

PUMMERER-LIKE REACTION OF SULPHINAMIDES

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Summary Treatment of secondary sulphinamides (1), bearing one hydrogen atom at α -carbon to nitrogen, with electrophilic reagents leads in some cases to formation of N-sulphenylimines (2), via a Pummerer-like reaction.

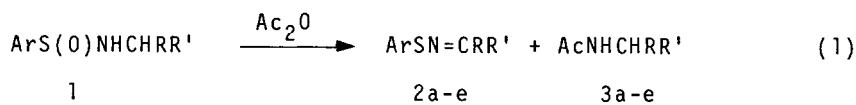
The Pummerer rearrangement of sulfoxides with acetic anhydride and other electrophilic reagents is well known and extensively studied¹

Other compounds of tricoordinate sulphur are reported to undergo Pummerer-type rearrangement, namely the alkoxysulphonium salts² and the N-p-tosylsulphylimines³

Within the category of sulphinyl derivatives, secondary sulphinamides (1) bearing one hydrogen atom at α -carbon to nitrogen appear as promising compounds for this type of reaction. Despite this, no systematic studies have appeared in the literature and only o-nitrophenylsulphinyl derivatives of two γ - β -aminocephalosporins have been mentioned⁴ to react with thionyl chloride and quinoline to give the corresponding N-sulphenylimines

In order to obtain new information pertaining to this reaction, we have investigated the reactivity of a variety of appropriate secondary sulphinamides towards electrophilic reagents


Treatment of sulphinamides 1a-e⁵ with acetic anhydride at room temperature led to N-sulphenylimines 2a-e⁵ and acetamides 3a-e (eq 1). The results are shown in Table 1



a, Ar = 4-CH₃C₆H₄, R = R' = 4-ClC₆H₄

b, Ar = 4-CH₃C₆H₄, R = R' = C₆H₅

c, Ar = 4-CH₃C₆H₄, R = R' = 4-CH₃C₆H₄

d, Ar = 4-CH₃C₆H₄, R, R' = 

e, Ar = 4-ClC₆H₄, R = R' = 4-ClC₆H₄

f, Ar = 4-CH₃C₆H₄, R = H, R' = C₆H₅

g, Ar = 4-CH₃C₆H₄, R, R' = -(CH₂)₅-

h, Ar = 4-CH₃C₆H₄, R = H, R' = n-C₃H₇

i, Ar = 4-CH₃C₆H₄, R = R' = CH₃

l, Ar = 4-ClC₆H₄, R = H, R' = C₆H₅

Table I - Products of the reaction of sulphinamides with acetic anhydride^a

Sulphinamide	Time, h	Products (yields %)	Ratio <u>2/3</u>
<u>1a</u>	45	<u>2a</u> (45), <u>3a</u> (26)	1 7
	70	<u>2a</u> (48), <u>3a</u> (43)	1 1
<u>1b</u>	45	<u>2b</u> (23), <u>3b</u> (30)	0 77
	70	<u>2b</u> (32), <u>3b</u> (42)	0 76
<u>1c</u>	45	<u>2c</u> (10), <u>3c</u> (25)	0 40
	70	<u>2c</u> (14), <u>3c</u> (37)	0 38
<u>1d</u>	45	<u>2d</u> (25), <u>3d</u> (35)	0 71
	70	<u>2d</u> (33), <u>3d</u> (48)	0 69
<u>1e</u>	30	<u>2e</u> (55), <u>3e</u> (25)	2 2
	45	<u>2e</u> (58), <u>3e</u> (38)	1 5

^aYields of isolated compounds

Substitution of acetic anhydride for acetyl chloride and pyridine in diethyl ether did not appreciably affect the yields of 2a and 3a (49% and 48%, respectively)

From the reaction mixture of 1a-e with acetic anhydride, p-tolyl p-toluenethiolsulphonate were identified by TLC and IR analysis. For 1a, p-toluenesulphonic acid was separated in the form of its acetamide 3a-salt⁵ in addition to the major products 2a and 3a. These sulphur-containing compounds, often reported as final products in the disproportionation of sulphinyl derivatives,⁶ evidently arise from a complex process involving the sulphinyl moiety of the sulphinamide.

The data in Table I, although obtained for a limited number of sulphinamides, indicate that the yields of N-sulphenylimines and the molar ratio 2/3 increase with the electron-withdrawing power of the para-substituents on the aromatic rings. For 1a and 1e, longer reaction times significantly decrease the molar ratio 2/3. This fact suggests the idea that one mechanistic pathway to acetamides involves acetic acid, whose production parallels that of the imines (eq 2), possibly via a protonation equilibrium of the sulphinamides.⁷



The fact that the reaction of the sulphinamides 1a or 1e with acetic anhydride in the presence of acetic acid produces only acetamide 3a but no imines 2a or 2e, respectively, supports this hypothesis.

When the reaction was carried out, under identical experimental conditions,

with N-alkyl or N-benzylsulphinamides (1f-1)⁵, we were not able to identify the corresponding N-sulphenylimines in the reaction mixture, the only identifiable products were disulphides and thioisulphonates. A control experiment, performed adding the sulphenimine 2i⁸ to a mixture of the sulphinamide 1i and acetic anhydride, revealed that the sulphur-nitrogen bond in the imine is cleaved under the reaction conditions. In fact, the recovered reaction mixture did not contain the starting imine but p-tolyl disulphide and p-tolyl p-toluenethiosulphonate. Consequently, if a similar decomposition occurs with the other alkyl (or cycloalkyl) and benzyl imines, the lack of these products in the reaction mixture does not necessarily reflect the inability to undergo the Pummerer-like reaction of the parent sulphinamides.

Similar results were obtained when thionyl chloride in pyridine was used at 0°C as electrophilic agent against the N-sulphenylimines 2 were isolated only from reaction mixtures with sulphinamides 1a-e and in comparable yields with those obtained using acetic anhydride (Table II).

Table II - Products of the reaction of sulphinamides with thionyl chloride in pyridine^a

Sulphinamide	Products (yields %)
<u>1a</u>	<u>2a</u> (55)
<u>1b</u>	<u>2b</u> (19)
<u>1c</u>	<u>2c</u> (16)
<u>1d</u>	<u>2d</u> (23)
<u>1e</u>	<u>2e</u> (64)

^aYields of isolated compounds

The knowledge of the factors governing the formation of the N-sulphenylimines is also important from a preparative point of view. In fact, although these compounds appear to be synthetic intermediates of considerable interest,⁹ they have rarely been used in organic synthesis because of the lack of convenient preparative methods⁹⁻¹¹. This is especially true for the N-sulphenyldiarylimines such as 2a-e, for which only one specific synthetic procedure is presently available¹⁰, while others failed¹¹. Thus, synthetic procedure based on the Pummerer-type reaction of sulphinamides may be considered a useful alternate route to these compounds.

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