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Reactions of 1-Arenesulfonyl-4-nitroimidazoles with Aniline in Aqueous Methanol Solution

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Abstract: Several 1-arenesulfonyl-4-nitroimidazoles were obtained and reacted with aniline in methanol-water medium at 65-70°C to yield mixtures of 1-arenesulfonylamide, 1-arenesulfonylanilide, 4-nitro-1-phenylimidazole and 4(5)-nitroimidazole in varied proportions depending on the arenesulfonyl group.

A contemporary synthesis of oligodeoxyribonucleotides is based on the so called triester method developed about twenty years ago[1]. In this method, arenesulfonylazoles are used as condensing agents. They are: imidazolides[2], 1,2,4-triazolides[3], tetrazolides[4], 4-nitroimidazolides[5-7], 3-nitro-1,2,4-triazolides[8] or their mixtures with N-methylimidazole[4] or tetrazole[6]. It is assumed that the condensing action of azolides consists in the formation of a reactive intermediary phosphinyloxysulfonate[9]. The condensing capability of the azolides will, therefore, depend on the susceptibility of the sulfur atom in the arenesulfonyl group to the attack of the nucleophilic reagent on the one hand and the leaving ability of the azole anion on the other.

The first work on application of arenesulfonylazoles concentrated on improving their condensing capabilities by adequate selection of pK_a of the azole (the leaving group). Generally, less attention was paid to the effect of the arenesulfonyl group and 2,4,6-triisopropylbenzenesulfonyl or mesitylenesulfonyl groups[4] were used. The selection of sterically developed arene substituents was aimed at restricting side reactions like arenesulfonation of 5'-hydroxyl groups in a sugar fragment. In further work, attention was paid to the potential influence of the substituents in the arenesulfonyl part of azolides on the rate of the condensation reaction. The latter considerably increased, when electron acceptor substituents were introduced into the arenesulfonyl group.

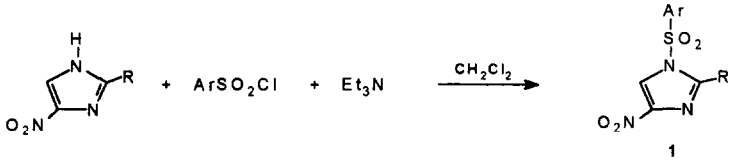
The basic problems in selection of a condensing reagent in the triester method concern achievement of a high condensation rate and high yields of oligoesters (without the use of reagents in excess) and elimination of side reactions. In spite of the fact that the above problems have been only partly solved,

more extensive studies on reactions of 1-arenesulfonylazolides with nucleophilic reagents have not been published. A few scattered reports concern their susceptibility to hydrolysis[7].

In this work, we have undertaken studies on the behaviour of 1-arenesulfonyl-4-nitroimidazoles in the presence of typical nucleophilic reagents like water and aniline. We have discovered that in certain 1-arenesulfonylazoles (especially where the azole group has a strong electron withdrawing nitro group) not only the sulfur atom of the sulfonyl group can be susceptible to nucleophilic attack, but also the carbon atom of the azole group. This was shown by us, when 4-nitro-1-(p-toluenesulfonyl)imidazole was reacted with aniline[10], and this paper is a continuation of our earlier brief communication.

RESULTS

1-Arenesulfonyl-4-nitroimidazoles were obtained with yields usually exceeding 70% by reaction of 4(5)-nitroimidazoles with 25% excess of arenesulfonyl chloride and triethylamine, in methylene chloride at 25°C for 24 hours, followed by solvent removal under reduced pressure and rinsing the residue twice with anhydrous methanol (scheme 1). This method was found to be more advantageous than that recently proposed, where tetraalkylammonium salts of nitroimidazole[11] were used.



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	Ar	R			Ar	R	
1a	p-$NO_2C_6H_4$	H	70.5%	**1h**	2,4,6-$(CH_3)_3C_6H_2$	H	57.6%
1b	p-ClC_6H_4	H	74.2%	**1i**	2,4,6-$(CH_3)_3C_6H_2$	CH_3	87.1%
1c	C_6H_5	H	68.1%	**1j**	2,4,6-$(iPr)_3C_6H_2$	H	85.7%
1d	p-$CH_3C_6H_4$	H	87.9%	**1k**	2,4,6-$(iPr)_3C_6H_2$	CH_3	77.6%
1e	p-$CH_3OC_6H_4$	H	91.9%	**1l**	p-$CH_3C_6H_4$	Cl	71.1%
1f	C_6H_5	CH_3	82.3%	**1m**	2,4,6-$(iPr)_3C_6H_2$	Cl	62.2%
1g	p-$CH_3C_6H_4$	CH_3	86.6%				

