Chemistry of Heterocyclic Compounds, Vol.35, No. 2, 1999

REACTIONS OF 5-DIAZO-4-NITROIMIDAZOLE WITH HYDROCHLORIC ACID

E. V. Sadchikova, V. S. Mokrushin, T. A. Pospelova, and I. S. Selezneva

Reaction of 5-diazo-4-nitroimidazole with concentrated hydrochloric acid leads to 4-chloro-5-diazoimidazole. The same product is formed together with a small quantity of 5-chloro-4-nitroimidazole with 1 N hydrochloric acid, but with 0.1 N hydrochloric acid only chloronitroimidazole was isolated. The results obtained are explained with the aid of quantum chemical calculations.

Previous investigations of the acid—base properties of 5-diazo-4-nitroimidazole (Ia) showed that in 50 and 20% solutions of sulfuric acid (H_0 -3.38; -1.01 respectively) this compound exists predominantly in the form of 4-nitroimidazole-5-diazonium sulfate (IIa) ($X = HSO_4^-$). At pH 0 an equilibrium between compounds (Ia), (IIa), and 4-nitro-5-nitrosaminoimidazole (III) was observed. At pH 1-5 diazo compound (Ia) and nitrosamine (III) were present in solution [1]. It is known that heterocyclic nitrosamines are converted in 1-10% hydrochloric acid into the corresponding halo derivatives. An increase in acid concentration leads to a reduction of their yield [2]. Decomposition of aromatic diazonium salts in the absence of catalyst by an S_N1 mechanism also leads to a haloarene [3].

The aim of the present work was to study the reactions of compound (Ia) in concentrated, 1 N, and 0.1 N hydrochloric acid.

On solution in concentrated hydrochloric acid (H_0 -3.95) diazoimidazole (Ia) is converted practically instantaneously into another diazo derivative of the imidazole series giving a yellow coloration on chromatograms when treated with m-phenylenediamine. 2-Nitrobenzenediazonium chloride reacts with concentrated hydrochloric acid forming 2-chlorobenzenediazonium chloride [4]. By analogy with this we propose that replacement of the nitro group by chlorine occurs in the salt (IIb) $X = Cl^-$, formed initially from imidazole (Ia), with the formation of 4-chloro-5-diazoimidazole (Ib). To confirm this structure azo couplings with ß-naphthol and dimethylamine, characteristic of diazo compounds, were carried out.

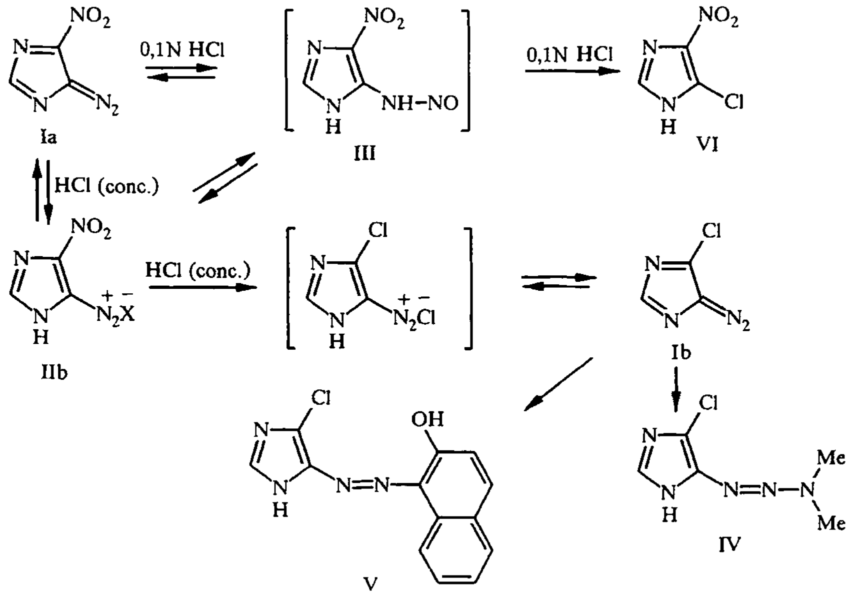
As a result individual products were obtained and characterized by elemental analysis, PMR and IR spectroscopy data as 4-chloro-5-(3,3-dimethyl-1-triazeno)-imidazole (IV) and 4-chloro-5-(2-hydroxy-1-naphthalene-diazo)imidazole (V). There were bands in the IR spectra of these compounds for the stretching vibrations of N=N and C—Cl bonds but the bands characteristic of nitro group absorption were absent. In the PMR spectra signals for the imidazole ring protons were observed, in the case of azo compound (V) a multiplet signal for the naphthalene ring protons was also present, and in the spectrum of triazene (IV) there was a singlet for the methyl group protons.

