2,2'-DIALKOXY, 2,2'-DIHYDROXY, and 2,2'-DIAMINO DERIVATIVES OF 1,1'-AZOBENZIMIDAZOLE. THE FIRST SYNTHESIS OF HETEROCYCLIC TETRAZENES BY MEANS OF A NUCLEOPHILIC SUBSTITUTION REACTION

V. V. Kuz'menko, I. M. Nanavyan, and A. F. Pozharskii

2,2'-Dimethanesulfonyl-1,1'-azobenzimidazole is prepared by the oxidation of 1-amino-2-methanesulfonylbenzimidazole with lead tetaacetate. The reaction of this tetrazene with alkali in DMSO, with sodium alkoxides in the corresponding alcohol or ammonia, or with primary or secondary amines leads to the formation of 2,2'-dihydroxy, 2,2'-dialkoxy, or 2,2'-diamino derivatives of 1,1'-azobenzimidazole.

Earlier we showed that 1-aminobenzimidazole and its 2-methyl, 2-phenyl, and 2-chloro derivatives are converted to the corresponding 1,1'-azobenzimidazoles by oxidation with lead tetraacetate and a number of other oxidants [1]. At the same time, the sole products of the oxidation of 1,2-diaminobenzimidazole and 1-aminobenzimidazole are the corresponding 3-aminobenzo-1,2,4-triazene and benzo-1,2,4-triazen-3-one, which are formed by expanding the imidazole ring [1, 2]. In the present work we set the goal of developing an alternate method of synthesizing the unknown tetrazenes of the benzimidazole series containing hydroxy, alkoxy, or amino groups in the 2-position.

It seemed possible to us to first synthesize a 1,1'-azobenzimidazole containing a functional group in the 2- and 2'-positions that readily undergoes nucleophilic substitution and then to replace it by OH, OAlk, NH₂, etc., groups. As such a compound, we selected 2,2'-dimethanesulfonyl-1,1'-azobenzene (II). Such an approach to the synthesis of tetrazenes has not been used before, possibly because of the well-grounded opinion that heterocyclic and, in particular, nonheterocyclic tetrazenes must be unstable toward nucleophilic or electrophilic reagents.

1-Amino-2-methanesulfonylbenzimidazole (I) was obtained in a 35% yield by the amination of 2-methanesulfonylbenzimidazole with hydroxylamine-O-sulfonic acid in aqueous alkali. Its oxidation with lead tetraacetate in methylene chloride gives tetrazene II in a 26% yield. The use of N-bromosuccinimide as the oxidant increases the yield of compound II to 50%.

The action of excess sodium methylate or ethylate in the corresponding alcohol on tetrazene II replaces the methanesulfonyl groups even at 20-50°C. As a result, 2,2'-dialkoxy derivatives of 1,1'-azobenzimidazole IIIa and IIIb are obtained in yields of 41 and 54%, respectively. We also attempted to synthesize tetrazenes IIIa and IIIb by the traditional method of oxidizing 1-amino-2-alkoxybenzimidazoles. However, the synthesis of the latter by the action of the sodium alkoxides on compound I did not succeed; only the deamination of I was observed. On treatment of tetrazene II with an excess of sodium hydroxide in

DMSO at room temperature, compound IV was obtained. Judging from the IR spectrum (the presence of an intense ν_{C=O} band at 1745 cm\(^{-1}\)) it exists in the oxo form, IVa, not in the hydroxy form, IVb, which would seem able to be stabilized by an intramolecular hydrogen bond. With the use of 1 equiv. of alkali, we obtained unsymmetrical tetrazene V.

Replacement of the methanesulfonyl groups in tetrazene II by amino, methylamino, and dimethylamino groups was accomplished by heating II in a sealed ampul with an aqueous solution of ammonia, methylamine, or dimethylamine at 95-100°C. Yields of compounds IIIc-e were 63, 87, and 69%, respectively. On attempting to carry out the analogous replacement of the methanesulfonyl groups by piperidino or morpholinono groups, we observed only the destruction of the azo group and obtained in high yield the 2-piperidino- and 2-morpholinobenzimidazoles. Compound IIIf was successfully synthesized by the action of potassium piperidide on tetrazene II in dimethoxyethane at 85°C. Note that the replacement of the methanesulfonyl groups is not brought about by the action of potassium amide on tetrazene II in liquid ammonia at \(-70 \text{ to } -30°C\).

The structure of the compounds obtained was established with the aid of the UV, PMR, and mass spectra. The UV spectra were especially informative since all 1,1'-azobenzimidazoles have an absorption band at 340 nm which is missing in initial benzimidazoles. In addition, a characteristic qualitative reaction for the tetrazene structure is the energetic, explosive decomposition of tetrazenes when they are introduced into a flame on the tip of a spatula.

