BENZO[1,2-d:3,4-d']DIIMIDAZOLE DERIVATIVES

III.* REACTION OF 3,6-DIMETHYL- AND 2,3,6,7-TETRAMETHYLBENZO[1,2-d:3,4-d']DIIMIDAZOLE WITH ELECTROPHILIC REAGENTS

A. M. Simonov, Yu. V. Koshchienko,
and T. G. Belenko

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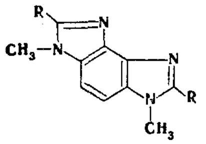
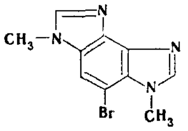
Bromination of 3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (Ia) in chloroform with bromine and dioxane dibromide in dioxane leads, through the intermediate formation of perbromides, to the 4-bromo-substituted derivative; 4,5-dibromo-3,6-dimethylbenzo[1,2-d:3,4-d']dimidazole is formed in addition to a monobromo-substituted derivative by the action of potassium bromate in hydrobromic acid on Ia. Nitration of Ia and its 2,7-dimethyl-substituted derivative (Ib), even under severe conditions, leads to the 4-mononitro derivatives. Only one of the pyridine nitrogen atoms is quaternized by the action of excess methyl iodide on Ia, b.

Continuing our investigation of benzo[1,2-d:3,4-d']diimidazole derivatives, we subjected 3,6-dimethyl- (Ia) and 2,3,6,7-tetramethylbenzo[1,2-d:3,4-d']diimidazole (Ib) to the action of electrophilic agents. According to the results of molecular orbital calculations [1] for Ia, the 4 and 5 positions are characterized by increased electron density. It is natural to assume that electrophilic substitution will proceed at these positions also.

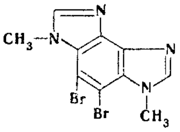
Bromination of Ia in chloroform with molecular bromine and dioxane dibromide in dioxane gives perbromides, which are converted to 4-bromo-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (II) in 66-74% yield on refluxing with water. The action of potassium bromate on Ia in hydrobromic acid initially leads to the perbromide hydrobromide, which forms two substances on refluxing with water. One of them is the monobromo-substituted derivative and is identical to II, obtained during bromination in neutral solvents; the yield was 36%. The second compound, obtained in 26% yield, contains two bromine atoms and may be either dibromo-substituted III or the product of the addition of two bromine atoms (IV), as observed for phenanthrene and 1,2-naphthimidazole [2, 3]. The latter assumption must be rejected, since III is also formed during the bromination of II. This conclusion confirms a study of the PMR spectrum of the dibromo derivative. This spectrum contains signals of protons in the 2 and 7 positions at 8.93 ppm and signals of protons of methyl groups at 4.20 ppm, while signals of alicyclic protons and protons of a benzene ring in the 4 and 5 positions are absent. The UV spectra recorded for II and III proved to be similar to one another. These results demonstrate that 4,5-dibromo-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (III) (see [4]) is formed along with 4-bromo-substituted II in the bromination of Ia with potassium bromate in hydrobromic acid.



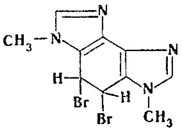
I



II



III



IV

a R=H; b R=CH$_3$

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*See [1] for communication II.

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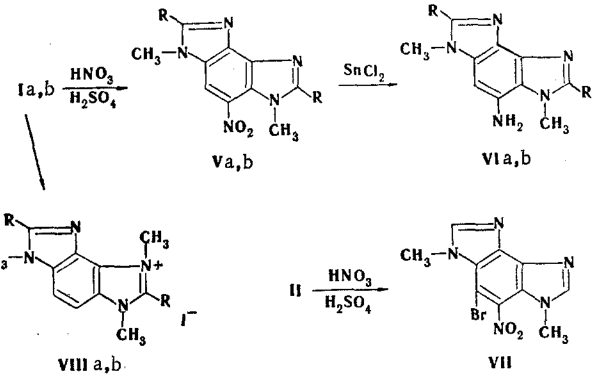
Only mononitro derivatives Va, b were obtained by the action of a nitrating mixture on Ia, b at 10-15°C. We were unable to introduce a second nitro group, even under severe conditions. Thus compounds Va, b were isolated reversibly in quantitative yields when a solution of Va was refluxed in a mixture of nitric acid (sp. gr. 1.5) and concentrated H_2SO_4. On the other hand, a second substitutent can be introduced into the benzene ring in the case of the 4-bromo-substituted derivative; the action of a nitrating mixture on II leads to 4-bromo-5-nitro-3,6-dimethylbenzo[1,2-d : 3,4-d']diimidazole (VII) in 79% yield.



