New 2-Pyrone-Based Hydrazones: Synthesis, spectral Characterisation, UV-visible Study and Evaluation of the Antiradicalar Activity

Djamila Oukacha-Hikem^{1,2}, Malika Makhloufi-Chebli^{1,2}, Anissa Amar^{3,4}, Houria Bouherrou², Yahia Rachedi², Hacène Meghezzi⁴, Artur M. S. Silva⁵, Maamar Hamdi²

¹Laboratoire de Physique et Chimie des Matériaux LPCM, Faculté des Sciences, Université Mouloud Mammeri, Tizi-Ouzou, Algeria, ²Laboratoire de Chimie Organique Appliquée (Groupe Hétérocycles), Faculté de Chimie, Université des Sciences et de la Technologie Houari Boumediène, Alger, Algeria, ³Département de Chimie, Université Mouloud Mammeri, Tizi-Ouzou, Algeria, ⁴Laboratoire de Thermodynamique et Modélisation Moléculaire, Faculté de Chimie, Université des Sciences et de la Technologie Houari Boumediène, Alger, Algeria, ⁵QOPNA, Department of Chemistry, University of Aveiro, Aveiro, Portugal

Abstract

The synthesis of new 2-pyrone-based hydrazones have been prepared by the coupling of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione with diazonium salts, obtained by diazotization of aniline derivatives. The structure of all compounds was established by spectroscopic methods and the structure of the more stable conformer was theoretically confirmed by potential energy profile analysis. The prepared 2-pyrone-based hydrazones dyes were acetylated and both groups of compounds showed moderate to good radical scavenging activity (DPPH).

Graphical Abstract:



2-Pyrone-based hydrazones have been prepared and acetylated. The structure of the more stable hydrazone *anti*-conformer of the 2-pyrone-based azo dyes was theoretically confirmed using the B3LYP/6-31G* level of theory. The acetyl-2-pyrone-based hydrazones presented good DPPH radical scavenging activity **KEYWORDS:** Pyran-2-ones, Diazonium salts, Hydrazones, Theoretical calculations, Antiradicalar activity

1. INTRODUCTION

Hydrazones and their derivatives constitute a versatile class of compounds in organic chemistry and they are characterized by the presence of –NH–N=CH– group in their molecules [1-2]. These compounds have interesting biological properties, such as anti-inflammatory, analgesic, anticonvulsant, antituberculosis, antitumor, anti-HIV and antimicrobial activity [3-6]. Hydrazones are also important compounds for drug design, as possible ligands for metal complexes, organocatalysis, and also for the syntheses of heterocyclic compounds [7-9]. Due to these important potential applications, hydrazones have been under study for a long time, but much of their basic chemistry remains unexplored. On the other hand, the presence of heterocyclic rings in many synthetic hydrazones plays a main role in their pharmacological properties [8].

2-Pyrones demonstrate a whole spectrum of biological properties, such as antibiotic, antifungal, cytotoxic, neurotoxic, and phytotoxic activities. Simple change in the substitution pattern on the 2-pyrone ring often leads to compounds possessing new biological activity. Indeed, some of the 4-alkyl/aryl/alkenyl/hydroxy-substituted-6-methyl-2-pyrones show remarkable biological effects, such as antimicrobial activity, human chronic myelogenous leukemia, and human ovarian carcinoma inhibitory properties [10-20].

2

The afore mentioned biological activities of hydrazone and 2-pyrone derivatives led us to prepare some dyads by the coupling of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione with diazonium salts and to evaluate their radical scavenging activity (DPPH radical).

2. RESULTS AND DISCUSSION

6-Methyl-4*H*-furo[3,2-*c*]pyran-3,4(2*H*)-dione **3** is obtained by the reaction of 3-(2bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one **2** with aliphatic amines [21]. The required α -haloketone **2** is easily obtained via the selective α -monobromination of dehydroacetic acid (DHAA) **1** in 70% yield according to a known procedure (Scheme 1) [21, 22].

