## DIAZO COMPOUNDS OF THE HETEROCYCLIC SERIES.

## II.\* 1,3 DI(2-BENZIMIDAZOLYL)TRIAZENES

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2-(N-Nitrosamino)benzimidazoles in aqueous solutions or in organic solvents are spontaneously converted to 1,3-di(2-benzimidazolyl)triazenes. Other methods for the synthesis of triazenes of the benzimidazole series and their properties are examined.

The possibility of spontaneous conversion of primary nitrosamines to triazenes, which was first pointed out by Grachev [2], has been experimentally confirmed only in the case of thiadiazole [3]. We have found that the ability to undergo conversion to symmetrical diazoamino compounds is also a characteristic property of 2-(N-nitrosamino)benzimidazoles (I-IV) [1].

In aqueous solutions the reaction proceeds over a broad range of acidities — from weakly acidic to 50% sulfuric acid solutions. The process takes place slowly and is catalyzed by acids in organic solvents (chloroform, acetone, and alcohol) and on heating in benzene. At the same time, dry nitrosamines I-IV can be stored for more than a year without alteration.



I, V a R=CH<sub>3</sub>; b R=C<sub>2</sub>H<sub>5</sub>; c R=CH(CH<sub>3</sub>)<sub>2</sub>; d R=CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>; R<sub>1</sub>=R<sub>2</sub>=H; II, VI R<sub>1</sub>=OCH<sub>3</sub>, R<sub>2</sub>=H; III, VII R<sub>1</sub>=H, R<sub>2</sub>=Br; IV, VIII R<sub>1</sub>=R<sub>2</sub>=Br;  $R=CH_3$ 

The effect of substituents on this conversion is ambiguous: the presence of bromine atoms in the 5 and 6 positions of III and IV facilitates the reaction; on the other hand, when there is an isopropyl grouping in the 1 position of benzimidazole the process takes place so readily that nitrosamine Ic cannot be isolated in the free state.

Better yields of the triazenes can be obtained when the reaction is carried out in alcohol solution at 20° in the presence of catalytic amounts of sulfuric acid. It might have been assumed that the process takes place via denitrosation with subsequent condensation of the resulting 2-aminobenzimidazole (IX) with a second molecule of nitrosamine. However, the addition of amine IX to the reaction mixture promotes only stabilization of nitrosamines I-IV, apparently through suppression of acid catalysis.

The assumption of conversion of the nitrosamines to triazenes through a step involving the formation of a diazonium salt, which then couples with the amine arising as a result of denitrosation of the nitrosamine, seems unlikely. We have shown that 1-methylbenzimidazole-2-diazonium tetrafluoroborate (X) reacts with amine IX or with 2-(N-methylamino)-substituted

\*See [1] for communication I.

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compounds XI in acetonitrile to give triazenes Va and XII only in low yields, whereas diazoamino coupling of this salt with 1,3-dimethyl-2-iminobenzimidazoline or p-nitroaniline readily gives triazenes XIII and XIV. The reduced activity of the amino group in the 2 position of benzimidazole in diazoamino coupling is in good agreement with its behavior in several other electrophilic substitution reactions [4].



The Grachev scheme [5], which includes the intermediate formation of an N-nitrosotriazene from the nitrosamine anion and diazonium cation, seems a more likely scheme for the conversion of the nitrosamine to a triazene. Thus the ability of the nitrosamine to act simultaneously as a proton donor and acceptor is important. A mixture of 2-(N-methyl-Nnitrosamino)-1-methylbenzimidazole and nitrosamine Ia in alcohol therefore forms only symmetrical triazene Va. Moreover, this scheme is also in agreement with the previously noted effect of bromine atoms in the rings of nitrosamines III and IV, which is due to an increase in the acidities of the corresponding nitrosamines.

The formation of triazene Va was also observed in the reaction of sodium 1-methyl-2benzimidazolyldiazotate with acetic anhydride in a dry nitrogen atmosphere with subsequent exposure of the intermediate to air. The intermediate apparently has the XV structure,\* and the role of air moisture reduces to partial hydrolysis of XV to nitrosamine Ia.



In fact, the reaction of XV with Ia even in the absence of moisture gives Va, i.e., it proceeds in conformity with the Grachev scheme, inasmuch as diazoacetates exist in organic solvents as a mixture of the covalent and ionic forms [6].

The Va structure was confirmed by alternative synthesis from 2-azido-1-methylbenzimidazole and 2-sodio-1-methylbenzimidazole.

The triazenes of the benzimidazole series (V-VIII) are yellow crystalline substances that decompose on melting and are moderately soluble in alcohol and chloroform (and in benzene on heating). They form stable salts with mineral acids; they give sodium salts in an alcohol solution of sodium hydroxide. On reduction with zinc dust in dilute acetic acid they are converted to amine IX and 2-hydrazino derivatives of benzimidazole. However, they are not reduced by tin salts in hydrochloric acid even on prolonged heating.

