole establishing that reaction (9) as written above takes place.

The extent to which any phenyl radicals might be derived from the solvent benzene, where used, was checked by performing the reaction between non-labelled phenylhydrazine and non-labelled sulphamyl chloride in C^{14} -labelled benzene. No incorporation of radioactive material was observed in the hydrazide isolated. Thus this reaction of phenylhydrazine appears to be a diffusion-controlled cage process.

References

- (1) L. F. Audrieth and M. v. Brauchitisch, J.Org.Chem. 21, 426 (1956).
- (2) S. Kubota and T. Akita (univ. Tokushima) Yakugaku Tasshi 81, 502 (1961) : Chem. Abs. 55 19925 (1961).
- (3) Compare R.L. Hardie and R.H. Thomson, J.Chem.Soc. 2512 (1957).
- (4) Radioactive assays were carried out in a Nuclear-Chicago model D-470 gas-flow counter with a "Micromil Window" on samples of finite thickness, with appropriate corrections for efficiency and self-absorption.