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SYNTHESIS OF AMINOARYLSULPHONANILIDES DERIVED FROM *o*-CHLOROTOLUENE

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SUMMARY

Fifteen new arylsulphonanilide amines containing at least one o-*chlorotoluene residue in a molecule have been synthesized. Their compositions have been confirmed by elementary analysis and infrared spectrophotometry. These amines can be used to synthesize acid and reactive dyes.*

1. INTRODUCTION

The rapid growth of polyamide fibre production has brought about a great demand in the textile industry for supplies of specially selected groups of the acid dyes. At present, such dyes are the most commonly used for dyeing polyamide fibres and consequently, research institutions have recently shown a great interest in them.[1–12] The primary emphasis has been on the search for new intermediates for the synthesis of acid dyes which would have high light fastness, bright colours, freedom from toxicity (both in the intermediates and the dyes), good application properties and low production costs.

The subjects of our study were several amines derived from arylsulphonanilides, illustrated by formulae **1**, **2** and **3**, containing at least one *o*-chlorotoluene residue in the arylsulphonyl or arylamine molecule.

The compounds were selected for several reasons. First, aminoarylsulphonanilides were expected to have no toxicity since some compounds with sulphonamide groups are utilized as chemotherapeutic agents. Another important reason to undertake this study was the need for the more extensive use of *o*-nitrotoluene and its derivatives for the synthesis of intermediates. A great

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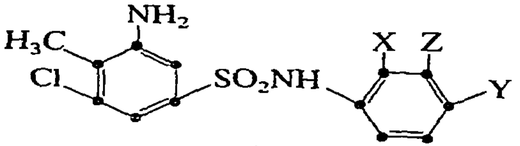

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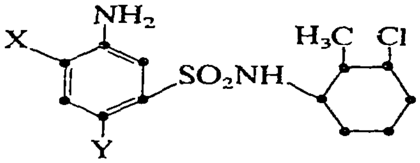

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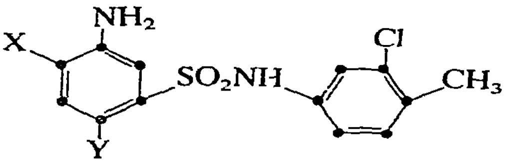


3

where X and Y = —H, $—CH_3$, $—OCH_3$ and —Cl
Z = —H or —Cl

deal of *o*-nitrotoluene is formed *in* nitration of toluene ($\frac{2}{3}$ of *ortho* isomer). As yet *o*-nitrotoluene is used in chemical technology only to a small extent and often it is treated as a waste product during the production of *p*-nitrotoluene.

2. DISCUSSION OF THE RESULTS

An important stage of the synthesis of aminoarylsulphonanilides **1–3** is the condensation reaction of arylsulphonylchlorides with aromatic amines. Carrying out the process in a water–organic solvent system enabled a high yield to be obtained with the use of only stoichiometric quantity of amine. Under such conditions the condensation reaction takes place in organic solvent in which the reactants are soluble or very soluble. On the other hand, the product is not soluble in organic solvent at the reaction temperature and goes to the aqueous phase. The temporarily formed amine hydrochloride dissolves well in water in which it is systematically neutralized, the amine dissolving in the organic solvent. The water solubility of the amines used is also very low. It should be noted that dissolution or dispersion of arylsulphonylchloride in the organic solvent with partial dissolution limits, to a considerable extent, the degree of hydrolysis of chloride to the sulphonic acid, since the concentration of hydroxyl ions in the organic layer is much lower than in water. This allows the process to be carried out within a wider range of pH without the risk of rapid hydrolysis of arylsulphonylchloride, which can be of great importance in industrial conditions of this type of reaction.

The condensation experiment in an aqueous medium using some amines (*o*- and *p*-toluidine and *o*- and *p*-anisidine) gave much worse results. In the case of the liquid amines (*o*-toluidine and *o*-anisidine) the product underwent caking, which made it difficult to carry out the process further in the heterogeneous system. The yields were about 20% lower than those in the presence of chlorobenzene. On the other hand, the results with the solid amines were still worse, even when using an excess of amine (at least 50%).