The most peculiar property of triazenes V-VIII is their extremely high stability with respect to cleavage by acids. It is characteristic that V-VIII in this respect surpass all of the previously noted triazenes of the azole series [2, 7]. Concentrated hydrochloric acid does not cleave V-VIII even on refluxing for many hours, and concentrated sulfuric acid at 20° partially converts V to a mixture of isomeric 5- and 6-azobenzimidazoles only after a week.

<sup>\*</sup>Because of its instability in air, the compound was not isolated in analytically pure form. It was shown that XV, in contrast to the diazotate and nitrosamine, couples quite readily with dimethylaniline to give the corresponding azo compound.

A second important peculiarity of triazenes V-VIII is the absence in their IR spectra of the absorption band of stretching vibrations of the NH group characteristic for aromatic [8] and heterocyclic [3] triazenes. The broad absorption at 2500-3500 cm<sup>-1</sup>, which appears in the spectra of both the solid compound and dilute solutions of it in chloroform, indicates the possible existence of an intramolecular hydrogen bond. Our next communication will be devoted to an examination of this problem.

## EXPERIMENTAL METHOD

1,3-Di(2-benzimidazoly1)triazenes (V-VIII). A) A 1-ml sample of concentrated sulfuric acid was added to an ice-cooled suspension of 10 mmole of 1-alky1-2-nitrosaminobenzimidazole in 25 ml of ethanol, after which the mixture was held at room temperature for 5-6 h. It was then treated with 10 ml of concentrated ammonium hydroxide, and the precipitated yellow crystals of the triazene were removed by filtration (see Table 1).

B) A mixture of 2-sodio-1-methylbenzimidazole, obtained by the method in [9] from 0.8 g (8 mmole) of sodium and 0.6 g (6 mmole) of chlorobenzene, was stirred in a nitrogen atmosphere at  $-15^{\circ}$ , after which 1 g (6 mmole) of 2-azido-1-methylbenzimidazole in absolute toluene was added. After all of the azide had been added, the temperature was raised to room temperature and kept at room temperature for 1 h, after which 5 ml of water was added. The yellow precipitate was removed by filtration and suspended in water, and the suspension was treated with carbon dioxide gas until it was weakly acidic. Workup gave 1 g (62%) of product. The product was purified by reprecipitation from chloroform solution by the addition of petroleum ether.

C) A 0.9-ml (10 mmole) sample of acetic anhydride was added to a cooled (to  $-10^{\circ}$ ) suspension of 1.98 g (10 mmole) of sodium 1-methyl-2-benzimidazolyldiazotate in 30 ml of absolute ether, after which the mixture was held at  $-10^{\circ}$  for 1 h. The temperature was then raised to room temperature, and the light-colored crystals of XV that had formed after 2 h were removed by filtration and allowed to stand in air for 24 h. The resulting triazene was obtained as yellow plates with mp 217° (dec.).

D) The light-colored crystals of diazoacetate XV obtained in experiment C were mixed with 1.76 g (10 mmole) of 2-(N-nitrosamino)benzimidazole, and the mixture was allowed to stand for 1 h, after which 1.1 g (73%) of the triazene was removed by filtration.

<u>1,3-Di(1-isopropy1-2-benzimidazoly1)triazene (Vc).</u> A) A 2.3-g sample of 1-isopropy1-2-benzimidazolyldiazotate [3] was dissolved in the minimum amount of water, and the solution was acidified to pH 4 with acetic acid. The reaction product was then extracted with chloroform and purified by chromatography with a column filled with aluminum oxide and elution with chloroform to give 1.1 g (60%) of yellow plates of Vc with mp 214.5° (dec., from benzene). Found: C 66.1; H 6.2; N 27.3%.  $C_{20}H_{23}N_7$ . Calculated: C 66.5; H 6.4; N 27.1%.

B) A solution of 1.4 g (20 mmole) of sodium nitrite in 5 ml of water was added in the course of 30 min to a cooled (from -5 to  $-10^{\circ}$ ) solution of 1.75 g (10 mmole) of 2-amino-1-isopropylbenzimidazole in 15 ml of 60% phosphoric acid, after which the mixture was held at this temperature for another 30 min. It was then diluted with water and made alkaline to pH 8 with ammonium hydroxide. The reaction product was extracted with chloroform and purified as described above to give 0.9 g (50%) of pure product.

Reduction of 1,3-Di(1-methyl-2-benzimidazolyl)triazene. A mixture of 0.3 g (1 mmole) of triazene Va and 0.3 g (5 mmole) of powdered zinc in 10 ml of 20% acetic acid was maintained at room temperature until it was completely decolorized. The unchanged zinc was then removed by filtration, 0.2 g (2 mmole) of benzaldehyde was added, and the mixture was made weakly alkaline and stirred at 40° for another hour. The reaction product was extracted with chloroform, the chloroform was evaporated, and the residue was separated with a column filled with aluminum oxide and elution by chloroform; the leading fraction was collected to give 0.12 g (50%) of the benzylidene derivative of 2-hydrazino-1-methylbenzimidazole, after which the column of aluminum oxide was extruded from the column and extracted with hot alcohol to give 0.12 g (80%) of 2-amino-1-methylbenzimidazole.

