

anhydride (20 ml) was refluxed for 1 h and then evaporated under vacuum to half volume. The precipitate that formed on cooling was filtered off and washed with water, alcohol, and ether to give compound (VI) (0.2 g, 76%), mp above 330°C (decomposition; from alcohol). IR spectrum: 1660, 1710 (C=O), 3390 cm^{-1} (NH). UV spectrum, λ_{max} : 210, 235, 247, 258, 279, 289, 302, 313, 339, 358, 379, 389 nm ($\log \epsilon$ 4.41, 4.33, 4.45, 4.38, 4.36, 4.31, 4.21, 4.30, 4.42, 4.25, 4.15, and 3.97). PMR spectrum (in DMSO- d_6): 2.37 (s, 2COCH₃), 3.28 (s, CH₃), 7.15-8.35 (m, aromatic protons), 11.75 ppm (s, NH). Found: C 71.0; H 4.8; N 15.1%; M^+ 370. $\text{C}_{22}\text{H}_{18}\text{N}_4\text{O}_2$. Calculated: C 71.3; H 4.9; N 15.1%; M 370.

LITERATURE CITED

1. A. Buzas, C. Herisson, and G. Lavielle, *Synthesis*, No. 2, 129 (1977).
2. J. R. Piper and F. J. Stevens, *J. Org. Chem.*, **27**, 3134 (1962).
3. C. D. Nenitzescu and D. Raileanu, *Chem. Ber.*, **91**, 1141 (1958).
4. V. S. Velezheva, V. P. Sevodin, Yu. V. Erofeev, N. K. Genkina, T. A. Kozik, V. V. Vampilova, and N. N. Suvorov, *Khim. Geterotsikl. Soedin.*, No. 3, 360 (1977).
5. D. H. R. Barton, R. E. O'Brien, and S. Sternhell, *J. Chem. Soc.*, 473 (1962).
6. V. I. Shvedov, G. N. Kurilo, A. A. Cherkasova, and A. N. Grinev, *Khim. Geterotsikl. Soedin.*, No. 8, 1096 (1975).
7. V. I. Shvedov, G. N. Kurilo, A. A. Cherkasova, and A. N. Grinev, *Khim. Geterotsikl. Soedin.*, No. 3, 377 (1977).

SUBSTITUTED AZAINDOLES.

58.* COMPARATIVE KINETICS OF THE NITRATION OF ISOMERIC 4-, 5-, 6-, AND 7-AZAINDOLES

V. A. Azimov, A. A. Prokopov,
I. S. Zhivotovskaya, M. K. Polievktov,
and L. N. Yakhontov

UDC 547.751'821.07:541.127:542.958.1

The distinctive features of the interaction of π -electron-deficient pyridine and π -electron-excessive pyrrole rings in the condensed systems of isomeric pyrrolopyridines (aza-indoles) have been discussed on several occasions [2, 3]. Hückel and PPP calculations of the indices of the electronic structure of isomeric azaindoles [4, 5] have revealed that the π -electron density distribution, ionization potential, and electron affinity vary only slightly on going from one isomer to another: the electron affinity increases slightly in the order 5-, 6-, 7-, and 4-azaindole and the ionization potential in the order 5-, 7-, 6-, and 4-azaindole.

Purely qualitative comparisons of the reactivity of the isomeric azaindoles in electrophilic substitution reactions have also failed to clarify the marked differences among these compounds [6]. Study of the kinetics of acid-catalyzed hydrogen exchange at position 3 of the isomeric 4-, 5-, and 7-azaindoles has revealed that 4-azaindole is more reactive than the 5-aza isomer, in which the electron-accepting effect of the pyridine nitrogen atom, which is para to the pyrrole nitrogen atom, is more effective [7].

In the work described here we have sought a more quantitative comparison of the reactivity by using a more complete series of the isomeric azaindoles, which included 6-azaindole in addition to 4-, 5-, and 7-azaindoles. Moreover to ascertain the generality of the correlations found earlier [7] we used another electrophilic substitution reaction, nitration, which under first-order reaction conditions takes place exclusively at position 3 and proceeds reasonably here to completion [6].

*For Communication 57 see [1].

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical Chemistry Institute, Moscow 119815. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 11, pp. 1489-1491, November, 1979. Original article submitted May 29, 1978; revision submitted December 15, 1978.

