DIAZO COMPOUNDS OF THE HETEROCYCLIC SERIES. 6.* AMINATION OF METHOXY-SUBSTITUTED 2-NAPHTHYL- AND 2-ARYLAZOBENZIMIDAZOLES

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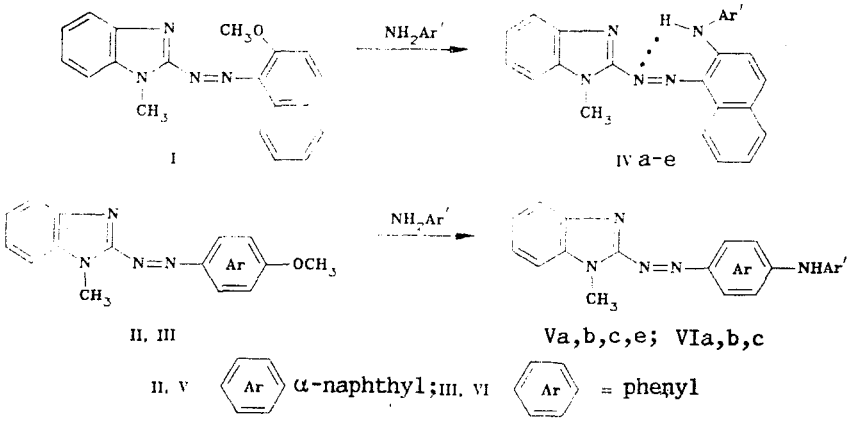
The amination of azo compounds inactivated by quaternization was carried out for the first time using 4-methoxyphenyl-, 2- and 4-methoxynaphthylazobenzimidazoles as examples. In contrast to the quaternary salts of 2-arylazobenzimidazoles, during the amination of the above bases of azo compounds, the substitution of the methoxy group rather than of the hydrogen atom was observed. The anomalous ease of substitution of the methoxy group, located in the naphthalene ring in a position adjacent to the azo bridge was attributed to the manifestation of an ortho-effect, discovered in the series of azo compounds for the first time.

The amination of the quaternary salts of 2-arylazobenzimidazoles results in deeply colored compounds of the benzimidazole series, which are difficult to obtain by other methods [2]. In addition, this reaction is interesting as an example of a nucleophilic substitution reaction in the series of azo compounds, which has not been much investigated. We therefore continued the investigation of this reaction by introducing 2- and 4-methoxy-substituted 2-naphthylazobenzimidazoles I and II into the reaction with arylamines, as well as 2-(4-methoxyphenylazo)benzimidazole (III), the latter to clarify the role of annelation of the benzene ring.

The principal difference of the amination reaction studied in the present work from similar transformations previously studied [2, 3] consists in the absence of preliminary activation of the azo compounds, usually realized by the quaternization of the N-hetero ring. The amination is carried out by the reaction of azo compound bases I-III with a 3- to 5-fold excess of arylamine in a chloroform solution.



IV—VI a $Ar'=p\text{-}CH_3OC_6H_4$, b $Ar'=p\text{-}CH_3C_6H_4$, c $Ar'=C_6H_5$, d $Ar'=\alpha$-нафтил, e $Ar'=p\text{-}CH_3OCOC_6H_4$

*For Communication 5, see [1].

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TABLE 1. Arylamination of Azobenzimidazoles I-III in Chloroform*

Compound	Arylamine	T_r, °C	t_r, h	Yield, %
I	p-Anisidine	20...25	12	93
	p-Toluidine	20...25	20	89
	Aniline	20...25	38	77
	α-Naphthylamine	20...25	100	62
	p-Aminoacetophenone	20...25	140	61
II	p-Anisidine	Boiling	40	92
	p-Toluidine	Boiling	67	96
	Aniline	Boiling	110	73
	α-Naphthylamine	Boiling	200	DSM
	p-Aminoacetophenone	30...35	360	21
III	p-Anisidine	Boiling	58	88
	p-Toluidine	Boiling	72	77
	Aniline	Boiling	130	67
	α-Naphthylamine	Boiling	200	DSM
	p-Aminoacetophenone	Boiling	200	DSM

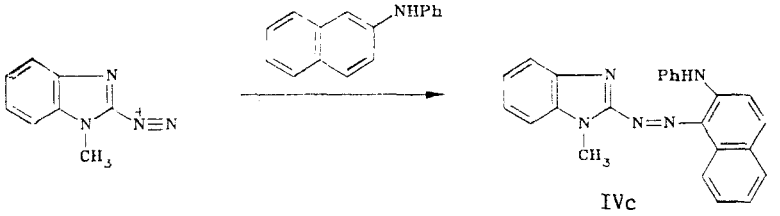
*T_r) temperature of reaction; t_r) time of reaction; DSM) difficultly separable mixture.

