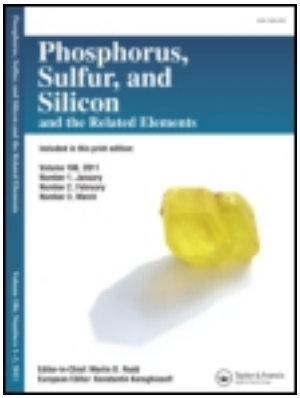


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

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

I. L. Odinets [a], M. V. Makarov [a], O. I. Artyushin [a], E. Yu. Rybalkina [b], K. A. Lyssenko [a], T. V. Timofeeva [c] & M. Yu. Antipin [a]

[a] A.N.Nesmeyanov Institute of Organoelement Compounds RAS, Moscow, Russia

[b] Institute of Carcinogenesis, Blokhin Cancer Research Center, RAMS, Moscow, Russia

[c] New Mexico Highlands University, Las Vegas, NM, USA

Available online: 20 Jun 2008

To cite this article: I. L. Odinets, M. V. Makarov, O. I. Artyushin, E. Yu. Rybalkina, K. A. Lyssenko, T. V. Timofeeva & M. Yu. Antipin (2008): Phosphoryl Substituted 3,5-Bis(Arylidene)-4-Piperidones Posessing High Antitumor Activity, Phosphorus, Sulfur, and Silicon and the Related Elements, 183:2-3, 619-620

To link to this article: http://dx.doi.org/10.1080/10426500701793246

Phosphorus, Sulfur, and Silicon, 183:619–620, 2008

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701793246

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

I. L. Odinets,[1] M. V. Makarov,[1] O. I. Artyushin,[1] E. Yu. Rybalkina,[2] K. A. Lyssenko,[1] T. V. Timofeeva,[3] and M. Yu. Antipin[1]

[1]A.N.Nesmeyanov Institute of Organoelement Compounds RAS, Moscow, Russia
[2]Institute of Carcinogenesis, Blokhin Cancer Research Center, RAMS, Moscow, Russia
[3]New Mexico Highlands University, Las Vegas, NM, USA

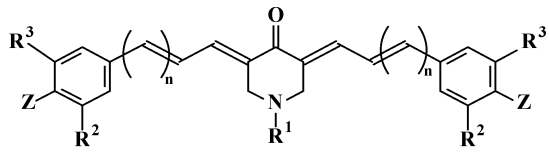
Keywords N-(phosphoryl)-3,5-bis(arylidene)-4-piperidones; N-(phosphorylalkyl)-3,5-bis(arylidene)-4-piperidones; alkylation; phosphorylation; cytotoxity

3,5-Bis(arylidene)-4-piperidones and related compounds **1** possess anticancer 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 R^1 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

We are thankful for our financial support from the Russian Basic Research Foundation (05-03-32692).

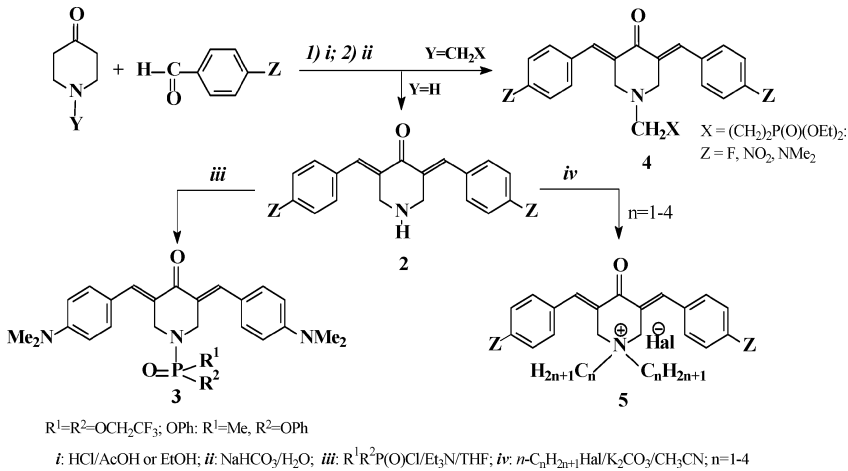
Address correspondence to I. L. Odinets, A. N. Nesmeyanov Institute of Organoelement Compounds RAS, Vavilova Str. 28, Moscow, 11991 Russia, E-mail: odinets@ineos.ac.ru



1, R^1 = alkyl, R^2, R^3=H, OH; n = 0, 1;
Z = NMe_2, NO_2

SCHEME 1

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



i: HCl/AcOH or EtOH; *ii*: $NaHCO_3/H_2O$; *iii*: $R^1R^2P(O)Cl/Et_3N/THF$; *iv*: *n*-$C_nH_{2n+1}Hal/K_2CO_3/CH_3CN$; n=1-4

SCHEME 2

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

REFERENCES

[1] J. R. Dimmock, A. Jha, G. A. Zello, J. W. Quail, E. O. Oloo, K. H. Nienaber, E. S. Kowalczyk, T. M. Allen, Ch. L. Santos, E. De Clercq, J. Balzarini, E. K. Manavathu, and J. P. Stables, *Eur. J. Med. Chem.*, **37,** 813 (2002).

[2] K. M. Yisef and M. A. El-Sherbeny, *Arch. Pharm. Chem. Life Sci.*, **338,** 181 (2005).

[3] V. N. Nesterov, T. V. Timofeeva, S. S Sarkisov, A. Leyderman, Ch. Y.-C. Leed, and M. Yu. Antipin, *Acta Cryst.*, C**59,** 605 (2003).