SYNTHESIS AND REACTIONS OF 1-(2-PYRIDYL)-3-METHYL-4-CHLORO-5-FORMYL-6,7-DIHYDROINDAZOLES

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The Vilsmeier formylation of 1-(2-pyridyl)-3-methyl-4-oxo-4,5,6,7-tetrahydroindazole and its 6-phenyl derivative gives 1-(2-pyridyl)-3-methyl-4-chloro-5-formyl-6,7-di hydroindazoles. Reactions of these derivatives with different N- and C-nucleophilic agents, including bisnucleophiles, were studied as a means of obtaining new 4- and 5-functional derivatives of indazole and its condensed systems.

In the development of work on the modification of the carbocyclic part of 1-(2-pyridyl)-4,5,6,7-tetrahydroindazoles [1, 2], the formylation of 1-(2-pyridyl)-3-methyl-4-oxo-4,5,6,7-tetrahydroindazole (IIIa) and its 6-phenyl derivative (IIIb) was carried out.

Using the examples of 1-phenyl-4-oxo-4,5,6,7-tetrahydrobenzazoles [3-5], the dependence of the structure of the formylation products on the character of substitution at the C(6) atom was found previously, whereby the 6,6-disubstituted derivatives form 4-oxo-5-chloromethylene derivatives, and the 6-unsubstituted and 6-monosubstituted derivatives form 4-chloro-5-formyl-6,7-di hydrobenzazoles. The last are more reactive [6-9], and therefore we subjected just the indazoles (IIIa, b) to formylation. The indazoles (IIIa, b) were synthesized by the reactions of 2-acetyl-1,3-cyclohexanedione (Ia) and 2-acetyl-5-phenyl-1,3-cyclohexanedione (Ib) with 2-hydrazinopyridine (II). Formylation of the indazoles (IIIa, b) by the method of [3] leads to 1-(2-pyridyl)-3-methyl-4-chloro-5-formyl-6,7-di hydroindazoles with the yield of 85% for (IVa) and 65% for (IVb). The frequency of the carbonyl group in the IR spectra of these β-chlorovinylaldehydes (the IR and PMR spectral data are presented in Table 1) is observed at 1660-1654 cm⁻¹, and the signal of the proton of the aldehyde function is characterized by the chemical shift of 10.18-10.20 ppm in the PMR spectra.


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The boiling of the dihydroindazole (IVA) in the aqueous-ethanolic solution of sodium hydroxide results in its hydrolysis to the ketoaldehyde, for which three tautomeric forms (VA-C) are allowable. In the IR spectrum of compound (V) above 1600 cm\(^{-1}\), only one absorption maximum is found at 1648 cm\(^{-1}\), which excludes the structure (VB). The choice in favor of (VC) was made on the basis of the PMR spectrum in which the doublet signal of the methylene proton is observed at 7.27 ppm, and the doublet signal of the hydroxyl proton involved in the intramolecular hydrogen bond is observed at 13.81 ppm. The reaction of the \(\beta\)-chlorovinylaldehydes (IVA) with a series of N- and C-nucleophiles was investigated. The corresponding 5-hydrazone methyl derivatives (VI)-(X) were obtained in the reactions with phenyl- and 2-pyridylhydrazines, and hydrazides of isonicotinic acid, salicylic acid, and p-toluene sulfonic acid.

Reaction of the \(\beta\)-chlorovinylaldehyde (IVA) with hydrazine hydrate using the reagent molar ratio of both 2:1 and 1:1 only leads to the formation of the azine (XII), and the boiling in ethanol with hydrazine hydrochloride in the presence of potassium carbonate leads to 6-(2-pyridyl)-8-methyl-4,5-dihydro-1H-indazolo[4,5-c]pyrazole (XII).

Reaction of the chlorovinylaldehyde (IVA) with o-phenylenediamine leads to 1-methyl-3-(2-pyridyl)-4,5-dihydro-7H-benzo[b]indazolo[4,5-e][1,4]diazepine hydrochloride (XIII), in the PMR spectrum of which the signals of the protons of the NH groups are observed at 9.09 and 10.09 ppm.

Reactions of the chlorovinylaldehyde (IVA) with ethyl cyanoacetate and cyanacetamide, as well as malonodinitrile, were performed in the presence of triethylamine. The structure of the resulting 4-chloro-5-ethenyl-6,7-dihydroindazoles (XIV)-(XVI) was confirmed by the combination of IR and PMR spectral data. Thus, the ester carbonyl of compound (XIV) is characterized by the frequency 1726 cm\(^{-1}\), and the amide carbonyl of (XV) is characterized at 1698 cm\(^{-1}\). The vibration frequencies of the nitrile groups of compounds (XIV)-(XVI) are observed in the range of 2220-2208 cm\(^{-1}\), and the chemical shift of the proton at the C(1) atom of the ethenyl group is observed at 8.27-8.56 ppm.

The reaction of (IVA) with potassium thiocyanate leads to the 4-thiocyanato-5-formyl derivative (XVII), the structure of which was confirmed by spectral data (\(\nu_{\text{SCN}} \) 2160 cm\(^{-1}\); \(\delta_{\text{CHO}} \) 10.38 ppm).

**EXPERIMENTAL**

The IR spectra were taken on the Specord-75 IR spectrometer using suspensions of substances in mineral oil (1800-1500 cm\(^{-1}\)) and hexachlorobutadiene (3600-2000 cm\(^{-1}\)). The vibration frequencies of the C–H bonds in the region of 3050-2800 cm\(^{-1}\) were not indicated. The PMR spectra were taken in CDCl\(_3\) and DMSO-D\(_6\) on the Bruker WH-90/DS spectrometer (90 MHz) with the internal standard TMS.