www.ijcps.org

IJCPS Vol. 7, Special Issue
ICAFM - March 2018

ISSN:2319-6602
International Journal of Chemical and Physical Sciences

Study of Density Functional Theory of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile

J.S.Aher[1*], A.V.Kardel[1], M.R.Gaware[2], D.D.Lokhande[3]
1Organic Chemistry Research Centre, Department of Chemistry, K.R.T. Arts, B.H. Commerce and A.M. Science College, Shivaji Nagar, Gangapur Road Nashik 422 002, (MS), India
2Department of Chemistry, Arts, Commerce and Science College, Nandgaon, Dist. Nashik, (MS)
3Department of Chemistry, KPG Arts, Commerce and Science College Igatpuri, Nashik (MS), India
Affiliated to Savitribai Phule Pune University (Formerly University of Pune), M.S., India
*Email: js_aher@rediffmail.com

ABSTRACT

4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile was synthesized from the 4-hydroxybenzaldehyde, malanonitrile and urea followed by characterization using IR spectroscopic technique. Quantum chemical calculations were performed to optimize geometry of the title compound by density functional theory method at B3LYP level and 6-311++G (d, p) as basis set. Fundamental vibrational frequencies were calculated theoretically by DFT and HF method and compared with experimental data. The small difference between observed and scaled theoretical frequencies were recorded. Absorption maxima (λ max) is calculated with the help of HOMO-LUMO energy gap. Small energy gap implies an electron density transfer from HOMO to LUMO and implies the reactivity of the title compound.

Keywords: DFT study, HOMO-LUMO, IR spectrum, 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile, vibrational frequencies

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INTRODUCTION

Pyrimidine and its derivatives are incessantly pulling attention of the medicinal chemists from the first day of their discovery as important constituents of nucleic acid and are known to have diverse pharmacological activities [1,2] like antimicrobial, antiviral, antifilarial, antimalarial, analgesic, anthelmintic, antihypertensive, anti-HIV and anticancer activity. Certain pyrimidine derivatives are also reported to possess anti-inflammatory [3,4] and antioxidant [4-6] activity. Recently it has been reviewed that pyrimidine and its fused derivatives are widely used as drugs to treat various diseases [7]. Pyrimidines are important heterocyclic moiety in many organic compounds and contributed due importance in pharmacological applications [7] biological uses [8-18], herbicidal effects [19], pesticidal impact [20], synthetically applications [21], polymeric and material sciences. [22-25].The various synthetic routes for pyrimidine derivatives have been extensively reviewed [8-18]. Various reports are also available on one pot synthesis [11-14] of pyrimidine by three component condensation reaction using aromatic aldehydes, ethyl cyanoacetate or malononitrile and urea or thiourea or guanidine using various catalysts. These single step methods are more convenient as compared with two step strategies as it is selective, less time consuming and produce higher yields. Density functional theory (DFT) is a quantum mechanical modelling method used to investigate the electronic structure in the ground state of many systems, particularly atoms, molecules and condensed phase. Using this theory many properties can be evaluated using functional that is functions of another. Application of density functional theory to UV, IR spectroscopies gives clear interpretations λ max values, modes of vibrations, vibrational frequencies, coupling constant etc. In the present work, we have correlated experimental and theoretical IR spectrum along with molecular structure of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile (Figure 1) investigated by determining the chemical indexes using density functional theory (DFT) at the B3LYP/6- 311++G (d, p) level. To the best of our knowledge the structural and thermodynamic parameters of this compound has not been reported earlier in open literature.

MATERIALS AND METHOD

Computational studies of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile was performed on lenovo intel core i3 personal computer using the Gaussian 09 software package program. Geometries were optimized using DFT/B3LYP level at 6-311++G (d, p) basis set and applied in calculations for vibrational frequencies to confirm the stationary point as minima by utilizing GaussView 5.0 visualization program

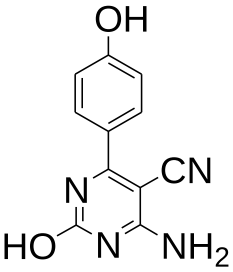
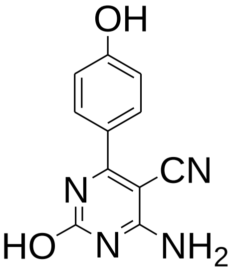


Figure 1: Structure of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile.