<u>1-Methylbenzimidazole-2-diazonium Tetrafluoroborate (X).</u> A 1.76-g (10 mmole) sample of 2-nitrosamino-1-methylbenzimidazole was mixed at 0° with 3.1 g (25 mmole) of boron trifluoride etherate in 20 ml of absolute alcohol. After 1 h, the temperature was raised to room temper-

TABLE 1. Triazenes of the Benzimidazole Series

Com-	mp(dec.)	Empirical formula	Found, %			Calc., %			Yield.
pound	°Ċ		с	н	N	С	Н	N	%
Va* Vb* Vd* VII VIII VI	217 <b>†</b> 208 <b>†</b> 213 <b>†</b> 246 262 215	$\begin{array}{c} C_{16}H_{14}N_7Na\\ C_{18}H_{18}N_7Na\\ C_{28}H_{22}N_7Na\\ C_{16}H_{13}N_7Br_2\\ C_{16}H_{11}N_7Br_4\\ C_{18}H_{19}N_7O_2 \end{array}$	58,6 60,5 70,6 41,3 31,2 59,6	4,7 5,1 4,6 3,2 1,7 5,2	30,0 28,0 20,0 21,0 15,6 26,8	58,7 60,8 70,1 41,5 30,9 59,2	4,3 5,1 4,6 2,8 1,8 5,2	30,0 27,6 20,5 21,2 15,8 26,8	74 70 75 81 78 62

\*The compounds were analyzed in the form of their sodium salts, inasmuch as the extremely rapid decomposition of the triazenes themselves on heating makes it impossible to obtain sufficiently accurate results.

<sup>†</sup>The melting points are presented for the triazenes themselves.

ature and held at room temperature for another 3 h. The 1-methyl-2-benzimidazolyldiazonium tetrafluoroborate was then removed by filtration and washed thoroughly with dry ether. The absorption band of an N=N bond was observed in the IR spectrum of this compound at 2260 cm<sup>-1</sup> after vacuum drying over calcium chloride.

The yield of diazonium salt X in this reaction was determined by diazo coupling of it with dimethylaniline: X was added to a solution of 2 ml of dimethylaniline in 30 ml of absolute acetonitrile. After 5 h, the mixture was treated with ammonium hydroxide, and the reaction product was extracted with chloroform. Purification with a column filled with aluminum oxide and elution with chloroform gave 2.5 g (80%) of red crystals with mp 223° (from benzene). Found: C 69.0; H 6.2; N 25.0%.  $C_{16}H_{17}N_{5}$ . Calculated: C 68.8; H 6.1; N 25.1%.

Reaction of Diazonium Salt X with Amines. A 10-mmole sample of diazonium salt X was mixed with 20 mmole of amine (imine) in 20 ml of absolute acetonitrile, and the mixture was allowed to stand for 24 h. The acetonitrile was then removed by vacuum distillation, and the residue was treated with ammonium hydroxide and extracted with chloroform. The reaction product was isolated by chromatography on aluminum oxide.

1,3-Di(1-methy1-2-benzimidazoly1)triazene (Va). This compound was obtained in 10% yield from 2-amino-1-methylbenzimidazole IX and diazonium salt X.

<u>1-(1-Methylbenzimidazolyl)-3-(1,3-dimethylbenzimidazolidene)triazene (XIII).</u> This compound was obtained from diazonium salt X and 1,3-dimethyl-2-iminobenzimidazoline. The reaction product was purified by chromatography with a column filled with aluminum oxide and elution with chloroform; the second fraction was collected to give yellow crystals, with mp 198° (from alcohol), in 64% yield. Found: C 64.0; H 5.3; N 30.4%.  $C_{17}H_{17}N_7$ . Calculated: C 63.9; H 5.4; N 30.7%.

<u>1,3-Di(1-methyl-2-benzimidazolyl)-2-methyltriazene (XII)</u>. This compound was obtained from X and 2-(N-methylamino)-1-methylbenzimidazole via the method described above. It was purified by chromatography in a thin layer of aluminum oxide in chloroform; the second fraction, with  $R_f$  0.7, was collected to give yellow plates with mp 165° (dec., from benzene) in 10% yield. Found: C 64.0; H 5.7; N 30.7%. C<sub>17</sub>H<sub>17</sub>N<sub>7</sub>. Calculated: C 63.9; H 5.4; N 30.7%.

<u>l-(1-Methyl-2-benzimidazolyl)-3-(4-nitrophenyl)triazene (XIV)</u>. This compound was obtained from X and p-nitroaniline. It was purified with a column filled with aluminum oxide and elution by chloroform to give bright-yellow needles with mp 180° (from ethanol) in 54% yield. Found: C 56.9; H 3.8; N 27.9%.  $C_{14}H_{12}N_6O_2$ . Calculated: C 56.8; H 4.1; N 28.4%.

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