Nucleophilic Attack of Azide at Electrophilic Azides: Formation of $\text{N}_6$ Units in Hexazene and Aminopentazole Derivatives**

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In memory of Professor Rolf Huisgen
Initial attempts to generate an all-nitrogen five-membered ring were performed more than a hundred years ago. But the first report with evidence of the arylpentazole \(2\) dates back from the year 1956 when Huisgen and Ugi described experiments with such intermediate species in the transformation of aryldiazonium salts \(1\) to prepare aryl azides \(3\) (Scheme 1a). Later, isolation and even characterization of pentazole \(2\) \((\text{Ar} = 4-\text{Me}_2\text{NC}_6\text{H}_4)\) with the help of single-crystal X-ray diffraction analysis were successful. However, attempted modification of the aryl group of \(2\) have usually resulted in destruction of the pentazole ring, which degraded rapidly at ambient temperature with evolution of dinitrogen. To our knowledge, the reaction of substrates \(1\) with azide salts proves to be the only method for the synthesis of pentazoles, and aryl derivatives of type \(2\) are the only representatives which could be prepared so far.

After a long period of unsuccessful attempts and hundreds of experiments, reaction conditions were recently found for the cleavage of arylpentazole \(2\) \((\text{Ar} = 3,5-\text{dimethyl-4-hydroxyphenyl})\) in the presence of \(m\)-chloroperbenzoic acid (\(m\)-CPBA) and ferrous bisglycinate \([\text{Fe}(\text{Gly})_2]\). This transformation led to the salt \(5\) \((\text{M} = \text{NH}_4)\) and effected a breakthrough in pentazolate chemistry and also in the synthesis of other salts of type \(5\). Nearly simultaneously, the products \(5\) \((\text{M} = \text{Cs, Li})\) were generated by laser heating of alkali azides in the presence of dinitrogen under very high pressure (Scheme 1a). Currently, polynitrogen compounds, such as pentazoles and pentazolate salts, attract attention because they are assumed to have important applications as high energy density materials (HEDMs).

Herein, we report an unprecedented synthesis of the aminopentazole derivative \(7\), which is available by treating the commercial Vilsmeier reagent \(6\) with sodium azide (Scheme 2). The reaction

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**Abstract:** With the help of selective \(^{15}\text{N}\) labeling experiments, it has been confirmed that nucleophilic attack of azide at iminium-activated organic azides leads to short-lived hexazene intermediates. Such species do not only tend to a cleavage reaction with formation of N-azido compounds, but also undergo ring closure to generate unprecedented amidino-functionalized pentazoles. Thus, treatment of the parent Vilsmeier reagent with two equivalents of sodium azide creates an aminopentazole derivative as the main product, which is easily characterized by NMR spectroscopy.

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[\(\text{Ar} \rightarrow \text{N}_2\)]

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**Scheme 1.** Synthesis of penzatoles \(2\) and \(7\) as well as pentazolate salts \(5\).

**Scheme 2.** Generation of the \(N\)-azido compound \(13\).
of 9 with lithium azide in dimethylformamide led to the highly unstable N-azido compound 13. The salt 10, which should establish an equilibrium with the covalent diazide 11,[11] and the hexazene derivative 12 were postulated as short-lived intermediates to explain the formation of the unusual final product 13.[10]

Quite recently, it was shown that the structures of several N-azidoamines, which were previously reported in the literature, are not correct and have been revised.[13] Thus, we assumed that structural verification of the N-azido compound 13 might be useful since the former characterization was mainly based on IR data[10] owing to the low stability of this substance. The reaction mechanism including nucleophilic attack of azide at the terminal nitrogen atom of the iminium-activated azido group of 10 and formation of intermediate 12 is plausible but also an unprecedented case. We thought that migration of an azido group of diazide 11 accompanied by liberation of dinitrogen may alternatively lead directly to 13 without the creation of 12. If hexazole intermediate 12 is really generated, however, cyclization to produce the corresponding aminopentazole derivative is possibly observable at low temperature. This assumption is based on the well-known ring closure of pentazenes to yield pentazoles.[5,14]

When we treated the substrate 9 in d7-DMF with hexadecyltributylphosphonium azide (Scheme 3), which includes a 15N label at one of the terminal nitrogen atoms (98%)[15] we obtained the desired N-azido compound 14N3-13 quantitatively (1H NMR spectroscopy at -60°C). The 15N NMR spectrum of this product indicated that the label was distributed among the imino group as well as N-β and N-γ of the azido group. Both signals of the azido group were accompanied by small doublets, which revealed a direct coupling of the two nitrogen atoms with 1J(15N,15N) = 9.3 Hz. These results show that the equilibration of isotopically labeled intermediates 10 and 11 led to such species with two, one, or zero 15N atoms. The distribution of the 15N label, observed in 14N3-13, is only compatible with formation of 13 via cleavage of 12.[10] In the alternative case with liberation of dinitrogen from 11, the isotopically isomeric product 14N3-13' should be generated. We treated 13 and 14N3-13 with cyclooctyne[17] in order to confirm the N-azido structure and the distribution of the 15N label. The product 14N3-14 was formed quantitatively (1H NMR spectroscopy) and led to 15N NMR signals at δ = -158.7, -48.7, and -44.7 ppm, which were

Scheme 3. Synthesis of the 15N-labeled compounds 13 and 14 as well as 15N NMR chemical shifts (δ) of 14.