The investigations showed that all the arylsulphonylchlorides used have similar reactivity. This is illustrated by their rates of condensation with 6-chloro-2-toluidine nitro-compounds from N-8 to N-11 and 2-chloro-4-toluidine nitro-compounds N-12 and N-15. Only 6-chloro-2-nitrotoluene-4-sulphonylchloride reacted slightly slower with 6-chloro-2-toluidine, although this did not affect the reaction yield (88·7%) which is of the same order as that of the remaining arylsulphonylchlorides. As was expected[13–15] a variation in the condensation process was observed depending on the properties of the amines. Amines of higher nucleophilicity reacted faster. It was also observed that aniline derivatives containing *p*- or *p*- and *m*-substituents reacted somewhat faster than their isomers containing *o*-substituents in relation to the amine group. In an aqueous medium the course of these reactions was reversed; the *o*-derivatives reacted faster.

The reduction of the nitroarylsulphonanilides (N-1 to N-15) was carried out in 50% dimethylformamide (DMF) by the Beschamps method. The DMF solution was selected for the reason that after the completion of the reaction and precipitation of iron salt, all the amines prepared in the alkaline medium were soluble at the boiling point and so were easy to separate from the iron oxides formed in the process. The amines were separated from the reaction medium by further dilution to about 20% relative to DMF, and neutralization with acetic acid. In the cases where amines were obtained as oils, they were separated as the hydrochlorides by acidifying the reaction medium with hydrochloric acid to pH 1–2. The processes of synthesis of the amines are protected by Polish Patent 216344.

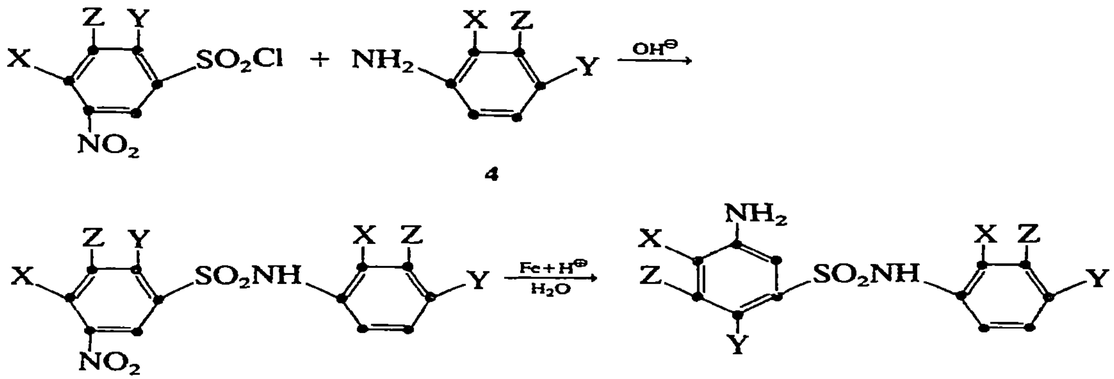
Preliminary trials have shown that the monoazo and disazo dyes prepared using the amines A-1 to A-15 are suitable for dying polyamide and protein fibres. The results of this evaluation will be published elsewhere.

3. EXPERIMENTAL

The amines illustrated by the general formulae **1–3** were prepared according to the general reaction scheme shown overleaf.

For X, Y and Z see formulae **1–3**.

The following sulphonylchlorides were selected for the study: 2-nitro-6-chlorotoluene-4-sulphonylchloride (**5**), 2-nitrotoluene-5-sulphonylchloride



4

4A

(6),[16] 4-nitrotoluene-2-sulphonylchloride (7),[17] 2-nitrochlorobenzene-4-sulphonylchloride (8),[18] 3-nitrobenzene-sulphonylchloride (9).[19] Sulphonylchlorides **5–9** were condensed with *o*- and *p*-toluidines. Fifteen isomeric nitroarylsulphonanilides (**4A**) were obtained which after reduction gave fifteen amines as illustrated by formulae **1–3**. The prepared nitrocompounds are specified in Tables 1 and 2.