The coupling of diazonium salts, obtained by diazotization of aniline derivatives in presence of sodium nitrite and concentrated hydrochloric acid, with pyran-3,4-dione **3** in the presence of sodium acetate gives (*E*)-6-methyl-2-(2-phenylhydrazono)-4*H*-furo[3,2*c*]pyran-3,4(2*H*)-diones **4a,b** in moderate to good yields (51-60%) (Scheme 2).The structure of these dyes may exist in four possible tautomeric forms, namely hydrazoneanti **T**₁, hydrazone-syn**T**₂, azo-keto **T**₃ and azo-enol **T**₄ (Scheme 3).

The ¹H NMR spectra of pyran-3,4(2*H*)-diones **4a,b** showed the presence of singlet signal at δ 11.2 ppm, which fits with a strongly deshielded chelated NH or OH proton. As so, it can be suggested that these dyes exist as the hydrazone **T**₁ or azo-enol **T**₄ forms. However the former hydrazone **T**₁ form is amply confirmed using HSQC and HMBC correlations (NH \rightarrow C-1' and C-2',6'). The referred intramolecular hydrogen bond implies that pyran-3,4(2*H*)-diones **4a,b** present a (*E*)-configuration.

Determination of energy barriers of the hydrazone form to internal rotation has been made possible by quantum chemical methods. Contributions from steric and electrostatic attractive and repulsive interactions become important in determining the rotational barrier and equilibrium conformation when the molecule is substituted with various groups.

Conformational analysis of the obtained product **4a** was carried out at the PBE1PBE [23] level combined with the LANL2DZ [24] basis set, using Gaussian 09 [25] program, in order to determine the most stable isomer. Note that the nature of the different isomers relative to the N-N bond was confirmed by the frequencies calculation of the normal modes of vibration. The most stable structure is determined by rotating the phenyl group along N-N bond using the dihedral angle C-N-N-C; the more stable structure belongs to the minimum in the potential energy surface. The initial value of the dihedral angle C-N-N-C was set to 180° and for every 1° the energies of the isomers are determined. The obtained potential energy surface is presented in Figure 1. In addition, the (*E*)- and (*Z*)-isomers/N-N bond of the hydrazone form of pyran-3,4(2*H*)-diones **4a,b** with the relative energy are shown in Figure 2. The (*E*)-isomer (A) with a C-N-N-C dihedral angle equal to 180° is found to be more favoured relatively to the (*Z*)-isomer (B) with C-N-N-C of 0° by 15.67 kcal/mol. It is worth noting that for (*E*)-isomer, an intramolecular hydrogen bond exists between respectively carbonyl group of the furanone and NH of the

4

hydrazone moiety, which is responsible for the higher stability of this structure. The distance between atoms O…H– N equals 1.95Å, which supports stabilizing of the investigated compounds in the form of the (*E*)-isomer relative to the N-N bond. Indeed, NBO analysis (Natural Bond Orbital) [26] indicate a significant hydrogen bond type interaction between LP(O) and $\mathbf{6} * (N-H)$, with a stabilization energy E^2 of 8.61 kcal/mol. In the other hand, steric repulsion effects between the phenyl ring and the rest of the molecule destabilize the (*Z*)-isomer compared to the (*E*)-one.

In addition, (E)/(Z)-isomerism of the C=N bond of **4a** have been analysed using the same level of theory considering the most stable (*E*)-isomer relative to the N-N bond (A). A recent study of Maiorova et al. [9] on similar compounds have shown that these types of isomerism are related and depend substantially on the structural fragments in the hydrazone molecule, namely in the introduction of additional substituents containing heteroatoms and double bonds capable of participating in the formation of intramolecular hydrogen bonds. The PBE1PBE/LANL2DZ results indicate that the (*E*)-isomer/C=N bond (A') is slightly less stable than the (*Z*)-isomer/C=N bond (A) (Figure 2) by 4.06 kcal/mol. These results show the importance of the intramolecular hydrogen bond in the stability of these compounds.

The UV-vis absorption spectra of azo dyes **4a,b** were recorded immediately after product dissolution in various solvents at a concentration of 10^{-6} M in the range 260-600 nm. The absorption maxima of these azo compounds in various organic solvents are given in Table 1 and also presented in Figure 3 and 4 respectively.