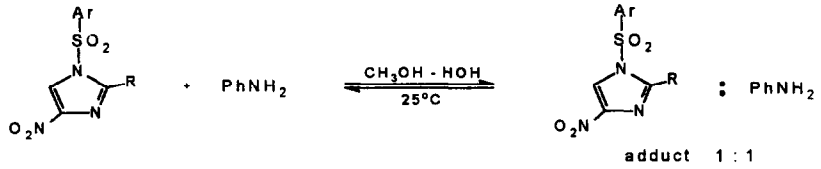
Scheme 1

Crude products had sharp melting points and their ^1H NMR spectra were in conformance with expectations. For analytical purposes, the samples of azolides were crystallized from organic solvents eg. anhydrous ethyl acetate or chloroform. The melting points of crystallized compounds were about 1 to 2°C higher than

those of crude azolides. The mass spectra of these compounds showed molecular ion peaks and intensive peaks for $ArSO_2^+$ and Ar^+ ions.

Azolides underwent hydrolysis under the influence of water to the corresponding arenesulfonic acids and 4(5)-nitroimidazoles. In solutions of dimethylsulfoxide-water or pyridine-water, a considerable quantity of 4(5)-nitroimidazoles appeared just after a dozen minutes. In aqueous methanol solutions, the azolides were relatively stable allowing the recording of their UV spectra. The solvolysis reaction in these solutions was greatly accelerated, when strong protonic acids of a concentration exceeding 0.1M were introduced. Isosbestic points were present in the UV spectra of the reaction mixtures, and their presence seemed to show that the solvolysis was not accompanied by side reactions. The effect of substituents in the 4 position of the benzene ring of the azolides on the acidic solvolysis rate was insignificant. The presence of methyl group in the 2 position of the imidazole ring also had little effect. Azolides 2,4,6-trisubstituted in benzene ring, especially mesitylenesulfonyl derivatives, underwent solvolysis rapidly. Kinetic data will be published in a separate paper. The samples of azolides underwent gradual changes even on storage in closed vials. The corresponding 4(5)-nitroimidazoles appeared (TLC) and melting points were found to be broadened. Crude azolides were used for syntheses and crystallized compounds in kinetic studies.

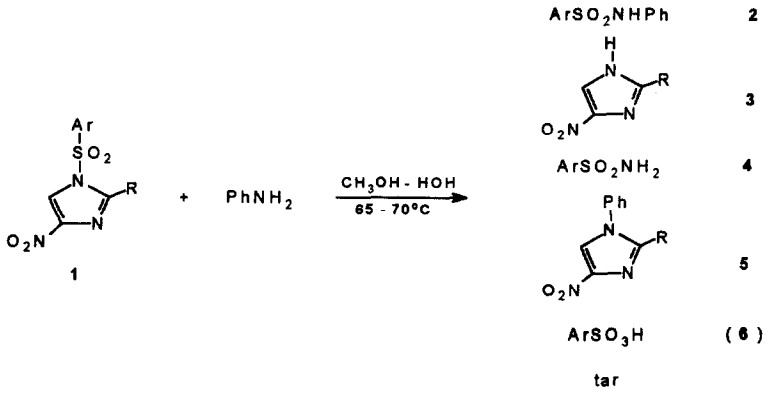
Some 1-arenesulfonyl-4-nitroimidazoles, obtained as described above, were reacted with excess aniline in methanol-water suspension (1:1) at 25°C yielding coloured azolide - aniline adducts (1:1) very sparingly soluble in the reaction mixture (scheme 2). The structure of these adducts has not been yet fully examined.



Scheme 2

It was found that contrary to 1,4-dinitroimidazole - aniline adducts[12], the 1-arenesulfonyl-4-nitroimidazole - aniline adducts remained in equilibrium with starting materials in organic solvents. Therefore, they can be charge transfer complexes by nature.

Adducts heated at 65-70°C in methanol-water solution (1:1) underwent complex transformations. Corresponding arenesulfonanilides, arenesulfonamides and nitroimidazoles were detected in the products. Also tars were found. Similar product mixtures were obtained from the reactions of 1-arenesulfonyl-4-nitroimidazoles with an excess of aniline in methanol-water medium carried out at once at 65-70°C. The yields of products were now much higher suggesting that the adducts were not intermediates in their formation. Generally, the reaction of 1-arenesulfonyl-4-nitroimidazoles with aniline in methanol-water medium at 65-70°C yielded a mixture of compounds as presented in scheme 3.



Scheme 3

Hence, arenesulfonanilides **2**, 4(5)-nitroimidazoles **3**, arenesulfonamides **4** and 4-nitro-1-phenylimidazoles **5** were obtained. Arenesulfonic acids **6**, were not separated. The yields and mutual proportions of the products varied within wide ranges depending on the arene group and possibly an additional substituent in the 4-nitroimidazole group. More important results are collected in table 1 (preparative data). They can be understated with errors of even a dozen percent due to the occurence of tar-like substances in certain reactions that render difficult the separation of the products from reaction mixtures.

