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A ONE-STEP TRANSFORMATION OF AROMATIC ALDEHYDES TO NITRILES, USING S,S-DIMETHYLSULFURDIIMIDE AS IMINATING AGENT. ISOLATION OF DITHIATETRAZOCINES AS REACTION INTERMEDIATES.

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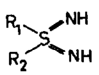
Abstract
S,S-Dimethylsulfurdiimide is explored as a novel and effective reagent for the direct synthesis of aromatic nitriles from aldehydes. A novel eight-membered heterocycle is isolated as a reaction intermediate and a mechanism for this reaction is discussed.

Sulfurdiimides **1** belong to a relatively new class of sulfur nitrogen compounds, which have been recognized as valuable intermediates in organic synthesis.[1]



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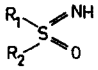

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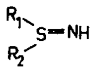

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Sulfoximides **2** and sulfilimines **3** have been subject to rather intensive studies, whereas little attention has focused so far on the chemistry of sulfurdiimides.[2] However, with the development of several effective methods for the synthesis of sulfurdiimides, they have now become readily available starting materials.[2,3] S-Imides are weakly basic compounds, which also display nucleophilic properties. S,S-Diphenylsulfilimine[4] adds to α,β-unsaturated carbonyl compounds to form aziridines and enamines[5] and is also known to react with aldehydes to form nitriles in high yields.[6]

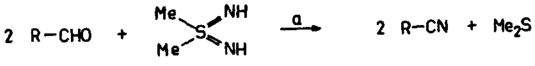
We have now found that sulfurdiimides **1** are also powerful iminating agents. Thermal reactions between several sulfurdiimides **1a-1e** and benzaldehyde (eq. 1) in refluxing benzene (overnight) quantitatively yielded in benzonitrile and the corresponding sulfides. S,S-Dimethylsulfurdiimide[7] **1a** was explored as an iminating agent with the aldehydes listed in

1 (1)

(a) R_1 = Me, R_2 = Me (b) R_1 = CH_2Ph, R_2 = CH_2Ph (c) R_1, R_2 = $(CH_2)_4$
(d) R_1 = Me, R_2 = p-Me-Ph (e) R_1 = Ph, R_2 = Ph

Table I; the corresponding nitriles were obtained in high yields. The nitriles (Table I) were characterized by ^{1}H NMR, IR, MS, mp or bp and compared with those of authentic samples.[8] The advantages of this novel approach for the facile formation of nitriles from aryl aldehydes are: (1) S,S-dimethylsulfurdiimide is readily available on a large scale through a one-step synthesis from dimethylsulfide and tert-butyl hypochlorite/ammonia[2]; (2) the required ratio between S,S-dimethylsulfurdiimide and aldehyde is 0.5:1; (3) only mild thermal reaction conditions are required; (4) the resulting nitriles are easily separated from the volatile dimethyl sulfide.

Table I. Conversion of aromatic aldehydes to nitriles with *S,S*-dimethylsulfurdiimide.



1a

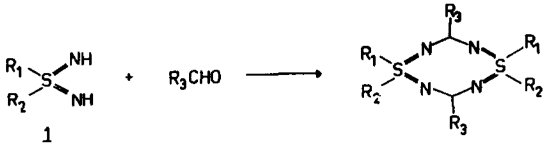
R	Time (h)	Yield[b] (%)	IR[d] ν_{CN}(cm^{-1})
Phenyl	8	100	2240
p-Methoxyphenyl	15	95	2240
p-Nitrophenyl	7	100	2400
p-Nitrophenyl	7	95[c]	2400
p-Chlorophenyl	8	100	2410
p-Chlorophenyl	8	95[c]	2410
m-Hydroxyphenyl	15	95	2250
trans-anisyl	7	95	2230
3,4,5-Trimethoxy-phenyl	15	95[c]	2240

[a] The reactions were run at 0.5-10 mmol substrate in refluxing acetonitrile for 7-15 h.
[b] Yield determined by GC analysis.
[c] Isolated yield.
[d] Chloroform solution.