The absorption spectra of **4a**, showed an intense absorption maxima in DMSO, which mean that the latter is present in only one tautomeric form. In toluene, chloroform, methanol acetonitrile and acetic acid, they exhibit two absorption maxima; indicate the presence of two tautomeric forms. For the compound **4b** only one absorption wavelength was observed in all the solvents. Except in the chloroform, two wavelengths were observed. As shown in Table 1, the electronic absorption spectra of the two studied compounds in different polar aprotic solvents did not significantly change. Strong evidence that this dyes exist in equilibrium is provided by the two absorption maxima and isobestic points in the visible spectra of (Figure 3). This equilibrium may exist between tautomeric forms.

NH-function of the pyran-3,4(2*H*)-diones **4a,b** has been acetylated with acetic anhydride leading to the formation of *N*-acetyl-hydrazones **5a,b** (Scheme 2). The structure of these acetyl derivatives is confirmed by IR, ¹H and ¹³C NMR, and mass spectra and in an indirect way confirms the structure of the starting materials **4a,b**.

2.4 Antiradicalar Activity

The 2,2-diphenyl-1-picrylhydrazyl radical (DPPH[•]) is a stable free radical, which has been widely accepted as a tool for estimating the free radical scavenging activities of potential antioxidants [27, 28]. The lower IC_{50} value indicates a stronger ability of the tested compound to act as a DPPH scavenger while the higher IC_{50} value indicates a lower scavenging activity of the scavengers. On electron or hydrogen reception the purple colour of DPPH radical fades or disappears due to its conversion to 2,2-diphenyl-1-picrylhydrazine resulting in decrease in absorbance at λ 517 nm. The more decrease the absorption in the presence of scavengers the more effective is its radical scavenging activity. Herein the antiradicalar activity of compounds **1-5** was expressed as IC₅₀ (Figure 5). The IC₅₀ values vary between 38.91 and 24.09 µg/mL for compounds **1-5** while butylhydroxytoluene (BHT, positive control) presented a value of 10.46 µg/mL. After the acylation of NH group in **4a,b** the scavenging activity of **5a,b** increased. This seems indicate that the radical scavenging activity of compounds **5a,b** is due to an electron donating mechanism and not an hydrogen donating mechanism since there no hydrogen atoms to be given [29].

3. CONCLUSION

New 2-pyrone-based hydrazones **4a,b** have been prepared by the coupling of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione with diazonium salts and then acetylated with acetic anhydride giving the acetyl-2-pyrone-based dyes **5a,b**. The structure of the more stable isomer of the 2-pyrone-based hydrazone **4a** was confirmed theoretically using the PBE1PBE/LANL2DZ level of theory. The calculated potential energy profile indicates the stability of the hydrazone (*E*)-isomer by 15.67 kcal/mol over the (*Z*)-one. The obtained results showed the importance of the intramolecular hydrogen bond in the stability of these compounds. The acetyl-2-pyrone-based hydrzones **5a,b** presented good DPPH radical scavenging activity.

4. EXPERIMENTAL

4.1. Materials And Method

Melting points were determined on a Stuart scientific SPM3 apparatus fitted with a microscope and are uncorrected. ¹H and ¹³C NMR spectra were recorded in CDCl₃ or DMSO-d₆ solutions on a Bruker Avance 300 (300.13 MHz for ¹H and 75.47 MHz for ¹³C) spectrometer. Chemical shifts are reported in ppm (δ) using tetramethylsilane (TMS) as internal reference and coupling constants (J) are given in Hz. ¹³C assignments were made using gradient selected heteronuclear single quantum coherence (gHSQC) and gradient selected heteronuclear multiple quantum coherence (gHMBC) (delays for one bond and long-range $J_{C/H}$ couplings were optimized for 145 and 7 Hz, respectively) experiments. Positive-ion electrospray ionization (ESI) mass spectra were acquired using a QTOF 2 instrument [diluting 1 μ L of the sample chloroform solution (~10⁻⁵M) in 200 μ L of 0.1% trifluoroacetic acid/methanol solution. Nitrogen was used as nebulizer gas and argon as collision gas. The needle voltage was set at 3000 V, with the ion source at 80°C and desolvation temperature at 150°C. Cone voltage was 35 V]. Infrared spectra (KBr) were determined as KBr pellets of the solids on a Magna- IR 550 series II Nicolet apparatus. UV spectra were recorded on Cary 50 Scan UV-vis spectrometer in acetonitrile solutions.

