Synthesis, spectroscopic characterization and DFT calculation of 6-substituted 3-R-2H-[1,2,4]triazino[2,3-c]quinazolin-2-ones

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The large spectrum of biological effects is reported for compounds containing the quinazoline ring system. Moreover, the quinazoline core is the versatile synthetic platform to access a wide rang of condensed heterocyclic compounds such as triazino[c]quinazolines. Literature examination provided numerous methods for their synthetic preparation. However, most of them particularly focused on [4+2]-cyclocondensation. In our previous research we reported the results of 3-substituted 3-R-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones synthesis via condensation of 4-hydrazinoquinazoline with α-ketocarboxilic acids esters. The main purpose of the presented investigation is elaboration of preparative methods for 6-substituted 3-R-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-2-ones.

It has been found that formation of mentioned substances resulted from specific Dimroth type rearrangement of [4,3-*c*] intermediate. This recyclization process makes the system more complicated for studying due to easily rotation of the ring. For better understanding of particularities of NMR spectra of 2,3- and 4,3-isomers of quinazolin-2-ones we have performed quantum-chemical calculations of ^{1}H chemical shifts of isomeric 3-methyl-6-phenyl-2H-[1,2,4]triazino[4,3-c]quinazolin-2-one and 3-methyl-6-phenyl-2H-[1,2,4]triazino[4,3c]quinazolin -2-one.

For calculations we have used DFT approach with B3LYP, PBE1PBE and M06L functionals in combination with CSGT and GIAO techniques for geometry optimized at the same levels of theory. Magnetically consistent 6-31G$^{\#\#}$ (I) basis set, proposed by us lately and tested for calculations of chemical shifts in numerous organic compounds has been used herein. The calculations have been performed with taking into account the effect of solvent (DMSO) via PCM method. Chemical shifts were obtained by subtracting the calculated magnetic shielding for the corresponding nuclei of interest from the shielding of the reference compound (TMS). All calculations have been performed using Gaussian 09 program. The Stampede computing system of Texas Advanced Computing Center was used. Stampede is the Dell PowerEdge C8220 Cluster where each node contains two Xeon Intel 8-Core 64-bit E5-2680 processors and 61 cores Intel Xeon Phi coprocessors. Operating system: Linux (CentOS distribution), number of nodes: 6.400, number of processing cores: 102.400, total memory: 205TB, total disk: 14PB(shared); 1.6PB (local).

The results of calculations showed that B3LYP and PBE1PBE functionals, in contrast to M06L, give good agreement with experiment and could be used for signal assignments and identification of the structure of such heterocyclic compounds. Calculations clearly demonstrate that difference of chemical shifts of *orto*- and *meta*-protons of 6-phenyl fragment could be used for unambiguous assignment of isomers.