

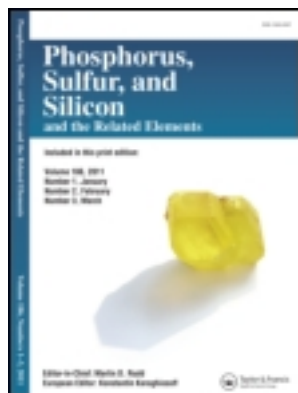
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Phosphoryl Substituted 3,5-Bis(Arylidene)-4-Piperidones Possessing High Antitumor Activity

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Phosphoryl Substituted 3,5-Bis(Arylidene)-4-Piperidones Possessing High Antitumor Activity

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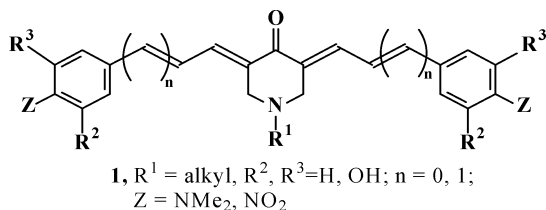
Keywords N-(phosphoryl)-3,5-bis(arylidene)-4-piperidones; N-(phosphorylalkyl)-3,5-bis(arylidene)-4-piperidones; alkylation; phosphorylation; cytotoxicity

3,5-Bis(arylidene)-4-piperidones and related compounds **1** possess anti-cancer and antioxidant activity (Scheme 1).^{1,2} Some of these compounds are also fluorescent, which makes possible to use them as dyes for tracing their cellular pathways during chemotherapy and as agents for photodynamic therapy.³ The important way to regulate the bioavailability and drug delivery of these compounds to target organs is an introduction of different substitutes R¹ to the N-atom of a piperidone moiety. Phosphorus-containing groups are prospective as such modifiers and may contribute to the biological activity. Therefore, we investigated synthetic approaches to phosphorylated arylidenepiperidones and “structure-activity-fluorescence properties” relationship in this series.

Direct phosphorylation of NH-precursor **2** by phosphorus(IV) acid chlorides afforded N-phosphorylated compounds **3**. Derivatives **4** with elongated alkylene-phosphoryl linker could be synthesized only by condensation of aldehydes with phosphorylated N-alkylpiperidones as

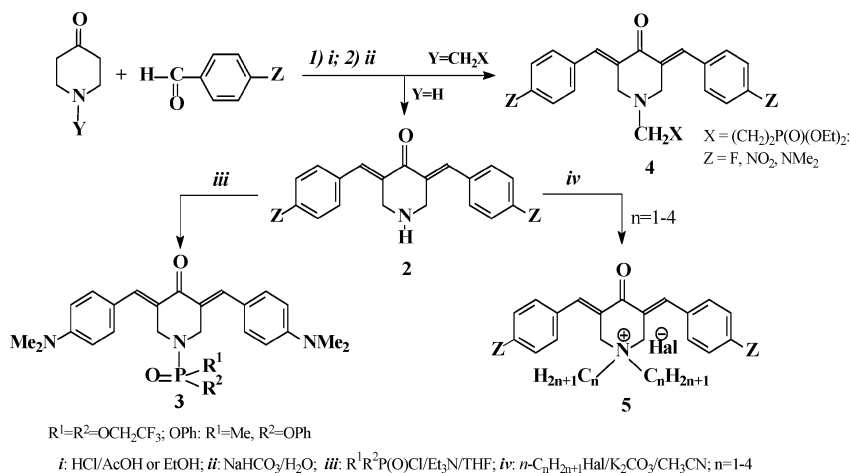
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SCHEME 1

alkylation of the NH-precursor **2** with alkyl halides surprisingly resulted in quaternary salts **5** as the only reaction products (Scheme 2).



SCHEME 2

Compounds **3–5** demonstrate high antitumor activity against a number of human cancer cell lines with IC₅₀ values in the range of 0.3–50·10^{−6} M including resistant lung carcinoma cell line A549 (compounds **5**).

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