**EXPERIMENTAL**

The PMR spectra were recorded on Tesla BS-487 (compound I), Tesla BS-567 (compounds II, IIIa, b, e, IV, and V), and Bruker WH-90 (compounds IIIId and IIIIf) spectrometers with working frequencies of 80, 100, and 90 MHz, respectively, and a TMS internal standard. The IR spectra were measured on a Specord IR-75 instrument in mineral oil, and the electronic spectra on a Specord M-40 spectrometer in methanol (IIIId, e, f) and DMSO (II, IIIa, b, and IV). The mass spectra were obtained on a Finnigan 4021 spectrometer by direct introduction into the ion source; accelerating potential 1 kV, ionizing electron energy 70 eV. The course of the reactions and the purity of compounds obtained were checked by TLC on standard activity Brokman chromatographically on a column with Al2O3 (chloroform eluent), the first fraction, with Rf 0.55, being taken. Colorless crystals with T\text{mp} 245-247°C (decomp., from aqueous DMF). IR spectrum: 1620, 3220, 3287, 3330 cm\(^{-1}\); PMR spectrum (CDCl\(_3\)): 3.53 (3H, s, CH\(_3\)); 6.45 (2H, bd s, disappears on deuteration, NH\(_2\)); 7.30-7.85 ppm (4H, m, 4-7-I-I).

1-Amino-2-methanesulfonylbenzimidazole (I, C\(_6\)H\(_7\)N\(_6\)O\(_2\)). A solution of 33.9 g (340 mmole) of sodium hydroxylamine-O-sulfonate in 25 ml of water is added to a solution of 19.6 g (0.1 mole) of 2-methanesulfonylbenzimidazole \([3]\) and 14.8 g (370 mmole) of NaOH in 100 ml of water at 40-45°C with stirring. After 5-10 min a precipitate forms in the orange solution. The mixture is stirred for 1 h at 40-45°C, then cooled. The crystals that separate are filtered off, washed with 30 ml of cold water, and dried at 100°C. The dry residue is extracted with chloroform in a Soxhlet extractor, and the solvent distilled off to obtain 7.4 g (35%) of amine I. Colorless prisms with T\text{mp} 192-193°C (decomp., from chloroform). IR spectrum: 1620, 3220, 360 nm (3.30). PMR spectrum (DMSO-d\(_6\)): 3.75 (3H, s, CH\(_3\)); 7.64 (2H, m, 5,6-H); 8.0 (tH, m, 4-H); 8.61 ppm (1H, m, 7-H). Yield 1.4 g (26%).

2,2'-Dimethanesulfonyl-1,1'-azobenzimidazole (II, C\(_{16}\)H\(_{14}\)N\(_6\)O\(_4\)S\(_2\)). A. Over a 30-min period 12.4 g (28 mmole) of lead tetraacetate is gradually poured into a solution of 5.35 g (25 mmole) of sodium amide in 120 ml of absolute dichloromethane at 0-4°C. The solution gradually becomes yellow, then brown. The mixture is stirred for 1 h at 0-8°C, 3 ml of ethylene glycol are then added and, over another 15 min, 60 ml of water. The precipitate that forms is filtered off and washed with 50 ml of water. Colorless crystals with T\text{mp} 245-247°C (decomp., from aqueous DMF). IR spectrum: 1593, 1673 cm\(^{-1}\); UV spectrum, \(\lambda_{\text{max}} (\log \varepsilon)\): 270 (3.63), 295 (3.30), 360 nm (3.30). PMR spectrum (DMSO-d\(_6\)): 3.75 (3H, s, CH\(_3\)); 7.64 (2H, m, 5,6-H); 8.0 (1H, m, 4-H); 8.61 ppm (1H, m, 7-H). Yield 1.4 g (26%).

B. In portions, 1.78 g (10 mmole) of N-bromosuccinimide is added to a suspension of 1.05 g (5 mmole) of amine I in 50 ml of absolute methylene chloride at 5-10°C, upon which the solid dissolves. A finely crystalline precipitate then separates from the red solution, is filtered off after 40 min, and washed with water. Colorless crystals with T\text{mp} 245-247°C (decomp., from aqueous DMF), identical in physical chemical properties with the sample from experiment A. Yield 0.52 g (50%).

2,2'-Dimethoxy-1,1'-azobenzimidazole (IIIa, C\(_{16}\)H\(_{14}\)N\(_6\)O\(_2\)). To a solution of sodium methanolate, prepared from 0.12 g (5 mmole) of metallic sodium in 10 ml of methanol, is added 0.22 g (0.5 mmole) of compound II. The suspension is stirred for 45 min at 20°C. After being filtered off and washed with 5 ml of methanol, the solid weighs 0.18 g. It is purified chromatographically on a column with Al2O3 (chloroform eluent), the first fraction, with R\text{f} 0.55, being taken. Colorless crystals with T\text{mp} 213-214°C (decomp., from a mixture of alcohol with chloroform). IR spectrum: 1567, 1620 cm\(^{-1}\); UV spectrum, \(\lambda_{\text{max}} (\log \varepsilon)\): 270 (3.60), 340 nm (3.60). Mass spectrum, m/e (rel. %): 322 (39) M\(^+\), 294 (6.7) [M - N\(_2\)]\(^+\); 279 (2.4) [M - N\(_2\)-CH\(_3\)]\(^+\); 147 (100) [(M - N\(_2\))/2]\(^+\); 132 (20); 119 (44.6); 104 (15.5); 92 (23.4); 90 (26.9). PMR spectrum (DMSO-d\(_6\)): 3.75 (3H, s, OCH\(_3\)); 7.26-7.62 (2H, m, 5,6-H); 8.0 (1H, m, 4-H); 8.60 ppm (1H, m, 7-H). Yield 0.07 g (41%).