TABLE 1

THE STRUCTURE OF NITROARYLSULPHONANILIDES AND SOME PARAMETERS OF REACTION

Number of nitro-compound	*Structure of nitro-compounds*				*Time of reaction* (h)	*Yield* (%)	*Melting point* (°C)
	Formula number	*Substituents*					
		X	*Y*	*Z*			
N-1	1	H	H	H	9·0	83·5	160–161·5
N-2	1	CH_3	H	H	8·5	87·4	130–131
N-3	1	H	CH_3	H	8·0	93·4	160–161
N-4	1	CH_3	CH_3	H	8·0	92·8	167–168·5
N-5	1	CH_3	H	Cl	11·5	88·7	124–126
N-6	1	OCH_3	H	H	8·0	86·9	105–106
N-7	1	H	OCH_3	H	7·5	83·9	139–140
N-8	2	H	H	—	7·5	91·4	150–151·5
N-9	2	CH_3	H	—	7·5	93·4	122–123
N-10	2	H	CH_3	—	7·5	92·3	173–174
N-11	2	Cl	H	—	7·5	90·5	129·5–131
N-12	3	H	H	—	6·5	92·7	145–146
N-13	3	CH_3	H	—	6·5	95·2	115–116
N-14	3	H	CH_3	—	6·5	97·4	127–128
N-15	3	Cl	H	—	6·5	94·0	115–116

TABLE 2

ELEMENTAL ANALYSIS DATA OF NITROARYLSULPHONANILIDES AND THEIR SPECIFIC ABSORPTION BANDS OF INFRARED SPECTRA

Number of nitro-compound	*Elemental analysis data (%)*										*The specific absorption bands of i.r. spectra in* cm^{-1}					
	C		*H*		*N*		*S*		*Cl*							
	calc.	*found*	*calc.*	*found*	*calc.*	*found*	*calc.*	*found*	*calc.*	*found*	*NH*	SO_2	$C—NO_2$	CH_3	$C—OCH_3$	*Aromatic C—H*
N-1	47·79	47·90	3·39	3·37	8·57	8·45	9·81	9·87	10.85	10·93	3250	1340 1160	1540 1350 895	2930 2870		710 770 870
N-2	49·34	49·35	3·84	3·85	8·22	8·02	9·41	9·55	10·40	10·43	3200	1350 1160	1530 1350 890	2890 2820		760 850
N-3	49·34	49·45	3·84	3·87	8·22	8·11	9·41	9·45	10·40	10·58	3200	1340 1160	1530 1350 890	2930 2850		820 850
N-4	50·79	50·80	4·26	4·19	7·90	7·92	9·04	9·15	9·99	10·07	3300	1350 1160	1540 1350 890	2950 2880		830 850 880
N-5	44·81	44·79	3·22	3·21	7·47	7·57	8·54	8·37	18·90	18·96	3250	1330 1160	1530 1340 890	2930 2850		720 790 810
N-6	47·13	47·30	3·67	3·65	7·85	7·79	8·99	8·95	9·94	10·15	3250	1350 1160	1540 1350 890	2930 2850	2820 1250 1030	760 850
N-7	47·13	47·40	3·67	3·61	7·85	7·86	8·99	9·19	9·94	10·00	3250	1350 1160	1540 1350 890	2950 2850	2820 1250 1030	700 720 790 870
N-8	47·83	47·84	3·39	3·32	8·57	8·51	9·81	9·92	10·85	10·91	3300	1350 1160	1540 1360 890	2950 2870		700 720 790 870
N-9	49·34	49·55	3·84	3·80	8·22	8·20	9·41	9·46	10·40	10·44	3300	1340 1160	1530 1350 895	2950 2850		720 780 810 880
N-10	49·34	49·33	3·84	3·80	8·22	8·19	9·41	9·42	10·40	10·50	3350	1330 1160	1520 1350 890	2930 2850		720 780 810 880
N-11	43·23	43·40	2·79	2·80	7·75	7·78	8·88	8·97	19·63	19·74	3250	1330 1160	1530 1350 890	2930 2850		720 780 810 880
N-12	47·83	47·89	3·39	3·34	8·57	8·54	9·81	10·03	10·85	10·78	3300	1340 1160	1530 1350 890	2930 2850		690 790 820 870 880
N-13	49·34	49·45	3·84	3·77	8·22	8·14	9·41	9·42	10·40	10·47	3250	1340 1160	1530 1350 890	2950 2870		830 880
N-14	49·34	49·33	3·84	3·80	8·22	8·08	9·41	9·35	10·40	10·51	3300	1345 1160	1530 1350 890	2930 2870		820 880
N-15	43·23	43·40	2·79	2·80	7·75	7·78	8·88	8·93	19·63	19·61	3250	1340 1160	1540 1350 890	2930 2870		830 880