4.2. Synthesis Of (E)-6-Methyl-2-(2-Phenylhydrazono)-4H-Furo[3,2-C]Pyran-3,4(2H)-Diones 4a,B.

The appropriate aromatic amine (5 mmol) was dissolved in HCl (20 mL, 10%) and cooled in an ice-salt bath to $0-5^{\circ}$ C. The mixture was then added in portions to a cold

solution of NaNO₂ (345 mg, 5 mmol) in water (20 mL) and stirred for 30 min. This diazonium salt solution was added to a vigorously stirring solution of 6-methyl-4*H*-furo[3,2-*c*]pyran-3,4(2*H*)-dione **3** (830 mg, 5 mmol) in sodium acetate (4.1 g, 50 mmol) and water (20 mL). The reaction mixture stirred for 4 h. The coloured products obtained were filtered, washed with water, dried and then recrystallized from ethanol.

(*E*)-6-*Methyl*-2-(2-*phenylhydrazono*)-4*H*-*furo*[3,2-*c*]*pyran*-3,4(2*H*)-*dione* **4a**: Brown powder (0.81 g, 60%). mp 135°C; IR: (v) 3100, 3350, 2980, 1750, 1640, 1574, 1515, 1425, 1350, 750 cm⁻¹; ¹H NMR (DMSO-d₆): δ 2.29 (s, 3H, 6-C*H*₃), 6.74 (s, 1H, H-7), 7.50-7.53 (m, 3H, H-2',4',6'), 7.21-7.24 (m, 2H, H-3',5'), 11.15 (s, 1H, NH); ¹³C NMR (DMSO-d₆): δ 21.1 (6-CH₃), 95.8 (C-7), 101.2 (C-3a), 115.8 (C-2',6'), 120.1 (C-4'), 129.6 (C-3',5'), 141.7 (C-1'), 155.2 (C-6), 171.9 (C-2), 174.7 (C-4), 184.9 (C-7a), 190.1 (C-3); ESI⁺-MS: m/z 293 [(M+Na)⁺, 100], 271 [(M+H)⁺, 12]. Anal. Calcd. For C₁₄H₁₀N₂O₄: C 62.2; H 3.7; N 10.4. Found: C 62.3; H 3.6; N 10.5%.

4.3. Synthesis Of (E)-N'-(6-Methyl-3,4-Dioxo-4H-Furo[3,2-C]Pyran-2(3H)-Ylidene)-N-Phenylacetohydrazides 5a,B.

A solution of the appropriate (*E*)-6-methyl-2-(2-phenylhydrazono)-4*H*-furo[3,2-*c*]pyran-3,4(2*H*)-dione **4a,b** (5 mmol) and pyridine (0.01 mL) in acetic anhydride (20 mL) was refluxed with stirring, for 30 min. After cooling at room temperature, the obtained solid was filtered and recrystallized from ethanol. (*E*)-*N*'-(6-*Methyl-3,4-dioxo-4H-furo[3,2-c]pyran-2(3H)-ylidene*)-*N-phenylacetohydrazide* **5a**: Brown powder (0.57 g, 37%); mp 178°C; IR: (v) 2982, 1750, 1640, 1572, 1425, 1368, 750 cm⁻¹; ¹H NMR (DMSO-d₆): δ 2.29 (s, 3H, 6-*CH*₃), 2.32 (s, 3H, COC*H*₃), 6.74 (s, 1H, H-7), 7.61-7.64 (m, 3H, H-2',4',6'), 7.72-7.78 (m, 2H, H-3',5'); ¹³C NMR (DMSO-d₆): δ 20.6 (6-*C*H₃), 21.1 (COCH₃), 95.8 (C-7), 101.2 (C-3a), 120.8 (C-2',6'), 124.5 (C-4'), 129.6 (C-3',5'), 138.5 (C-1'), 155.2 (C-6), 168.8 (N-C=O), 171.9 (C-2), 174.7 (C-4), 187.4 (C-7a), 190.1 (C-3); ESI⁺-MS: m/z 335 [(M+Na)⁺, 45], 313 [(M+H)⁺, 100]. Anal. Calcd. For C₁₆H₁₂N₂O₅: C 61.5; H 3.9; N 8.9. Found: C 61.4; H 3.7; N 8.8%.

