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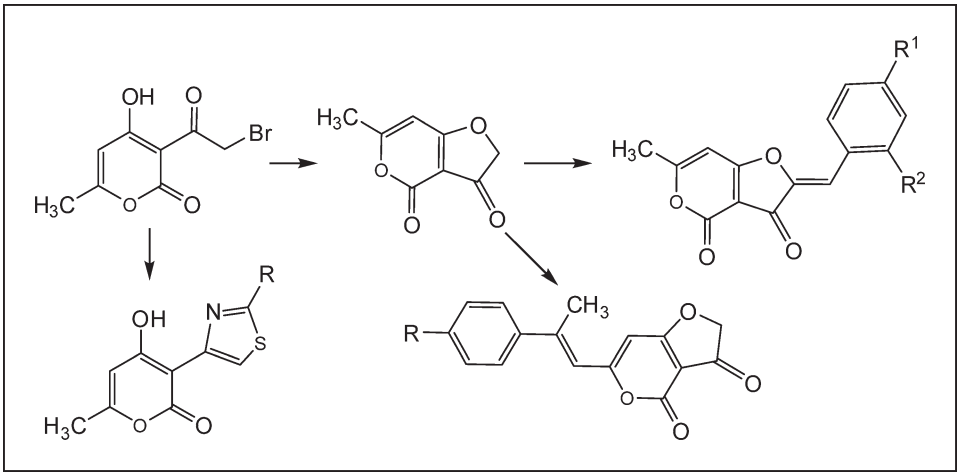

An efficient synthesis of 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one by bromination of dehydroacetic acid in glacial acetic acid is described. Novel 4-hydroxy-6-methyl-3-(2-substituted-thiazol-4-yl)-2*H*-pyran-2-ones have been prepared from the reaction of 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one with thioamides, thiourea, and diphenylthiocarbazone. The condensation reaction of 6-methyl-4*H*-furo[3,2*c*]pyran-3,4-dione, obtained from the reaction of 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one with aliphatic amines, with benzaldehydes and acetophenones led to novel 2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-diones and 6-(2-arylprop-1-enyl)-2*H*-furo[3,2-*c*]pyran-3,4-diones. The structure of all compounds was established by elemental analysis, IR, NMR, and mass spectra.

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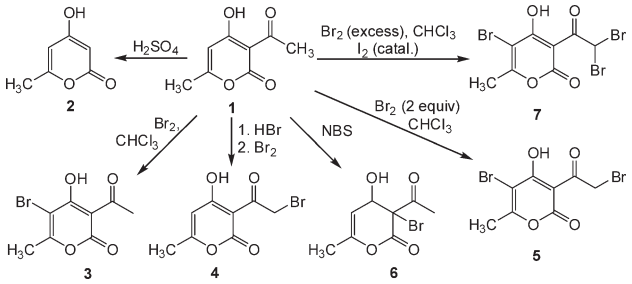
INTRODUCTION

2-Pyrone, a six-membered cyclic unsaturated ester, and its derivatives constitutes a large family of biologically active natural products, abundantly found in animals, insects, plants, bacteria, and microbial systems [1–7]. Small changes in the substitution pattern on the 2-pyrone ring often lead to diverse biological properties. For instance, 4-hydroxy-2-pyrones are considered as one important classes of anti-HIV agents and exhibit a wide range of antifungal, phytotoxic, antimicrobial, cytotoxic, and neurotoxic activities [8–10]. Other 2-pyrone derivatives have shown a huge potential in the treatment of Alzheimer's and other dementia diseases [11,12].