Some 1-arenesulfonyl-4-nitroimidazoles were reacted with other compounds having primary amine groups in methanol-water medium at elevated temperatures. The reaction of 4-nitro-1-(p-toluenesulfonyl)imidazole with p-N,N-diethylaminoaniline yielded a mixture of N-(p-N,N-diethylaminophenyl)-p-toluenesulfonamide and 4(5)-nitroimidazole (approx. 65% yields). Neither 1-(p-N,N-diethylaminophenyl)-4-nitroimidazole nor p-toluenesulfonamide were found. In a similar reaction of 4-nitro-1-(p-toluenesulfonyl)imidazole with p-anisidine, a mixture of different products was obtained containing both 1-(p-methoxyphenyl)-4-nitroimidazole and p-toluenesulfonamide, but their yields were lower than those of the corresponding reaction products from aniline. The reaction of 4-nitro-1-(p-toluenesulfonyl)imidazole with 2,2-diethoxyethylamine yielded approx. 100% 4(5)-nitroimidazole.

4-Nitro-1-(p-toluenesulfonyl)imidazole was reacted with aniline also in such organic solvents as anhydrous pyridine, dimethylsulfoxide and chloroform p-Toluenesulfonanilide and 4(5)-nitroimidazole were obtained with 25 to 50% yields, when reactions were carried out in pyridine or dimethylsulfoxide. Neither 4-nitro-1-phenylimidazole nor p-toluenesulfonamide were found in the reaction mixtures. Separation and identification of the products were rendered difficult by tars. In chloroform, the reagents did not undergo any change.

The structure of the products was determined after isolation by their physico-chemical and spectroscopic properties and comparison with those of the compounds prepared by independent methods. The absence of

certain products was confirmed by TLC analysis of post-reaction mixtures.

Table 1. Yields of the Products from Reactions of Selected 1-Arenesulfonyl-4-nitroimidazoles with Aniline in Methanol-water Medium at 65-70°C after 2 hours

Azolide			Yields [%] and m.p's. [°C]			
No	Ar	R	Ar SO_2NHPh (2)	4(5)-NO_2I (3)	$ArSO_2NH_2$ (4)	1-Ph-4-NO_2I (5)
1a	p-$NO_2C_6H_4$	H	21; 162-166 (169-170)[a]	36; 282-287 (308-310)[16]	30; 174-177 (179-180)[a]	42; 183-185 (186-187)[14]
1b	p-ClC_6H_4	H	30; 100-103 (104-105)[a]	43; 240-260	55; 143-146 (146-147)[a]	57; 183-185
1c	C_6H_5	H	-	28; 290-292	25; 147-149 (151-153)[a]	30; 182-184
1d	p-$CH_3C_6H_4$	H	-	28; 280-290	46; 136-137 (138-139)[a]	42; 183-185
1e[b]	p-$CH_3OC_6H_4$	H	3; TLC	18; 290-292	25; 105-110 (112-113)[a]	30; 179-183
1f[c]	p-$CH_3C_6H_4$	CH_3	-	traces	-	-
1h	2,4,6-$(CH_3)_3C_6H_2$	H	70; 109-112 (112-114)[a]	85; 293-296	8; 135-140 (142-144)[a]	-
1l	p-$CH_3C_6H_4$	Cl	90; 99-101 (102-103)[a]	70; 217-219 (218-219)[17]	-	-
1m[d]	2,4,6-$(iPr)_3C_6H_2$	Cl	87; 159-161 (163-164)[a]	68; 216-218	-	-

a) Arenesulfonanilides and arenesulfoamides obtained in a reaction of amine or ammonia with adequate arenesulfony chlorides. Melting points acc.to literature.
b) After 30 minutes of reaction.
c) A large quantity of tars rendering the separation impossible.
d) After 2 hours of reaction at 25°C.

DISCUSSION OF RESULTS

The following conclusions can be drawn from the data collected in table 1 and numerous observations made by us during studies. In the reaction medium composed of 1-arenesulfonyl-4-nitroimidazole + aniline + water + methanol, generally, at least three simultaneous processes occur at 65-70°C as mentioned below:

a) solvolysis of 1-arenesulfonyl-4-nitroimidazole to arenesulfonic acid, methyl arenesulfonate and 4(5)-nitroimidazole;

b) aminolysis of 1-arenesulfonyl-4-nitroimidazole to arenesulfonanilide and 4(5)-nitroimidazole;

