New Synthesis and Reactivity of 3-Bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one with Binucleophilic Amines

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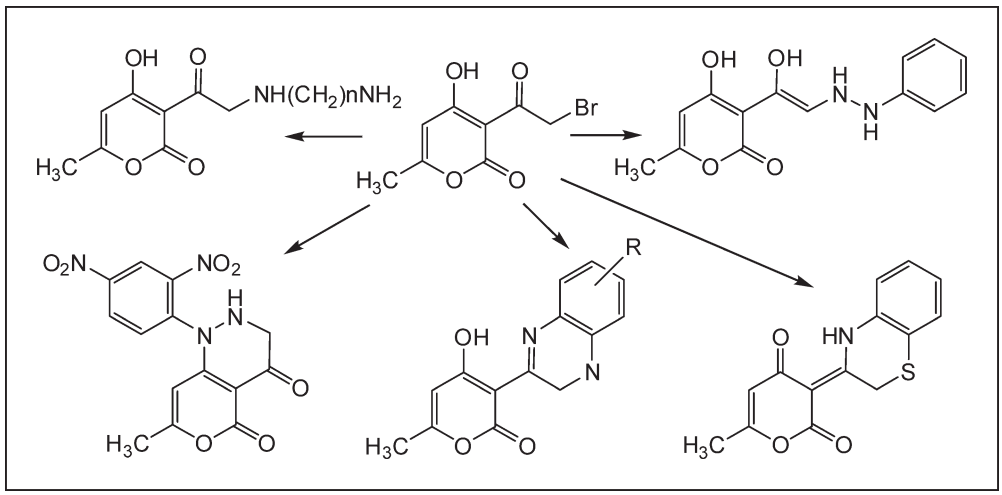

3-(Bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one was synthesized by the reaction of dehydroacetic acid (DHAA) with bromine in glacial acetic acid. Novel heterocyclic products were synthesized from the reaction of bromo-DHAA with alkanediamines, phenylhydrazines, *ortho*-phenylenediamines, and *ortho*-aminobenzenethiol. The obtained new products 3-(2-*N*-substituted-acetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-ones, 4-hydroxy-3-[1-hydroxy-2-(2-phenylhydrazinyl)vinyl]-6-methyl-2*H*-pyran-2-one, 1-(2,4-dinitrophenyl)-7-methyl-2,3-dihydro-1*H*-pyrano[4,3-*c*]pyridazine-4,5-dione, 3-(3,4-dihydroquinoxalin-2-yl)-4-hydroxy-6-methyl-2*H*-pyran-2-one/3-(3,4-dihydroquinoxalin-2-yl)-6-methyl-2*H*-pyran-2,4(3*H*)-dione, 6-methyl-3-(3,4-dihydroquinoxalin-2-yl)-2*H*-pyran-2,4(3*H*)-dione, and (*E*)-3-(2*H*-benzo[b][1,4]thiazin-3(4*H*)-ylidene)-6-methyl-2*H*-pyran-2,4(3*H*)-dione were fully characterized by IR, ^{1}H and ^{13}C NMR, and mass spectra.

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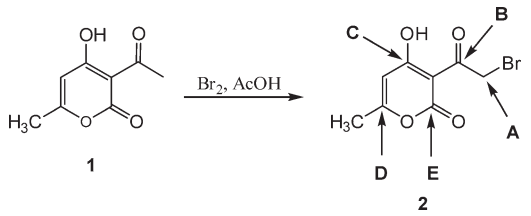
INTRODUCTION

2-Pyrones demonstrate a whole spectrum of bioactivity and have shown 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-hydroxy/alkyl/aryl/alkenyl-substituted-6-methyl-2-pyrones show remarkable biological effects, such as antimicrobial activity, human chronic myelogenous leukemia, and human ovarian carcinoma inhibitory properties [1–3].

The referred biological potential of 2-pyrones let us to start a research program towards the synthesis of 3-substituted-4-hydroxy-6-methyl-2-pyrones. 3-Acetyl-4-hydroxy-6-methyl-2-pyrone (dehydroacetic acid, DHAA) **1** is an industrial available product and the chemistry of this compound was extensively investigated [4–11]. For this reason, we decided to investigate the bromination of the acetyl DHAA group [12–19], since α-bromoketone **2** has been attracting our attention due to its high reactivity as building blocks for the preparation of several classes of compounds and its selective transformations with various nucleophiles. Therefore, DHAA has been reported to generate a number of heterocyclic compounds through ring opening and recyclization upon treatment with a variety of binucleophiles [20,21].