Refluxing imidazole (Ia) in 1 N hydrochloric acid gave diazo compound (Ib) together with an insignificant quantity of 5-chloro-4-nitroimidazole (VI) identical (TLC, mp, IR spectrum, and PMR data) with a sample of known structure synthesized by the procedure of [5]. Refluxing of compound (Ia) in 0.1 N hydrochloric acid for 6 h or leaving the solution at room temperature for a month (until disappearance of the compound (Ia) from the reaction mixture according to TLC) leads mainly to chloronitroimidazole (VI). We also confirmed the presence of a small

---

Urals State Technical University - Urals Polytechnical Institute (UPI), Ekaterinburg 620002, Russia; e-mail: mokr@tos.rcupi.E-burg.ru Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 199-202, February, 1999. Original article submitted March 25, 1998.

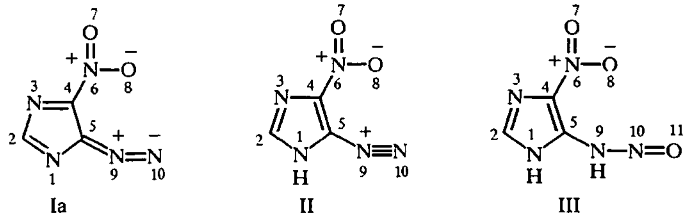
quantity of diazoimidazole (Ib) in the reaction mixture with the aid of TLC. This compound is probably subject to extensive decomposition under the reaction conditions to unstable products with undetermined structure. On refluxing in absolute dioxan for 72 h compound (Ia) remained unchanged and the formation of products (VI) and (Ib) was not observed.



$$\text{Ia} + \text{II} + \text{III} \xrightarrow{\text{1N HCl}} \text{VI} + \text{Ib}$$

We have carried out quantum chemical calculations on compounds (Ia), (IIb), and (III) by the AM-1 method (Table 1) to explain the results obtained.

TABLE 1. Electron Densities on C, N, and O Atoms and Energies of Frontier Orbitals in Compounds (Ia), (II), and (III)



Atom	Compound, atom charge		
	Ia	II	III
$N_{(1)}$	-0,077	-1,140	-0,244
$C_{(2)}$	-0,122	0,064	-0,074
$N_{(3)}$	-0,066	-0,037	-0,056
$C_{(4)}$	-0,087	0,003	-0,212
$C_{(5)}$	-0,214	-0,121	0,154
$N_{(6)}$	0,598	0,605	0,618
$O_{(7)}$	-0,282	-0,185	-0,324
$O_{(8)}$	-0,397	-0,354	-0,362
$N_{(9)}$	0,239	0,189	-0,336
$N_{(10)}$	0,190	0,391	0,372
$O_{(11)}$	—	—	-0,237
E_{LUMO}, eV	-2,239	-7,150	-1,034
E_{HOMO}, eV	-10,194	-15,520	-9,799

It is seen from Table 1 there is a positive charge on $C_{(4)}$ linked to the nitro group in diazonium salt (II) while $C_{(5)}$ carries a negative charge. This is possible since nucleophilic substitution of nitro group by chlorine occurs and diazoimidazole (Ib) is formed. In difference to diazo compound (Ia) and salt (IIb) the carbon atom at position 5 in nitrosamine (III) carries a positive and not a negative charge. This permits nucleophilic substitution of the nitrosamino group and the formation of chloronitroimidazole (VI).

The experimental and calculated data obtained by us therefore confirm that the nitrosamine (III) is present as a third partner in the equilibrium between diazonium salt (IIb) and diazo compound (Ia), and the direction of the reaction with hydrochloric acid depends on the concentration of the predominating form of the diazo compound.

EXPERIMENTAL

Analytically and chromatographically pure samples were used for spectral investigations. The IR spectra of compounds were recorded on a Specord IR 75 instrument (in KBr disks). The PMR spectra were taken on a Bruker WR 80 (80 MHz) in DMSO-d_6, internal standard TMS. A check on the progress of reactions and the purity of the compounds obtained was made using TLC on Silufol UV 254 and on Sorbfil UV 254 plates (sorbent was silicagel CTX-1A) in the system chloroform—ethanol 3 : 1.

5-Diazo-4-nitroimidazole (Ia) and the authentic sample of 4-chloro-5-nitroimidazole (VI) were obtained by the procedures described previously in [5] and [6] respectively.