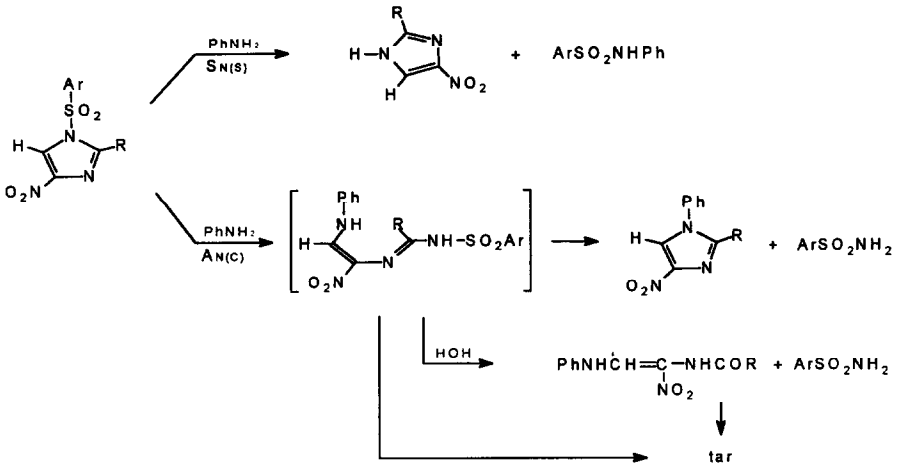
c) reactions yielding the arenesulfonamide and 4-nitro-1-phenylimidazole and possibly tars.

The contents of the products from each process in the reaction mixture depend to a great extent on the substituents both of the benzene ring of the arenesulfonyl group and of the imidazole ring.

To reduce the solvolysis process, the reactions were carried out in anhydrous organic solvents. In pyridine or dimethylsulfoxide solutions, considerable quantities of tars were obtained rendering it difficult to separate the products. It is worthy of mention that 1,4-dinitroimidazoles (similar behaviour to 1-arenesulfonyl-4-nitroimidazoles) in anhydrous pyridine under the influence of anilines, undergo decomposition to 4(5)-nitroimidazoles, whereas in anhydrous dimethylsulfoxide they form the corresponding 4-nitro-1-phenyl-imidazoles in high yields comparable to those obtained in methanol-water solutions. Based on spectrophotometric determinations of the solvolysis rates of 1-arenesulfonyl-4-nitroimidazoles in methanol-water solution in the absence of acids and the data collected in table 1 we are of the opinion that the contribution of solvolysis (process "a") in reactions of azolides with aniline in neutral methanol-water solution was insignificant in most cases, hence, it can be practically neglected in further cosiderations.

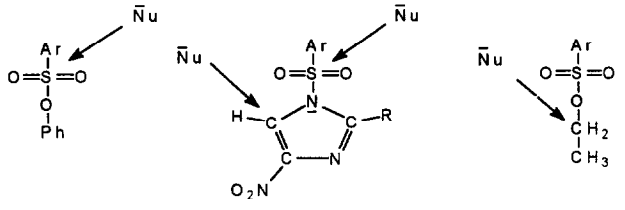
To analyze the effects of the substituents on mutual proportions of the products formed in the processes "b" and "c", it is necessary to assume reaction mechanisms. We assume that arenesulfonanilides and 4(5)-nitroimidazoles are formed in paralell in a nucleophilic substitution reaction at the sulfur atom ($S_{N(S)}$), whereas arenesulfonamides and 4-nitro-1-phenylimidazole are obtained in the reaction initiated by a nucleophilic attack of aniline on the 5 carbon atom of the imidazole ring ($A_{N(C)}$). Tars can be also formed as by-products (scheme 4).

In the literature[13], one may find the kinetic data on hydrolysis of ethyl- and phenyl arenesulfonates. It was proved that ethyl arenesulfonates undergo hydrolysis by nucleophilic attack of water on the alkyl carbon atom combined with oxygen ($S_{N(C)}$), while phenyl arenesulfonates hydrolyze by attack on the sulfur atom ($S_{N(S)}$). The effect of substituents in both reactions is described by the Hammett equation (ρ_c= +1.425, ρ_s= +2.24). In a neutral strongly polar medium, some aryl arenesulfonates, especially those containing 2,4,6-trialkyl substituents, can also hydrolyze according to the $S_{N(S)}1$ mechanism. We have tried to use the cited literature data in analysis of the results obtained in this work. Aminolysis of 1-arenesulfonyl-4-nitroimidazoles (process "b") was considered as analogous to the hydrolysis of phenyl arenesulfonates. Furthermore, the reactions yielding arenesulfonamides and 4-nitro-1-phenylimidazole (process "c") were considered as a



Scheme 4

fair analogy to the hydrolysis of ethyl arenesulfonates.The scheme 5 shows the most probable sites of the first nucleophilic attack on the compounds under consideration, justifying the mentioned analogies.



Scheme 5

Based on the assumed similarities and considering the nature of our preparative results, far from their quantitative estimation, the ratios of the sum of the yields in the process "c" to the sum of the yields in the process "b" (neglecting the process "a") were compared with ratios of the hydrolysis rate constants of the similarly substituted ethyl and phenyl arenesulfonates in a neutral medium (see table 2).