Inspection of the structure **2** suggests that it would be susceptible for the attack of amines at five sites (A, B, C, D, or E) leading to quite different products (Scheme 1). Transformations involving the three reactive sites of

Scheme 1



the pyrone ring and the direct condensation in the bromoacetyl group, in particular with binucleophilic reagents, offer a versatile approach to synthesize of a plethora of 4-hydroxy-6-methyl-2*H*-pyran-2-one analogs [22]. In that way, we decided to study the reactivity of bromo-DHAA **2** with several binucleophilic amines.

RESULTS AND DISCUSSION

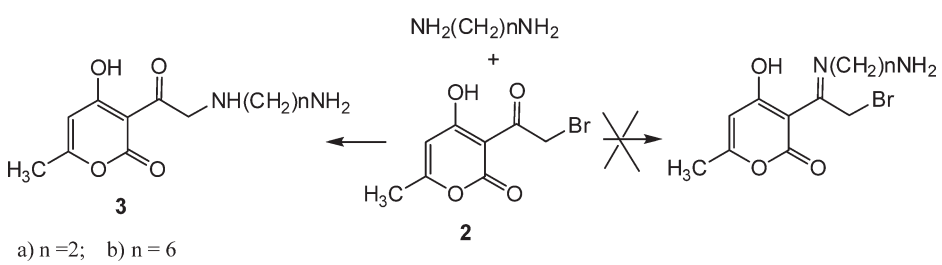
Studies of Harris *et al*. [23] on the bromination of DHAA under different experimental conditions describe a method for the preparation of bromo-DHAA **2**. We have found some difficulties in reproducing this reaction, as the bromination at the acetyl group gives a viscous oil; render the method quite difficult to be scaled up. A modification of this method gives very good results. It involves the treatment of DHAA with one equivalent of bromine in refluxing glacial acetic acid to afford **2** in 70% yield. This method is superior to the one based on the use bromine in an HBr-saturated solution [23].

We started our reactivity studies by refluxing **2** with an equimolecular amount of 1,2-ethanediamine **2** in ethanol. A large amount of product, whose structure was subsequently determined, was isolated on filtration the reaction mixture. Two possibilities of the diamine attack without pyrone ring opening may occur, but only one was observed (Scheme 2). The elemental analysis and the mass spectra of **3** [*m/z* at 227 $(M+H)^+$ and 249 $(M+Na)^+$ for **3a**, *m/z* at 283 $(M+H)^+$ and 305 $[M+Na]^+$ for **3b**] indicate the absence of bromine in the structure and that one molecule of **2** reacted with diamine. These structures were also supported by its ^{1}H NMR spectra, especially by the singlets at δ 2.36–2.38, 6.02, and 12.11–12.12 ppm due to the 6-CH_3, H-5, and 4-OH protons of the 2-pyrone moiety. We also observed the signals from the 1,2-ethanediamine moiety, multiplets at δ 1.35–2.83 ppm from methylene groups, and two three-singlets at δ 4.84–4.85, 7.70–7.72, and 8.90–8.92 ppm due to the α-methylene, NH_2, and NH protons. The existence of the 4-hydroxy-6-methyl-2-pyrone moiety was also confirmed by ^{13}C NMR, mainly by the carbonyl carbon resonances at δ 165.9 (ester) and 196.4–196.5 (ketone) ppm. All these spectroscopic features confirm the generality of the reaction for aliphatic diamines.