The amination of 2-methoxynaphthylazo compound I proceeds with unusual ease with p-anisidine and p-toluidine, which are most basic in the series of arylamines, studied at room temperature takes only a few hours (see Table 1). The reaction time increases to several days with decrease in the basicity of the amine. Thus, the increase in temperature is undesirable here because of intensification of side reactions leading to the formation of weakly-colored products.

In contrast to the 2-methoxy-substituted I, the 4-methoxyisomer II and its benzene analog III undergo the reaction with aromatic amines only on prolonged boiling of the reaction mixtures. Since, as has been found, an autocondensation process predominates for p-aminoacetophenone under these conditions, the amination product could be isolated only in the case of the azo compound II in a low yield after prolonged holding of the reaction mixture at 30-35°C. Positive results could not be obtained for 4-methoxy-substituted II and III in the reaction with α-naphthylamine. The data in Table 1 show that the amination of 4-methoxy naphthyl-substituted II proceeds somewhat more easily compared with the benzene analog, which agrees with the known influence of the annelation of rings on the aromatic substitution reactions [4, 5].

It has previously been found that the arylamination of the quaternary salts of heterocyclic azo compounds proceeds at the free p-position of the benzene ring of the azo component, even in the presence of an ortho-methoxyl group in it [2, 3, 6]. This observation, together with the above-described difference in the reaction conditions with amines of 2-methoxy- and 4-methoxy-substituted compounds, did not eliminate the possibility of the substitution of a hydrogen atom at 4-position of the azo compound I by the arylamine residue. However, the study of the structure of the products of the amination of compounds IV-VI showed that both in the case of 2-methoxynaphthylazobenzimidazole I, and in the case of the 4-methoxy-substituted isomer II and its benzene analog III, the substitution of the methoxy group takes place.

The structure of the product of amination of 2-methoxynaphthylazo compound I by aniline was verified by a countersynthesis by an azo coupling of benzimidazole-2-diazonium salt with phenylaminonaphthalene.