A comparison of pK_a values for phenol (9.8) with those for 4(5)-nitroimidazole (9.2) and 2-methyl-4(5)-nitroimidazole (9 7) shows a similar nucleofugicity of phenolate and nitroimidazole ions. The nucleophilic substitution at the sulfur atom in 1-arenesulfonyl-4-nitroimidazoles should, therefore, proceed according to the

$S_{N(S)}2$ mechanism characteristic for hydrolysis of most phenyl arenesulfonates. The effect of substituents in the arenesulfonyl group on the susceptibility of the 5 carbon atom in compounds **1** and of the OCH_2 - carbon atom in ethyl arenesulfonates to nucleophilic agents should be similar (in spite of differences in the constitution of the attacked compounds). A similarity consists in the same number of bonds between

Table 2. A Comparison of the Ratios of the Yields in "b" and "c" Processes of 1-Arenesulfonyl-4-nitroimidazoles with Aniline and the Ratios of the Hydrolysis Rate Constants for Ethyl and Phenyl Arenesulfonates

Ar SO_2	$\frac{\text{yields in process "c" [\%]}}{\text{yields in process "b" [\%]}} = \frac{4+5}{2+3}$	$\frac{k_{Et}}{k_{Ph}}$
p-$NO_2C_6H_4SO_2$	~ 1.3	0.85
p-$ClC_6H_4SO_2$	~ 1.5	1.29
$C_6H_5SO_2$	~ 2.0	1.59
p-$CH_3C_6H_4SO_2$	~ 3.1	2.01
p-$CH_3OC_6H_4SO_2$	~ 2.6	3.26
2,4,6-$(CH_3)_3C_6H_2SO_2$	~ 0.05	0.02

k_{Et} - the hydrolysis rate constant of ethyl arenesulfonates in dioxane-water solution at 50°C
k_{Ph} - the hydrolysis rate constant of phenyl arenesulfonates in dioxane-warer solution at 50°C

substituents and reaction centres in both cases. It explains in our opinion, the consistent effect of the substituents in the reactions under discussion as presented in table 2. The ratio of the yields in "c" to "b" processes, for the reaction of the azolide with p-methoxy substituent are lower than expected and can be explained by slightly different reaction conditions (table 1). 4-Nitro-1-(2,4,6-trialkylbenzenesulfonyl)imidazoles probably react according to the $S_{N(S)}1$ mechanism. Even in such case, the attack of aniline on the 5 carbon atom of the imidazole ring is possible as indicated by the 2,4,6-trimethylbenzenesulfonamide **(8)** obtained in reaction of aniline with **1h**. A lack of 4-nitro-1-phenylimidazole in products of this reaction (as in other reactions of aniline with 4-nitro-1-(2,4,6-trialkylbenzenesulfonyl)imidazoles can be easily explained by steric hindrance making difficult the recyclization of the linear intermediate.

From our observations a considerable quantity of tar-like substances results, when the methyl group is introduced into the 2 position of an azolide reacted with aniline. The above can be hardly explained, since 1,4-dinitro-2-methylimidazole reacts with aniline to give the corresponding 1-aryl-2-methyl-4-nitroimidazoles

in high yields. When the methyl group in the 2 position of azolides **1** is replaced by a chlorine atom, the reaction of **1** with aniline gives the products of the attack on the sulfur atom with high yields already at 25°C with no products from the attack on the imidazole ring. This result can be easily associated with the easy abstraction of 2-chloro-4-nitroimidazole anion (pK_a= 5.85 for 2-chloro-4(5)-nitroimidazole). Due to considerable differences in the conditions of the reactions studied in this work and the synthesis of oligodeoxyribonucleotides, it is not possible to indicate unequivocally the best condensing agent among the examined azolides. In the author's opinion, the use of 1-arenesulfonyl-2-chloro-4-nitroimidazoles for this purpose may bring satisfactory results.

Most results presented in this work concerned the reactions of azolides **1** with aniline. Only in a few cases, were other compounds with primary amine group used instead of aniline. In view of our experiments, one may believe that the increase in basicity (nucleophilicity) of the amine nitrogen promotes the attack on the sulfur atom.

EXPERIMENTAL

The purity of all the compounds described was examined by melting points and thin-layer chromatography. Melting points (not corrected) were determined in open capillaries. TLC chromatograms were developed on the plates covered with silica gel 60 F_{254} with solvents as follows: benzene-ethyl acetate (1:1), acetone-chloroform (2:1) or chloroform-methanol (9:1), observed under UV light and then in a chamber saturated with iodine vapors. ^{1}H NMR spectra were determined on a type Tesla BS-587 (80 MHz) spectrometer in $CDCl_3$ or $(CD_3)_2CO$ with TMS as an internal standard. EI MS spectra were determined on a type LKB-2091 spectrometer at 70eV.