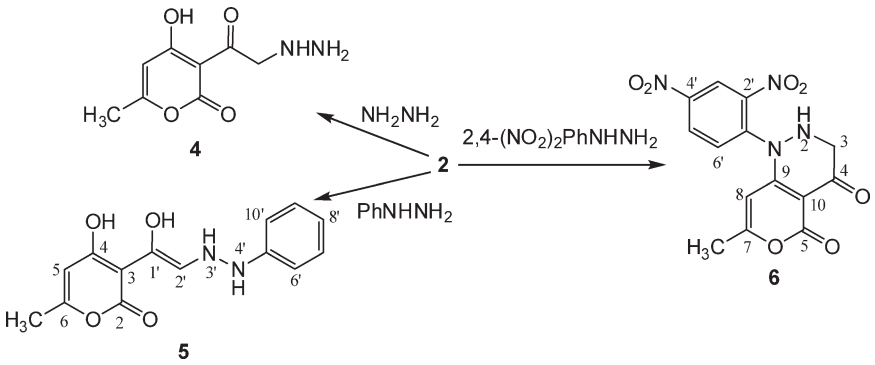
Treatment of **2** with an equimolecular amount of hydrazine gave only one pure product. The analytical data of this product indicate that the reaction took place with the loss of one HBr molecule and keeping a 2-pyrone skeleton. Its mass spectra [molecular ion at *m/z* 199 $(M+H)^+$ and 221 $(M+Na)^+$] indicate the incorporation of one hydrazine molecule. The ^{1}H NMR spectrum of this compound presents three singlets at δ 4.98 (CH_2), 7.66 (NH), and 8.54 (NH_2) ppm, typical signals of the 3-(2-substituted-acetyl)-4-hydroxy-6-methyl-2-pyrone moiety. Its spectrum ^{13}C NMR also confirms the presence of 2-pyrone ring [δ 165.2 (ester) and 183.8 (ketone) ppm]. The referred spectroscopic data are only compatible with the structure of 3-(2-hydrazinylacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** (Scheme 3).

Then we investigated the reaction of phenylhydrazine with **2**, under similar conditions to those reported above, but the transformation did not produce the analog of **4** but a new compound **5**. The molecular ion at *m/z* 275 $(M+H)^+$ and 297 $(M+Na)^+$ suggests the formation of **5** by incorporation of one phenylhydrazine molecule and the elimination of one HBr molecule. The ^{1}H NMR spectrum of **5** presents the typical three signals of 6-CH_3, H-5, and OH of the 2-pyrone moiety. Therefore, other signals are observed at δ 8.81, 9.28, 12.57, and 12.77 ppm, due to resonances of four exchangeable protons, then assigned to the two NH and OH protons, respectively. The connectivities found in the HMBC spectrum of **5** [H-5 (δ 6.95 ppm)→C-6, C-7, and C-3; OH-1′ and H-2′→C-1′] allowed the unequivocal assignments of some of their quaternary carbon resonances and at the same time support the proposed structure **5**.

Scheme 2



Scheme 3

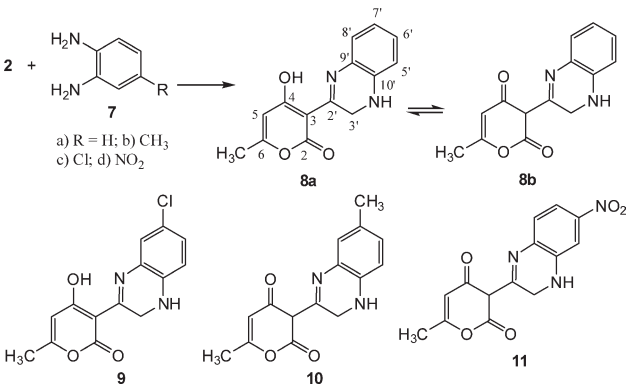


The reaction of **2** with 2,4-dinitrophenylhydrazine (DNPH) in ethanol gave only one pure product **6** (Scheme 3). The mass spectrum of compound **6** and elemental analysis indicates a molecular formula of $C_{14}H_{10}N_4O_7$, which are only compatible with the incorporation of one DNPH molecule and the elimination of single HBr and water molecules relatively to the starting material **2**. The NMR spectra of **6**, namely the singlets at δ 2.32 (7-C*H*$_3$) and 6.06 (H-8) ppm, and those at δ 161.7 (C-7), 165.7 (C-5), 173.9 (C-9), and 189.3 (C-4) support the presence of a 2,3-dihydro-1*H*-pyrano[4,3-*c*]pyridazine-4,5-dione ring. The connectivities found in the HMBC spectrum of **6** (N*H*→C-3 and C-9) also support the proposed structure. The formation of this compound would be explained through the formation of an unstable intermediate (analog of the ketone form of **5**) and gives **6** after a cyclocondensation reaction.