TABLE 1. Rate Constants for Nitration of Azaindoles at Position 3

Substrate	k , min ⁻¹	Dispersion, s ²	Number of degrees of freedom, f
4-Azaindole	0.0380	0.00035	16
5-Azaindole	0.0985	0.00125	23
6-Azaindole	0.0352	0.00006	21
4-Methyl-7-azaindole	0.0652	0.00003	10

The high rate of nitration of the isomeric azaindoles required that quantitative measurements be carried out with cooling to $-10 \pm 1^\circ\text{C}$. Nitration proceeds smoothly in concentrated sulfuric acid but is almost stopped by dilution of the reaction mixture with water. We determined the isomeric 3-nitroazaindoles by polarography in all cases. As a preliminary we established that under the conditions of polarographic analysis used in our work the reduction waves of the 3-nitroazaindoles have similar values of $E_{1/2}$ (≈ -0.1 V), while their heights depend linearly on the depolarizer concentration. We calculated the rate constants for the nitration of the isomeric 4-, 5-, 6-, and 7-azaindoles from plots of the height of the polarographic wave of the 3-nitro product against time under first-order reaction conditions. The rate constants for nitration and their dispersions are summarized in Table 1.

Table 1 shows that 5-azaindole is nitrated most rapidly; 4-methyl-7-azaindole reacts more slowly, but faster than 4- and 6-azaindoles, nitration of which is very slow.

Thus, like the greatest combined effect of the pyridine and pyrrole nitrogen atoms in the *o* and *p* positions on the basicity of these compounds [2], the possibility of resonance effects in 5- and 7-azaindoles has a marked effect on the reactivity of these compounds in an electrophilic substitution reaction, nitration at position C(3).

Among the theoretical indices of the electronic structure of the isomeric azaindoles, the ionization potential, which characterizes the energy of the highest occupied orbital on the C(3) atom, correlates most closely with the rate parameters for the nitration process.

The nature of the junction of the five- and six-membered rings in 4- and 5-azaindoles remarkably has a directly opposite effect on the rate of acid-catalyzed deuterium exchange at position 3 as it does on the rate of nitration in sulfuric acid at the same position.

EXPERIMENTAL

The methods of synthesis, purification, physical constants, and elemental analyses of the azaindole derivatives used in this work have been described earlier: 4-azaindole [8], 5-azaindole [6], 6-azaindole [9], 4-methyl-7-azaindole [10], 3-nitro-4-azaindole [6], 3-nitro-5-azaindole [6], 3-nitro-6-azaindole [11], and 3-nitro-4-methyl-7-azaindole [12]. We used 96% sulfuric acid (chemically pure grade), 99% nitric acid, and nitrogen (ultrapure grade) from a cylinder. Polarographic determinations were carried out on an RO-4 instrument (Radiometer, Denmark). The rate constants were calculated from the results of several runs (2-4).

Kinetic Measurements on the Nitration of Isomeric Azaindoles. The azaindole (≈ 0.007 g, accurately weighed) was added to a conical flask containing sulfuric acid (10 ml). Nitrogen was passed through. After dissolution of the azaindole the flask was immersed in a bath filled with chloroform, to which dry ice was added with stirring so that the temperature in the bath was maintained constant at $-10 \pm 1^\circ\text{C}$. After 20 min at this temperature fuming nitric acid (0.1 ml) was added to the flask with a micropipet and timing was started. The initial concentration of the azaindole was 0.006 mole/liter, of nitric acid 0.24 mole/liter. After 1, 2, 3, 5, 10, and 15 min, 0.5 ml of the reaction mixture was removed from the flask with a pipet and transferred to a weighed beaker containing distilled water (10 ml). The beaker with this sample of the reaction mixture was then weighed. Its contents were next diluted with distilled water on the basis that 1 g of the reaction mixture would be contained in 25 ml of water. The resulting solutions were transferred to a thermostated cell ($+25 \pm 1^\circ\text{C}$), nitrogen was passed through to remove dissolved oxygen, and the polarogram was recorded, starting from +0.2 V relative to the saturated calomel electrode.

The error of the determination at 0.95 reliability did not exceed 4%.