Scheme 4. Synthesis of aminopentazole derivatives 7 from Vilsmeier reagent 6 and sodium azide.
additionally verify the 15N NMR data of create an aminopentazole derivative was not observed.

The signals of 15N3-azides is possible since nucleophilic attack of azide at iminium-activated organic azido structure of 13. Disappointingly, cyclization of short-lived 12 to create an aminopentazole derivative was not observed.

Our investigations allow the drawing of the following interim conclusions: The 15N NMR data and the trapping reaction of 13 with the help of cyclooctyne confirm the N-azido structure of 13. Moreover, it is demonstrated that nucleophilic attack of azide at iminium-activated organic azides is possible since 13 was generated from 9 via hexazene derivative 12. Disappointingly, cyclization of short-lived 12 to create an aminopentazole derivative was not observed.

When we planned and performed final experiments to additionally verify the 15N NMR spectrum of 14 measured with natural abundance (Scheme 3). The signals of 15N14 with δ = -48.7 and -44.7 ppm were accompanied by small doublets with J(15N,15N) = 18 Hz. Whereas the 2D-15N1H shift correlation spectrum of 14 showed cross signals for N-3/4'-H as well as N-1'/9'-H, the corresponding spectrum of 15N-14 indicated the former cross signal only, and a correlation of the 9'-H signal with nitrogen signals was not observed.

The 15N NMR spectrum of 15N7 and 15N17 in d7-DMF measured at -60°C (61 MHz, reference MeNO2 with δ = 0; J values in Hz).

Figure 1. 15N NMR spectrum of 15N7 and 15N17 in d7-DMF measured at -60°C (61 MHz, reference MeNO2 with δ = 0; J values in Hz).

compared with the 15N NMR spectrum of 14 measured with natural abundance (Scheme 3). The signals of 15N-14 with δ = -48.7 and -44.7 ppm were accompanied by small doublets with J(15N,15N) = 18 Hz. Whereas the 2D-15N1H shift correlation spectrum of 14 showed cross signals for N-3/4'-H as well as N-1'/9'-H, the corresponding spectrum of 15N-14 indicated the former cross signal only, and a correlation of the 9'-H signal with nitrogen signals was not observed.

The N-azido compound 17 can easily be handled in solution at -40°C; however, rapid decay with a half-life of around 16 min, which was measured by collecting the liberated dinitrogen gas, was observed at -30°C. Hence, 17 is significantly less stable than 13, and consequently, 17 did not undergo a clean trapping reaction with cyclooctyne. On the other hand, solutions of the aminopentazole derivative 7 can be utilized for NMR spectroscopy at +10°C, and a half-life of around 11 min was roughly estimated at 21°C. The identification of 17 and 17 was mainly based on NMR spectroscopy and especially 15N NMR data. The 15N NMR data of 15N-17 and those of 15N13 are very similar. The 15N NMR chemical shifts and the 15N15N coupling constants of 15N7 and 15N17 are in excellent agreement with those published for several other pentazoles. To our knowledge, 15N-7 is the first pentazole derivative in which all members of the ring are labeled by 15N atoms. Therefore, there is no need to compare with known data of other pentazoles since the coupling patterns alone are unequivocal proof of the structure with an all-nitrogen five-membered ring connected with a sixth nitrogen atom. As depicted in Figure 1, the imine nitrogen atom couples with N-1 (J = -14.3 Hz), and a direct coupling with N-2 and N-5 is responsible for the additional triplet splitting of the N-1 signal (J = -18.0 Hz). Other triplet splittings were detected for the N-1 signal by...
geminal coupling with N-3 and N-4 (\(J = 0.8\) Hz) and also for the imine signal by geminal coupling with N-2 and N-5 (\(J = 2.2\) Hz). Finally, N-2, N-5, N-3, and N-4 create an AA’XX’ system, which was analyzed by iterative simulation of the \(^{15}\)N NMR spectrum.[16]

In conclusion, we confirmed the nucleophilic attack of azide at the terminal nitrogen atom of iminium-activated organic azides. Clearly, the resulting short-lived hexazene derivatives undergo not only a cleavage reaction to generate \(N=\)azido compounds, but also a cyclization leading to unprecedented aminopentazole[23] structures. This simple access to amidino-substituted pentazoles is remarkable, especially as the precursor 6 is a commercial substance known as the Vilsmeier reagent and isolated in 1959 for the first time.[21] Currently, we investigate whether the new approach to functionalized pentazoles can be transferred to other chloroiminium substrates. Preliminary experiments have shown that pentazolate salts are also available by similar reactions. Moreover, we assume that the decay of 7 and 17 will offer an access to dimethylaminomethylidene, a rarely studied carbene.[23] This expectation is based on the known decomposition reaction of 13, which led to the corresponding short-lived benzo[1,2-c]thiazol-2-ylidene.[19]

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Conflict of interest

The authors declare no conflict of interest.

Keywords: azides · isotopic labeling · nitrogen heterocycles · reaction mechanisms · reactive intermediates

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