For the condensation with amines (**4**), sulphonylchlorides (**5**–**9**) were used directly after their separation from the reaction mixture and after quantitative determination by potentiometric titration of chlorine after hydrolysis, or the nitrogroups (after hydrolysis) by reduction and diazotization.

The condensation of arylsulphonylchlorides and aromatic amines with high nucleophilicity and fairly good water solubility can be carried out in an aqueous medium using an excess of amine and at the same time neutralizing the produced hydrogen chloride with alkali.[20] As was shown in preliminary experiments, the use of chlorotoluidines and solid amines for the condensation caused the process to run slowly. Raising the reaction temperature gave accelerated hydrolysis of the sulphonylchlorides into sulphonic acids, and consequently, the reaction yield was decreased.

The experiments showed that the addition to the reaction medium of organic solvents immiscible with water but partly dissolving the arylsulphonylchlorides and amines, such as chlorobenzene, dichlorobenzene, tetrachloroethylene and others, allowed the condensation process to be carried out with stoichiometric quantities of amine and products of high purity to be obtained in high yields. It is interesting to note that the used solvent can be reused for a subsequent reaction directly after distilling off with steam. Such a procedure was used in the synthesis of all nitrocompounds. The pH value of the reaction medium was kept at 7·0–7·4. The reaction temperature was about 10°C in the initial stage, then it was raised to 20–25°C, and in the final stage to 45–50°C. The process was considered complete when both the pH value and the amount of unreacted amine, determined by diazotization of successive samples, did not change any more. Some properties and reaction parameters of the prepared nitrocompounds are given in Tables 1 and 2.

The reduction of the prepared nitrocompounds was carried out using the Beschamps method in a water–DMF system, using such a concentration of DMF as to get complete dissolution of amine in the reaction medium after completing the reduction at boiling temperature, which allowed for easy separation of amine from the reduction sludge. Amines were separated from the prepared solution in the form of free bases (pH 7) or hydrochlorides (pH 1–2). Some properties of aminoarylsulphonanilides obtained by reduction are given in Table 3.

The obtained nitrocompounds and amines were crystallized from 80% ethanol solutions.

The composition of nitrocompounds and amines was confirmed by elementary analysis and i.r. spectra[21] obtained on a Specord 71-i.r. (Carl Zeiss, Jena). The results of determinations and i.r. spectrum analysis are given in Tables 2 and 3. The melting points were determined by a Boetius microscope without any corrections.