LITERATURE CITED

1. V. A. Azimov, D. M. Krasnokut-skaya, I. N. Palant, and L. N. Yakhontov, *Khim. Geterotsikl. Soedin.*, No. 3, 375 (1979).
2. R. E. Willette, *Adv. Heterocycl. Chem.*, **9**, 27 (1968).
3. L. N. Yakhontov, *Usp. Khim.*, **37**, 1258 (1968).
4. D. A. Bochvar, A. A. Bagatur'yants, A. B. Turkevich, L. N. Yakhontov, M. Ya. Uritskaya, D. M. Krasnokut-skaya, and M. V. Rubtsov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 354 (1966).
5. D. A. Bochvar and A. A. Bagatur'yants, *Teor. Eksp. Khim.*, No. 6, 793 (1967).
6. L. N. Yakhontov, V. A. Azimov, and E. I. Lapan, *Tetrahedron Lett.*, 1909 (1969).
7. A. El-Anani, S. Clementi, A. R. Katritzky, and L. N. Yakhontov, *J. Chem. Soc., Perkin Trans. II*, No. 7, 1072 (1973).
8. V. A. Azimov and L. N. Yakhontov, *Khim. Geterotsikl. Soedin.*, No. 10, 1425 (1977).
9. A. A. Prokopov and L. N. Yakhontov, *Khim. Geterotsikl. Soedin.*, No. 8, 1135 (1977).
10. L. N. Yakhontov, M. Ya. Uritskaya, and M. V. Rubtsov, *Zh. Obshch. Khim.*, **34**, 1449 (1964).
11. A. A. Prokopov and L. N. Yakhontov, *Khim. Geterotsikl. Soedin.*, No. 4, 496 (1978).
12. L. N. Yakhontov, M. Ya. Uritskaya, and M. V. Rubtsov, *Zh. Org. Khim.*, **1**, 2032 (1965).

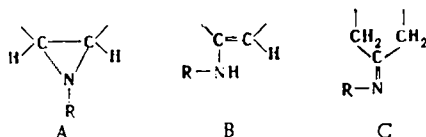
SYNTHESIS AND REACTIONS OF AZIDOPOLYBROMOPYRIDINES

S. D. Moshchitskii, A. A. Zeikan',
A. F. Pavlenko, and V. P. Kukhar'

UDC 547.822.5

Azido derivatives of organic compounds are interesting and highly reactive reagents. Recently the chemistry of aromatic azides, and particularly that of azidotetrafluoro(chloro)-pyridines, has been intensively studied [1-3]. Seeking to synthesize 4-azido-2,3,5,6-tetrabromopyridine (I), we have examined the reaction of pentabromopyridine with sodium azide in DMSO. We found that at 20°C the attack of azide ion is directed exclusively at position 4 and compound (I) is formed quantitatively. We verified the absence of the isomeric product by TLC and established the position of substitution of the bromine atom by independent synthesis of azide (I) by substitution of azido for the methylsulfonyl group in 4-methylsulfonyl-2,3,5,6-tetrabromopyridine. Reaction of pentabromopyridine with excess sodium azide at 20°C forms 2,4,6-triazido-3,5-dibromopyridine (II). Azides (I) and (II) are stable in the dark at room temperature, melt without exploding or decomposing, and decompose at 150-155°C with evolution of nitrogen.

Thermal decomposition of aromatic azides is known to generate nitrenes, which are capable either of conversion to primary amines or of insertion into the C-H bond of hydrocarbons. Consequently we subjected azide (I) to thermolysis in N,N-dimethylaniline at a temperature close to its decomposition point. Analysis by gas-liquid chromatography (GLC) identified the major thermolysis product as 4-amino-2,3,5,6-tetrabromopyridine (III). When heated in excess cyclohexene, azide (I) gave an oily product with the formula $C_{11}H_{10}Br_4N_2$, which could have three possible structures:



R = 2,3,5,6-tetrabromo-4-pyridyl

The IR and PMR parameters unequivocally support structure B, i.e., 4-(1-cyclohexenyl)amino-2,3,5,6-tetrabromopyridine (IV). After several hours enamine (IV) crystallized and the IR and PMR spectra of the crystalline product now lacked the band and signal of the NH group, which had been replaced by a band and signals typical of structure C, implying the isomerization of enamine (IV) to 4-cyclohexylideneamino-2,3,5,6-tetrabromopyridine (V). Since the

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660.
Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 11, pp. 1492-1495, November, 1979. Original article submitted July 17, 1978; revision submitted January 16, 1979.