ACYLATION OF BENZIMIDAZOLE BY THE REGEL-BUECHEL METHOD.

2.* DEACYLATION AND DISSOCIATION OF 1-METHYL-3-ACYL-2-(1'-METHYL-2'-BENZIMIDAZOLYL)-4-BENZIMIDAZOLINES

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With excess acyl halide l-methyl-3-acyl-2-(l'-methyl-2'-benzimidazolyl)-4benzimidazoline is converted to an unstable l-methyl-3-acyl-2-(l'-methyl-3acyl-4'-benzimidazolin-2'-yl)benzimidazolium chloride, which undergoes intramolecular redox cleavage with the formation of 1,l'-dimethyl-2,2'-dibenzimidazolyl and an aldehyde and dissociates at the C-C bond that connects the benzimidazolium and benzimidazoline fragments into a carbene yield and a l-methyl-3-acylbenzimidazolium chloride.

It has been previously shown that the direct acylation of benzimidazole (Ia) [2] and 1-methylbenzimidazole (Ib) [1] in the 2 position by the action of aroyl halides via the Regel-Buechel method [3, 4] leads to the formation of chiefly coupling products II, which can be converted to 2-acyl-benzimidazoles III by heating with the corresponding acyl halides in acetonitrile in the presence of triethylamine [1].



I a R=H, b R=CH₃; II a R=C₆H₅CO, R¹=C₆H₅; b R=CH₃, R¹=C₆H₅; c R=CH₃, R¹=4-CH₃OC₆H₄; d R=CH₃, R¹=2-fury1, III a R=C₆H₅; b R=4-CH₃OC₆H₄; c R= =2-fury1

We have observed that the conversion of l-methyl-3-acyl-2-(1'-methyl-2'-benzimidazolyl)-4-benzimidazolines IIb-d to 2-acylbenzimidazoles III is invariably accompanied by the formation of 1,1'-dimethyl-2,2'-dibenzimidazolyl (IV). The latter is readily formed in the alcoholic alkaline hydrolysis of bis compounds II; its formation under conditions that exclude such hydrolysis therefore remained incomprehensible. The present research was devoted to a study of the mechanism of the formation of deacylated product IV.

*See [1] for communication 1.

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TABLE 1. Deacylation of Bis Products IIb-d

Com- pound	т _{тр} , °С	In benzene		In acetonitri1e	
		yie1d of IV, %	II isolated, %	yie1d of IV, %	II isolated, 🕫
IIb IIC IId*	170—171 [1] 168—169 [1] 145—147	.44 41 48	48 53 47	18 15 24	49 58 36

*This compound was crystallized from aqueous alcohol.

A priori this product could have been formed by thermal decomposition of II with the splitting out of an aldehyde. However, this assumption was not confirmed experimentally (acetonitrile, $100^{\circ}C$, 2 h); this indicated the decisive role of the acyl halide in this process. In fact, the addition of 1-2 moles of the acyl halide to a suspension of II in absolute benzene (toluene) led to the formation of IV when the reaction mixture was shaken for 2 days at 20°C (see Table 1).

In acetonitrile one observes a decrease in the yield of the deacylated product by a factor of more than two, and 1-methylbenzimidazole I is formed.

Regarding the acyl halide as an oxidizing agent, we attempted to replace it with nitrobenzene; however, we observed virtually no formation of deacylation product IV (70°C, 1 h, in solution in acetonitrile). This constitutes evidence that a decisive role in the deacylation of II is played by their prior coordination with the acyl halides, as a result of which V is formed. Its structure is confirmed by the corresponding absorption frequencies of the carbonyl group in the IR spectrum of a mixture of starting compound IIb and benzoyl chloride in a molar ratio of 1:2 in solution in chloroform: 1660 (CO group of the imidazoline fragment of V), 1740 (CO group attached to the imidazolium N heteroatom), 1790 cm⁻¹ (absorption of the carbonyl group of benzoyl chloride, which is present in excess amounts). The last two assignments were confirmed by the IR spectrum of a mixture of 1methylbenzimidazole and benzoyl chloride at a molar ratio of 1:2.

We assume that the mechanism of the deacylation of intermediate V consists in hydride migration from the imidazoline fragment to the imidazolium carbonyl carbon atom with the formation of VI. The fact of the deacylation of IIb by the action of trifluoroacetic acid was unexpected. The transformation proceeds smoothly in ~80% yield at 20°C after 5-6 h. Let us note that dilute mineral acids lead to the complex transformation of IIb to give a number of products, among which 1-methylbenzimidazole, 1-methyl-2-formylbenzimidazole, bis product IV, and unidentified compounds were detected.