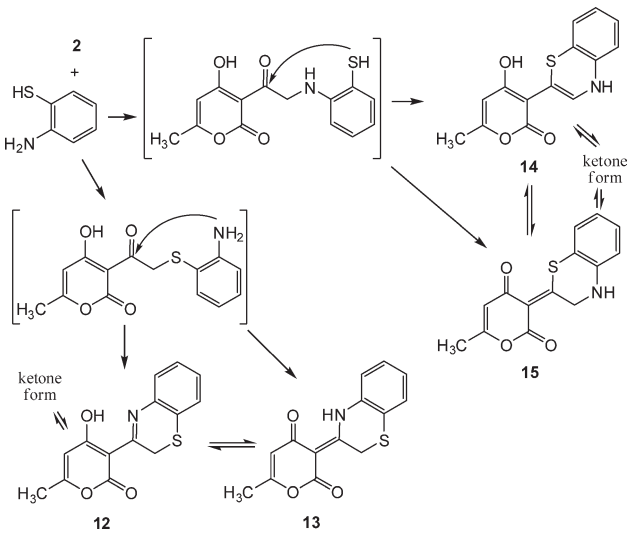
Thereafter, we investigated the reaction of equimolar amounts of **2** with 1,2-phenylenediamines **7a–d** in refluxing ethanol, which gave products **8–11** in excellent yields (Scheme 4). The mass spectrum of the product **8** reveals a molecular ion at *m/z* 257 $(M+H)^+$ and 279 $(M+Na)^+$ indicating the incorporation of one 1,2-phenylenediamine molecule and the elimination of HBr and water molecules. This result would be explained through the cyclocondensation of an α-haloketone. However, the NMR spectra revealed the existence of a keto–enolic equilibrium in a 30:70 ratio. The ^{1}H NMR spectrum showed three signals at δ 15.20, 5.88, and 2.12/2.26 ppm corresponding to the expected 4-OH, H-5, and 6-CH_3 protons of a 2-pyrone moiety. The signal of the major species at δ 4.74 ppm is assigned to the methynic group of the ketone system **8b**. The ^{13}C NMR spectrum of **8** confirms all the carbon resonances of tautomers **8a** (enol form) and **8b** (ketone form) (Scheme 4). The reaction of **2** with 1,2-phenylenediamines **7b–d**, bearing CH_3, Cl, and NO_2 as substituents, yielded in each case a single pure product **9–11** in high yields (confirmed by single resonances in the ^{1}H and ^{13}C NMR), even in the case of electron-withdrawing NO_2 group, which is attenuated by the nucleophilicity of the NH_2 groups. The structure of the obtained products **9–11** was determined by reference to the ring substituents and are a consequence of the starting 1,2-phenylenediamines **7b–d**. When an electron-donating group is present (CH_3, Cl), the 1-NH_2 reacts first, whereas for an electron-withdrawing substituent (NO_2), the 2-NH_2 group reacts first, giving products **9–11** after a cyclocondensation reaction [24–26]. The ^{13}C NMR spectrum of **9** confirms a 4-hydroxy-2-pyrone ring whereas in compounds **10** and **11**, the presence of the methine group of a β-ketoester system is amply confirmed using HSQC and HMBC correlations (H-3→C-3 and C-2′; H-3′→C-3 and C-10; NH→C-5′).

To confirm the formation mechanism of **8–11** and generalize this method of synthesis, we investigated the condensation reaction of **2** with *ortho*-aminobenzenethiol. This transformation can afford the six-membered heterocyclic compounds **12–15**, resulting from the first thiol or amino attack on the bromomethylenic group (Scheme 5). The tlc analysis of the reaction mixture showed that only a single product was formed. The mass spectrum of this product reveals a molecular ion at *m/z* 274 $(M+H)^+$ and 296 $(M+Na)^+$, which is consistent with the molecular formula $C_{14}H_{11}NO_3S$. The ^{1}H

Scheme 4



Scheme 5



NMR spectrum showed the presence of one signal at δ 16.12 ppm, which fits with a strongly deshielded chelated OH or NH proton. The ^{13}C NMR spectrum gives rise to only one resonance for each carbon atom, indicating that only one species is observed in $CDCl_3$ solution. The proton and carbon resonances at δ 4.56 and 24.7 ppm confirms the presence of a thiomethylenic group. Among the possible structures **12–14**, only **13** is confirmed by the connectivities found in their HMBC spectrum (NH→C-3 and C-3′).

