9. V. G. Koshechko, E. P. Platonova, V. Yu. Atamanyuk, and V. D. Pokhodenko, Elektrokhimiya, 16, 620 (1980).
10. H. Gilmann and J. J. Dietrich, J. Am. Chem. Soc., 79, 6178 (1957).
11. S. Hünig, H. Quarst, W. Brenninger, and E. Schmitt, Chem. Ber., 102, 2874 (1969).
12. W. Michler and H. Pattinson, Chem. Ber., 17, 115 (1884).
13. A. Weissberger, A. Proskauer, D. Riddick, and A. Toops, Organic Solvents [Russian translation], Inostr. Lit., Moscow (1958), pp. 283, 345, 419.

ELECTROPHILIC SUBSTITUTION AND ELECTRONIC STRUCTURE OF INDOLO[2,3-b]QUINOXALINE

V. T. Grachev, S. P. Ivashchenko,
O. A. Ivanova, B. G. Gerasimov,
A. Ts. Sarkisyan, A. D. Vasil'eva,
V. N. Lisyutenko, A. V. Ivashchenko,
and T. A. Mikhailova

UDC 547.863.1'866'752:542.944.2:543.87

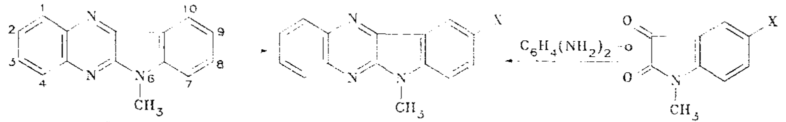
The nitration and bromination of 6-methylindolo[2,3-b]quinoxaline take place in the 9 position. The reactivity indexes were calculated within the framework of the Hückel MO and CNDO (complete neglect of differential overlap) methods. Only the π-charge distribution is in satisfactory agreement with the experimental data on electrophilic substitution in the investigated compound.

Indolo[2,3-b]quinoxalines and their analogs are attracting considerable attention [1]. In the present research we investigated the reactivity of 6-methylindolo[2,3-b]quinoxaline (I) in electrophilic substitution reactions.

In the theoretical investigation of the reactivity of I within the framework of the Hückel MO and CNDO (complete neglect of differential overlap) methods we used the following reactivity indexes [2]: the localization energy (L_r), the superdelocalizability (S_r), the boundary electron density (f_r), the distribution of the π-electron charge [$Q_r(\pi)$], and the total electron charge [$Q_r(\pi + \sigma)$] with allowance for the π and σ electrons.

It follows from an examination of the $Q_r(\pi)$ values of I (Table 1) that the aromatic ring of the indole fragment (the 7 and 9 positions) should be the most reactive, whereas, on the other hand, from the L_r, S_r, and f_r values it follows that the aromatic ring of the quinoxaline fragment (the 1 and 4 positions) should be most reactive.

We carried out two electrophilic substitution reactions (nitration and bromination) for I and found that they lead to 9-nitro- (IV) and 9-bromo-6-methylindolo[2,3-b]quinoxaline (V). The structures of IV and V were confirmed by alternative synthesis, IR and PMR spectroscopy, and mass spectrometry.



I IV,V VI,VII

IV,VI X=NO$_2$; V,VII X=Br

Thus of the calculated reactivity indexes for I, only the $Q_r(\pi)$ values are in satisfactory agreement with the experimental data on the direction of electrophilic substitution. Let us note that the formation as a result of the nitration and bromination of I of 9-nitro (IV) and 9-bromo (V) derivatives rather than 7-substituted 6-methylindolo[2,3-b]-quinoxalines, as follows from the calculated $Q_r(\pi)$ values [$Q_{(7)}(\pi) = -0.027$ and $Q_{(9)}(\pi) = -0.021$], can evidently be explained by the steric effect of the methyl substituent in I.

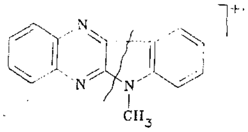
Scientific-Research Institute of Organic Intermediates and Dyes, Moscow 103787. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 840-842, June, 1984. Original article submitted January 13, 1983; revision submitted September 13, 1983.