Spectral Data

The spectral data of the compound is shown below. The experimental IR spectral data of the compound is listed in table 1 and theoretical IR spectral data of compound is listed in figure 2 while experimental and theoretical IR spectrum are shown in figure 3.

Table 1: Experimental and theoretical spectral data of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile.

	Experimental data	**Theoretical data**
 $C_{10}H_8N_4O_2$	3471:-NH_2 stretching 2225:- CN symmetric stretching 1562:-Aromatic Stretching 3348:-OH Stretching , 1627,-NH_2 bending	3963:- NH_2 Stretching 2551:- CN Symmetric starching 1676:- Aromatic hydrogen 3300:- -OH of pyrimidine ring 1600:- NH_2 bending

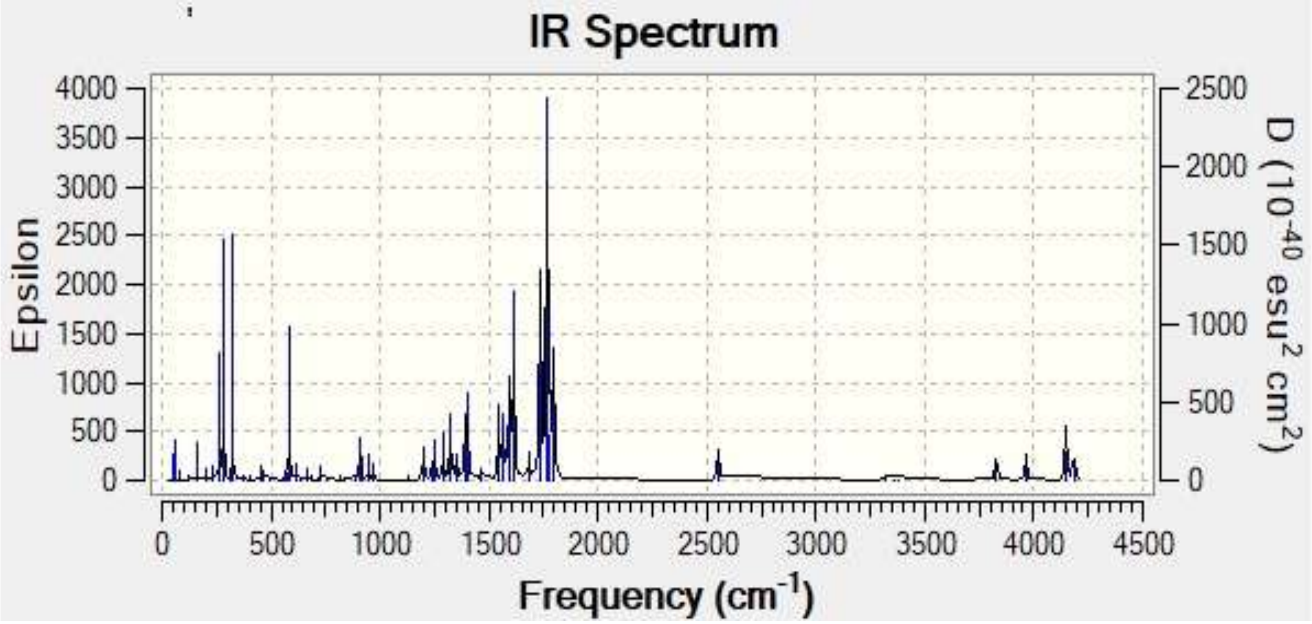


Figure 2: Theoretical IR spectrum of 14-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile

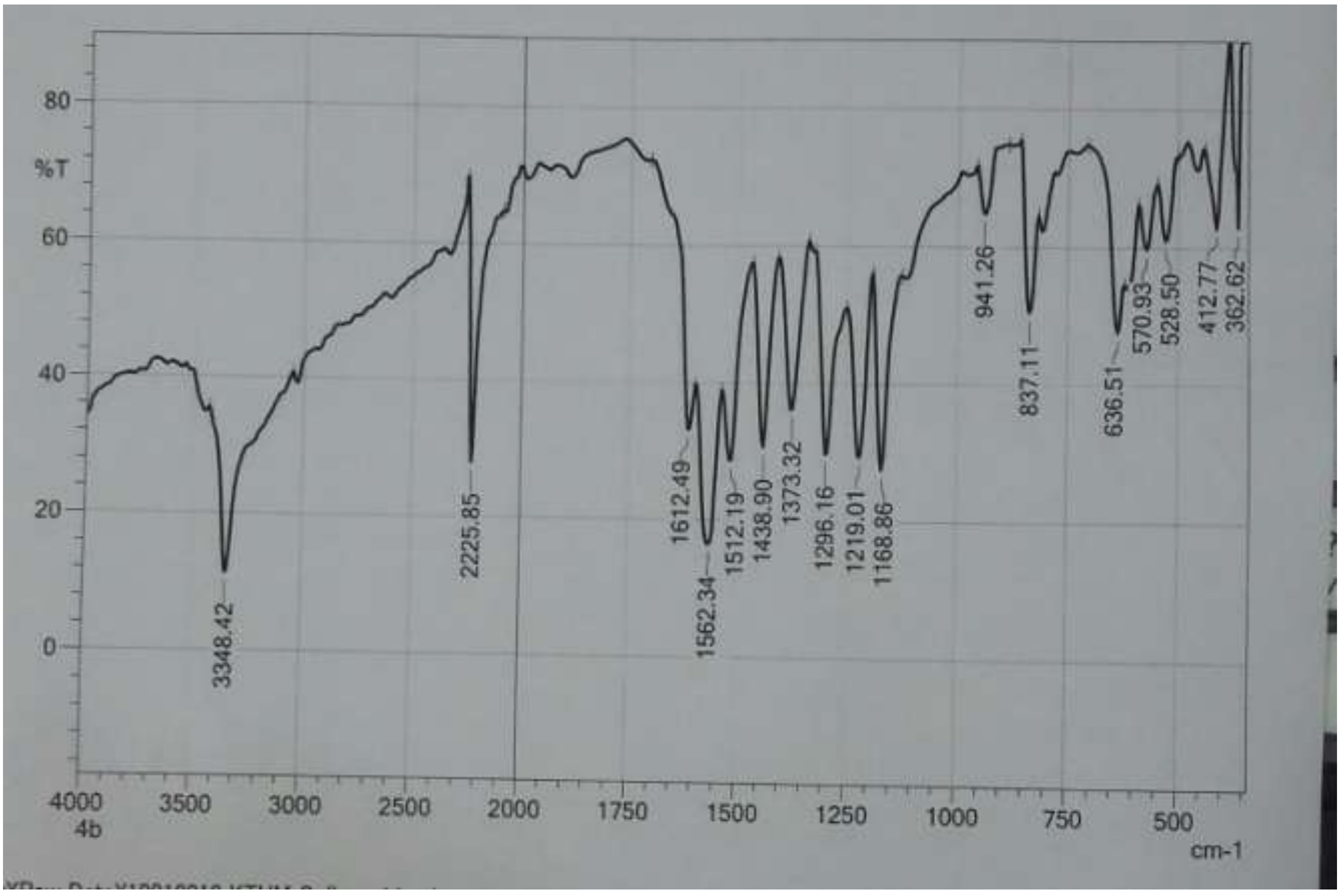


Figure 3: Experimental IR spectrum of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile

RESULT AND DISCUSSION:

Molecular geometry:

Theoretical calculations related to geometry optimization were `performed by DFT method with the B3LYP level at 6-311G++ (d, p) basis set in the ground state. According to the numbering reported in optimized structure (Figure 1) of the compounds 1, the optimized geometry parameters (bond lengths and bond angles) are listed in Table 2. The self-consistent field (SCF) energy of 1 and 2 was found to be -788.96 a.u . While dipole moment was found 2.6872 D respectively. The point group symmetry of the planar structure of the compound is C1. The compound possess 25 atoms hence there 69 normal modes of fundamental vibrations are expected. Slight variation has been observed in experimental and theoretical IR data for the said compound. For better upgradation across agreement between observed and calculated vibrational frequencies, calculated absorption frequencies were adjusted by multiplying with scaling factor 0.9631 for density functional theory resulting in computed absorption frequencies. The scaled vibrational frequencies are listed in table 1.