ACKNOWLEDGMENTS

Thanks are due to University of Aveiro, FCT/MEC for the financial support to the QOPNA research Unit (FCT UID/QUI/00062/2013), through national funds and where applicable co-financed by the FEDER, within the PT2020 Partnership Agreement, and also to the Portuguese NMR Network. We thank Cristina Barros and Hilário Tavares (Department of Chemistry, University of Aveiro, 3810-193, Aveiro, Portugal) for performing the mass and NMR spectra.

Supporting Information: Full experimental detail, ¹H and ¹³C NMR spectra, evaluation of the free-radical-scavenging activity by using 1,1-diphenyl-2-picryl-hydrazyl radical. This material can be found via the "Supplementary Content" section of this article's webpage.

REFERENCES

- [1] Angelusiu, M. V.; Barbuceanu, S. F., Draghici, C.; Almajan, G. L. Eur. J. Med.
- Chem. 2010, 45, 2055-2062.
- [2] Belskaya, N. P.; Dehaen, W.; Bakulev, V. A. Arkivoc 2010, *i*, 275-332.
- [3] Rollas, S. Kucukguzel, S. G. Molecules 2007, 12, 1910-1939.
- [4] Ozkay, Y.; Tunah, Y.; Karaca, H.; Isikdag, I. Eur. J. Med. Chem. 2010, 45, 3293-3298.
- [5] Candéa, A. L. P.; Ferreira, M. L.; Pais, K. C.; Cardoso, L. N. F.; Kaiser, C. R.;
- Henriques, M. G. M. O.; Lourenço, M. C. S.; Bezerra, F. A. F. M.; Souza, M. V. N.
- Bioorg. Med. Chem. Lett. 2009, 19, 6272-6274.
- [6] Joshi, S. D.; Vagdevi, H. M.; Vaidya, V. P.; Gadaginamath, G. S. *Eur. J. Med. Chem.*2008, 43, 1989-1996.
- [7] Sreeja, P. B.; Sreekanth, A.; Nayar, C. R.; Kurup, M. R. P.; Usman, A.; Rasaz, I. A.;
 Chantrapromma, S.; Fun, H. K. J. Mol. Struct. 2003, 645, 221-226.
- [8] Kuriakose, M.; Kurup, M. R. P.; Suresh, E. Spectrochim. Acta Part A 2007, 66, 353-358.
- [9] Maiorova, O. A.; Babkina, N.V.; Egorova A.Yu. *Chem. Heterocycl. Compd.* **2015**, *51*, 514-517.
- [10] Schäberle, T. F. Beilstein J. Org. Chem. 2016, 12, 571-588.
- [11] Lee, J. S. Mar. Drugs 2015, 13, 1581-1620.
- [12] Sucipto, H.; Sahner, J. H.; Prusov, E.; Wenzel, S. C.; Hartmann, R. W.; Koehnke, J.;Müller, R. *Chem. Sci.* 2015, *6*, 5076-5085.