The decrease in the yields of deacylated product IV on passing from benzene to acetonitrile and the invariable formation in a solution of the latter of 1-methylbenzimidazole constitute evidence for dissociation of quaternary salt V at the C-C bond joining the benzimidazolium and benzimidazoline fragments into carbene yield VII and quaternary salt VIII. This assumption is also confirmed by the formation of 1,3-dimethylbenzimidazolium iodide in the reaction of IIb with methyl iodide both in acetonitrile and chloroform.

Let us note that both the hydride migration, which leads to deacylated product IV, and dissociation of quaternary salts V and IX are due to the same reason — the tendency of the imidazoline fragment of the molecule to undergo aromatization (which is accompanied by oxidation here) — and, consequently, are competitive processes. Deacylation is suppressed in polar solvents, which facilitate dissociation, whereas dissociation is suppressed in nonpolar solvents, and deacylation increases.

Taking into account the fact that quaternary salt V can be converted to 1-methyl-2acylbenzimidazole only when it dissociates (both as a consequence of intramolecular stabilization of carbene yield VII and by way of its reaction with the acyl halide), one can understand the decisive role of the polarity of the solvent and high temperatures (above 140°C) in its conversion to 2-acyl derivatives. The higher the temperature, the higher the rate at which carbene yield VII undergoes intramolecular conversion to the 2-acyl derivative and the smaller the likelihood of its conversion (via the reaction with quaternary salt VIII) to bis compound V and irreversible conversion of the latter to deacylated coupling product IV.

EXPERIMENTAL

The melting points are indicated without correction. The IR spectra of solutions of the compounds in chloroform were recorded with a UR-20 spectrometer. The PMR spectrum of a solution in $CDCl_3$ was obtained with a Tesla BS-467 spectrometer (80 MHz) with hexamethyl-disiloxane (HMDS) as the internal standard.

<u>1-Methyl-3-furoyl-2-(1'-methyl-2'-benzimidazolyl)-4-benzimidazoline (IIc)</u>. A 1.96-g (15 mmole) sample of furoyl chloride was added in three portions while maintaining the temperature at no higher than 30°C to a solution of 1.98 g (15 mmole) of 1-methylbenzimidazole [5] and 3.03 g (30 mmole) of triethylamine in 12 ml of dry acetonitrile, after which the reaction mixture was shaken for 25 min in a tightly sealed vial and then allowed to stand for 30 min. Water (60 ml) was then added, and the aqueous mixture was extracted with toluene. The extract was evaporated, and the residue (2.8 g) was chromatographed with a column packed with low-activity aluminum oxide (adsorbent volume 50 cm × 3 cm) with elution by toluene with chloroform. The following three substances were isolated: 1-methyl-2-furoylbenzimidazole (IIIc) [0.43 g, mp 126-127°C (mp 128°C [6]). IR spectrum: 1655 cm⁻¹ (CO)], bis compound IV [0.39 g, mp 204-206°C (mp 210-211°C [7]). The IR spectrum was identical to that of the sample in [7]], and bis compound IId [0.92 g, mp 146-147°C, yellow prisms. IR spectrum: 1650 cm⁻¹ (CO). PMR spectrum: 2.75 (3H, s, CH₃), 3.60 (3H, s, CH₃), 6.25-7.75 ppm (12H, m). Found, %: C 70.1, H 4.48, N 15.4. C₂₁H₁₈N₄O₂. Calculated, %: C 70.4, H 5.1, N 15.6].

Deacylation of Bis Products IIb-d. A) In benzene. A 3 mmole sample of the corresponding acyl halide was added to a suspension of 2.5 mmole of bis product IIb-d in 40 ml of dry benzene, and the reaction mixture was shaken at 25°C in a sealed ampul for 2 days. In the experiments with IIb, c the precipitates (0.44 and 0.53 g, respectively) of the unchanged starting compounds were removed by filtration, the filtrates were evaporated to one third of their original volumes at 20°C, and bis compound IV (0.29 and 0.27 g, respectively) was separated from the starting compounds with a column packed with aluminum oxide (toluene with chloroform). In the case of IId the reaction mixture was separated with a column packed with aluminum oxide with the same eluent without prior filtration. This procedure gave 0.32 g of IV and 0.42 g of the starting compound.

<u>B) In acetonitrile.</u> A 2.5-mmole sample of IIb-d was shaken in an ampul with 3 mmole of the acyl halide in 30 ml of absolute acetonitrile for 2 days, after which the reaction mixture was evaporated in a stream of exhaust-hood air, and the residue was chromatographed with a column packed with low-activity aluminum oxide (50 cm \times 3 cm) with elution by toluene with chloroform. See Table 1 for the yields of I and IV. The products were identified from the IR spectra of genuine samples.