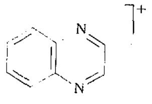
TABLE 1. Reactivity Indexes for 6H-Indolo[2,3-b]quinoxaline

Position	L_r (HMO)	S_r (HMO)	f_r (HMO)	f_r (CNDO)	$Q_r(\pi)$ (HMO)	Q_r (π) (CNDO)	Q_r ($\pi+\sigma$) (CNDO)
1	2,317	0,972	0,191	0,394	−0,002	+0,006	−0,009
2	2,517	0,862	0,063	0,334	+0,004	−0,004	−0,035
3	2,505	0,849	0,070	0,157	+0,010	−0,019	−0,022
4	2,309	0,983	0,187	0,431	−0,008	−0,019	−0,025
7	2,354	0,914	0,004	0,177	−0,027	−0,027	−0,012
8	2,511	0,846	0,025	0,154	+0,005	+0,013	−0,046
9	2,455	0,898	0,028	0,074	−0,021	−0,020	−0,009
10	2,468	0,866	0,002	0,211	+0,007	−0,005	−0,034

Let us now turn to the experimental proof for nitration and bromination in the 9 position of I.

Cleavage of the C–N and C–C bonds with the formation of a fragment with m/z 129, which is accompanied by migration of hydrogen from the indole fragment, is observed in the mass spectrum of I.





129

The formation of this intense fragment ion (m/z 129), which constitutes evidence that nitration and bromination take place in the indole fragment of I rather than in the quinoxaline fragment, is also observed in the mass spectra of IV and V.

In the PMR spectra, the aromatic protons of the indole and quinoxaline fragments of I give signals corresponding to two four-spin ABCD systems. For one of these groups of signals the constant of spin–spin coupling between the ortho protons is 7.5–8.0 Hz, as compared with 5.5–6.0 Hz for the other. This makes it possible to reliably assign the signals. The signal at weakest field at ~8.21 ppm is related to the 10-H proton. The signals of the 7-H proton are found at strongest field at ~7.25 ppm. Signals with an overall integral intensity corresponding to two protons are observed at 7.9–8.1 ppm; these signals can be separated into two groups with the largest spin–spin coupling constants (SSCC), viz., 5.5–6.0 Hz and 7.5–8.0 Hz. They are related to the 1-H and 8-H protons. The signals of the 9-H proton (~7.40 ppm) can be isolated by means of $J_{9,10}$ = 7–8 Hz. The 2-H, 3-H, and 4-H protons resonate at 7.4–7.7 ppm in the form of complex signals that are superimposed on one another and are partially overlapped with the signals of the 8-H proton. The methyl protons give a narrow singlet at 3.80 ppm.

In the PMR spectrum of IV the signals of the 10-H proton show up in the form of a doublet of doublets with SSCC of 2.5 Hz and 0.5–1.0 Hz, and signals of a 9-H proton are absent. Consequently, replacement of the hydrogen atom in the 9 position occurs in the case of nitration.

The PMR spectrum of V shows that the bromine atom also replaces the hydrogen atom in the 9 position. In fact, in the spectrum of this compound the signals of the 10-H proton show up at 8.48 ppm in the form of a doublet of doublets with meta and para SSCC of 2.0 Hz and 1.0 Hz, and signals of a 9-H proton are absent.

Compounds IV and V obtained by alternative synthesis [3, 4] have identical spectral characteristics, and no melting-point depressions were observed for mixtures of the appropriate samples.

EXPERIMENTAL

The IR spectra of solutions of the compounds in carbon tetrachloride [$2 \cdot 10^{-4}$ to 10^{-1} mole/liter] at layer thicknesses ranging from 0.4 to 5 cm were recorded at 35°C with a UR-20 spectrometer. As compared with the IR spectrum of I, absorption bands at 1520, 1289, 860, and 610 cm^{-1}, which, with respect to their positions and intensities, correspond to stretching vibrations of a nitro group (1520 and 1289 cm^{-1}) [5], vibrations of a $C-NO_2$ bond (860 cm^{-1}) [5, 6], and deformation vibrations of a C–NO group (610 cm^{-1}) [5], appear in the IR spectrum of IV. The mass spectra were measured with a Varian MAT CH-6 spectrometer with direct introduction of the samples into the ion source at an accelerating voltage of 1.75 kV, a cathode emission current of 100 μA, and an ionizing-electron energy of 70 eV. The PMR spectra of I (in deuterated methanol) and IV and V (in deuterated DMF) were recorded with a WR-80 spectrometer; the chemical shifts were determined relative to tetramethylsilane.