1-Arenesulfonyl-4-nitroimidazoles (1)

Triethylamine (12.5 mmol) and arenesulfonyl chloride (12.5 mmol) were successively added in several portions to a mixture of 4(5)-nitroimidazole (10 mmol) suspended in dichloromethane (20 cm^3). The prepared mixture was stirred at 25°C for two hours and then left overnight. The solvent was removed under reduced pressure at 25°C and the residue shaken twice with methanol (2x10 cm^3). After filtration of the undissolved sediment and washing it with methanol (5 cm^3), colourless 1-arenesulfonyl-4-nitroimidazoles (**1**) were obtained. They melted sharp and were used for further reactions without additional purification. For analytical purposes, the products were recrystallized.

4-Nitro-1-(p-nitrobenzenesulfonyl)imidazole (1a): yield 70.5%, m.p. 193-195°C. After crystallization from ethyl acetate m.p. 195-197°C. Found: C, 36.14; H, 1.90; N, 19.15; $C_9H_6N_4O_6S$ requires: C, 36.25; H, 2.03; N, 18.79. UV (CH_3OH): λ_{max} (ε_{max}) 271 nm (6700). ^{1}H NMR [$(CD_3)_2CO$] δ: 8.42 (d, J=1.8 Hz, 1H, CH imid); 8.52 (broad s, 4H, CH arom); 8.69 (d, J=1.8 Hz, 1H, CH imid).

1-(p-Chlorobenzenesulfonyl-4-nitroimidazole (1b): yield 74.2%, m.p. 164-167°C. After crystallization from

chloroform m.p. 167-168°C. Found: C, 37.32; H, 1.93; N, 14.55; $C_9H_6N_3O_4ClS$ requires: C, 37.57; H, 2.10; N, 14.61. UV (CH_3OH): λ_{max} (ε_{max}) 271 nm (8300). ^1H NMR ($CDCl_3$,) δ: 7.55 (broad d, J=9 Hz, 2H, CH arom); 7.88 (d, J=1.5 Hz, 1H, CH imid); 7.92 (broad d, J=9 Hz, 2H, CH arom); 8.00 (d, J=1.5 Hz, 1H, CH imid).

1-Benzenesulfonyl-4-nitroimidazole (1c): yield 68.1%, m.p. 155-160°C. After crystallization from ethyl acetate m.p. 160-161.5°C. Found: C, 42.58; H, 2.60; N, 16.42; $C_9H_7N_3O_4S$ requires: C, 42.69; H, 2.79; N, 16.59. UV (CH_3OH): λ_{max} (ε_{max}) 272 nm (7200). ^1H NMR ($CDCl_3$) δ: 7.50-7.82 (m, 5H, CH arom); 7.94 (d, J=1.6 Hz, 1H, CH imid); 8.02 (d, J=1.6 Hz, 1H, CH imid). MS (m/z): 253 (9%, M^+), 141 (63%, $C_6H_5SO_2^+$), 77 (100%, $C_6H_5^+$), 51 (25%).

4-Nitro-1-(p-toluenesulfonyl)imidazole (1d): yield 87.9%, m.p. 166-167°C. After crystallization from chloroform m.p. 168-169°C. Found: C, 44.77; H, 3.28; N, 15.67; $C_{10}H_9N_3O_4S$ requires: C, 44.94; H, 3.39; N, 15.72. UV (CH_3OH): λ_{max} (ε_{max}) 273 nm (6600). ^1H NMR ($CDCl_3$) δ: 2.43 (s, 3H, CH_3); 7.39 (broad d, J=11 Hz, 2H, CH arom); 7.88 (broad d, J=11 Hz, 2H, CH arom); 7.91 (d, J=1.6 Hz, 1H, CH imid); 8.04 (d, J=1.6 Hz, 1H, CH imid). MS (m/z): 267 (40%, M^+), 155 (80%, $H_3CC_6H_4SO_2^+$), 91 (100%, $H_3CC_6H_4^+$), 65 (20%), 39 (12%).

1-(p-Methoxybenzenesulfonyl)-4-nitroimidazole (1e): yield 91.9%, m.p. 169-172°C. After crystallization from ethyl acetate m.p. 170-172°C. Found: C, 42.37; H, 3.16; N, 14.91; $C_{10}H_9N_3O_5S$ requires: C, 42.40; H, 3.20; N, 14.83. UV (CH_3OH): λ_{max} (ε_{max}) 262 nm (19000). ^1H NMR [$(CD_3)_2CO$] δ: 3.39 (s, 3H, CH_3O); 7.19 (broad d, J=10 Hz, 2H, CH arom); 8.14 (broad d, J=10 Hz, 2H, CH arom); 8.25 (d, J=1.6 Hz, 1H, CH imid); 8.52 (d, J=1.6 Hz, 1H, CH imid).

