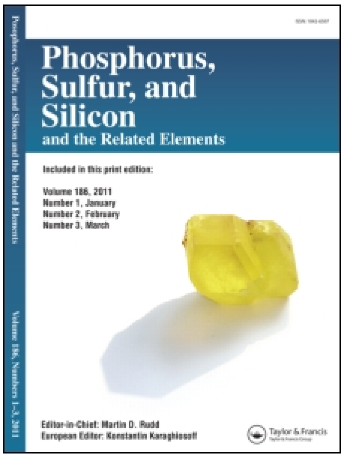

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ON SOME INCORRECTNESS IN THE INTERPRETATION OF RESULTS OF THE REACTION OF SULPHINYLAMINES WITH ALDEHYDES

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ON SOME INCORRECTNESS IN THE INTERPRETATION OF RESULTS OF THE REACTION OF SULPHINYLAMINES WITH ALDEHYDES

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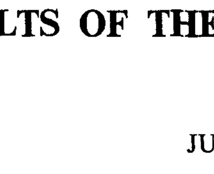
In contradiction to reports by others, it was shown that sulphinylamines do not give products of cycloaddition on reaction with aldehydes in aprotic solvents. However, in the presence of a protonogenic agent, crystalline products were precipitated for which an ammonium α-aminosulphonate salt structure was confirmed. These salts are formed as a result of consecutive hydrolysis of sulphinylamines, condensation of aldehydes with the resulting amines, and bisulphite anion addition to Schiff bases.

INTRODUCTION

Certain authors[1,2,3] report the reaction of sulphinylamines with aldehydes in anhydrous ether, with formation of cycloaddition products (A).

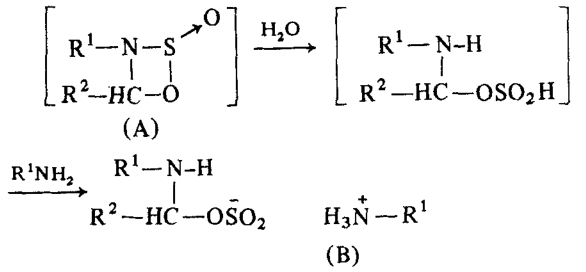


(A)

One author[1] suggests crystallization of these products from 96% alcohol, from which it could be inferred that they can resist hydrolysis.

Another publication[4] describes the reactions of sulphinylamines with aldehydes in the presence of water and assumes the formation of intermediate cyclic adducts (A), which undergo hydrolysis to the respective acids. These acids form crystalline salts (B) with amines resulting from the independent hydrolysis of sulphinylamines.

$R^1\text{-}N{=}S \rightarrow O + R^2\text{-}CH{=}O \rightarrow$



(A) (B)

Despite the mild reaction conditions (37°C, 40 min), the authors were unable to prove the existence of the cyclic product (A).

These contradictory reports encouraged us to pursue the problem further. After careful survey of literature, we concluded that products of a similar structure and physico-chemical properties to (B) had been investigated previously. They had either been obtained in reaction of sulphinylaniline with benzaldehyde in the presence of water,[5] or in other reactions: *N*-benzylideneaniline with sulphurous acid;[6] *N*-benzylideneaniline with sodium sulphite and water;[7] aniline with benzaldehyde, water and sulphur dioxide;[8] benzaldehyde with sodium bisulphite and aniline;[9] and aniline sulphite with benzaldehyde.[10,11] The question of their structure had nevertheless remained open, with almost every worker in the field proposing a different solution to the problem.

In this paper we have determined the correct structure of products precipitated from the solution of sulphinylamines with aldehydes in the presence of water (or even alcohol or amine), and explained how they are formed.

RESULTS AND DISCUSSION

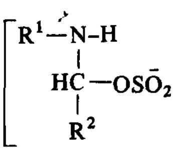
The first stage of our work dealt with the reactions of sulphinylamines with aldehydes in an aprotic solvent, which proved disappointing in that in no case were four-membered cyclic adducts found to be formed. The solutions of sulphinylamines with aldehydes appeared to be stable and ir spectra taken after several weeks storage showed only the slow transformation of Scheme 1.

$$R^1\text{—N=S}\rightarrow O + R^2\text{—CH=O}\rightarrow R^1\text{—N=CH—}R^2 + SO_2$$

SCHEME 1

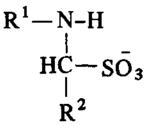
On addition of even small amounts of water, a crystalline precipitate was deposited after some time, the ir spectra of which showing that it was the salt of the respective amine. The salt nature of these products was confirmed by the fact that their cations were easily exchangeable with other ammonium ions by crystallization from methanol with excess of the desired amine. Exchange was particularly easy if the added amine was a stronger base than that giving rise to the original salt. Addition of alkali metal bases did not cause the exchange of ammonium for metal ions, but rather decomposition with formation of metal sulphites.