IVc

TABLE 2. Characteristics of Aminophenyl(naphthyl)azobenzimidazoles IV-VI

Compound	Empirical formula	mp, °C (from alcohol)	IR spectrum, ν, cm^{-1}*	PMR spectrum, δ, ppm (J, Hz)**				
				NCH_3 (s, 3H)	OCH_3 (s, 3H)	CCH_3 (s, 3H)	H_{arom}, M	$^{8\text{-}H}$ (d, d, 1H)
IV a	$C_{25}H_{21}N_5O$	229...230	710, 820, 1027, 1140, 1240, 1315, 1345, 1605 s.	3,97	3,75	—	7,22...7,85 (13H);	8,90 (J=8,4)
IV b	$C_{25}H_{21}N_5$	234...235	705, 1135, 1190, 1250, 1270, 1330, 1395, 1607 s.	3,98	—	2,34	7,20...7,90 (13H);	8,88 (J=8,5)
IV c	$C_{24}H_{19}N_5$	216...217	726, 940, 1123, 1206, 1260, 1314, 1607 s.	3,90	—	—	7,18...7,85 (14H)	8,88 (J=8,4)
IV d	$C_{28}H_{21}N_5$	219...220	730, 780, 1060, 1133, 1180, 1286, 1315, 1607 s.	3,82	—	—	6,92...8,03 (16H);	8,98 (J=8,3)
IV e	$C_{26}H_{21}N_5O$	223...224	706, 815, 1135, 1160, 1225, 1313, 1607 s., 1660 s.	4,22	—	2,61	7,26...8,15 (13H);	8,98 (J=8,6)
V a	$C_{25}H_{21}N_5O$	205...206	715, 1140, 1160, 1260, 1325, 1615 w., 3175 br.	4,02	3,70	—	6,83...8,46 (13H);	8,86 (J=8,3)
V b	$C_{25}H_{21}N_5$	212...213	715, 1140, 1160, 1260, 1273, 1600 w., 3180 br.	4,08	—	2,25	6,98...8,45 (13H);	8,85 (J=8,5)
V c	$C_{24}H_{19}N_5$	228...230	713, 1126, 1260, 1313, 1602 s, 3380 br..	4,03	—	—	7,02...8,04 (14H)	8,80 (J=8,4)
V e	$C_{26}H_{21}N_5O$	195...196	708, 1140, 1215, 1315, 1607 w., 1658 s., 3310 br.	4,12	—	2,54	7,05...8,14 (13H),	8,85 (J=8,6)
VI a	$C_{21}H_{19}N_5O$	227...228	730, 1130, 1240, 1330, 1605, 3160, 3270 br.	3,95	3,70	—	6,83...8,08 (12H)	-
VI b	$C_{21}H_{19}N_5$	284...285	725, 1104, 1127, 1297, 1330, 1602 w., 3280 br.	4,05	—	2,27	6,90...8,08 (12H)	-
VI c	$C_{20}H_{17}N_5$	255...256	728, 1064, 1140, 1228, 1312, 1607 w., 3320 br.	4,10	—	—	7,01...8,38 (13H)	- -

*s) Strong band; w) weak band; br.) broad.

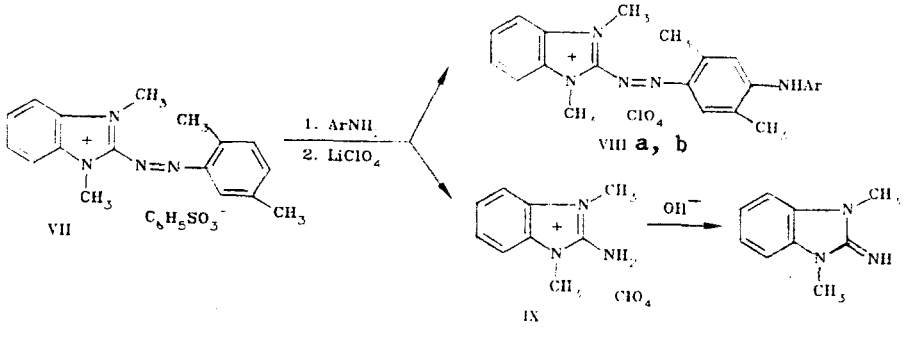
**In DMFA-D_7, compound VI — in $CDCl_3$.

In the remaining cases, the structure of the amino-substituted IV-VI was confirmed by the elemental analysis data and physicochemical methods. In the IR spectra of the amino-substituted IV-VI, the region of the extraplanar deformational vibrations of the C—H bonds of the aromatic ring is characteristic. Together with the bands of the starting azo compounds I-III [1], there appear absorption peaks of the aromatic ring introduced with the arylamine residue (Table 2). The most intense absorption in the IR spectra of the azo compounds IV-VI is observed in the 1140-1127 cm^{-1} region. A similar band has been noted for a large number of amino-substituted azo compounds of the benzene series, without their being assigned to any given grouping [7]. The difference in the amination products at the ortho- (IV) and para-positions (V, VI) is manifested by the presence in the former of an intense peak at 1607-1605 cm^{-1}, while the para-substituted compounds (V, VI) give only a weak absorption in this region. Moreover, the 4-amino-substituted compounds V, VI are characterized by weak bands of the ν_{N-H} stretching vibrations at 3380-3360 cm^{-1}, while the 2-substituted IV do not show any noticeable absorption either in solutio or on fluorinated hydrocarbon oil mulls. A similar behavior was noted by the authors of [7] for aminoazo compounds possibly having an intramolecular hydrogen bond.