The 3-acetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **1** [dehydroacetic acid (DHA)] is converted into 4-hydroxy-6-methyl-2*H*-pyran-2-one **2** (triacetic lactone) by the action sulfuric acid (Scheme 1) [8]. These two natural occurring 2-pyrones have been extensively studied as building blocks for a wide range of important biologically active heterocyclic compounds, such as pheromones, pyridones, styrylpyrones, pyrazoles, benzodiazepines, and coumarins [13–23]. Therefore, these studies, an efficient synthetic methodology allowing a simple introduction of a plethora of substituents into the structures of these 2-pyrones still constitutes a challenge for the scientific community. Following our interest in the use of DHA as a building block for the synthesis of other heterocyclic compounds, we focused our attention on the selective α-monobromination of DHA, trying to prepare 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4**. Indeed, α-haloketones are versatile building blocks for the preparation of several classes of compounds due to their high reactivity and selective transformation [24]. It is already known that the reaction of DHA with a stoichiometric amount of bromine in

Scheme 1



chloroform yielded the corresponding 5-bromo-DHA **3**, while when the reaction media was saturated with hydrogen bromide prior to the addition of bromine 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** (50% yield) was obtained (Scheme 1). The reaction of DHA with two molar equivalent of bromine gave the 5-bromo-3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **5**, while the reaction with *N*-bromosuccinimide yielded a mixture of compounds (e.g., 3-bromo-DHA **4** and **6**) [25]. Recently, Prakash and coworkers found 5-bromo-3-(dibromoacetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one **7** as the result of the bromination of DHA with an excess of bromine in chloroform and in the presence of a catalytic amount of iodine (Scheme 1) [26,27].

In the present manuscript, we describe a selective monobromination of DHA and the reactivity of the obtained 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** with aliphatic amines, thioamides, thiourea, and diphenylthiocarbazone. We will also report the study on the condensation reaction of 6-methyl-4*H*-furo[3,2-*c*]pyran-3,4-dione **8** with benzaldehydes and acetophenones.

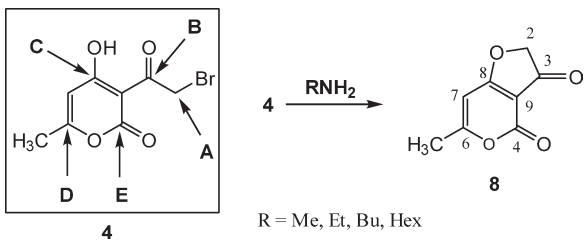
RESULTS AND DISCUSSION

3-Bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** was firstly synthesized by Harris *et al*. [25], but our studies on this hard procedure proved that it did not give reproducible results. Therefore, the knowledge that acidic medium favour α-bromination at the acetyl group led us to consider the treatment of a DHA solution in glacial acetic acid with a stepwise addition of bromine in glacial acetic acid. This new synthetic method afforded pyranone **4** in a simple and reproducible way (Scheme 2). The structure of compound **4** was confirmed by elemental analysis, mass spectra, and ^{1}H and ^{13}C NMR data. Compound **4** was clearly distinguishable from other monobromo derivatives on the basis of its NMR spectra, namely by the resonances of the acetyl methylene group [δ_H 4.71 (s, 2H, CH_2Br), δ_C 35.2 (*C*H_2Br)] suggesting an α-bromination on the methyl group of DHA. The HSQC spectrum allowed the assignment of all protonated carbon resonances while the connectivities found in the HMBC spectrum (e.g., O*H* → C-3, C-4, and C-5; 6-CH_3 → C-5 and C-6) supports the structure of **4**.

Besides the work of Rao and coworkers [28] on the transformation of **4** into the corresponding mercapto derivative, and of Briel *et al*. [29] on their transformation into furanones and other DHA derivatives, the possible reactive sites of compound **4** [26] (Scheme 2) led us to start a program to study their reactivity toward aliphatic amines, thioamides, thiourea, and diphenylthiocarbazone, which will allow the synthesis of a wide range of new heterocyclic compounds. The initial experiments considered the reaction with aliphatic primary amines (methylamine, ethylamine, butylamine, and hexylamine). Heating **4** with an equimolar amount of a primary amine in ethanol for 1 h led to the formation of a single product. The mass spectra of the obtained compound **8** revealed the presence of the peaks at *m*/*z* 167 [(M + H)$^+$] and 189 [(M + Na)$^+$], suggesting the elimination of one HBr molecule relatively to the starting material **4**. On the other hand, the OH resonance was not observed in the ^{1}H NMR spectrum and the two signals at δ_H 2.39 and 4.75 ppm in a 3:2 proportion, assigned to the proton resonances of the methyl and methylene groups, supports the structure of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione (**8**, Scheme 2). The formation of **8** can be envisaged by an intramolecular cyclocondensation assisted by aliphatic amines. The formation of this type of compound has been already reported by heating DHA in the presence of several aliphatic and aromatic amines [30].