From the results of elemental analysis, and ir and nmr spectra, (B), (C), and (D) could be given as possible structures for the salts.



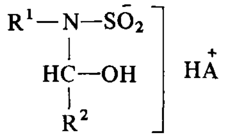
(B)

or



(C)

or



(D)

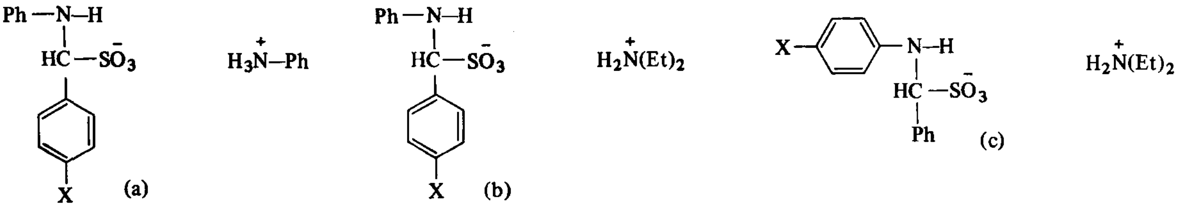
Where: A = amine

The ir spectra of these compounds showed an intense absorption band in the 3400 cm^{-1} region. In order to determine whether this was due to N—H or O—H stretching vibrations, a series of para-substituted derivatives were prepared.

It is evident that substituents on the R^1 phenyl exert a considerable influence on the position of this band, whereas there is no corresponding effect for the R^2 substituents. This indicates that the active proton is

TABLE I

Spectral data for the compounds of the following types:



Type of Compound	Compound No	X	δ H-C-SO$_3^-$ (ppm)	Δδ δ(X)—δ(H) (ppm)	ν N—H^a (cm^{-1})	Δν N—H ν(X)—ν(H) (cm^{-1})
a	1	H	5.49	0	3397	0
	6	Cl	5.46	−0.03	3396	−1
	7	OMe	5.42	−0.07	3397	0
	8	NO$_2$	5.67	+0.18	3399	+2
b	19	H	5.52	0	3410	0
	21	Me	5.38	−0.14	3410	0
	22	Cl	5.52	0	3410	0
	23	OMe	5.39	−0.13	3410	0
	24	N(Me)$_2$	5.27	−0.25	3411	+1
	25	NO$_2$	5.62	+0.10	3411	+1
c	19	H	5.52	0	3410	0
	18	Me	5.36	−0.16	3408	−2
	17	Br	5.43	−0.09	–	–
	16	OMe	5.34	−0.18	3402	−8
	15	N(Me)$_2$	5.27	−0.25	3395	−15
	20	NO$_2$	5.74	+0.22	3422	+12

[a] ± 2 cm^{-1}, because the bands were comparatively broad.

located in the region of strong R^1 influence, i.e. adjacent to nitrogen, and not oxygen where predominance of the influence of the R^2 ring would be expected. Thus structure (D) must be rejected.

This dependence of the N—H stretching vibrations on the substituent on the R^1 ring may be expressed by the Hammet equation, and this had been done on the plot. These conclusions on structure have been supplemented by graphical representation on the plot (Figure 1) of a similar relation for N—H stretching vibrations for derivatives of the model substance *N*-phenylbenzylamine.[12]

Table I also lists positions of nmr signals for protons originating from the aldehyde group. The similar effect of substituents from both rings is noteworthy here. Analysis of the molecular model showed that substitution of one hydrogen by large substituent on the benzyl carbon in *N*-phenylbenzylamine forces the molecule to assume a structure in which the remaining hydrogen on the benzyl carbon is pushed in the direction of the phenyl ring bound to nitrogen. As a result of this situation, π-electron density changes on either phenyl ring give rise to similar magnetic field changes in the region in which this proton is situated and hence also to changes in the position of its nmr signal.