TABLE 3

SOME PROPERTIES OF AMINOARYLSULPHONANILIDES, ELEMENTAL ANALYSIS DATA AND SPECIFIC ABSORPTION BANDS OF INFRARED SPECTRA

Number of amine[*]	*Yield of reaction* (%)	*Melting point of aminohydrochloride* (°C)	*Melting point* of amine (°C)	*Elemental analysis data of aminohydrochloride* (%)										*The specific absorption bands of* i.r. *spectra in* cm^{-1}	
				C		*H*		*N*		*S*		*Cl*			
				calc.	*found*	*calc.*	*found*	*calc.*	*found*	*calc.*	*found*	*calc.*	*found*	NH_3^+	NH_2
A-1	89·7	161–162·5	133–134	46·86	47·00	4·23	4·13	8·41	8·23	9·62	9·70	21·28	21·39	2600–3500 1900–2000	3550 3450 1640
A-2	91·8	154–155	—	48·42	48·40	4·64	4·67	8·07	7·89	9·23	9·07	20·42	20·43	2600–3500 1900–2000	3550 3450 1640
A-3	92·3	169–171	149–151	48·42	48·60	4·64	4·60	8·07	8·05	9·23	9·15	20·42	20·43	2600–3500 1900–2000	3550 3450 1640
A-4	86·3	146–147	129–131	49·87	49·74	5·02	4·85	7·75	7·53	8·87	8·88	19·63	19·60	2600–3500 1900–2000	3500 3400 1630
A-5	84·2	166·5–168	—	44·05	44·27	3·96	3·84	7·34	7·16	8·40	8·20	27·86	27·82	2600–3500 1900–2000	
A-6	90·6	141–142·5	—	46·29	46·39	4·44	4·40	7·71	7·66	8·33	8·97	19·52	19·51	2600–3500 1900–2000	
A-7	92·6	138·5–140	—	46·29	46·30	4·44	4·24	7·71	7·53	8·83	8·73	19·52	19·36	2600–3500 1950–2000	
A-8	87·5	181·5–183	139–140·5	46·86	46·90	4·23	4·15	8·41	8·27	9·62	9·64	21·28	21·40	2600–3500 1950–2000	3550 3450 1640
A-9	86·1	168–170	147–148	48·42	48·25	4·64	4·70	8·07	8·08	9·23	9·28	20·42	20·40	2600–3500 1900–2000	3500 3400 1640
A-10	74·6	205–206	—	48·42	48·31	4·64	4·60	8·07	8·13	9·23	9·07	20·42	20·29	2600–3500 1900–2000	
A-11	81·3	114–116	—	42·47	42·50	3·56	3·55	7·62	7·62	8·72	8·88	28·93	28·79	2600–3500 1900–2000	
A-12	81·6	173–174·5	148–149	46·88	47·01	4·23	4·20	8·41	8·41	9·62	9·84	21·28	21·48	2600–3500 1900–2000	3550 3450 1640
A-13	78·9	170–171·5	145–147	48·42	48·30	4·64	4·80	8·07	8·08	9·23	9·45	20·42	20·38	2600–3500 1900–2000	3500 3450 1640
A-14	75·4	171–173	—	48·42	48·56	4·64	4·67	8·07	8·09	9·23	9·30	20·42	20·32	2600–3500 1900–2000	
A-15	80·7	143–144·5	—	42·47	42·58	3·56	3·55	7·62	7·43	8·72	8·58	28·93	28·90	2600–3500 1900–2000	

[*] Number of amine corresponds to number of nitro-compound

Preparative details were as follows.

3.1. 6-*Chloro-2-nitrotoluene-4-sulphonanilide* (*N*-1)

70 cm^3 of water, 10 cm^3 of chlorobenzene and 9·3 g (0·1 mole) of aniline were put into a three-necked flask provided with a fast stirrer. 27·0 g (0·1 mole) of 6-chloro-2-nitrotoluene-4-sulphonylchloride were added, keeping a temperature of 10°C and pH 7·0–7·4 and adding 10% solution of sodium carbonate. After 3 h, the reaction mixture was heated up to 20–25°C and such a temperature was maintained for 6 h. After this period, the pH value of the reaction medium did not change. The completion of reaction was ascertained by diazotization of successive samples from the reaction mixture. Then, the flask content was heated and boiled for 1 h and chlorobenzene and residual aniline (1·5 g) were distilled off with steam. After cooling to room temperature, the crystalline precipitate was filtered off and dried at 70–75°C. 27·3 g of product was obtained with a melting point of 158–160°C. The reaction yield was 83·5%. The raw product was crystallized from 80% ethanol at a yield of 79%. The crystallization was repeated until a constant melting point of 160–161·5°C was achieved.