4-Chloro-5-(3,3-dimethyl-1-triazeno)imidazole (IV). Mixture of compound (Ia) (0.1 g, 0.72 mmol) and concentrated hydrochloric acid (5 ml) was diluted with water (15 ml), and then extracted with chloroform. Saturated solution of dimethylamine in alcohol was added dropwise to chloroform solution of 4-chloro-5-diazoimidazole (Ib) until a negative test for the diazo compound with *m*-phenylenediamine was obtained. The reaction mixture was left for 15 min, and the chloroform evaporated in vacuum without heating. The residue was dissolved in water (10 ml) and an aqueous solution of sodium hydroxide added to pH 8. The solid was filtered off and dried. Product (IV) (0.09 g: 72%) was obtained having mp 162°C, R_f 0.6. IR spectrum: 3120 (C—H), 1580 (N=N), 640 cm^{-1} (C—Cl). PMR spectrum (DMSO-d_6): 12.33 (1H, br. s, NH); 7.36 (1H, s, 2-H); 3.27 ppm (6H, s, $2CH_3$). Found, %: C 34.3; H 4.5; N 40.3; Cl 20.9. $C_5H_8ClN_5$. Calculated, %: C 34.6; H 4.6; N 40.3; Cl 20.5.

4-Chloro-5-(2-hydroxy-1-naphthalenediazo)imidazole (V). Suspension of β-naphthol (0.14 g, 0.97 mmol) in 10% Na_2CO_3 solution (5 ml) was added to mixture of compound (Ia) (0.1 g, 0.72 mmol) and concentrated hydrochloric acid (10 ml) and the mixture boiled for 15 min. The precipitate was filtered off, crystallized from ethyl alcohol, and dried. Product (V) (0.15 g, 76%) was obtained; mp 247°C, R_f 0.51. IR spectrum: 3130 (C—H), 1600 (N=N), 625 cm^{-1} (C—Cl). PMR spectrum (DMSO-d_6): 13.01 (1H, br. s, NH); 8.08 (1H, s, 2-H); 7.27-9.04 ppm (6H, m, $C_{10}H_6$). Found, %: C 57.7; H 3.1; N 20.1; Cl 13.8. $C_{13}H_9ClN_4O$. Calculated, %: C 57.6; H 3.3; N 20.5; Cl 13.0.

5-Chloro-4-nitroimidazole (VI). A. Mixture of compound (Ia) (0.1 g, 0.72 mmol) and 0.1 N hydrochloric acid (10 ml) was left at room temperature for a month. The solid was filtered off, the filtrate evaporated, the residue was washed with water, crystallized from ethyl alcohol, and dried. Product (VI) (0.06 g: 56%) was obtained; mp 246°C, R_f 0.47. Found, %: C 24.3; H 1.4; N 28.9; Cl 23.5. $C_3H_2ClN_3O_2$. Calculated, %: C 24.4; H 1.4; N 28.5; Cl 24.1.

B. Mixture of compound (Ia) (0.1 g, 0.72 mmol) and 0.1 N hydrochloric acid (10 ml) was refluxed for 6 h, evaporated, the residue was washed with water, crystallized from ethyl alcohol, and dried. Product (VI) (0.05 g, 47%) was obtained.

C. Mixture of compound (Ia) (0.1 g, 0.72 mmol) and 1 N hydrochloric acid (10 ml) was refluxed for 2 h. After cooling, the reaction mixture was extracted with chloroform. The extract was treated with saturated alcoholic solution of dimethylamine as described above for the synthesis of compound (IV), and product (IV) (0.12 g, 63%) was obtained. The remainder was evaporated, the residue was washed with water, crystallized from ethyl alcohol, and dried. Product (VI) (0.02 g, 18%) was obtained.

REFERENCES

1. V. S. Mokrushin, I. S. Selezneva, T. A. Pospelova, and V. K. Usova, Khim. Geterotsikl. Soedin., No. 9, 1245 (1997).
2. H. Gehlen and J. Dost, Justus Liebigs Ann. Chem., 665, 144 (1963).
3. S. Patai (editor), Chemistry of Diazonium and Diazo Groups, Interscience, Chichester, New York, Brisbane, Toronto (1978), p. 1099.
4. A. Oku and A. Matsui, J. Org. Chem., 44, 3342 (1979).
5. G. P. Sharnin, R. Kh. Fassakhov, T. A. Eneikina, and P. P. Orlov, Khim. Geterotsikl. Soedin., No. 5, 653 (1977).
6. V. S. Mokrushin, I. S. Selezneva, T. A. Pospelova, V. K. Usova, S. M. Malinskaya, G. M. Anoshina, T. E. Zubova, and Z. V. Pushkareva, Khim.-farm. Zh., No. 3, 303 (1982).