After rejection of structure (D), a decision had to be reached whether the system was of structure (B) or structure (C). Here previous papers[6,7,8] and the author's own work, based on ir spectra, supplied a helpful point: that the same product is formed in the reaction of aniline bisulphite with *N*-benzylideneaniline, as in the reaction of sulphinylaniline with benzaldehyde in the presence of water.

Additions of bisulphite anion to multiple bonds, and in particular to the carbonyl group, have been extensively described and the structure of resulting products thoroughly investigated.[15] They proceed by the joining of the sulphur of the bisulphite anion to an electrophilic centre. The sulphinic acids undergo similar addition reactions[16] and, for Schiff base additions, give α-aminosulphones.[17] All these facts indicate that the same type of addition is involved in the reaction of sulphinylamines with aldehydes in the presence of a protonogenic agent, and that the resulting salts have the structure (C).

The compounds obtained by us are listed in Table II. All decompose on melting, as shown in Scheme 2.

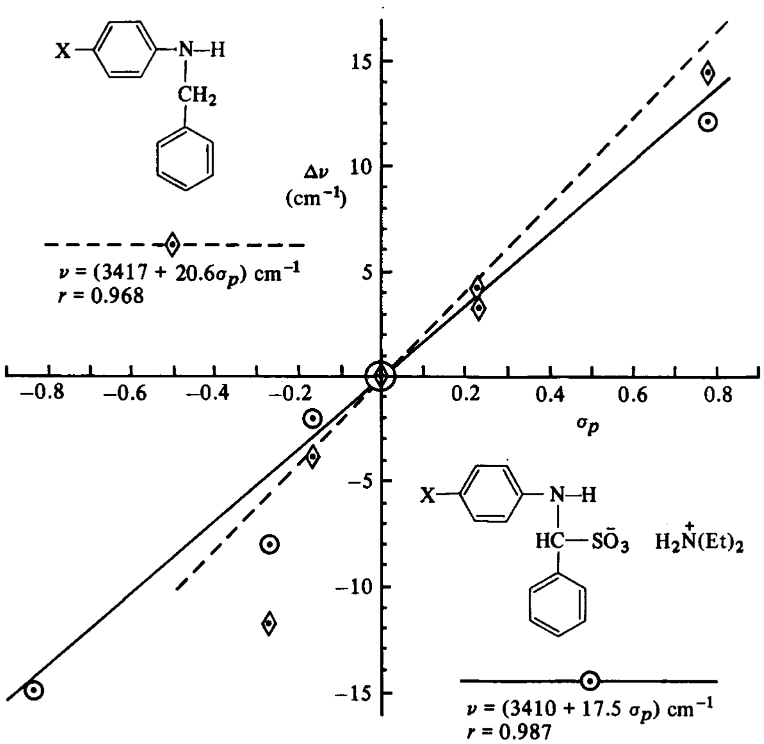


FIGURE 1 Plot of shifts ($\Delta\nu$) in infrared N–H stretching frequencies of above compounds *vs.* σ_p-constants of substituents (taken from Refs. 13 and 14).

TABLE II

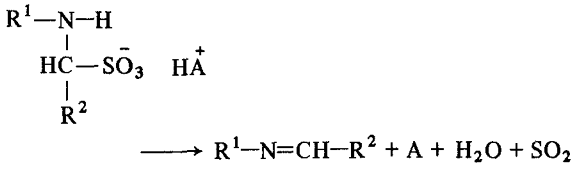
Analytical data, yields and melting points of the investigated compounds $R^1NH—CH(R^2)SO_3^-HA^+$