The major drawback of this novel method for the synthesis of nitriles[9] is the fact that aliphatic aldehydes give a complex mixture of several reaction products. Therefore this procedure is not suitable for the formation of aliphatic nitriles. Reaction between sulfurdiimides and aromatic aldehydes in acetonitrile at room temperature (overnight) gave little conversion to nitriles. In some instances, however, a novel eight-membered heterocyclic ring system **4a-4c** could be isolated after reacting benzaldehyde and sulfurdiimides **1a**, **1c**, and **1d**. We were also able to isolate the heterocycles **4d-4g** with formaldehyde as the carbonyl component.[10] Sulfurdiimides could produce several intra- or intermolecular condensation products, when reacted with aldehydes. The absence of OH or NH absorptions in the infrared spectra of **4** indicated the presence of a cyclic structure. The ^{1}H NMR spectra of **4d-4f** show signals between 4.03-4.6 ppm typical for methylene protons. Chemical ionisation of **4e** produced M$^+$ *m/e* 512 as required for the formation of the dithiatetrazocine **4e**.

All isolated products **4a-4g** exhibited satisfactory elemental analyses. The novel dithiatetrazocines **4** are crystalline compounds, which are stable for about 10 to 14 days at room temperature and then start to decompose. **4a-4c** are insoluble; **4d-4g** are very soluble in solvents such as chloroform and methylene chloride. Thermal decomposition of **4a-4c** in refluxing benzene overnight gave quantitative conversion to benzonitrile, which strongly suggests that **4** is a reaction intermediate.

Table II. Formation of **4** from sulfurdiimides and aldehydes.



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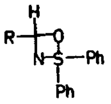
4	R$_1$	R$_2$	R$_3$	Yield %
a	Me	Me	Ph	74
b	Me	p-Tolyl	Ph	31
c	(CH$_2$)$_4$		Ph	23
d	Me	Me	H	34
e	CH$_2$Ph	CH$_2$Ph	H	27
f	CH$_2$Ph	Et	H	16
g	Ph	Ph	H	43

Several reaction mechanisms and intermediates 5-7 have been suggested for the formation of nitriles from aldehydes and S,S-diphenylsulfilimine **3a**, [1a,6]; similar mechanisms could



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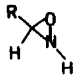

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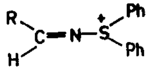

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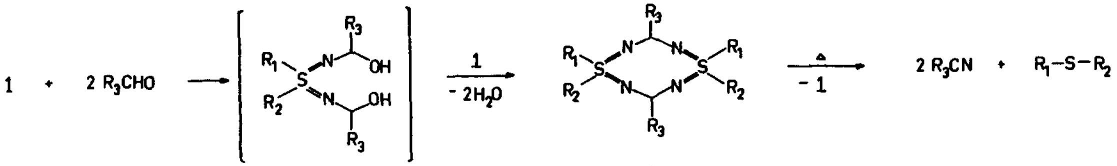
explain the formation of nitriles with sulfurdiimides. However, in light of the isolation of **4**, which seem to be a reaction intermediate, we suggest the pathway shown in Scheme I.

Scheme I. Mechanism for the nitrile formation from aldehydes and sulfurdiimides.



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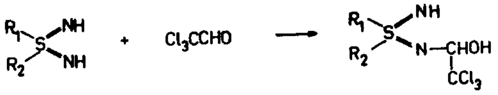
The first step of the reaction presumably involves carbonyl addition of the sulfurdiimide to the carbonyl group of the aldehyde to form 8. Adducts of type 8 (semi-aminal) between S,Sdiarylsulfilimines and chloral have been described[11]; we have observed that sulfurdiimides also form monoadducts **9** with chloral (Table III).

Table III. Adducts between chloral and sulfurdiimides.



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9	R_1	R_2	Yield %
a	CH_2Ph	CH_2Ph	56
b	Me	p-Me-Ph	44
c	CH_2Ph	Ethyl	58
d	$(CH_2)_4$		60

The next step in this reaction would be the addition of another sulfurdiimide with elimination of water to form the heterocyclic ring system **4** (aminal). Elimination of a thioether accompanied by simultaneous elimination of sulfurdiimide would result in formation of the nitrile.

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