a R=H; b R=CH_3

Compound Va can be reduced with stannous chloride in hydrochloric acid to 4-amino derivative VIa, which differs markedly in properties from the isomeric 2-amino-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole [1]; for example, it is readily diazotized under the usual conditions, and the diazonium salt reacts with β-naphthol to give a brightly colored azo compound. Thus substitution during nitration indisputably proceeds at the 4 position.

Bisquaternization of bases Ia, b does not occur when alcohol solutions of Ia, b are refluxed with excess methyl iodide, and only monomethyl derivatives VIIIa, b are obtained. Monomethylation is also observed when Ib is mixed with 2 mole of methyl benzenesulfonate. This phenomenon is probably associated with the steric hindrance that develops after the addition of the first methyl group, which hinders attack of a second pyridine nitrogen atom (see [5]).

EXPERIMENTAL

The PMR spectrum of III in trifluoroacetic acid was recorded with a PE-2305 spectrometer with an operating frequency of 60 MHz with hexamethyldisiloxane as the internal standard. The UV spectra of methanol solutions were recorded with an SF-4 spectrophotometer. The IR spectra of mineral oil suspensions were recorded with a UR-20 spectrometer.

2,3,6,7-Tetramethylbenzo[1,2-d:3,4-d']diimidazole (Ib). A 1.9-g (0.01 mole) sample of 4-amino-5-methylamino-1,2-dimethylbenzimidazole [1] was refluxed in 10 ml of glacial acetic acid for 6 h, after which 20 ml of water was added, and the mixture was neutralized with concentrated ammonium hydroxide solution. The resulting precipitate was removed by filtration to give 1.7 g (80%) of colorless crystals (from water) with mp 359-360°. Found: C 67.5: H 6.4; N 26.3%. $C_{12}H_{14}N_4$. Calculated 67.3; H 6.6; N 26.2%.

4-Bromo-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (II). A. A solution of 0.23 ml (4.5 mmole) of bromine in 5 ml of dry chloroform was added to a solution of 0.85 g (4.5 mmole) of Ia in 15 ml of dry chloroform at 20-30°, and the mixture was stirred for 2 h. The precipitated yellow-green perbromide was removed by filtration, washed with chloroform, and dried in a vacuum desiccator over phosphorus pentoxide to give 1.45 g of a product with mp 236-239° (dec.). The perbromide was quite stable in air, but it reacts with an aqueous solution of phenol to give 2,4,6-triboromophenol. On the other hand, the benzene ring of benzo[1,2-d:3,4-d']diimidazole undergoes bromination to give II when the perbromide is refluxed with acetone, and bromination of the acetone is not observed.

The perbromide was refluxed with 60 ml of water for 2 h, and the mixture was cooled, neutralized with concentration ammonium hydroxide, and extracted with chloroform to give 0.91 g (74%) of product.