The calculation of the L_r, S_r, f_r and $Q_r(\pi)$ reactivity indexes within the framework of the Hückel MO method was carried out with the following coulombic (h_r) and resonance (k_{rs}) parameters: $h_{\dot{N}} = 0.4$, $h_{\ddot{N}} = 2.0$, $k_{C \overset{---}{-} C} = k_{C \overset{---}{=} N} = 1.0$, and $k_{C-C} = k_{C-N} = 0.7$.

The calculation of the compounds within the CNDO/S approximation was carried out from the program in [7] with the parametrization in [8] and allowance for 21-fold excited electron configurations. It was assumed that the molecules are planar, and the geometries reported in [9, 10], respectively, were used for the quinoxaline and indole fragments.

The course of the reaction and the purity of the products were monitored by TLC on Silufol UV-254 plates with chloroform–acetone (4:1) as the eluent.

9-Nitro-6-methylindolo[2,3-b]quinoxaline (IV). A) A 0.43-g (4.3 mmole) sample of potassium nitrate was added in portions with stirring at 0°C to a solution of 1 g (4.3 mmole) of I [11] in 40 ml of 96% sulfuric acid at such a rate that the temperature did not exceed 5°C, after which the mixture was maintained at room temperature for 1 h and poured into water. The aqueous mixture was neutralized with 20% aqueous KOH solution, and the precipitate was removed by filtration, washed with water until the wash water was neutral, and dried at 60°C to give 0.9 g (76%) of a product with mp 296.5-297.5°C. Crystallization from DMF gave a product with mp 299.0-299.5°C. Found: C 64.7; H 3.6; N 20.0%. $C_{15}H_{10}N_4O_2$. Calculated: C 64.8; H 3.6; N 20.1%.

B) A hot solution of 1.05 g of o-phenylenediamine in 10 ml of glacial acetic acid was added to a hot solution of 2 g (9.7 mmole) of VI in 55 ml of glacial acetic acid, and the mixture was refluxed for 1 h. The precipitate was removed by filtration and dried to give 1.29 g (48%) of a product with mp 299.0-299.5°C (from DMF).

9-Bromo-6-methylindolo[2,3-b]quinoxaline (V). A) A 1.5-g (9.4 mmole) sample of bromine was added gradually at 60°C to a solution of 1.68 g (7.2 mmole) of I in 25 ml of chloroform, and the mixture was stirred until the color of the solution changed from dark red to yellow. The solution was cooled, and the precipitate was removed by filtration, dried, and crystallized from benzene to give 1.17 g (52%) of a product with mp 187-188°C. Found: C 57.5; H 3.2; N 13.4%. $C_{15}H_{10}BrN_3$. Calculated: C 57.7; H 3.2; N 13.5%.

B) A solution of 1.4 g (5.8 mmole) of VII in 40 ml of glacial acetic acid was added to a hot solution of 0.63 g of o-phenylenediamine in 10 ml of glacial acetic acid, and the solution was refluxed for 3 h. It was then cooled to room temperature and poured into water, and the precipitate was removed by filtration, dried, and crystallized from DMF to give 0.93 g (51%) of a product with mp 185.5-186.5°C. Crystallization from benzene gave a product with mp 187-188°C.

LITERATURE CITED

1. A. V. Ivashchenko and V. M. Dziomko, Usp. Khim., 46, 244 (1977).
2. A. R. Katritzky (editor), Physical Methods in the Chemistry of Heterocyclic Compounds, Academic Press (1963).
3. W. Borsche and N. Jacobs, Chem. Ber., 47, 354 (1914).
4. H. O. Calvery, C. R. Noller, and R. Adams, J. Am. Chem. Soc., 47, 3059 (1925).
5. R. Silverstein, G. Bassler, and T. Morrill, Spectroscopic Identification of Organic Compounds, Wiley (1974).
6. K. Nakanishi, Infrared Spectra and Structure of Organic Compounds [Russian translation], Mir, Moscow (1965), p. 61.
7. R. L. Ellis, G. Kuehnlenz, and H. H. Jaffe, Theor. Chim. Acta, 26, 131 (1972).
8. V. M. Ryaboi and I. N. Fundlyer, Algoritmy Programmy, No. 3, P 001396, 48 (1975).
9. M. M. Kaganskii, G. G. Dvoryantseva, I. V. Sokolova, and V. I. Danilov, Khim. Geterotsikl. Soedin., No. 1, 118 (1975).
10. E. M. Evleth, Theor. Chim. Acta, 16, 22 (1970).
11. G. M. Badger and P. Nelson, J. Chem. Soc., No. 10, 3930 (1962).