Synthesis of 1-phenylindoles derivatives

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Abstract

The growing needs of medicine and pharmacology induce synthetic organic chemistry to constantly be in the process of modernizing existing methods of synthesis and developing new ones.

Since ancient times, the high physiological activity of indole derivatives has been widely known. Indole is a heterocyclic condensed aromatic compound that is part of the molecules of a multitude of compounds with biochemical and physiological value. A large number of drugs of the indole group obtained synthetically are derivatives of arylindols.

One of the most common methods of obtaining arylindoles is the use of Ulman reaction conditions. However, this technique involves the use of high temperatures and a large amount of aryl halide to obtain optimal yields. Some classical methods suggest the use of palladium compounds as a catalyst, which are highly prices and require inert conditions, which limits their uses in the syntheses and reduces the overall synthetic attraction.

In order to mitigate the conditions of the Ulman reaction and increase the reaction yields, methods have been proposed for the synthesis of 1-phenylindole derivatives based on the introduction of phenyldiodide by arylating the nitrogen atom in position 1 of the 5-methoxyindole indole ring in the presence of monovalent copper chloride using phenanthroline and anthracene as ligands, followed by heteroarylation the compounds obtained quinoline and isoquinoline in the presence of benzoyl chloride and 2-bromo-3-methylbutanoyl chloride.

The physical and chemical characteristics of the compounds obtained were determined. Installed using ¹H NMR spectroscopy and elemental analysis of the structure of the obtained derivatives are in good agreement with the proposed structural formulas.

According to a review of literature data, the obtained structures can be supposedly used to research their physiological activity.

References

- [1] R.J. Sundberg. The chemistry of Indoles. *N.Y.: Academic Press.* **1970.** 489p.
- [2] G.I. Zhungietu. Preparative Indole Chemistry. *Kishinev: Shtiintsa.* **1975.** 262p.
- [3] G.I. Zhungietu, M.A. Rechter. Isatin and its derivatives. *Kishinev: Shtiintsa.* **1977.** 288p.
- [4] J. Joule, K. Mills. Chemistry of heterocyclic compounds. *Moscow: Mir.* **2004.** 728p. (russian)
- [5] R. Elderfield. Heterocyclic compounds. *Moscow: Foreign Literature.* **1954.** 359p. (russian)
- [6] N.P. Maxutina Herbal medicines. *Kiev: Zdorovie.* **1985.** 280p.
- [7] M.D. Mashkovsky. USSR State Pharmacopoeia. *Moscow: Medicine.* **1968.** 1086p. (russian)
- [8] M.D. Mashkovsky. Medicines. *Moscow: Medicine.* **2001.** 1216p. (russian)
- [9] A.D. Turova. Medicinal plants of USSR and their application. *Moscow: Medicine.* **1974.** 289p. (russian)
- [10] S.I. Sokolov. Handbook of medicinal plants. Phytotherapy. *Moscow: Medicine.* **1988.** 464p. (russian)
- [11] E.S. Selezneva, and Z.P. Belousova. Concerning the study of genotoxicity effect of indole derivatives on *Allium cepa*. *Butlerov Communications.* **2016.** Vol.47. No.7. P.21-25. DOI: 10.37952/ROI-jbc-01/16-47-7-21
- [12] I.V. Mikhura, A.A. Formanovsky, M.M. Rumyantseva, and G.A. Borisova. *N*-Ethylamide 3-indolcarboxylic acid derivatives. *Butlerov Communications.* **2016.** Vol.46. No.6. P.71-73. DOI: 10.37952/ROI-jbc-01/16-46-6-71
- [13] A.V. Syromolotov, A.A. Kimyashov, and D.R. Khafizova. Synthesis of *N*-substituted 1-piperazinoalkylindoles. *Butlerov Communications.* **2018.** Vol.54. No.4. P.94-98. DOI: 10.37952/ROI-jbc-01/18-54-4-94

- [14] J.C. Antilla, A. Klapars, S.L. Buchwald. The Copper-Catalyzed *N*-Arylation of Indoles. *JACS*. **2002**. Vol.124. No.39.P.11684-11688. DOI: 10.1021/ja027433h
- [15] E.V. Larina, A.A. Kurokhtina, E.V. Yarosh. Operando study of the coupling reactions using ligand-free palladium catalysts. *Bulletin of the Buryat State University. Chemistry. Physics*. **2016**. No.5. P.26-36. DOI:10.18101/2306-2363-2016-4-26-36
- [16] K.V. Vatsiro, G.L. Mishchenko. Nominal reactions in organic chemistry. *Moscow: Mir*. **1976**. 528p. (russian)
- [17] V.Yu. Gorokhov, and L.P. Unicov. Xanthynilation of arylamines: synthesis and structure of new reaction products. *Butlerov Communications*. **2015**. Vol.43. No.7. P.154-160. DOI: 10.37952/ROI-jbc-01/15-43-7-154