B. A solution of 0.99 g (4 mmole) of dioxane dibromide in 5 ml of dioxane was added in small portions with stirring to a solution of 0.74 g (4 mmole) of Ia in 40 ml of dioxane, and the mixture was held at 20-25°

TABLE 1. Amino, Bromo, and Nitro Derivatives of Benzo[1, 2-d:3, 4-d']diimidazole

Compound	mp, °C[*]	Crystallization solvent	Empirical formula	Found, %				Calc., %				Yield, %
				C	H	Br	N	C	H	Br	N	
II	198—199	Dioxane—ether	$C_{10}H_9BrN_4 \cdot 1/2H_2O$	43,8	3,9	29,1	20,4	43,9	3,7	29,2	20,4	74[†]
III	283—284	Chloroform—ether	$C_{10}H_8Br_2N_4$	35,2	2,3	46,3	16,1	34,9	2,3	46,5	16,3	69[‡]
Va	267	Water	$C_{10}H_9N_5O_2$	51,9	3,9	—	30,1	51,9	3,9	—	30,3	78
Vb	231—232	Acetone	$C_{12}H_{13}N_5O_2$	55,4	5,3	—	27,0	55,6	5,1	—	27,0	86
VIa	253—254	Butanol	$C_{10}H_{11}N_5$	59,4	5,4	—	34,5	59,7	5,5	—	34,8	64
VII	276	Butanol	$C_{10}H_8BrN_5O_2$	38,6	2,7	25,9	22,9	38,7	2,6	25,8	22,6	79

[*] Compounds III and IVa were obtained as colorless prisms, Va and VII were obtained as yellow needles, Vb was obtained as bright-yellow prisms, and II was obtained as yellowish crystals.

[†] In the bromination of Ia with bromine in chloroform.

[‡] In the bromination of II.

for 30 min. The precipitated perbromide was removed by filtration, washed with dioxane, dried, and worked up as in the preparation of the perbromide in experiment A to give 0.68 g (66%) of II. UV spectrum, λ_{max}, nm (log ε): 270 (3.34), 278 (3.45), 283 (3.39), 289 (3.39).

4-Bromo-3,6-dimethyl- (II) and 4,5-Dibromo-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (III). A solution of 1.3 g (7 mmole) of Ia in 17 ml of hydrobromic acid (sp. gr. 1.4) was cooled rapidly to 0-5°, and a solution of 0.39 g (2.3 mmole) of potassium bromate in 30 ml of water was added by drops with vigorous stirring. The mixture was held at 20° for 2 h and at 60° for 2 h. The resulting bright-yellow precipitate of the perbromide hydrobromide of Ia was removed by filtration and dried in a vacuum desiccator over phosphorus pentoxide to give 2.6 g of a product with mp 256-258° (dec.). The perbromide hydrobromide of Ia was dissolved in the minimum amount of water by heating, and the solution was refluxed for 2 h. After prolonged standing, the hydrobromide of III (1.2 g) precipitated; it had mp 261°. The hydrobromide of III was dissolved in water and converted to 0.62 g (26%) of the base by the action of 20% alkali. The filtrate from the separation of the hydrobromide of III was treated with alkali, and II [0.65 g (36%)] was extracted with chloroform. The compound was hygroscopic; it absorbed moisture from the air and melted.

The properties of II and III are presented in Table 1.

4,5-Dibromo-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (III). The bromination of II was carried out in hydrobromic acid with potassium bromate, as in the bromination of Ia. The perbromide hydrobromide of II was dissolved in the minimum amount of water, and the mixture was refluxed for 2 h. It was then neutralized with concentrated ammonium hydroxide solution, and the precipitate was removed by filtration to give 0.36 g (69%) of a product with mp 283-284°. UV spectrum, λ_{max}, nm (log ε): 273 (3.41), 280 (3.50), 292 (3.46), 296 (3.46).

4-Nitro-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (Va). A mixture of 0.13 ml (3 mmole) of nitric acid (sp. gr. 1.52) and 0.5 ml of sulfuric acid (sp. gr. 1.82) was added by drops with stirring to a cooled (0-5°) solution of 0.56 g (3 mmole) of Ia in 5 ml of concentrated H_2SO_4, and the mixture was held at this temperature for 30 min and then at 20-30° for 1.5 h. It was then poured over ice, and the aqueous mixture was neutralized with concentrated ammonium hydroxide. The resulting precipitate was removed by filtration and washed with ice water to give 0.53 g of product.