The PMR spectra of the amination products IV-VI indicate a substitution of the methoxy group in the initial azo compounds, and the retention of the azo structure, characterized by a weak-field doublet of doublets of the 8′-H peri-proton in compounds IV, V (cf. [1]). The azo compounds IV with an amino group in a position adjacent to the azo bridge give a singlet of the N-CH_3 group protons in a weaker field than the 4-amino-substituted V, VI. The product of amination by α-naphthylamine IVe, in which this singlet is shifted to a strong field, is an exception (see Table 2).

In the UV region the introduction of the amino group is accompanied by an intensification of the color, such that the greatest bathochromic shift of the long-wave band is observed for the II → V transitions from 430 to 640 nm. Introduction of an amine residue into the ortho-position to the azo group is characterized by a considerably smaller bathochromic effect from 438 nm for compound I to 490-550 for compound IV.

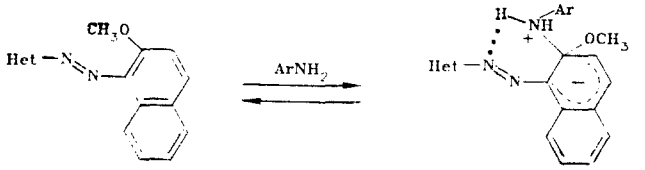
Thus, the reaction of 2- and 4-methoxy-substituted naphthylazobenzimidazoles I and II, and also of 4-methoxyphenylazobenzimidazole III with aromatic amines proceeds by a substitution path of the methoxyl grouping by an arylamino group. The ortho-amination observed for the first time in the azo-compounds series was found to be for the 2-methoxynaphthylazo-substituted I not only simply possible, but proceeding with anomalous easiness: under the conditions of amination of the azo compound I, its 4-methoxyisomer II forms only traces of amino-substituted products. The reactivity of the 2-methoxynaphthylazo compounds I with respect to aromatic amines was found to be comparable with that observed for a 1,3-dimethyl-2-(2,5-dimethylbenzenazo)benzylimidazolium quaternary salt (VII); the latter is aminated with p-anisidine and p-toluidine in 10 and 17 h, respectively. In the IR spectra of the amino-substituted VIIIa, b there are absorption bands of the NH group at 3260 and 3190 cm^{-1}, respectively, and there is also a band at 1140 cm^{-1} characteristic for the phenylamino derivatives of the azo compounds [7]. At the same time, in the PMR spectra of the amination products of VIII, proton signals appear of the methoxyl (3.75 ppm for VIIIa) and methyl (2.50 ppm for VIIIb) groups, which are absent in the spectrum of the initial quaternary salt VII. It is of interest that the amination of salt VII is accompanied by the formation of product of a reductive uncoupling — the 1,3-dimethyl-2-aminobenzylimidazolium salt (IX), which is probably due to the participation of the initial compound VII in the oxidation of a hydride σ-complex. In none of the reactions of the methoxy-substituted azo compounds I-III was the assumed product of the reductive splitting detected.



VIII a Ar=*p*-$CH_3OC_6H_4$; b Ar=*p*-$CH_3C_6H_4$

The high reactivity of 2-methoxynaphthylazobenzimidazole I in the amination reaction, and also the previously noted [1] ease of the hydrolytic splitting of the ether group in this compound can be considered as a

manifestation of the ortho-effect of the azo group. The probable reason for the anomalous ease of substitution of the 2-methoxy group in the naphthalene ring of the azo compound I is clearly its S,Z-conformation [1], which is favorable for the formation of the energetically convenient cyclic transition state with a delocalized 6π-electronic system.



The correctness of this explanation is confirmed by the results of the amination of ortho-methoxyphenylazobenzimidazoles, which will be discussed in the next article in this series.

EXPERIMENTAL

The IR spectra were obtained on a Specord IR-75 spectrophotometer in mineral oil, chloroform, and on fluorinated hydrocarbon oil mulls. The UV spectra were measured on a Specord M-40 spectrometer in methanol. The PMR spectra were run on Tesla BS 487 (80 MHz) and Varian XL (100 MHz) with accumulation in a Fourier trap. The monitoring of the course of the reactions and the preparative chromatographic separation of the products were carried out on Al_2O_3 grade II of activity using chloroform as eluent.