Analysis for $C_{13}H_{11}ClN_2O_4S$ (326·73)

Calculated:	C = 47·79	H = 3·39	N = 8·57	S = 9·81	Cl = 10·85%
Found:	C = 47·90	H = 3·35	N = 8·45	S = 9·87	Cl = 10·93%

The remaining nitrocompounds were prepared in the same way.

3.2. 2-*Amino-6-chlorotoluene-4-sulphonanilide* (*A*-1)

80 cm^3 of 50% DMF, 2 cm^3 30% hydrochloric acid, and 18 g of iron powder were put into a three-necked flask provided with a stirrer, reflux condenser and thermometer. The flask was heated up to a temperature of 90°C and during 1 h 0·1 mole of 6-chloro-2-nitrotoluene-4-sulphonanilide was added, maintaining the temperature at 95–98°C. After the addition of the nitrocompound was completed, the reaction mixture was further stirred at the boil for 1 h. After completion of the reduction process, the mixture was cooled to 70°C and 5 g of soda were added to render the system alkaline to Brilliant Yellow paper in order to precipitate dissolved iron salts. The solution was tested with sodium sulphide. Then, the reaction mixture was reheated to the boil, the precipitated iron oxides were filtered off and washed on the filter with 50 cm^3 of hot water. The combined filtrate and washings were cooled down to the room temperature and neutralized with acetic acid (30%) to pH 7.

At the first stage the product was obtained in the oily form, which then crystallized in the form of an easily filtered precipitate. After filtration and drying, 26·6 g of product with a melting point of 130–132°C were obtained. The reaction yield was 89·7%. The raw product was crystallized from 80%

ethanol. The crystallization yield was 92% and the purified product had a melting point of 133–134°C.

Elementary analysis involved amine hydrochloride.

Analysis for $C_{13}H_{14}Cl_2N_2O_2S$ (333·22)
Calculated: C = 46·86 H = 4·23 N = 8·41 S = 9·62 Cl = 21·28%
Found: C = 47·00 H = 4·13 N = 8·23 S = 9·70 Cl = 21·39%

Amines A-3, A-4, A-8, A-9, A-12 and A-13 were prepared by the same procedure.

3.3. 2-*Amine*-3′, 6-*dichloro*-2′-*methylotoluene*-4-*sulphonalilide* (A-5)

Reaction was carried out using a three-necked flask provided with a stirrer, reflux condenser and thermometer. 40 cm^3 of water and 3 cm^3 of hydrochloric acid were poured in and 21 g of iron powder were added; the mixture was heated to 90°C and over 1·5 h, 37·5 g of 3′,6-dichloro-2′-methyl-2-nitrotoluene-4-sulphonanilide in 80 cm^3 of DMF were added using a dropping funnel, maintaining mild boiling all the time. After the addition, stirring was continued for another hour. Then, the reaction mixture was cooled down to 60°C and 14 cm^3 of 30% NaOH were added. After complete precipitation of the iron salts, the iron oxides and hydroxides were filtered off. The precipitate was washed on the filter with 100 cm^3 of hot water. The combined filtrates were cooled down to room temperature and neutralized with 30% acetic acid to pH 7. The product separated as an oil. Then, the supernatant liquid was removed, the product was dissolved in 120 cm^3 of ethanol and 12 cm^3 of 30% hydrochloric acid were added. A white precipitate of the amine hydrochloride was rapidly formed which after cooling down to 5–10°C was filtered off and washed with 20 cm^3 of 50% ethanol. After drying, 32·1 g of product were obtained, with a melting point of 163–165°C. After crystallization from 80% ethanol solutions, the product had a melting point of 166·5–168°C. The crystallization yield was 75%.

The amine hydrochloride was subjected to elementary analysis.

Analysis for $C_{14}H_{15}Cl_3N_2O_2S$ (381·71)
Calculated: C = 44·05 H = 3·96 N = 7·34 S = 8·40 Cl = 27·86%
Found: C = 44·77 H = 3·84 N = 7·16 S = 8·20 Cl = 27·82%

Amines A-2, A-6, A-7, A-10, A-11, A-14 and A-15 were prepared in the same way.

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