C≡N stretching vibrations:

Stretching frequency of nitriles group occurs in the region 2220-2260 cm^{-1}. Theoretical C≡N stretching frequency was seen at 2247 cm^{-1} whereas experimentally it is seen at 2225 cm^{-1}.

Aromatic C=C stretching vibrations:

Aromatic C=C stretching is observed in range between 1585-1600cm^{-1} and 1400-1500 cm^{-1}. Experimental C=C stretching absorbs in the range 1473 cm^{-1} while theoretically aromatic C=C stretching absorption bands is seen at 1580 cm^{-1}.

N-H stretching vibrations:

1^{0} amine shows N-H stretching between 3400-3200 cm^{-1}.For compounds it is observed at 3471 cm^{-1} bending nearly equal to 1600 cm^{-1} .Experimentally it is observed at 1612 cm^{-1}

O-H stretching vibrations:

Stretching frequency of OH observed in range between 3400-3200cm^{-1} very broad. Experimentally OH starching range at 3348 cm^{-1}.

Optimised Structure

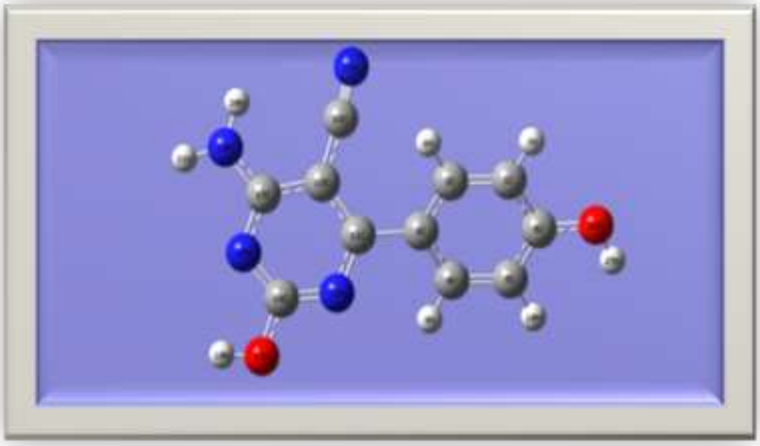


Figure 3: Optimized Structure of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile

Bond Length

Table 2: Optimized bond lengths (A^{o}) of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile by DFT method at B3LYP level using 6-311++G (d, p) basis sets

Atoms	Bond Length (A^{0})
C1-C2	1.3788
C1-C6	1.3867
C1-H7	1.0737
C2-C3	1.3935
C2-H8	1.0726
C3-C4	1.3915
C3-C11	1.4823
C4-C5	1.3801
C4-H9	1.0727
C5-C6	1.3878
C5-H10	1.0767
C6-O24	1.344
C11-N12	1.3249
C11-C13	1.3986
N12-C14	1.3119
C13-C15	1.4143
C13-C22	1.4277
C14-C16	1.3156
C14-O17	1.3158
C15-N16	1.323
C15-N19	1.3375
O17-H18	0.9441
N19-H20	0.9923
N19-H21	0.9922
C22-N23	1.133
O24-H25	0.941

Bond Angles:

Table 3: Optimized bond angles of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile by DFT method at B3LYP level using 6-311++G (d, p) basis sets

Atoms	Bond Angles
C2-C1-C6	119.7
C2-C1-H7	120.9
C6-C1-H7	119.2
C1-C2-C3	121.1
C1-C2-H8	118.1
C3-C2-H8	120.6
C2-C3-C4	118.2

C2-C3-C11	122.9
C4-C3-C11	118.7
C3-C4-C5	121.0
C3-C4-H9	119.2
C5-C4-H9	119.6
C4-C5-C6	119.7
C4-C5-H10	119.9
C6-C5-H10	120.2
C1-C6-C5	119.9
C1-C6-O24	117.6
C5-C6-O24	122.4
C3-C11-N12	115.5
C3-C11-C13	123.8
N12-C11-C13	120.6
C11-N12-C14	117.0
C11-C13-C15	116.8
C11-C13-C22	125.2
C15-C13-C22	117.8
N12-C14-N16	128.1
N12-C14-O17	115.4
N16-C14-O17)	116.4
C13-C15-N16	121.0