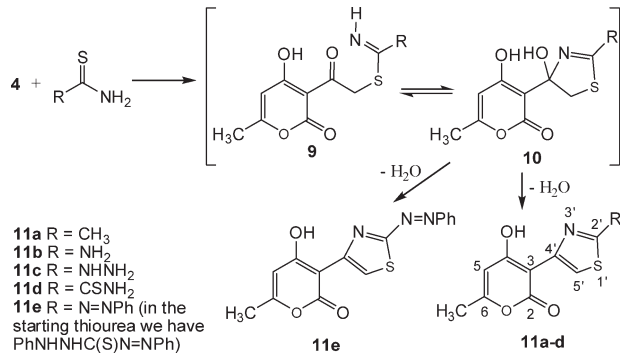
In the second part of our study, we investigated the reactivity of 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** toward various substituted thioamides, thiourea, and diphenylthiocarbazone (Scheme 3). This transformation gives rise to thiazoles, a class of heterocyclic compounds possessing important biological activities [2,3,6,7,9,10,16–22]. Three different procedures (A–C) have been applied in the Hantzsch reaction. The first one (A) consider the conventional Hantzsch reaction [1,4,5,31–45], by refluxing an ethanol solution of **4** with thioamides, thiourea, and diphenylthiocarbazone for 4–6 h, being the reaction products obtained in good yields

Scheme 2



R = Me, Et, Bu, Hex

Scheme 3



and without need of purification. Microwave irradiation was used as an alternative source of heating in the other methods, using ethanol as solvent (B) or in the solvent-free reaction conditions (C). In the latter case, the solid support of neutral aluminium oxide was impregnated with the appropriate thioamides, thiourea, and diphenylthiocarbazone and of **4**. The three methods yielded the same solid compounds **11a–e** (Scheme 3). The main advantage of microwave irradiation was the shortening of the reaction time, from 5 h in the case of procedure A for 5–10 min in procedures B and C, since comparable yields were obtained in all of them (Table 1).

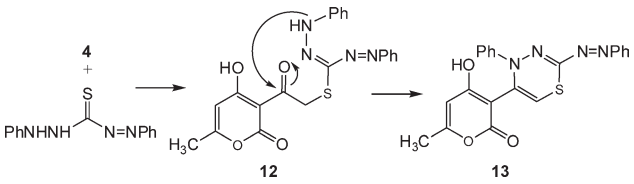
Structure of **11e** was unequivocally determined and suggests the loss of an aniline molecule during its formation. In fact the ^{1}H and ^{13}C NMR spectra support the presence of only one phenyl ring from the starting diphenylthiocarbazone. From the HSQC spectrum, one can conclude that H-5′ (δ_H 8.48 ppm) is bonded to the carbon appearing at δ_C 117.9 ppm, typical of a 2,4-disubstituted thiazole ring. Elemental analysis and mass spectrometry also confirms the presence of an odd number of nitrogen atoms; being the peaks at *m/z* 314 and 336 corresponding to the ions $(M + H)^+$ and $(M + Na)^+$ of a molecule with the formula $C_{15}H_{11}N_3O_3S$. We have tried to isolate some reaction intermediates, but none of our attempts to isolate a six-membered heterocyclic compounds **13** with three heteroatoms was successful (Scheme 4) [46,47]. The formation of a similar six-membered heterocyclic rings can be envisaged in the reaction leading to thiazoles **11b** and **11c** but none of them was observed and the expected compounds were obtained in good yields.

Table 1

Reaction conditions and yields obtained in the reactions of **4** with thioamides, thiourea, and diphenylthiocarbazone.