In summary, we have shown that the mechanism for the reaction of 3-(bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one **2** with binucleophilic amines involves an initial nucleophilic attack of the most reactive amino group at the bromomethylenic carbon, followed by the attack on the second amino group without opening of the pyrone ring. This condensation reaction gives substituted 2-pyrones in good yield. The results of biological study have shown that compound **10** have an antifungal action.

EXPERIMENTAL

General remarks. Melting points were determined on a Stuart scientific SPM3 apparatus fitted with a microscope and are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solutions on a Bruker Avance 300 (300.13 MHz for ^1H and 75.47 MHz for ^{13}C) spectrometer. Chemical shifts are reported in ppm (δ) using tetramethylsilane (TMS) as internal reference and coupling constants (*J*) are given in Hz. ^{13}C assignments were made using gradient selected heteronuclear single quantum coherence (*g*HSQC) and gradient selected heteronuclear multiple quantum coherence (*g*HMBC) (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 Q-TOF 2 instrument [diluting 1 μL of the sample chloroform solution ($\sim 10^{-5} M$) in 200 μL 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-Visible spectrometer in acetonitrile solutions.

3-(Bromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one (2). A glacial acetic acid solution (10 mL) of bromine (0.80 g, 5 mmol) was added to a hot solution of the DHA (0.84, 5 mmol) in glacial acetic acid (20 mL) and refluxed for 2 h [23]. The reaction mixture was poured in a mixture of water (100 mL) and ice (50 g) and the obtained solid filtered off and recrystallized from the 1:1 hexane–chloroform mixture. This compound was obtained as yellow small crystals. Yield: 70%; mp. 118–119°C (mp. 111–114°C); IR: 3160–3530, 1690–1735, 1717, 1641, 1350, 1260, 1240, 1180, 1150, 1070, 1020, 990 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.31 (d, 3H, $^4J_{5-7}$ = 0.6 Hz, 6-C*H*$_3$), 4.71 (s, 2H, H-2′), 6.03 (s, 1H, H-5), 15.51 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 20.8 (6-*C*H$_3$), 35.2 (C-2′), 99.4 (C-3), 101.3 (C-5), 160.6 (C-6), 170.1 (C-2), 180.9 (C-4), 197.2 (C-1′); ESI(+)-MS: *m/z* 271 [(M+Na)$^+$, ^{81}Br, 269 [(M+Na)$^+$, ^{79}Br, 18), 249 [(M+H)$^+$, ^{81}Br, 90), 247 [(M+H)$^+$, ^{79}Br, 95), 167 [(M-Br)$^+$, 100]. Anal. calcd. for $C_8H_7BrO_4$: C 38.89; H 2.86; Br 32.34. Found: C 39.10; H 2.80; Br 32.51.

General procedure for the synthesis of compounds 3–6, 8–12. A solution of **2** (2.47 g, 10 mmol) and the appropriate binucleophile (10 mmol) in ethanol (30 mL) was refluxed with stirring. After cooling at room temperature, the obtained solid was filtered and recrystallized from ethanol.

3-[2-(2-Aminoethylamino)acetyl]-4-hydroxy-6-methyl-2H-pyran-2-one (3a). This compound was obtained as yellow powder. Yield: 80%; mp. 132°C; IR: 3300, 2930, 1735, 1662, 1600, 1280 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.36 (s, 3H, 6-C*H*3), 2.71–2.74 (m, 2H, H-5′), 2.81–2.83 (m, 2H, H-4′), 4.84 (s, 2H, H-2′), 6.02 (s, 1H, H-5), 7.72 (s, 2H, N*H*$_2$), 8.90 (s, 1H, N*H*), 12.11 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 22.1 (6-*C*H$_3$), 27.1 (C-5′), 44.2 (C-4′), 74.6 (C-2′), 96.6 (C-3), 103.2 (C-5), 163.3 (C-6), 165.9 (C-2), 184.5 (C-4), 196.4 (C-1′); ESI(+)-MS: *m/z* 227 [(M+H)$^+$, 100], 249 [(M+Na)$^+$, 30]; UV: λ_{max} 284 (ε 5.710), 352 (ε, 10.110) nm. Anal. calcd. for C_{10} $H_{14}N_2O_4$: C, 53.09; H, 6.24. Found: C, 53.10; H, 6.26.