Mulliken atomic charges:

Atomic charges depends on the arrangement of atom and how the atoms are defined. Natural Population Analysis (NPA) is used to generate information on the electron densities of the atom. Mullikens charges are obtained using NPA based on the DFT/ B3LYP/ 6-311 ++ G (d, p) basis set and are listed in table 5. More positive charge is present on C13 (2.078) and C3 (0.924) while more negative charge is present on C6 (-2.086) and C2 (-0.197).

Table 4: Computed Mulliken Atomic Charges (a.u) by Natural Population Analysis (NPA) calculated by DFT at B3LYP/6-311++G (d, p) basis set

Atom	Charge
C1	-0.442
C2	-0.758
C3	0.924
C4	-0.036
C5	-0.081
C6	-0.438
H7	0.237
H8	0.267
H9	0.260
H10	0.184
C11	-0.369
N12	-0.197
C13	2.078

C14	0.605
C15	0.305
N16	-0.376
O17	-0.290
H18	0.340
N19	-0.579
H20	0.347
H21	0.340
C22	-2.086
N23	-0.221
O24	-0.294
H25	0.282

HOMO-LUMO energy and absorption maxima:

The HOMO is a highest occupied molecular orbital that can act as an electron donor and the LUMO is lowest unoccupied molecular orbital that can accept electron. HOMO-LUMO energy gap can be used to predict the absorption maxima (λ max) of the molecules by the following formula [26-27].

Energy gap (eV) = Energy gap (Hartree or a.u.) x 27.2113834

λ max =1240/Energy gap (eV)

For the compound λ_{max} was determined and found to be 67.7884 nm as shown in **Table 5.**

Table 5: HOMO, LUMO (a.u.), λmax, dipole moment (D) and SCF energy (a.u.) values of 4-amino-2-hydroxy-6-(4-hydroxyphenyl) pyrimidine-5-carbonitrile by DFT method at B3LYP level using 6-311++G (d, p) basis set.

Basis Set	**6.311++G(d,p)**
E (RB+HF-LYP) (au)	-788.9669 a.u.
HOMO (e v)	-8.7509
LUMO(e v)	9.5413
Energy gap (eV)	18.2922
Dipole moment (D)	2.6872
λ max nm	67.7884
Chemical hardness(η)	9.1461
Electronegativity(χ)	0.14348
Electronic chemical potential (μ)	-0.14348
Electron affinity	9.5413
Ionisation energy(I)	-8.7509
Global Electrophilicity Index (ω)	0.0112

CONCLUSION:

The optimized geometries were computed by DFT/ B3LYP at 6-311++G (d, p) basis set using Gaussian 09W package and Gauss A-5.0. Vibrational assignments were examined DFT methods of computation and the values predicted by DFT/B3LYP at 6-31++G (d, p) were found to be nearly in good agreement with the experimental values of the compound. The absorption maxima of the synthesized molecule are obtained from HOMO-LUMO energy gap.

ACKNOWLEDGEMENT

The authors are thankful to Maratha Vidya Prasarak Samaj Nashik for providing infrastructure, Principal, K. R. T. Arts B. H. Commerce and A. M. Science College, Gangapur Road, Nashik-422 002, (MS), India for providing the research facilities.

REFERENCE

[1] I. M. Lagoja, Chem Biodivers, **2005**, 2(1), 1-50.

[2] H. J. Dhongade, H. Dansena, K. K. Chandrakar, Asian J Pharm Clin Res, **2015**, 8(4), 171-7.

[3] M. Amir, S. Javed, H. Kumar, Indian J Pharm Sci, **2007**, 69(3), 337-43.

[4] S. Panda, P. Chowdary, Indian J Pharm Sci, **2008**, 70(2), 208-15.

[5] G. Vanessa, M. Sidnei, F. C. F. Alex, C. F. Darlene, C. Pio, P. Ernani, J Braz Chem Soc, **2010**, 21(8), 1477-83.