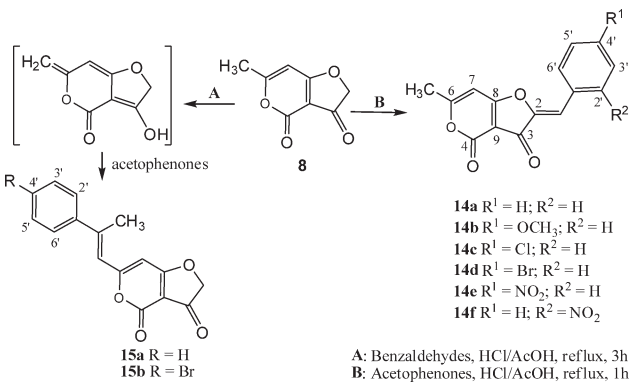
Obtained compounds	Procedure	Power (W)	Reaction time (min)	Yield (%)
11a	A	–	300	70
	B	200	5	82
	C	300	8	72
11b	A	–	240	79
	B	200	7	93
	C	300	10	84
11c	A	–	300	80
	B	200	10	92
	C	300	8	89
11d	A	–	300	75
	B	200	10	88
	C	300	10	82
11e	A	–	360	77
	B	200	5	89
	C	300	10	85

Scheme 4



6-Methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** has two susceptible sites to react with aldehydes and ketones. Following our previous work on this type of reactions [16], we decided to study the reactivity of **8** with benzaldehydes and acetophenones in acid conditions (in a 1:1 mixture of HCl:acetic acid) (Scheme 5). The mass spectra of the reaction products of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** with benzaldehydes prove there was the condensation with only one molecule of aldehyde, while the NMR data reveal the absence of the methylene group of the dihydrofuran ring and the presence of the methyl group ($\delta_H \sim 2.4$ ppm; δ_C 21 ppm) of the pyranone ring. All these data supports the structure of 2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-diones **14a–f**. Therefore, the NMR data of compounds obtained in the reaction of **5** with acetophenones, resulting from the condensation reaction of only one ketone molecule, present the methylene group ($\delta_H \sim 5$ ppm; δ_C 77 ppm) of the dihydrofuran ring and does not have the methyl group of the pyranone ring. The new vinylic

Scheme 5



bond was identified by their proton ($\delta_H \sim 7.5$ ppm;) and carbon [$\delta_C \sim 128$ (=CH) and 136–137 (=C) ppm] resonances. All these data and the connectivities found in the HMBC (=C*H* → =C, *C*H$_3$, C-1′, C-6, and C-7; C*H*$_3$ → vinylic carbons and C-1′) are only compatible with the structure of 6-(2-arylprop-1-enyl)-2*H*-furo[3,2-*c*]pyran-3,4-dione **15a**,**b**.

The reaction of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** with benzaldehydes gives rise to **14a–f** resulting from the condensation with the active methylene group of the furanone ring, while the reaction with acetophenones yielded **15a**,**b** as a result of the condensation with the active methyl group of the pyran ring (Scheme 5). This site selectivity is probably due to the steric hindrance from the acetophenone. These reactions were also carried out under microwave irradiation being obtained the same products in a slight high yield and a shorter reaction time (2–3 min). All the attempts to obtain a double condensation (at methylene and methyl groups) by using a bigger excess of the carbonyl compounds and longer reaction time in classic heating conditions and under microwave irradiation were unsuccessful.

According to the literature data, it is difficult to establish the stereochemistry of compounds similar to **15a–f** [48], but the *Z* isomer is generally the more stable (Austin Model) and more frequent found one [49,50]. Taken into consideration these data, we postulate that we have obtained (*Z*)-2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-diones **14a–f**. In the case of compounds **15a**,**b**, we postulate a (*E*)-stereochemistry based on the steric hindrance between the phenyl and the pyranone rings.

CONCLUSION

In summary, we report herein an efficient methodology for the synthesis of thiazoles **11a–e**, 2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-diones **14a–f**, and 6-(2-arylprop-1-enyl)-2*H*-furo[3,2-*c*]pyran-3,4-diones **15a**,**b**. The synthesis under microwave irradiation of these tethered compounds is straightforward with moderate yields and high purity of the final compounds.

