Chemistry of Heterocyclic Compounds, Vol. 31, No. 3, 1995

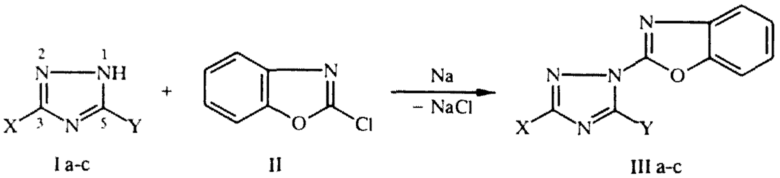
REACTION OF SOME AZOLES AND AZOLINTHIONES WITH 2-CHLOROBENZOXAZOLE

R. G. Aflyatunova, N. A. Aleiv, U. A. Abdullaev,
M. G. Levkovich, and N. D. Abdullaev

The reaction of 1,2,4-triazole and imidazolidin- and thiazolidin-2-thiones with 2-chlorobenzoxazole gave the corresponding 2-(heteryl)benzoxazoles and 2-(heterylthio)benzoxazoles.

In earlier years, interest has grown in new classes of compounds based upon 1,2,4-triazole, imidazole, and thiazole which rapidly break down in the environment [1-3]. Study of the alkylation of such heterocyclic compounds may allow new biologically active materials to be obtained, and in the case of their mercapto derivatives the possibility arises of obtaining derivatives with nitrogen as well as sulfur, or with both atoms [4].

The reaction of the sodium salt of 1,2,4-triazole (I) with 2-chlorobenzoxazole (II) in acetonitrile was used to synthesize 1-(2′-benzoxazolyl)-1,2,4-triazole (IIIa).



I, III a X = H; b, c X = NO_2; a, b Y = H; c Y = Br

In the mass spectrum of IIIa, the M^+ peak with m/z 186 possessed the maximum intensity, and fragmentation of the system took place through a deep rearrangement process with successive elimination of HCN and CO fragments, and also the radicals CN and NCO [5, 6]. As a result of this the mass spectrum showed ions with m/z 159, 133, 132, 104, 90, 78, 77, 64, and 63. It should be noted that the ions with m/z 78 and 77 have a pyridine structure and their source is the fragmentation of the m/z 104 ion, which as the result of the dissociation rearranges into a pyridine fragment.

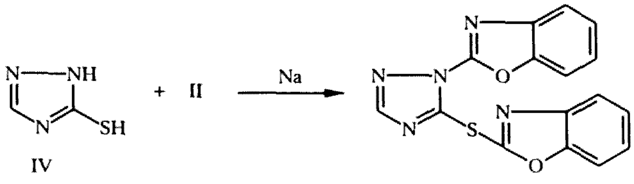
The ^1H NMR spectrum of IIIa in $CDCl_3$ shows two singlets; for 1H at 9.00 and at 8.17 ppm from the two protons of the triazole ring and a complex group of signals in the 7.25-7.80 ppm region for the four aromatic hydrogen atoms. The absence of symmetry in this group of signals confirms the *ortho*-substitution of benzene by nonequivalent substituents.

As indicated by the different chemical shifts of the ^1H NMR signals, the protons of the triazole ring of IIIa are nonequivalent. It is known that the π-electron densities of the C_3 and C_5 carbon atoms of 1,2,4-triazole are 0.144 and 0.64, respectively [7]. From the large π-electron density of C_5, the signal at 9.00 ppm relates to the H_5 proton and the signal at 8.17 ppm to H_3. This assignment corresponds with literature data [8].

Carrying out the reaction of II with 3-nitro- and 5-bromo-3-nitro-1,2,4-triazole gave 1-(2′-benzoxazolyl)-3-nitro-1,2,4-triazole (IIIb) and 1-(2′-benzoxazolyl)-5-bromo-3-nitro-1,2,4-triazole (IIIc) in very low yields, apparently a result of the low basicity of the N_1 nitrogen atom in the substituted 1,2,4-triazoles Ib and Ic. The structure of IIIb was proven by mass spectral data, which showed peaks with m/z 231 $[M]^{+\bullet}$, 153, 119, 114, 90, 78, 77, 64, and 63.

Institute for the Chemistry of Plant Materials, Academy of Sciences of the Republic of Izbekistan, Tashkent 700170. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 403-405, March, 1995. Original article submitted May 26, 1994.

Taking into account the relative mobility of the protons on mercapto groups, we examined the indicated reaction with 5-mercapto-1,2,4-triazole (IV). The reaction of II with IV under the earlier-indicated conditions gave 1-(2′-benzoxazolyl)-5-(2′-benzoxazolylthio)-1,2,4-triazole (V) in 34% yield together with probable monoalkylation products. Carrying out this reaction with excess II (1:2) led to an increased yield of product (68%).



IV

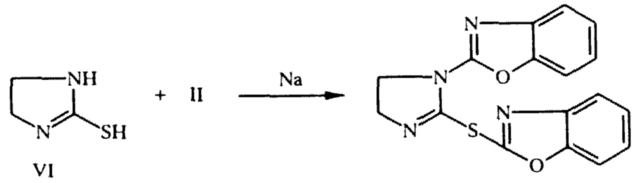
V

The mass spectrum of compound V showed the molecular ion peak with m/z 335 and fragments with 277, 191, and 150, as well as peaks for ions observed in the spectrum of III: 104, 90, 78, 77, 64, and 63. It is necessary in this particular case to note that the elimination of the bridging sulfur atom in the form of the isothiocyanate ($^{\bullet}$NCS) radical occurs with the formation of the fairly stable ion with m/z 277.