Compound	R^1	R^2	A	Formula	Analyses[a] % Found (Calculated) C	H	N	S	Mp.[b] °C	Yield, %
1	Ph	Ph	$PhNH_2$	$C_{15}H_{20}N_2SO_3$	64.0 (64.0)	5.9 (5.7)	7.7 (7.9)	9.0 (9.0	131-33	89
2	*p*Me—Ph	Ph	pMe—$PhNH_2$	$C_{21}H_{24}N_2SO_3$	65.4 (65.6)	6.5 (6.3)	7.2 (7.4)	8.3 (8.3)	126-28	76
3	mCl—Ph	Ph	mCl—$PhNH_2$	$C_{19}H_{18}N_2Cl_2SO_3$	53.5 (53.7)	4.3 (4.3)	6.5 (6.6)	7.5 (7.5)	104-07	89
4	*p*Me—Ph	*p*Cl—Ph	*p*Me—$PhNH_2$	$C_{21}H_{23}N_2ClSO_3$	60.3 (60.2)	5.8 (5.5)	6.6 (6.7)	7.5 (7.7)	127-29	92
5	*p*Br—Ph	Ph	*p*Br—$PhNH_2$	$C_{19}H_{18}N_2Br_2SO_3$	44.4 (44.4)	3.6 (3.5)	5.4 (5.5)	6.3 (6.2)	120-23	73
6	Ph	*p*Cl—Ph	$PhNH_2$	$C_{19}H_{19}N_2ClSO_3$	58.5 (58.4)	5.1 (4.9)	7.1 (7.2)	8.2 (8.2)	128-30	92
7	Ph	*p*(MeO)—Ph	$PhNH_2$	$C_{20}H_{22}N_2SO_4$	62.2 (62.2)	5.9 (5.7)	7.2 (7.3)	8.3 (8.3)	125-27	94
8	Ph	*p*(NO_2)—Ph	$PhNH_2$	$C_{19}H_{19}N_3SO_5$	56.6 (56.9)	5.0 (4.8)	10.4 (10.5)	8.2 (8.0)	127-29	99
9	Ph	Ph	piperidine	$C_{18}H_{24}N_2SO_3$	62.2 (62.0)	6.9 (6.9)	7.8 (8.0)	9.2 (9.2)	191-93	55
10	Ph	Ph	pyridine	$C_{18}H_{18}N_2SO_3$	63.1 (63.1)	5.5 (5.3)	8.2 (8.2)	9.5 (9.4)	126-28	88
11	Ph	Ph	*p*Me—PhNH2	$C_{20}H_{22}N_2SO_3$	64.7 (64.8)	5.9 (6.0	7.6 (7.6)	8.7 (8.7)	131-34	49
12	Ph	Ph	quinoline	$C_{22}H_{20}N_2SO_3$	67.3 (67.3)	5.2 (5.1)	7.1 (7.1)	8.4 (8.2)	123-25	94
13	Ph	Ph	morpholine	$C_{17}H_{22}N_2SO_4$	58.1 (58.3)	6.3 (6.3)	7.8 (8.0)	9.1 (9.2)	166-68	85
14	Ph	Ph	$CH_3(CH_2)_5NH_2$	$C_{19}H_{28}N_2SO_3$	62.4 (62.6)	7.7 (7.7)	7.5 (7.7)	9.2 (8.8)	129-30	99
15	*p*$(Me)_2N$—Ph	Ph	Et_2NH	$C_{19}H_{29}N_3SO_3$	60.0 (60.1)	7.7 (7.7)	10.8 (11.1)	8.5 (8.4)	142-43	55
16	*p*(MeO)—Ph	Ph	Et_2NH	$C_{18}H_{26}N_2SO_4$	59.2 (59.0)	7.2 (7.2)	7.4 (7.6)	9.0 (8.7)	149-51	82
17	*p*Br—Ph	Ph	Et_2NH	$C_{17}H_{23}N_2BrSO_3$	49.2 (49.2)	5.6 (5.6)	6.6 (6.7)	7.7 (7.7)	177-78	68
18	*p*Me—Ph	Ph	Et_2NH	$C_{18}H_{26}N_2SO_3$	62.0 (61.9)	7.5 (7.5)	8.0 (8.0)	9.3 (9.1)	160-61	82
19	Ph	Ph	Et_2NH	$C_{17}H_{24}N_2SO_3$	60.5 (60.7)	7.2 (7.2)	8.2 (8.3)	9.6 (9.5)	154-55	91
20	*p*(NO_2)—Ph	Ph	Et_2NH	$C_{17}H_{23}N_3SO_5$	53.5 (53.5)	6.1 (6.1)	11.1 (11.0)	8.5 (8.4)	168-71	69
21	Ph	*p*Me—Ph	Et_2NH	$C_{18}H_{26}N_2SO_3$	61.7 (61.9)	7.5 (7.5)	7.7 (8.0)	9.2 (9.1)	156-57	88
22	Ph	*p*Cl—Ph	Et_2NH	$C_{17}H_{23}N_2ClSO_3$	54.8 (55.1)	6.2 (6.3)	7.3 (7.6)	8.8 (8.6)	153-54	62
23	Ph	*p*(MeO)—Ph	Et_2NH	$C_{18}H_{26}N_2SO_4$	58.9 (59.0)	7.2 (7.2)	7.6 (7.6)	8.8 (8.7)	150-52	77
24	Ph	*p*$(Me)_2N$—Ph	Et_2NH	$C_{19}H_{29}N_3SO_3$	59.9 (60.1)	7.6 (7.7)	10.8 (11.1)	8.6 (8.4)	144-46	89
25	Ph	*p*(NO_2)—Ph	Et_2NH	$C_{17}H_{23}N_3SO_5$	53.4 (53.5)	6.2 (6.1)	1-.8 (11.0)	8.7 (8.4)	136-37	83
26	Ph	Pr	morpholine	$C_{14}H_{24}N_2SO_4$	53.2 (53.1)	7.6 (7.6)	8.6 (8.9)	10.2 (10.1)	151-53	42
27	Ph	Et	piperidine	$C_{14}H_{24}N_2SO_3$	55.9 (56.0)	7.8 (8.1)	9.2 (9.3)	10.8 (10.7)	122-23	89