EXPERIMENTAL

General remarks. Melting points were determined on a Stuart scientific SPM3 apparatus fitted with a microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solutions on a Bruker Avance 300 (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C) spectrometer. Chemical shifts are reported in ppm (δ) using TMS as internal reference and coupling constants (*J*) are given in Hz. ^{13}C assignments were made using *g*HSQC and *g*HMBC (delays for one bond and long-range *J* C/H couplings were optimized for 145 and 7 Hz, respectively) experiments. Positive-ion 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–vis spectrometer in acetonitrile solutions.

3-Bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one (4). A solution of bromine (0.27 mL, 5 mmol) in glacial acetic acid (10 mL) was added stepwise to a solution DHA **1** (0.84 g, 5 mmol) in glacial acetic acid (20 mL). After a reflux of 2 h, the reaction mixture was poured into H_2O (100 mL) and ice (50 g). The obtained solid was filtered off and recrystallized from a 1:1 mixture of hexane–chloroform, being 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **3** obtained as yellow crystals (0.75 g, 61%): mp 118–119°C (lit. 111–114°C [25]); IR (ν, cm^{-1}): 3160–3530, 1690–1735, 1717, 1641, 1350, 1260, 1240, 1180, 1150, 1070, 1020, 990; UV (λ_{max}, nm): 236 (ε, 3.289), 328 (ε, 3.223); NMR ($CDCl_3$): δ 2.31 (d, 3H, $J = 0.6$ Hz, 6-C*H*$_3$), 4.71 (s, 2H, C*H*$_2$Br), 6.03 (s, 1H, H-5), 15.51 (s, 1H, O*H*); ^{13}C NMR: δ 20.8 (6-*C*H$_3$), 35.2 (*C*H$_2$Br), 99.4 (C-3), 101.3 (C-5), 160.6 (C-6), 170.1 (C-2), 180.9 (C-4), 197.2 (C=O, ketone); ESI$^{(+)}$-MS: *m*/*z* 271 [(M + Na)$^+$, ^{81}Br, 18], 269 [(M + Na)$^+$, ^{79}Br, 20], 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. Found: C, 39.10; H, 2.80.

6-Methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione (8). A solution of 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** (1.24 g, 5 mmol) and primary aliphatic amines (5 mmol) in ethanol (20 mL) was refluxed, with stirring, for 1 h. After cooling the reaction mixture, the formed solid was filtered off and recrystallized from cold ethanol leading to 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** (0.54 g, 65%): mp 199–200°C; IR (ν, cm^{-1}): 1767, 1694, 1565, 1482, 1450, 1220, 1145; UV (λ_{max}, nm): 267 (ε, 1.228); ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 3H, 6-C*H*$_3$), 4.75 (s, 2H, H-2), 6.22 (s, 1H, H-7); ^{13}C NMR ($CDCl_3$): δ 21.4 (6-*C*H$_3$), 76.5 (C-2), 96.6 (C-7), 101.3 (C-9), 155.6 (C-6), 173.8 (C-4), 188.8 (C-8), 192.1 (C-3); ESI$^{(+)}$-MS: *m*/*z* 189 [(M + Na)$^+$, 64], 167 [(M + H)$^+$, 19]. Anal. Calcd. for $C_8H_6O_4$: C, 57.84; H, 3.64. Found: C, 57.90; H, 3.76.

General procedure for the synthesis of 4-hydroxy-6-methyl-3-(2-substituted-thiazol-4-yl)-2*H*-pyran-2-ones (11a–e). ***Procedure A.*** A solution of 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** (0.24 g, 1 mmol) and the appropriate thioamide, thiourea, and diphenylthiocarbazone (1 mmol) in ethanol (20 mL) was reflux until total consumption of the starting material (see Table 1).

Procedure B. Conditions similar to procedure A save the use of microwave irradiation as source of energy (power and reaction conditions in Table 1).

Procedure C. The mixture of ethyl ether (10 mL), neutral alumina (1 g), the appropriate thioamide, thiourea, or diphenylthiocarbazone (1 mmol) and 3-bromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **4** (0.24 mmol), in a mortar, is ground vigorously until total solvent evaporation. This solid mixture was submitted to microwave irradiation under conditions indicated in Table 1.