1-Benzenesulfonyl-2-methyl-4-nitroimidazole (1f): yield 82.3%, m.p. 133-135°C. After crystallization from chloroform m.p. 134-135°C. Found: C, 44.40; H, 3.29; N, 15.54; $C_{10}H_9N_3O_4S$ requires: C, 44.94; H, 3.39; N, 15.72. UV (CH_3OH): λ_{max} (ε_{max}) 277 nm (7350). ^1H NMR ($CDCl_3$) δ: 2.56 (s, 3H, CH_3); 7.6-8.0 (m, 5H, CH arom); 8.15 (s, 1H, CH imid). MS (m/z): 267 (10%, M^+), 141 (62%, $C_6H_5SO_2^+$), 77 (100%, $C_6H_5^+$), 51 (22%).

2-Methyl-4-nitro-1-(p-toluenesulfonyl)imidazole (1g): yield 86.6%, m.p. 147-150°C. After crystallization from benzene m.p. 148-150°C. Found: C, 46.92; H, 3.97; N, 14.72; $C_{11}H_{11}N_3O_4S$ requires: C, 46.97; H, 3.94; N, 14.94. UV (CH_3OH): λ_{max} (ε_{max}) 278 nm (7900). ^1H NMR ($CDCl_3$) δ: 2.43 (s, 3H, CH_3); 2.55 (s, 3H, CH_3); 7.38 (broad d, J=9 Hz, 2H, CH arom); 7.81 (broad d, J=9 Hz, 2H, CH arom); 8.13 (s, 1H, CH imid). MS (m/z): 281 (11%, M^+), 155 (68%, $H_3CC_6H_4SO_2^+$), 91 (100%, $H_3CC_6H_4^+$), 65 (17%).

1-Mesitylenesulfonyl-4-nitroimidazole (1h): yield 57.6%, m.p. 137-139°C. After crystallization from ethyl acetate m.p. 138-139°C. Found: C, 48.60; H, 4.40; N, 14.20; $C_{12}N_{13}N_3O_4S$ requires: C, 48.80; H, 4.44; N, 14.23. UV (CH_3OH): λ_{max} (ε_{max}) 280 nm (9900). ^1H NMR ($CDCl_3$) δ: 2.35 (s, 3H, CH_3); 2.61 (s, 6H, CH_3 + CH_3); 7.03 (s, 2H, CH arom); 7.86 (s, 2H, CH imid). MS (m/z): 295 (6%, M^+), 183 (46%, $MesSO_2^+$), 119 (100%, Mes^+), 91 (18%), 77 (9%).

1-Mesitylenesulfonyl-2-methyl-4-nitroimidazole (1i): yield 87.1%, m.p. 125-127°C. After crystallization from

benzene m.p. 126-127°C. Found: C, 50.38; H, 4.93; N, 13.53; $C_{13}H_{15}N_3O_4S$ requires: C, 50.47; H, 4.89; N, 13.58. UV (CH_3OH): λ_{max} (ε_{max}) 282 nm (10200). ^1H NMR ($CDCl_3$) δ: 2.31 (s, 3H, CH_3); 2.36 (s, 3H, CH_3); 2.53 (s, 6H, CH_3); 7.02 (s, 2H, CH arom); 8.07 (s, 1H, CH imid). MS (m/z): 309 (6%, $M^{+\cdot}$), 183 [39%, $(CH_3)_3C_6H_2SO_2^+$], 119 [100%, $(CH_3)_3C_6H_2^+$], 91 (12%).

4-Nitro-1-(2,4,6-triisopropylbenzenesulfonyl)imidazole (1j): yield 85,5%, m.p. 155156°C. After crystallization from cycloheksen-benzen (2:1) m.p. 156-157°C. Found: C, 56,84; H, 6.68; N, 10.96; $C_{18}H_{25}N_3O_4S$ requires: C, 56.97; H, 6.64; N, 11.07. UV (CH_3OH): λ_{max} (ε_{max}) 282 nm (12000). ^1H NMR ($CDCl_3$) δ: 1.18 (d, J=8 Hz, 12H, CH_3 izopr); 1.28 (d, J=8 Hz, 6H, CH_3 izopr); 2.93 (m, J=8 Hz, 1H, CH izopr); 3.95 (m, J=8 Hz, 2H, CH izopr); 7.25 (s, 2H, CH arom); 7.83 (d, J=1.6 Hz, CH imid); 7.90 (d, J=1.6 Hz, CH imid). MS (m/z): 379 (4%, $M^{+\cdot}$), 267 [100%, $(CH_3)_3C_6H_2SO_2^+$]; 203 [31%, $(CH_3)_3C_6H_2^+$]; 175 (28%); 119 (24%); 91 (32%); 43 (65%); 41 (21%).