The UV spectrum of compound I shows a maximum absorption in the 288 nm region, which is characteristic of 2-(alkylthio)benzoxazoles [7]. The ^{1}H NMR spectrum of V in trifluoroacetic acid shows two signals: a wide single-proton singlet at 9.02 ppm, corresponding to the single triazole proton, and a broad eight-proton multiplet from the aromatic protons in the 7.12-7.70 ppm region.

The reaction of 2-chlorobenzoxazole and imidazolidine-2-thione (VI) processes analogously to give 1-(2′-benzoxazolyl)-2-(2′-benzoxazolylthio)imidazole (VII) in 73% yield.

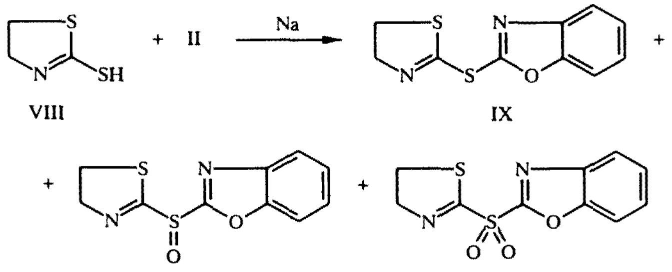
The mass spectrum of VII contained the molecular ion peak with m/z 336, and also characteristic peaks or the ions enumerated for compounds III and V. The presence of the saturated bridged imidazole system in the VII molecule introduces a specific contribution to the fragmentation, for example by the appearance in the spectrum of the ion $[M-CH_2CNS]^{+\bullet}$ with m/z 264 and the formation of ions with m/z 134, 105, and 92.



VI

VII

The reaction of II with thiazolidin-2-thione (VIII) also was carried out. In the mass spectrum of the product obtained was observed M$^+$ 236, and also peaks with m/z 252 and 268. It appears that in the course of the reaction the corresponding sulfoxide X (MW 252) and sulfone XI (MW 268) were formed in addition to the sulfide IX (MW 236).



VIII

IX

X

XI

The isolation from this reaction mixture of individual materials was not successful. On the basis of the above it follows that alkylation of 1,2,4-triazole with 2-chlorobenzoxazole gives monoalkylation and 5-mercapto-1,2,4-triazole and imidazolidine-2-thione undergo simultaneous N- and S-alkylation independently of the proportion of reagent.

EXPERIMENTAL

The mass spectra were obtained with a MS25RF (Kratos) instrument with direct introduction of the sample into the ion source, ionization energy 70 eV, ion chamber temperature 250°C, sample introduction system temperature 150°C. UV spectra were determined with a EPS-3T (Hitachi) spectrometer in ethanol, and ^{1}H NMR spectra were obtained on a Tesla 567a instrument with a working frequency of 100 MHz in $CDCl_3$, internal standard HMDS.

Control of the course of the reactions and the purity of the synthesized compounds was carried out by TLC on Silufol UV-254 plates in the solvent system benzene–ethanol, 1:2. A solution of 1 g $KMnO_4$ + 4 ml H_2SO_4in 96 ml of water was used for visualization.

Elemental analysis data corresponded with the calculated values.

2-Chlorobenzoxazole was obtained by the method of [10].

1-(2′-Chlorobenzoxazolyl)-1,2,4-triazole (III). To 0.46 g (0.02 mole) of metallic sodium and 20 ml of methanol was added 1.38 g (0.02 mole) of triazole Ia. The methanol was distilled and the residue was dried under vacuum. The salt was dissolved in 50 ml of acetonitrile and 3.06 g (0.02 mole) of II was added with stirring. The mixture was stirred for 1 h and boiled in a water bath for 5 h. The acetonitrile was evaporated and the residue was treated with 2% KOH solution, water, and then dried and crystallized from ethanol to give IIIa, 3 g (76%), mp 152-153°C.

Compounds IIIb, IIIc, V, VII and IX were prepared analogously. **IIIb** mp 280-282°C; IIIc, mp 228-230°C; V, VII, mp 282-284°C.

REFERENCES

1. N. N. Mel'nikov, Agrokhimiya, No. 5, 138 (1991).
2. N. N. Mel'nikov, Zashch. Rast., No. 7, 24 (1991).
3. A. F. Pozharskii, Theoretical Principles of the Chemistry of Heterocyclic Compounds [in Russian], Khimiya, Moscow (1985), p. 278.
4. O. S. Attaryan. G. V. Asratyan, G. A. Eliazyan, E. G. Dabrinyan, and S. G. Matsoyan, Arm. Khim. Zh., **39**, 630 (1986).
5. K. L. Lutfullin, M. M. Tadzhibaev, Y. A. Abdullaev, V. M. Malikov, and S. Yu. Yunusov, Khim. Prir. Soedin., No. 5, 625 (1976).
6. P. B. Terent'ev and A. P. Stankyavichus, Mass Spectrometric Analysis of Biologically Active Nitrogen Bases [in Russian], Mokslas, Vilnius (1987), p. 286.
7. B. F. Malichenko, Molecular Diagrams of Organic Compounds [in Russian], Naukova Dumka, Kiev (1982), p. 115.
8. M. C. Pevzner, T. P. Kofman, E. N. Kubasova, N. F. Sushchenko, and T. L. Uspenskaya, Khim. Geterotsikl. Soedin., No. 2, 257 (1980).
9. N. A. Aliev and N. S. Mukhamedov, Khim. Geterotsikl. Soedin., No. 9, 1289 (1989).
10. FRG Patent 1,201,617, Ref. Zh. Khim., 19H485 (1967).