3) Cyclohexanone oxime (25 g), 12.5 g of KOH, and 200 ml of DMSO were placed in a flask equipped with a stirrer, reflux condenser, thermometer, and bubbler, the mixture was heated with stirring to 90-95°C, and acetylene was admitted at atmospheric pressure for 4-5 h (until cyclohexanone oxime disappeared on the chromatogram). Standard workup gave 28.9 g (90%) of II.

LITERATURE CITED


BEHAVIOR OF N-ALKOXYBENZIMIDAZOLES WITH RESPECT TO NUCLEOPHILIC REAGENTS.

ATTEMPTS TO SYNTHESIZE N-HYDROXY-2-AMINOBENZIMIDAZOLES

M. M. Medvedeva, A. F. Pozharskii, V. V. Kuz'menko, V. V. Bessonov, and B. A. Tertov

Various possibilities for the synthesis of N-hydroxy- and N-alkoxy derivatives of 2-aminobenzimidazoles — reductive cyclization of o-nitrophenylureas, the action of sodium amide on 1-alkoxybenzimidazoles, the ammonolysis of 1-alkoxy-2-iodobenzimidazoles, etc. — were investigated. Organometallic compounds of 1-alkoxybenzimidazoles were obtained for the first time, and their reactivities with respect to benzophenone, iodine, and 1-substituted benzimidazoles were studied. 2,2'-Di-benzimidazolyls that contain an alkoxy group in the 1 position were synthesized.

The present research was undertaken in order to synthesize N-oxides of 2-aminobenzimidazoles — a class of compounds that heretofore has not been described in the literature. Two approaches based on the cyclization of suitable o-phenylenediamine derivatives and on the direct incorporation of an amino group in N-hydroxybenzimidazoles were studied.
It is known that the general method for the preparation of N-oxides of benzimidazole (IVa) is reduction of N-acyl derivatives of o-nitroaniline (I) with ammonium sulfide [1]; the N-hydroxyamino intermediates (III) undergo spontaneous cyclization to the final products.

We also developed a similar scheme for the synthesis of 2-aminobenzimidazole N-oxides (IVb), with the difference that we used o-nitrophenylureas (IIa-e) as the starting compounds instead of o-nitroaniline derivatives. Reduction of IIa-e with ammonium sulfide in alcohol gave high-melting colorless substances, which, according to the results of elementary analysis, IR spectral data, and the positive tests with a solution of FeCl₃ (red coloration), correspond to the desired 2-aminobenzimidazole N-oxides. However, it was found that the azomethines of the compounds obtained contain a carbonyl group, according to the IR spectroscopic data. This compelled us to assume that the products are actually o-aminophenylureas (V) rather than 2-aminobenzimidazole N-oxides. This assumption was confirmed by alternative synthesis of o-aminophenyl ureas V by the action of potassium cyanate on aqueous solutions of the corresponding o-phenylenediamines and their hydrochlorides. All of the properties of the compounds obtained by the two methods were identical. It is interesting to note that the two nitro groups are reduced immediately to give Vc in the case of the reaction of ammonium sulfide with IIc, although it is known that primarily the o-nitro group is reduced in 2,4-dinitroanilines under these conditions [2].

A characteristic feature of o-aminophenylureas is their easy conversion to benzimidazolones. This reaction takes place when they are heated in acids and alkalis and also during simple thermolysis. Compounds V initially melt with gas (ammonia) evolution, after which they solidify and remelt at the melting point of the corresponding benzimidazolone (VI).

The failure to obtain 2-aminobenzimidazole N-oxides from o-nitrophenylureas is evidently explained by the low rate of intramolecular cyclization to the corresponding hydroxyamino-phenylureas (III, R = NH₂), owing to which further reduction to an amino group occurs. In view of this, methods for the incorporation of an amino group in N-hydroxy- and N-alkoxy-benzimidazoles were studied.

There are no indications in the literature [3] regarding the successful Chichibabin amination of heteroaromatic N-oxides. The attempts by various researchers to accomplish this reaction with N-oxides were probably unsuccessful. We also were unable to thoroughly aminate the N-oxides of 1-methyl-, 1-ethyl-, and 1-benzylbenzimidazoles with sodium or potassium amide in xylene, dimethylaniline, or liquid ammonia. In all cases we observed pronounced destruction of the N-oxides to give six to eight difficult-to-separate and unstable substances, and the reaction mixture had a strong isocyanide odor.

The reaction of 1-alkoxybenzimidazoles with metal amides proceeds in an interesting manner. As demonstrated by Takahashi and Kano [4], 1-ethoxybenzimidazole (VIIb) is converted to 1-ethoxy-2,2'-dibenzimidazolyl (Xb) by the action of NaNH₂ in dimethylaniline. We confirmed these results for VIIb and also extended them to 1-methoxy- and 1-benzyloxybenzimidazoles.

This reaction proceeds exothermically at room temperature in both dimethylaniline and xylene (however, it does not take place in liquid ammonia). Dimers X are formed in xylene in 60-80% yield. The yield of dimers is somewhat lower in dimethylaniline. The structures of dimers X are in good agreement with the data from the IR and PMR spectra. The PMR spectra contain signals of corresponding integral intensity of an NH group at 5.0 ppm (this signal vanishes after deuteration) and of an alkoxy group. An interesting feature of the PMR spectra of dimers X is a pronounced paramagnetic shift of the protons of the alkoxy group in trifluoroacetic acid. Thus the signal of a CH₃ group appears in the spectrum of Xc in d₅-pyridine at 5.6 ppm, whereas it appears at 3.7 ppm in CF₃COOH. In addition to a band of stretching vibrations of free NH groups at 3450 cm⁻¹, the IR spectra of the dimers in CHCl₃ solution contain a strong broad band at 2500-3300 cm⁻¹, which corresponds to associated NH groups and is evidently due to the formation of an intramolecular hydrogen bond. The spectra of crystalline samples of the dimers do not contain bands of free NH groups, and only a broad band at 2550-3300 cm⁻¹ is present.

We assume that the mechanism of the dimerization includes the intermediate formation of 2-sodio compound VIII, which adds to the C=N bond of a molecule of the starting 1-alkoxybenzimidazole with subsequent aromatization of adduct IX by splitting out of a molecule of alcohol: