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1-Hydroxy-2-aryl(alkyl)-1*H*-naphto[2,3-*d*]imidasole-4,9-diones, their alkylation and tautomerism

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Abstract

Nitrogen-containing polycyclic quinoid compounds are of interest because some of them have various types of biological activity including antitumor activity. Particular attention is drawn to quinoid *N*-oxides, which are potential oxidizers and sources of nitric oxide. It is known that 1-*R*-4,9-dioxo-1*H*-naphtho[2,3-*d*]imidazole-4,9-diones and their oximation products, 1-*R*-4,9-dioxo-1*H*-naphtho[2,3-*d*][1,2,3]triazol-2-oxid-4-oximes, exhibit antitumor activity comparable with that of doxorubicin. In this regard, it is of interest to study other naphthoquinone derivatives that contain the *N*-oxide fragment. We have improved the method for the synthesis of 1-hydroxy-2-phenyl-1*H*-naphtho[2,3-*d*]imidazole-4,9-dione and increased its yield from 67% to 84%. Two-dimensional NMR spectroscopy has been used to refine the spectral parameters of phenyl-1*H*-naphtho[2,3-*d*]imidazole-4,9-dione. It has been shown that alkylation of this compound leads to the formation of 11-methoxy(ethoxy)-2-phenyl-1*H*-naphtho[2,3-*d*]imidazole-4,9-dione. We have analyzed the ^{1}H and ^{13}C NMR spectra of the synthesized alkylation products and electron absorption spectra of the studied initial compounds. Using the Gaussian-09 quantum chemical method DFT B3LYP/6-311++G(d,p), we have confirmed that 1-hydroxy-2-phenyl-1*H*-naphtho[2,3-*d*]imidazole-4,9-dione and 1-hydroxy-2-metyl-1*H*-naphtho[2,3-*d*]-imidazole-4,9-dione exists in two tautomeric forms, with the *N*-oxide form prevailing in dichloroethane.

References

[1] V.G. Granik, N.B. Grigoryev. Nitric oxide (NO). A new way to find drugs. *Moscow: High school book.* **2004**. P.180. (russian)
[2] T.M.B. Silva, N.T.V. Cerqueira, S.W.D. Silva. Theoretical Evaluation and Classifications of Potential Antimalarial Phenazine Compounds. *Lett. in Organic Chemistry.* **2011**. Vol.8. No.10. P.752-762.
[3] K. Kobayashi, N. Oda, J. Sakakibara. *Yakugaku Zasshi*. **1983**. Vol.103. P.165-172.
[4] L.M. Gornostaev, E.V. Arnold, D.S. Rudenko, Yu.G. Khalyavina, V.V. Chernyshev, O.A. Tyablikov, S.F. Dunaev, and G.A. Stashina. Synthesis of 5-hydroxy-10-*R*-benzo[*a*]phenazine-12-oxides by cyclization of 2-arylamino-1,4-naphthoquinone-1-oximes under the action of nitrating mixture. *Butlerov Communications.* **2020**. Vol.61. No.2. P.12-22. DOI: 10.37952/ROI-jbc-01/20-61-2-12
[5] L.M. Gornostaev, L.V. Dolgushina, Yu.G. Khalyavina, G.A. Stashina, S.I. Firgang. Transformation of 2-alkylamino-1,4-naphthoquinones into 2-alkylnaphtho[2,1-d][1,3]oxazole-4,5-dione 4-oximes by the action of nitrosylsulfuric acid. *Russ. Chem. Bull.*, Int. Ed. **2011**. Vol.60. No.1. P.157-159.
[6] *Pat. no. 2545091 RF.* 1-R-4,9-dioxo-1H-naphtho[2,3-d][1,2,3]triazol-4-oxime-2-oxides and their derivatives with cytotoxic activity. A.A. Shtil, V.A. Glazunova, T.I. Lavrikova, Yu.G. Khalyavina, L.M. Gornostaev. Publ. 27.03.**2015**. Byul. No.9. (russian)
[7] L.M. Gornostaev, T.I. Lavrikova, Y.G. Khalyavina, A.S. Kuznetsova, V.B. Tsvetkov, A.A. Markova, D.N. Kaluzhny, A.V. Shunayev, M.V. Tsvetkova, V.A. Glazunova, A.A. Shtil, V.V. Chernyshev. The oxime derivatives of 1-r-1h-naphtho[2,3-d][1,2,3]triazole-4,9-dione 2-oxides: Synthesis and properties. *Anti-Cancer Agents in Medicinal Chemistry.* **2017**. Vol.17. No.13. P.1814-1823.
[8] *Pat. № WO2012/021409* Anthraquinone Analogs. C.-W. T. Chang. Utah state university. **2012**.
[9] S.O. Chua, M.J. Cook, A.R. Katritzky. The Tautomerism of Heteroaromatic Compounds with Five-membered Rings. Part X1I. The lmidazole 3-Oxide versus 3-Hydroxy[3*H*]imidazole Equilibrium. *J. Chem. Soc.* B. **1971**. P.2350.

[10] S.S. Sabri, M.M. El-Abadelah, H.A. Yasin. *J. Heterocycl. Chem.* **1987**. Vol.24. P.165.
[11] M. Boiani, H. Cerecetto, M. Gonzalez, O.E. Piro, E.E. Castellano. *J. Phys. Chem.* A. **2004**. P.108, 11241.
[12] P.A. Nikitina, L.G. Kuzmina, V.P. Perevalov, I.I. Tkach. *Tetrahedron*. **2013**. Vol.69. P.3249.
[13] M.V. Gorelik. Chemistry of anthraquinones and their derivatives. *Moscow: Chemistry.* **1983**. 296p. (russian)
[14] Prech E. Determination of the structure of organic compounds. Tables of spectral data. E. This, p. bühlmann p., K., affolter C. structure determination. Per. with Anlg. *Moscow: BINOM. Laboratory of knowledge.* **2006**. 438p. (russian)
[15] R. Silverstein. Spectrometric identification of organic compounds. *Moscow: BINOM. Laboratory of knowledge*. **2012**. 557p. (russian)
[16] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.A. Robb, J.R. Cheeseman, T. Keith, G.A. Petersson, J.A. Montgomery, K. Raghavachari, M.A. Al-Laham, V. Zakrzewski, J.V. Ortiz, J.B. Foresman, J. Closlowski, B.B. Stefanov, A. Nanayakkara, M. Challacombe, C.Y. Peng, P.Y. Ayala, W. Chen, N.W. Wong, J.L. Andress, E.S. Replogle, R. Gomperts, R.L. Martin, D.J. Fox, J.S. Binkley, D.J. Defress, J. Baker, J.P. Stewart, C. Head-Gordon, Gonzales, J.A. Pople. *GAUSSIAN'09, Version C0.1, Gaussian Inc., Pittsburg, PA.* **2010.**
[17] A.D. Becke. *J Chem. Phys.* **1993**. Vol.98. P.5648-5662.
[18] N.C. Handy, A.J. Cohe. *Mol. Phys*. **2001**. Vol.99. P.403-410.
[19] O.Kh. Poleshchuk, A.V. Fateev, A.C. Legon, G. Frenking. Hyperfine interactions and DFT study of the bonding in complexes of metal halides, interhalogen diatomics in SO3 with Lewis bases. *Trends in Physical Chemistry*. **2014**. Vol.15. P.13-43.
[20] L.M. Gornostaev, E.V. Nuretdinova, T.I. Lavrikova, Yu.G. Khalyavina, I.S. Kryukovskaya, Yu.V. Gatilov. Transformations of 2-alkylamino-1,4-naphthoquinones under the action of nitrating mixture in acetic acid. *Russian Journal of Organic Chemistry*. **2015.** Vol.51. No.12. P.1733-1738.
[21] P.A. Nikitina, V.P. Perevalov. Methods of synthesis and physicochemical properties of 1-hydroxyimidazoles, imidazole 3-oxides, and their benzoannulated analogs. *Chemistry of Heterocyclic Compounds.* **2017**. Vol.53. No.2. P.123-149.
[22] G. Aguirre, M. Boiani, H. Cerecetto, A. Gerpe, M. González, Y.F. Sainz, A. Denicola, C.O. de Ocáriz, J.J. Nogal, D. Montero. *Escario. J. A. Arch. Pharm. Pharm. Med. Chem*. **2004**. Vol.337. P.259.
[23] N. Xi, Huang, Q., Liu L. In Comprehensive Heterocyclic Chemistry III; Katrizky A.R., Ramsden C.A., Scriven E.F.V., Taylor R.J.K. Eds. *Elsevie.* **2008**. Vol.4. P.143.
[24] P.A. Nikitina, A.S. Peregudov, T.Yu. Koldaeva, L.G. Kuz'mina, E.I. Adiulin, I.I. Tkach, V.P. Perevalov. Synthesis and study of prototropic tautomerism of 2-(2-hydroxyphenyl)-1-hydroxyimidazoles *Tetrahedron.* **2015**. Vol.71. P.5217.