[a] All compounds containing chlorine or bromine gave good elemental analyses for these elements.

[b] All compounds decomposed on melting (liberation of sulphur dioxide).

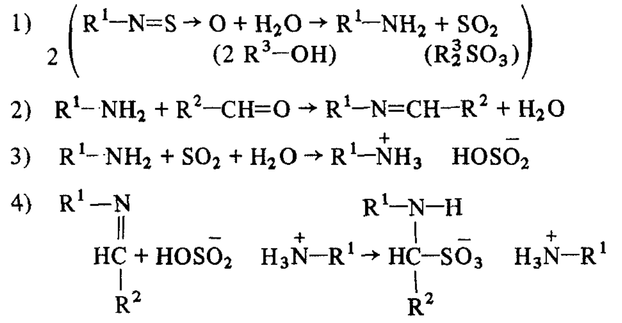
This was tested chemically and checked by mass spectrography.



$$\begin{array}{l} R^1{-}N{-}H \\ \quad | \\ HC{-}\overset{-}{S}O_3 \quad H\overset{+}{A} \\ \quad | \\ \quad R^2 \end{array} \longrightarrow R^1{-}N{=}CH{-}R^2 + A + H_2O + SO_2$$

SCHEME 2

It was found that these salts precipitate from solutions of aldehydes and sulphinylamines not only in the presence of water, but also with other protonogenic agents, e.g. amines or alcohols. This was taken into account in the reaction path suggested, described in Scheme 3.



1) $2\left(\begin{array}{l} R^1{-}N{=}S\rightarrow O + H_2O \rightarrow R^1{-}NH_2 + SO_2 \\ \qquad\qquad (2\,R^3{-}OH) \qquad\qquad (R^3_2SO_3)\end{array}\right)$

2) $R^1{-}NH_2 + R^2{-}CH{=}O \rightarrow R^1{-}N{=}CH{-}R^2 + H_2O$

3) $R^1{-}NH_2 + SO_2 + H_2O \rightarrow R^1{-}\overset{+}{N}H_3 \quad HOS\overset{-}{O}_2$

4) $\begin{array}{l} R^1{-}N \\ \quad \| \\ \quad HC \\ \quad | \\ \quad R^2 \end{array} + HOS\overset{-}{O}_2 \quad H_3\overset{+}{N}{-}R^1 \rightarrow \begin{array}{l} R^1{-}N{-}H \\ \quad | \\ \quad HC{-}\overset{-}{S}O_3 \\ \quad | \\ \quad R^2 \end{array} \quad H_3\overset{+}{N}{-}R^1$

SCHEME 3

Salts formation consists of a set of stages, each of which is a known reaction and in none of which a cyclic adduct of sulphinylamine and aldehyde is necessary. The first stage is the well-known hydrolysis[18] or alcoholysis[19, 20] of sulphinylamines. If the protonogenic agent added is an amine, the reaction begins from the second stage as shown in the scheme, and the sulphinylamines are hydrolysed only subsequently by the water produced. The crucial stage in the reaction is the final one, in which amine bisulphite is added to Schiff base and a precipitate of the corresponding ammonium salt of the α-aminosulphonic acid is formed.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were performed by SLAF, Cracow. The nuclear magnetic resonance spectra were taken on a Tesla BS-487 spectrometer, using HMDSO as the external reference and d_6-DMSO as solvent (15% solutions). Infrared spectra were recorded with a Zeiss UR-10 spectrophotometer for 0.01 M solutions in chloroform using 1.0 mm sodium chloride cells. Mass spectra were obtained with a LKB-9000 S mass spectrometer.