3-[2-(6-Aminohexylamino)acetyl]-4-hydroxy-6-methyl-2H-pyran-2-one (3b). This compound was obtained as colored powder. Yield: 84%; mp. 171°C; IR: 3299, 2919, 1727, 1653, 1601, 1255 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.35 (m, 4H, H-6′ and H-7′), 1.54–1.61 (m, 4H, H-5′, and H-8′), 2.38 (s, 3H, and 6-C*H*$_3$), 2.76–2.78 (m, 4H, H-4′, and H-9′), 4.85 (s, 2H, H-2′), 6.02 (s, 1H, H-5), 7.70 (s, 2H, N*H*$_2$), 8.92 (s, 1H, N*H*), 12.12 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 22.1 (6-*C*H$_3$), 25.4 (C-7′), 25.9 (C-6′), 26.9 (C-5′), 27.0 (C-8′), 38.7 (C-9′), 43.7 (C-4′), 74.8 (C-2′), 96.6 (C-3), 103.2 (C-5), 163.3 (C-6), 165.9 (C-2), 184.5 (C-4), 196.3 (C-1′); ESI(+)-MS: *m/z* 283[(M+H)$^+$, 100], 305 [(M+Na)$^+$, 25]; UV: λ_{max} 264 (ε 9.530), 369 (ε 11.550) nm. Anal. calcd. for $C_8H_{14}N_2O_4$: C 56.56; H 7.85. Found: C 56.50; H 7.81.

3-(2-Hydrazinylacetyl)-4-hydroxy-6-methyl-2H-pyran-2-one (4). This compound was obtained as yellow powder. Yield: 80%; mp. 137°C; IR: 3442, 2923, 1724, 1662, 1578, 1280 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.11 (s, 3H, 6-C*H*$_3$), 4.98 (s, 2H,

H-2′), 5.61 (s, 1H, H-5), 7.67 (s, 2H, 4′-N*H*), 8.54 (s, 1H, 3′-N*H*), 12.73 (s, 1H, 4-O*H*); ^{13}C NMR ($CDCl_3$): δ 19.3 (6-*C*H_3), 60.3 (C-2′), 95.1 (C-3), 105.1 (C-5), 166.0 (C-2), 163.1 (C-6), 188.5 (C-4), 194.7 (C-1′); ESI(+)-MS: *m/z* 199 [$(M+H)^+$, 100], 221 [$(M+Na)^+$, 55]; UV: λ_{max} 234 (ε 24.970), 313 (ε 17.920) nm. Anal. calcd. for $C_8H_{10}N_2O_4$: C 48.48; H 5.09. Found: C 48.50; H 5.10.

4-Hydroxy-3-[1-hydroxy-2-(2-phenylhydrazinyl)vinyl]-6-methyl-2H-pyran-2-one (5). This compound was obtained as colored powder. Yield: 85%; mp. 168°C; IR: 3453, 1717, 1660, 1555, 1261 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.09 (s, 3H, 6-CH_3), 5.75 (s, 1H, H-5), 6.95 (s, 1H, H-2′), 7.30–7.32 (m, 5H, Phenyl), 8.81 (s, 1H, 4′-N*H*), 9.28 (s, 1H, 3′-N*H*), 12.57 (s, 1H, 4-O*H*), 12.77 (s, 1H, 1′-O*H*); ^{13}C NMR ($CDCl_3$): δ 19.1 (6-*C*H_3), 94.3 (C-3), 107.7 (C-5), 113.9 (C-7′ and C-9′), 121.9 (C-2′), 128.3 (C-5′), 129.3 (C-6′, C-8′, and C-10′), 143.2 (C-1′), 162.2 (C-6), 165.2 (C-2), 183.8 (C-4); ESI(+)-MS: *m/z* 275 $[(M+H)^+$, 100], 297 $(M+Na)^+$, 84]; UV: λ_{max} 220 (ε 15.970), 313 (ε 11.980) nm. Anal. calcd. for $C_{14}H_{14}N_2O_4$: C 61.31; H 5.14. Found: C 61.30; H 5.12.

