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LETTERS TO THE EDITOR

Indole-Containing Bromonitroethylphosphonates

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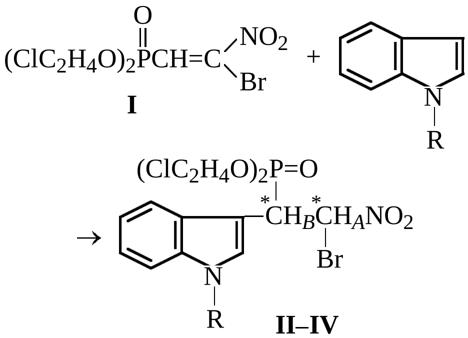
It is known that the indole system is a structural constituent of many biologically important natural compounds (tryptophan, heteroauxin, serotonin, etc.) and synthetic drugs (Mexamine, Indopan, Indomethacin, etc.) [1–3]. *gem*-Halonitroethenylphosphonates [4–6], the representatives of highly electrophilic functionalized nitroethenes [7, 8], may be used as convenient precursors for constructing practically valuable phosphorylated organic compounds, including those containing the indole ring.

We have found that bis(2-chloroethyl) 2-bromo-2-nitroethenylphosphonate **I** reacts with indole and its *N*-alkyl-substituted derivatives under very mild conditions, and the process as a whole is convenient for preparative synthesis.



R = H (**II**), CH_3 (**III**), C_2H_5 (**IV**).

Reactions proceed in carbon tetrachloride at 16–18°C in the absence of catalyst at 1 : 1 reactant ratio, yielding bis(2-chloroethyl)-1-(indol-3-yl)-2-bromo-2-nitroethylphosphonates **II**–**IV** isolated as mixtures of *erythro* and *treo* diastereomers in high yields.

The structure of compounds **II**–**IV** was determined by IR and ^{1}H and ^{31}P NMR spectroscopy, and their composition was confirmed by elemental analysis. For compound **III** the mass spectrum was also recorded. It contained a peak of the corresponding molecular ion.

The IR spectra of indolylbromonitroethenylphosphonates **II**–**IV** contain the bands of phosphoryl (1250–1280, 1030–1080 cm^{-1}) and nonconjugated nitro (1570–1575 and 1350–1355 cm^{-1}) groups. In the spectrum of **II** the absorption band of the NH group of the indole ring is characterized by the band at 3400 cm^{-1}. The ^{1}H NMR spectra of **II**–**IV** in $CDCl_3$ show the doubled set of signals, suggesting that the compounds exist as mixtures of diastereomers. For example, the spectrum of **III** contains the singlets of methyl protons at δ 3.73 and 3.82 ppm, and the methine protons are characterized by the doublets of doublets at δ 6.47 and 6.52 ppm (H_A), 4.57 and 4.51 ppm (H_B) with the coupling constants J_{AB} 9.5 and 8.1 Hz, J_{BP} 22 and 22.7 Hz, and J_{AP} 6.6 and 6.0 Hz. The multiplet at 7.15–7.73 ppm refers to the protons of the indole ring, and the protons of chloroethoxy group give the signals at 4.35 and 4.41 ppm (OCH_2); 3.72 and 3.75 ppm (CH_2Cl). The ^{31}P NMR spectra of indolylnitroethylphosphonates **II**–**IV** are characterized by the presence of two signals at 19.4–19.6 and 20.3–20.5 ppm.

The obtained compounds **II**–**IV** may be regarded as indole-containing bromonitro precursors of 2-aminoethylphosphonic acid which widely occurs in the nature and exhibits a high biological activity [9].

gem-Bromonitroethenylphosphonate **I** was prepaped according to the procedure in [10].

Bis(2-chloroethyl)-1-(indol-3-yl)-2-bromo-2-nitroethylphosphonate (II). *gem*-Bromonitroethenylphosphonate **I** (0.69 g) and indole (0.23 g) were dissolved in 10 ml of carbon tetrachloride, and the reaction mixture was kept at room temperature for a day. The solvent was evaporated to dryness on a rotary evaporator, and the residue was dissolved in benzene and chromatographed on silica gel, elution with chloroform and ether. From the chloroform–ether fraction 0.54 g (59%) of **II** was isolated as a mixture of two diastereomers with R_f 0.2 and 0.26. Found, %: C 35.17, 35.18; H 3.69, 3.71; N 5.78, 5.79; P 6.17, 6.25. $C_{14}H_{16}BrCl_2N_2O_5P$. Calculated, %: C 35.40; H 3.37; N 5.90; P 6.30.

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Compounds **III** and **IV** were prepared similarly.

Bis(2-chloroethyl)-1-(*N*-methylindol-3-yl)-2-bromo-2-nitroethylphosphonate (III). Yield 94%, R_f 0.31 and 0.38. Found, %: C 36.78, 36.81; H 3.95, 3.98; N 6.00, 5.99; P 6.64, 6.61. $C_{15}H_{18}BrCl_2N_2O_5P$. Calculated, %: C 37.00; H 3.70; N 5.70; P 6.20. Mass spectrum: m/z 490, 488, 486 (M^+). M_{calc} 488.

Bis(2-chloroethyl)-1-(*N*-ethylindol-3-yl)-2-bromo-2-nitroethylphosphonate (IV). Yield 87%, R_f 0.35 and 0.32. Found, %: C 38.22, 38.21; H 4.00, 4.02; N 5.60, 5.80; P 6.17, 6.19. $C_{16}H_{20}BrCl_2N_2O_5P$. Calculated, %: C 38.30; H 4.00; N 5.60; P 6.00.

The IR spectra were recorded on a Specord IR-75 spectrometer in chloroform in the frequency ranges of NaCl and LiF prisms. The ^1H and ^{31}P NMR spectra were measured on a Bruker AC-200 (200 MHz) spectrometer in $CDCl_3$; phosphoric acid (85%) was used as an external ^{31}P reference. The mass spectrum was taken on an MKh-1321 spectrometer (ionizing voltage 70 V, temperature of ionization chamber 150°C).

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