The starting naphthylazo compounds I and II were obtained by the methods described in [1], the phenylazo compound III according to [8]. The 2-arenazobenzimidazolium quaternary salt VII was synthesized by azo coupling of the benzimidazole-2-diazonium salt with p-xylene according to [9], followed by quaternization of the azo compound formed with methyl benzenesulfonate on boiling in benzene.

The data of the elemental analysis of compounds IV-VI for C, H, and N correspond to the calculated values.

Reaction of 2-(2-Methoxynaphthylazo)-1-methylbenzimidazole (I) with Aromatic Amines. A solution of 0.32 g (1 mmole) of azo compound I and 3 mmoles of an aromatic amine (5 mmoles in the case of a weakly basic arylamine) in 5 ml of chloroform was held at room temperature up to the disappearance of the starting azo compound in the chromatographic probe. A 2- to 3-fold volume of hexane was then added with stirring to the reaction mixture, the solution was decanted from the precipitate that separated out, and the latter was ground with ether to remove the excess of amine. Then the impure products of the amination of IVd with α-naphthylamine IVd and with p-aminoacetophenone IVe were purified by reprecipitation with ether from alcohol or by chromatography on a column (25 × 2.5 cm) filled with aluminum oxide in chloroform.

2-(2-Phenylaminonaphthylazo)-1-methylbenzimidazole (IVc). A solution of benzimidazole-2-diazonium salt, obtained from 0.147 g (1 mmole) of 2-amino-1-methylbenzimidazole in 7 ml of concentrated H_3PO_4 by diazotization according to a method described in [9], was added with vigorous stirring to a suspension of 0.22 g (1 mmole) of 2-phenylaminonaphthalene in 7 ml of concentrated CH_3COOH. The mixture was stirred at room temperature for 4 h, an equal volume of water (15 ml) was added, the mixture was acidified with an ammonia solution to pH 8-9. The crystals of the azo compound were filtered off and washed thoroughly with water. Yield 0.31 g (82%). Claret-colored crystals from ethanol. The compound is identical with the amination product of 2-methoxynaphthylazobenzimidazole IVc and the mixed sample does not give a depression of the melting point.

Reaction of 4-Methoxysubstituted II and III with Aromatic Amines. The reaction of compounds II and III with amines (with the exception of p-aminoacetophenone) was carried out by boiling a solution of the components in chloroform (see Table 1). After separation of the solvent the mixture was ground twice with ether, and the residue was chromatographed on a column with aluminum oxide (25 × 2.5 cm) in chloroform.

The reaction with p-aminoacetophenone was carried out at 30-35°C for 15 days, the chloroform was evaporated, and the residue was ground with ether and treated with a hot mixture of benzene and CCl_4 (1:1). The amination product Ve was purified chromatographically on a column. Yield 21%.

In the reaction of the phenyl derivative III with p-aminoacetophenone, traces of amino-substituted derivative VIe was formed, which could not be separated in a pure state.

Reaction of 1,3-dimethyl-2-(2,5-dimethylphenylazo)benzimidazolium benzenesulfonate (VII) with p-anisidine and p-toluidine was carried out at 20-25°C in a chloroform solution. At the end of the reaction the mixture was acidified by 1 drop of concentrated CH_3COOH, a twofold volume of ether was added, and the precipitate that separated out was filtered off. The precipitate was then dissolved in a minimal volume of warm

ethanol and the reaction products were isolated in the form of perchlorates, as described in [2]. To separate the product of the reductive uncoupling of IX the precipitate of the perchlorates was treated with 10-15 ml of boiling chloroform, and the amine salt IX was filtered off, and was converted by grinding with a KOH solution into the known 1,3-dimethyl-2-iminobenzimidazoline [10]. After evaporation the contents of the chloroform filtrate were crystallized from alcohol with ether. The dark-claret crystals with a green tinge comprise the 1,3-dimethyl-2-(2,5-dimethyl-4-p-methoxyphenylazo)benzimidazolium perchlorate. Mp 222-223°C (from acetone). Yield 63%.

The amination product of salt VII with p-toluidine — 1,3-dimethyl-2-(2,5-dimethyl-p-tolylaminophenylazo)imidazolium perchlorate, was isolated in a 58% yield. Dark-claret crystals, mp 227-228°C.

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