Compound Vb was similarly obtained by nitration of Ib.

4-Bromo-5-nitro-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (VIII). A 0.17-ml (4 mmole) sample of nitric acid (sp. gr. 1.52) in 0.4 ml of concentrated H_2SO_4 was added in the course of 5 min to a solution of 1.06 g (4 mmole) of II in 8 ml of concentrated H_2SO_4 at 0-5°. The temperature was raised to 20-30°, and the mixture was held at this temperature for 2 h. It was then poured over ice, and the aqueous mixture was neutralized with concentrated ammonium hydroxide to give 0.98 g of product.

4-Amino-3,6-dimethylbenzo[1,2-d:3,4-d']diimidazole (VIa). A 0.46-g (2 mmole) sample of Va was added in portions to a solution of 2.3 g (10 mmole) of stannous chloride in 10 ml of hydrochloric acid (sp. gr. 1.18), and the mixture was heated on a boiling-water bath for 2 h. It was then cooled, and the precipitated amine–tin salt complex was removed by filtration and dissolved in the minimum amount of water. The solution was made strongly alkaline by the addition of 40% sodium hydroxide solution and extracted with acetone to give 0.32 g of product. The product was soluble in water, ethanol, and dioxane and insoluble in benzene, ethyl acetate, and ether. IR spectrum, cm^{-1}: δ_{NH_2} 1660, ν_{NH_2} 3215, 3334.

The properties of Va, b, VIa, and VII are presented in Table 1.

4-Acetamido-3,6-dimethylbenzo[1,2-d;3,4-d']diimidazole. A solution of 0.40 g (2 mmole) of VIa in 1.5 ml of acetic anhydride was refluxed for 15 min, diluted with water, and neutralized with potassium carbonate to give 0.36 g (69%) of colorless hygroscopic crystals (from butanol) with mp 216°. Found: C 55.1; H 6.0%. $C_{12}H_{13}N_5O \cdot H_2O$. Calculated: C 55.2; H 5.8%.

3,6-Dimethylbenzo[1,2-d;3,4-d']diimidazole Methiodide (VIIIa). A solution of 0.37 g (2 mmole) of Ia and 1 ml of methyl iodide in 1.5 ml of ethanol was refluxed for 2 h and worked up to give 0.61 g (95%) of colorless needles (from alcohol) with mp 244-245°. Found: N 17.4%. $C_{11}H_{13}IN_4$. Calculated: N 17.1%.

2,3,6,7-Tetramethylbenzo[1,2-d;3,4-d']diimidazole Methiodide (VIIIb). A. This compound was obtained by a method similar to that used for the preparation of VIIIa by refluxing Ib with methyl iodide in alcohol solution. The yield of colorless needles (from water) with mp 320-321° (dec.) was 92%. Found: N 16.1%. $C_{13}H_{17}IN_4$. Calculated N 15.8%.

B. A mixture of 0.75 g (3.5 mmole) of Ib and 1.2 g (7 mmole) of methyl benzenesulfonate was held at 120-130° for 2 h. It was then triturated with acetone and filtered to give 1.2 g of product. The benzenesulfonate of Ib was dissolved in water, and the solution was treated with saturated potassium iodide solution to give 0.76 g (61%, based on Ib) of VIIb.

LITERATURE CITED

1. Yu. V. Koshchienko, A. M. Simonov, and A. F. Pozharskii, Khim. Geterotsikl. Soedin., 1132 (1971).
2. L. Fieser, Chemistry of Phenanthrene Derivatives [Russian translation], Goskhimizdat (1941), p. 19.
3. L. S. Éfros, L. N. Kononova, and Ya. Éded, Zh. Obshch. Khim., 24, 488 (1954).
4. S. S. Kolodyazhnaya and A. M. Simonov, Khim. Geterotsikl. Soedin., 714 (1969).
5. S. F. Torf and N. V. Khromov-Borisov, Zh. Obshch. Khim., 30, 1798 (1960).