Reaction of IIb with Methyl Iodide. A) In chloroform. A 0.68-g [0.3 ml (4.8 mmole)] sample of methyl iodide was added to a solution of 0.37 g (1 mmole) of IIb, and the mixture was allowed to stand in a sealed flask for 48 h. It was then evaporated in vacuo at 20°C, and 15 ml of toluene was added to the residue. The 1,3-dimethylbenzimidazolium iodide (XII) was removed by filtration and crystallized from aqueous alcohol to give 0.13 g (47%) of a product with mp 191-192°C. The IR spectrum was identical to the spectuum of a genuine sample [8].

B) In acetonitrile. A mixture of 0.37 g (1 mmole) of IIb, 0.68 g (4.8 mmole) of methyl iodide, and 2 ml of acetonitrile was heated in a sealed ampul for 10 min at 100°C, after which the acetonitrile was evaporated on a water bath, and the residue was worked up as in experiment A to give 0.24 g of XII with mp 191-192°C.

Deacylation of IIb in Solution in Trifluoroacetic Acid. A solution of 0.38 g (1 mmole) of IIb in 10 ml of trifluoroacetic acid was maintained at 20°C for 6 h, after which it was evaporated in vacuo, and the residue was washed with dilute sodium carbonate solution and crystallized from alcohol to give 0.12 g of IV with mp 204-206°C. The IR spectrum was identical to that of the sample obtained in [7].

Action of Dilute Acids on IIb. A 1-g sample of IIb was heated with 20 ml of 10% HCl solution on a boiling-water bath for 1 h, after which the mixture was cooled, filtered, and neutralized with a saturated solution of sodium bicarbonate. This solution was then extracted with chloroform, and the chloroform extract was chromatographed with a column packed with Al_2O_3 to give 0.35 g of IV, 0.34 g of 1-methyl-2-formylbenzimidazole [9], and

0.52 g of 1-methylbenzimidazole. The products were identified from the IR spectra of genuine samples.

LITERATURE CITED

- 1. B. I. Khristich, A. M. Simonov, E. N. Shepelenko, and V. A. Yatsimirskii, Khim. Geterotsikl. Soedin., No. 1, 98 (1983).
- 2. E. Regel, Ann., No. 1, 159 (1977).
- 3. E. Regel and K.-H. Buechel, German Offen. No. 1926206; Chem. Abstr., 74, 307 (1971).
- 4. E. Regel and K.-H. Buechel, German Offen., 1956711; Chem. Abstr., 75, 369 (1971).
- 5. A. F. Pozharskii and A. M. Simonov, Zh. Obshch. Khim., 33, 179 (1963).
- 6. E. Regel and K.-H. Büchel (Buechel), Ann. Chem., No. 1, 145 (1977).
- 7. B. A. Tertov, Yu. V. Kolodazhnyi, and A. V. Koblik, Tetrahedron Lett., 4445 (1968).
- 8. A. D. Garnovskii, Master's Dissertation, Kharkov State University, Kharkov (1962).
- 9. H. R. Hensel, Chem. Ber., 98, 1325 (1965).

EPR AND POLAROGRAPHY OF NITROAZOLES.

6.* 3-NITRO-1,2,4-TRIAZOLES

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The electrochemical reduction of eight 3-nitro-1,2,4-triazole derivatives in acetonitrile was investigated by polarography and EPR spectroscopy.

We have previously shown that N-unsubstituted 5(3)-substituted derivatives of 3(5)nitro-1,2,4-triazole are reduced in acetonitrile in two formally one-electron steps to stable dianion radicals (DAR), which are recordable in the EPR spectra [2].

However, the literature contains no information regarding the electrochemical behavior of dinitrotriazoles in aprotic media. In this connection, we undertook a study, by EPR spectroscopy and polarography, of the mechanism of the electrochemical reduction (ECR) in acetonitrile of dinitro-1,2,4-triazole derivatives I-III and model compounds IV-VIII.

The presence of two-nitro groups in the molecule substantially changes the polarographic behavior of I as compared with the behavior of its mononitro analog VII. Three waves are observed in the polarogram of 3,5-dinitro-1,2,4-triazole; the reduction is facilitated to such an extent that the first irreversible wave is observed at positive potentials (Table 1 and Fig. 1). Its intensity with respect to the current is markedly depressed and corresponds to the transfer of ~0.5 of an electron. The second wave has split character, and its overall current corresponds to an approximately one-electron level. The third wave is a multi-electron wave (virtually eight times higher than the first wave) and corresponds formally to the transfer of 4.4 electrons per molecule. Two different signals were recorded in the EPR spectra in the electrochemical reduction of I. The first signal shows up at the potentials of the second wave with a hyperfine structure (hfs) corresponding to coupling of an unpaired electron with five nitrogen atoms and to a symmetrical distribution of the spin density (Tables 1 and Fig- 2a). When the potential is increased to the values of the third wave, the indicated EPR signal vanishes, and another signal, the hfs of which corresponds to coupling of an unpaired electron with four nitrogen atoms (Table 1 and Fig. 2b), arises in place of it.

*See [1] for communication 5.

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