2-Methyl-4-nitro-1-(2,4,6-triisopropylbenzenesulfonyl)imidazole (1k): yield 77.6%, m.p. 113-115°C. After crystallization from cycloheksene m.p. 114-116°C. Found: C, 57.60; H, 6.93; N, 10.52; $C_{19}H_{27}N_3O_4S$ requires: C, 57.99; H, 6.92; N, 10.68. UV (CH_3OH): λ_{max} (ε_{max}) 284 nm (11300). ^1H NMR ($CDCl_3$) δ: 1.16 (d, J=7 Hz, 12H, CH_3 izopr); 1.27 (d, J=7 Hz, 6H, CH_3 izopr); 2.27 (s, 3H, CH_3); 2.95 (m, 1H, CH); 3.88 (m, 2H, CH); 7.21 (s, 2H, CH arom); 8.02 (s, 1H, CH imid). MS (m/z): 393 (3%, $M^{+\cdot}$), 267 [100%, $(CH_3)_3C_6H_2SO_2^+$], 203 [31%, $(CH_3)_3C_6H_2^+$], 43 (38%).

2-Chloro-4-nitro-1-(p-toluenesulfonyl)imidazole (1l): yield 71.1%, m.p. 124-126°C, without crystallization. Found: C, 39.98; H, 2.53; N, 13.86; $C_{10}H_8N_3O_4ClS$ requires: C, 39.81; H, 2,67; N, 13.93. UV (CH_3OH): λ_{max} (ε_{max}) 279 nm (8000). ^1H NMR ($CDCl_3$) δ: 2.50 (s, 3H, CH_3); 7.40 (broad d, J=9 Hz, 2H, CH arom); 7.80 (broad d, J=8 Hz, 2H, CH arom), 8.21 (s, 1H, CH imid).

Reactions of 1-arenesulfonyl-4-nitroimidazoles (1) with aniline

Reactions carried out at 25°C - adducts formation. Aniline (0,93 g, 10 mmol) was added to a suspension of 1-arenesulfonyl-4-nitroimidazole (5 mmol) in 20 cm^3 methanol-water solution (1:1) and then agitated for 24 hours at 25°C. The coloured sediment was filtered off and washed with methanol to yield an adduct. E.g. **1d** with aniline: yellow sediment, m.p. 98-99°C (decom.), yield 88.9%.

Reactions carried out at 65-70°C. Aniline (0.93 g, 10 mmol) was added to a stirred mixture of 1-arenesulfonyl-4-nitroimidazole (2.5 mmol) in 20 cm^3 methanol-water solution (1:1). The whole mixture was agitated for 2 hours at 65-70°C and then left at 25°C until next day. The precipitated sediment (A) was filtered off and washed with methanol. The filtrates were subjected to steam distillation. 250 cm^3 distillate was collected and then rejected. Hot aqueous solution from the destillation flask was separated from oil (B - which crystallized later on) and left until next day. The precipitated sediment (C) was filtered off and filtrate was evaporated under reduced pressure at a temperature below 80°C to dryness yielding the residue (D). From the sediments (A-D) after their crystallization, arenesulfonamides **(4)**, arenesulfonanilides **(2)**, 4(5)-nitroimidazoles **(3)** and 4-nitro-1-phenylimidazole **(5)** were obtained. These compounds were compared with standard compounds

prepared by other methods. Example:

Reaction of 1-(p-chlorobenzenesulfonyl)-4-nitroimidazole (1b) with aniline. From 0.72 g **(1b)** the following compounds were prepared: 0.27 g sediment (A) - 4-nitro-1-phenylimidazole contaminated with 4(5)-nitroimidazole (TLC). After crystallization from acetone, 4-nitro-1-phenylimidazole was obtained, m.p. 183-185°C (lit.[14] 186-187°C); 0.25 g sediment (B) - p-chlorobenzenesulfonanilide contaminated with tar-like substances (TLC). After crystallization from diluted methanol with activated carbon, p-chlorobenzenesulfonanilide was obtained, m.p. 100-103°C (lit.[15] 105°C); 0.15 g sediment (C) - a mixture of 4-nitro-1-phenylimidazole and p-chlorobenzenesulfonanilide (TLC); 0.39 g sediment (D) - a mixture of p-chlorobenzenesulfonamide and 4(5)-nitroimidazole (TLC). Anhydrous ether was added to D. Undissolved sediment was filtered off. After its crystallization from water, contaminated 4(5)-nitroimidazole was obtained, m.p. 240-260°C (lit.[16] 308-310°C). Ether was removed from ethereal filtrate and the residue was crystallized from diluted methanol with activated carbon. p-Chlorobenzenesulfonamide was obtained, m.p. 143-146°C (lit.[15] 146-147°C).

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