1-(2,4-Dinitrophenyl)-7-methyl-2,3-dihydro-1H-pyrano[4,3-c]pyridazine-4,5-dione (6). This compound was obtained as colored powder. Yield: 78%; mp. 150°C; IR: 3421, 2926, 1696, 1653, 1576, 1255 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.32 (s, 3H, 7-CH_3), 5.02 (s, 2H, H-3), 6.06 (s, 1H, H-8), 7.51 (m, 1H, H-6′), 8.45 (m, 1H, H-5′), 9.21 (s, 1H, H-3′), 14.12 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 20.3 (7-*C*H_3), 58.5 (C-3), 99.4 (C-10), 101.6 (C-8), 114.8 (C-6′), 123.7 (C-3′), 129.7 (C-2′), 130.1 (C-5′), 138.2 (C-4′), 143.0 (C-1′), 161.7 (C-7), 165.7 (C-5), 173.9 (C-9), 189.3 (C-4); ESI(+)-MS: *m/z* 347 $[(M+H)^+$, 45], 369 $[(M+Na)^+$, 100]; UV: λ_{max} 222 (ε 17.340), 312 (ε 16.050) nm. Anal. calcd. for $C_{14}H_{10}N_4O_7$: C 48.56; H 2.91. Found: C 48.51; H 2.88.

3-(3,4-Dihydroquinoxalin-2-yl)-4-hydroxy-6-methyl-2H-pyran-2-one (8a)/3-(3,4-dihydroquinoxalin-2-yl)-6-methyl-2H-pyran-2,4(3H)-dione (8b). This compound was obtained as colored powder. Yield: 79%; mp. 168°C; IR: 3442, 2923, 1724, 1662, 1578, 1280 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.12 (s, 3H, 6-CH_3 ketone), 2.26 (s, 3H, 6-CH_3 enol),4.70 (s, 2H, H-3′ ketone), 4.74 (s, 2H, H-3′ enol), 5.22 (s, 1H, H-3 enol), 5.88 (s, 2H, H-5), 6.22–6.99 (m, 8H, Phenyl), 11.25 (s, 1H, N*H* ketone), 11.22 (s, 1H, N*H* enol), 15.20 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.6 (6-*C*H_3 ketone), 20.7 (6-*C*H_3 enol), 43.9 (C-3′ ketone), 55.1 (C-3′ enol), 88.8 (C-3 ketone), 95.3 (C-3 enol), 101.2 (C-5 ketone), 99.4 (C-5 enol), 114.2 (C-5′ ketone), 118.6 (C-7′), 123.3 (C-8′), 128.8 (C-6′), 129.4 (C-9′ enol), 130.4 (C-9′ ketone), 139.3 (C-10′), 162.4 (C-6), 162.7 (C-2), 161.9 (C-2′ enol), 164.2 (C-2′ ketone), 175.1 (C-4 ketone), 188.6 (C-4 enol). ESI(+)-MS: *m/z* 257 $[(M+H)^+$, 100], 279 $[(M+Na)^+$, 40); UV: λ_{max} 224 (ε 24.060), 313 (ε 18.120) nm. Anal. calcd. for $C_{14}H_{12}N_2O_3$: C 65.62; H 7.72. Found: C 65.59; H 7.68.

3-(7-Chloro-3,4-dihydroquinoxalin-2-yl)-4-hydroxy-6-methyl-2H-pyran-2-one (9). This compound was obtained as colored powder. Yield: 84%; mp. 173°C; IR: 3453, 2919, 1717, 1660, 1555, 1261 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.12 (s, 3H, 6-CH_3), 4.76 (s, 2H, H-3′), 5.83 (s, 1H, H-5), 6.51–6.65 (m, 2H, H-6′ and H-8′), 7.07–7.09 (m, 1H, H-5′), 11.22 (s, 1H, N*H*), 15.53 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.6 (6-*C*H_3), 41.7 (C-3′), 96.6 (C-3), 103.3 (C-5), 112.8 (C-5′), 117.1 (C-7′), 120.3 (C-5′), 131.5 (C-9′), 133.6 (C-6′), 139.7 (C-10′), 162.4 (C-6), 162.8 (C-2), 164.2 (C-2′), 176.6 (C-4); ESI(+)-MS: *m/z* 291 $[(M+H)^+$, 100], 313 $[(M+Na)^+$, 70]; UV: λ_{max} 220 (ε 15.970), 313 (ε 11.980) nm. Anal. calcd. for $C_{14}H_{11}ClN_2O_3$: C 57.84; H 3.81. Found: C 57.80; H 3.82.