[6] A. Padmaja, T. Payani, G. D. Reddy, V. Padmavathi, Eur J Med Chem, **2009**, 44(11), 4557-66.

[7] T. P. Selvam, C. R. James, P. V. Dniandev, S. K. Valzita, Research in Pharmacy, **2015**, 2(4), 1-9.

[8] C. O. Kappe Tetrahedron. 49**, 1993**, 6937 and references cited therein.

(a) Patil A D, N. V. Kumar, W. C. Kokke, M. F. Bean,A. J. Freyer, De Brosse, C Mai, A.

[9] Truneh, D. J. Faulkner, B. Carte, A. L. Breen, R. P. Hertzberg P, R. K. Johnson, J. W.

[10] Westley and B. C. Potts, J. Org. chem. 60 **1995** 1182.

[11] B. B. Snider, C. J Patil, A D and A. Freyer Tetrahedron. Lett. 37, **1996** 6977.

[12] J. Clark, M. S. Shahhet, D. Korakas and G. J. Varvounis. Het. Chem. 30**, 1993**, 1065- 1072.

[13] K. Ogowva, I. Yamawaki, Y. I. Matsusita, N. Nomura, P. F. Kador and J. H.

[14] J. H. Kinoshita Eur. J. Med. Chem. 28 **1993**, 769-781.

[15] B. Tozkoparan, M. Ertan, P. Kelicen and R. Demirdar, Farmaco, 54, **1999**, 588-593.

[16] M. Santagati, M. Modica, A Santagati, F. Russo and S. Spampinato, Pharmazie. 51, **1996**, 7-11.

[17] V. K. Ahluwalia, M. Chopra and R. A. Chandra, J. Chem. Rs. 5, **2000**, 162-163.

[18] M. Van Laar, E. Volkerts and M. Verbaten, Psychopharmacology. 154 **2001**, 189-197.

[19] K. Danel, E. B. Pedersen and C. J. Nielsen. Med. Chem. 41, **1998**, 191-198

[20] O. A. Fathalla, S. M. Awad and M. S. Mohamed Arch. Pharm. Res. 28, **2005**, 205–1212.

[21] O. A. Fathalla, A. Zaghary, H. H. Radwan, S. M. Awad and M. S. Mohamed, Arch. Phar. Res 25, **2002**, 258-269.

[22] Y. Ding, J. Girardet, K. L. Smith, G. J. Prigaro, J. Z. Wu and N. Yao Bioorg. Chem. 34, **2006**, 26-38.

[23] T. Azza and M. A. Sahar, Molecules. 17, **2012,** 9868-9886.

[24] M. Kimura and M. Aizawa, USP 15005795497161A 5, **1998,** 795,497.

[25] P. Moreau, F. Anizon, M. Sancelme, M. Prudhomme, C. Bailly, C. Carrasco, M. Ollier, D. Severe, J. Riou, D. Fabbro, T. Meyer, A. Aubertin, A. J. Med. Chem. 41, **1998,** 1631.

[26] V. Danilenko, A. Simonov, S. Lakatosh, M. Kubbutat, F. Totzke, C. Schachtele, S. Elizarov, O. Bekker, S. Printsevkaya, Y. Luzikov, M. Reznikova, A. Shtil, S. Preobrazhenskaya, J. Med. Chem. 51, **2008,** 7731.

[27] A. Kozikowski, I. Gaisina, P. Petukhov, J. Sridhar, L. King, S. Blond, T. Duka, M. Rusnak, A. Sidhu, A., J. Med. Chem. 1, **2006,** 256.

[28] M. Coghlan, A. Culbert, D. Cross, S. Corcoran, J. Yates, N. Pearce, O. Rausch, G. Murphy, P. Carter, L. Cox, D. Mills, M. Brown, D. Haigh, R. Ward, D. Smith, K. Murphy, A. Reith, J. Holder, Chemistry and Biology, 7, **2000,** 793.

[29] F. Trager. Handbook of Lases and optics, Part A, 1st Edition, Springer Science Publisher; New York, 2007.

[30] K. Chen, T. Chow. “1,7-Dinitroperylene bisimides: facile synthesis and characterization as *n*-Type organic semiconductors”, Tetrahedron Lett. vol 51, pp. 5959-5963, 2010.