Sulphinylamines were prepared by the reaction of appropriate amines with thionyl chloride in boiling benzene according to Kresze and Smalla.[21] Commercial aldehydes were purified by distillation or crystallization from methanol.

Stability of Solutions of Sulphinylamines with Aldehydes in Aprotic Solvents

(a) A 1.0 M solution of carefully purified benzaldehyde[22] and sulphinylamine (equivalent quantities) in dry ether was sealed in vials and kept at room temperature. On several respective occasions the individual vials were opened one at a time and ir spectra were recorded for the solutions. The spectra showed the slow formation of *N*-benzylideneaniline and sulphur dioxide as the sole products according to Scheme 1. After 5 weeks the estimated molar ratio of substrate to products was 1.6 : 1, respectively.

(b) A mixture of 2.8 g (0.02 mol.) of *p*-chlorobenzaldehyde and 4.5 ml (0.04 mol.) of sulphinylaniline was kept at room temperature in sealed vials. Infrared spectra of this mixture were recorded after 1 hr and 1, 2, 3, and 12 weeks. These spectra showed the occurence of the corresponding Schiff base approximately in a 0, 20, 34, 42, and 55% yield, respectively.

(c) An equimolar solution of 5.6 ml (0.05 mol.) of sulphinylaniline and 7.0 g (0.05 mol.) of *p*-chlorobenzaldehyde in 70 ml of dry benzene was heated at reflux under nitrogen for 8 hr. The infrared spectrum of this solution was identical with that before heating.

Confirmation of structures and yields of products were obtained by comparison of spectra using authentic samples.

Reactions of Sulphinylamines with Aldehydes in the Presence of Water

To a solution of 0.025 mol of the appropriate aldehyde and 0.05 mol. of sulphinylamine in 1,4-dioxane (30 ml) was added 0.9 ml (0.05 mol.) of water, giving after a while precipitation of a white or yellow product. The mixture was left at room temperature overnight and then the precipitate was filtered off. Recrystallization from methanol gave the pure salt (compounds **1–8**, Table II).

Reactions of the Salts with Amines (Cation Exchange)

To a stirred warm solution of salt **1** in methanol was added an excess of the corresponding amine, and precipitation ensued. After cooling, the new salt (compound **9** and **10**, Table II) was filtered and recrystallized from methanol.

Derivatives of Two Different Amines. General Procedure

0.01 mol of the appropriate sulphinylamine and 0.01 mol. of aldehyde were dissolved in 10 ml of 1,4-dioxane. To this solution was added a solution of 0.012 mol. of amine and 0.18 ml of water in 5 ml of the same solvent. The mixture was set aside overnight. The precipitate was filtered off and recrystallized from methanol giving the pure salt (compounds **11–27**, Table II). These salts were dried under vacuum at room temperature.

Reaction in the Presence of Amine

To a mixture of 0.01 mol. of sulphinylaniline and 0.02 mol. of benzaldehyde was added 0.2 mol. of freshly distilled aniline. After 4 hr the mixture solidified. After 48 hr at room temperature the nmr spectrum of a solution of the resulting mixture in d_6-DMSO indicated the formation of salt 1 and *N*-benzylideneaniline as the exclusive products in 100% yield. This was determined by comparison of the spectrum with those of authentic materials.

Reaction in the Presence of Alcohol

0.48 ml (12 mmol.) of anhydrous methanol was added to a solution of 6 mmol of benzaldehyde in 9 mmol of sulphinylaniline. Within a few minutes the solution became warm and crystals began to precipitate. The nmr spectrum of a solution of the product mixture in d_6-DMSO was recorded after 24 hr. This spectrum showed that salt **1**, *N*-benzylideneaniline, and methyl sulphite were formed in the molar ratios of 1 : 1 : 2 (by comparison with spectra of authentic compounds).

Reaction of N-benzylideneaniline with Aniline Hydrosulphite

A solution of 1.82 ml (0.02 mol.) of aniline and 1.0 ml of water in 10 ml of methanol was saturated with sulphur dioxide. To the resulting solution was added a solution of 3.6 g (0.02 mol.) of *N*-benzylideneaniline in 20 ml of methanol, giving a precipitate. After 24 hr at −5°C, the precipitate was filtered off, washed with ether and dried under vacuum. The ir and nmr spectra of the obtained sample (6.6 g, 92%) and salt 1 were identical.

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