6-Methyl-3-(7-methyl-3,4-dihydroquinoxalin-2-yl)-2H-pyran-2,4(3H)-dione (10). This compound was obtained as colored powder. Yield: 82%; mp. 167°C; IR: 3462, 2925, 1712, 1642, 1549, 1270 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.11 (s, 3H, 6-CH_3), 2.17 (s, 3H, 6′-CH_3), 4.71 (s, 1H, H-3), 4.92 (s, 2H, H-3′), 5.82 (s, 1H, H-5), 6.45–6.46 (m, 1H, H-5′), 6.69 (s, 1H, H-8′), 6.93–6.96 (m, 1H, H-6′), 11.33 (s, 1H, N*H*); ^{13}C NMR (DMSO-d_6): δ 19.5 (6-*C*H_3), 21.0 (6′-*C*H_3), 55.8 (C-3′), 87.7 (C-3), 99.4 (C-5), 114.2 (C-5′), 118.7 (C-7′), 120.5 (C-8′), 134.0 (C-9′), 137.4 (C-6′), 143.3 (C-10′), 164.1 (C-2), 164.2 (C-2′), 173.9 (C-6), 188.6 (C-4); ESI(+)-MS: *m/z* 271 $[(M+H)^+$, 100], 293 $[(M+Na)^+$, 73]; UV: λ_{max} 218 (ε 26.190), 316 (ε 12.100) nm. Anal. calcd. for $C_{15}H_{14}N_2O_3$: C 66.66; H 5.22. Found: C 66.60; H 5.28.

6-Methyl-3-(6-nitro-3,4-dihydroquinoxalin-2-yl)-2H-pyran-2,4(3H)-dione (11). This compound was obtained as colored powder. Yield: 78%; mp. 182°C; IR: 3421, 2926, 1714, 1653, 1576, 1255 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.16 (s, 3H, 6-CH_3), 4.86 (s, 2H, H-3′), 5.21 (s, 1H, H-3), 5.96 (s, 1H, H-5), 7.73–7.76 (m, 1H, H-8′), 8.12–8.16 (m, 1H, H-7′), 8.48 (s, 1H, H-5′), 11.66 (s, 1H, N*H*); ^{13}C NMR (DMSO-d_6): δ 19.6 (6-*C*H_3), 56.9 (C-3′), 88.1 (C-3), 100.2 (C-5), 111.4 (C-5′), 114.9 (C-7′), 118.4 (C-8′), 143.1 (C-9′), 148.7 (C-6′), 154.9 (C-10′), 163.4 (C-2), 164.0 (C-2′), 170.6 (C-6), 187.1 (C-4); ESI(+)-MS: *m/z* 302 $[(M+H)^+$, 100], 324 $[(M+Na)^+$, 65]; UV: λ_{max} 220 (ε 25.390), 312 (ε 17.780) nm. Anal. calcd. for $C_{14}H_{11}N_3O_5$: C 55.82; H 3.68. Found: C 55.89; H 3.65.

(E)-3-(2H-Benzo[b][1,4]thiazin-3(4H)-ylidene)-6-methyl-2H-pyran-2,4(3H)-dione (13). This compound was obtained as yellow small crystals. Yield: 79%; mp. 177°C; IR: 3500–3300, 2925, 1730, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.18 (s, 3H, 6-CH_3), 4.56 (s, 2H, H-3′), 5.80 (s, 1H, H-5), 7.14–7.34 (m, 4H, H-5′, H-6′, H-7′, and H-8′) 16.12 (s, 1H, N*H*); ^{13}C NMR ($CDCl_3$): δ 20.0 (6-*C*H_3), 24.7 (C-3′), 95.0 (C-3), 107.4 (C-5), 120.8 (C-8′), 125.1 (C-10′), 127.0 (C-6′), 127.2 (C-7′), 127.9 (C-5′), 133.4 (C-9′), 162.9 (C-2), 163.4 (C-2′), 164.0 (C-6), 185.5 (C-4); ESI(+)-MS: *m/z* 274 $[(M+H)^+$, 100], 296 $[(M+Na)^+$, 45]; UV: λ_{max} 247 (ε 25.120), 313 (ε 18.600) nm. Anal. calcd. for $C_{14}H_{11}N_2O_3$: C 61.52; H 4.06. Found: C 61.50; H 4.00.

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