- [13] Brachmann, A.; Brameyer, S.; Kresovic, D.; Hitkova, I.; Kopp, Y.; Manske, C.;
- Schubert, K.; Bode, Heermann, H. R. Nature Chem. Biol. 2013, 9,573-578.
- [14] Fairlamb, I. J. S.; Marrison, L. R.; Dickinson, J. M.; Lu, F. J.; Schmidt, J. P. *Bioorg.Med. Chem.* 2004, *12*, 4285-4299.
- [15] McGlacken, G. P.; Fairlamb, I. J. S. Nat. Prod. Rep. 2005, 22, 369-385.
- [16] Hua, D. H.; Huang, X.; Tamura, M.; Chen, Y.; Woltkamp, M.; Jin, L.W.; Perchellet,

E. M.; Perchellet, J. P.; Chiang, P. K.; Namatame, I.; Tomoda, H.*Tetrahedron* **2003**, *59*, 4795-4803.

[17] Perchellet, E. M.; Ladesich, J. B.; Chen, Y.; Sin, H. S.; Hua, D. H.; Kraft, S. L.;

Perchellet, J.P. Anti-Cancer Drugs 1998, 9, 565-576.

- [18] Shin, J.; Paul, V. J.; Fenical, W. Tetrahedron Lett. 1986, 27, 43, 5189-5192.
- [19] Mayer, A. M. S.; Paul, V. J.; Fenical, W.; Norris, J. N.; Carvalho, M. S.; Jacobs, R.
- S. Hydrobiologia 1993, 260, 521-529.
- [20] Goel, A.; Ram, V. J. Tetrahedron 2009, 65, 7865-7913.
- [21] Hikem-Oukacha, D.; Rachedi, Y.; Hamdi, M.; Silva, A. M. S. *J. Heterocycl. Chem.***2011**, *48*, 31-37.
- [22] Hikem-Oukacha, D.; Hamdi, M.; Silva, A. M. S.; Rachedi, Y. *J. Heterocycl. Chem.***2011**, *48*, 63-68.
- [23] Perdrew, J. P.; Burke, K.; Ernzerhof, M. Phys. Rev. Lett. 1996, 77, 3865-3868.
- b) Perdew, J. P.; Ernzerhof, M.; Burke, K. J. Chem. Phys. 1996, 105, 9982-9985.
- [24] Hay, P. J.; Wadt, W. R. J.Chem. Phys. 1985, 82, 299-310.
- [25] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M.
- A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.;

- Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng,
- G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.;
- Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery Jr.,
- J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.;
- Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J.
- C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.;
- Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.;
- Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.;
- Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.;
- Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.;
- Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.
- [26] a) Foster, J. P.; Weinhold, F. J. Am. Chem. Soc. 1980, 102, 7211-7218. b) Reed, A.
- E.; Curtiss, L. A.; Weinhold, F. Chem. Rev. 1988, 88, 899-926.
- [27] Wang, M.; Li, J.; Rangarajan, M.; Shao, Y.; La Voie, E. J.; Huang, C. T.; Ho, C. T.*J. Agric. Food Chem.* **1998**, *46*, 4869-4873.
- [28] Brand-Williams, W.; Cuvelier, M.; Berset, C. Lebensmittel-Wissenschaft und-Technol. **1995**, 28, 25-30.
- [29] Lee, J. H.; Ozcelik, B.; Min, D. B. J. Food Sci. 2003, 168, 861-865.

Dye		λ_{max}/nm					
	DMSO	ACN	Ethyl	Acetic	Methanol	Chloroform	Toluene
			acetate	acid			
	307	351	352	348	346	351	360
4 a		438	442	463	442	444	463
4b	303	306	310	307	307	364	316 460

Table 1. Influence of solvent on λ max of dyes **4a,b**.





Scheme 2. Synthesis and acetylation of (E)-6-methyl-2-(2-phenylhydrazono)-4*H*-furo[3,2-*c*] pyran-3,4(2*H*)-diones **4a,b**.



Scheme 3. Possible tautomeric forms of (*E*)-6-methyl-2-(2-phenylhydrazono)-4*H*-

furo[3,2-*c*]pyran-3,4(2*H*)-diones **4a,b**.





Figure 1. PBE1PBE/LANL2DZ calculated potential energy profile of 4a.







Figure 3. Absorption spectra of dye 4a in various solvents.



Figure 4. Absorption spectra of dye 4b in various solvents



Figure 5. The DPPH radical scavenging activity (IC₅₀ μ g/mL) of compounds 1, 3, 4a,b