4-Hydroxy-6-methyl-3-(2-methylthiazol-4-yl)-2H-pyran-2-one (11a). This compound was obtained as a white solid with mp 140–141°C; IR (ν, cm^{-1}): 3100–3500, 2980, 1754, 1660, 1448, 1490, 1379, 990, 820, 735; UV (λ_{max}, nm): 344 (ε, 0.227); ^{1}H NMR (DMSO-d_6): δ 2.22 (s, 3H, 6-CH_3), 2.23(s, 3H, 6′-CH_3), 6.17 (s, 1H, H-5), 7.13 (s, 1H, H-5′), 14.13 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 20.5 (6-*C*H_3), 35.2 (2′-*C*H_3), 98.4 (C-3), 102.6 (C-5), 101.6 (C-5′), 140.2 (C-4′), 160.8 (C-6), 162.7 (C-2′), 168.7 (C-2), 181.0 (C-4); ESI$^{(+)}$-MS: *m/z* 224 [(M + H)$^+$, 100], 246 [(M + Na)$^+$, 10]. Anal. Calcd. for $C_{10}H_9NO_3S$: C, 53.90; H, 4.06; N, 6.27. Found: C, 53.82; H, 4.02; N, 6.15.

3-(2-Aminothiazol-4-yl)-4-hydroxy-6-methyl-2H-pyran-2-one (11b). This compound was obtained as a yellow solid with mp 290–292°C; IR (ν, cm^{-1}): 3100–3500, 2980, 1754, 1660, 1448, 1490, 1379, 990, 820, 735; UV (λ_{max}, nm): 344 (ε, 0.227); ^{1}H NMR (DMSO-d_6): δ 2.23 (s, 3H, 6-CH_3), 6.18 (s, 1H, H-5), 7.15 (s, 1H, H-5′), 8.40 (s, 2H, NH_2), 14.27 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.4 (6-CH_3), 92.7 (C-3), 101.3 (C-5), 101.9 (C-5′), 139.2 (C-4′), 162.0 (C-6), 168.0 (C-2′), 169.3 (C-2), 178.5 (C-4); ESI$^{(+)}$-MS: *m/z* ESI$^{(+)}$-MS: *m/z* 225 [(M + H)$^+$, 100], 247 [(M + Na)$^+$, 45]. Anal. Calcd. for $C_9H_8N_2O_3S$: C, 48.21; H, 3.60; N, 12.49. Found: C, 48.18; H, 4.00; N, 12.38.

3-(2-Hydrazinylthiazol-4-yl)-4-hydroxy-6-methyl-2H-pyran-2-one (11c). This compound was obtained as a yellow solid with mp 240–242°C; IR (ν, cm^{-1}) 3100–3500, 2980, 1754, 1660, 1448, 1490, 1379, 990, 820, 735; UV (λ_{max}, nm) 344 (ε, 0.227); ^{1}H NMR (DMSO-d_6): δ 2.23 (s, 3H, 6-CH_3), 6.20 (s, 1H, H-5), 7.43 (s, 1H, H-5′), 9.94 (s, 1H, N*H*), 14.02 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.4 (6-*C*H_3), 94.0 (C-3), 101.2 (C-5), 104.5 (C-5′), 141.6 (C-4′), 161.5 (C-6), 168.4 (C-2′), 169.9 (C-2), 179.6 (C-4); ESI$^{(+)}$-MS: *m/z* 240 [(M + H)$^+$, 100], 262 [(M + Na)$^+$, 60]. Anal. Calcd. for $C_9H_9N_3O_3S$: C, 45.18; H, 3.79; N, 17.56. Found: C, 45.01; H, 3.83; N, 17.46.

4-(4-Hydroxy-6-methyl-2-oxo-2H-pyran-3-yl)thiazole-2-carbothioamide (11d). This compound was obtained as a yellow solid with mp 268–269°C; IR (ν, cm^{-1}): 3100–3500, 2980, 1754, 1660, 1448, 1490, 1379, 990, 820, 735; UV (λ_{max}, nm): 344 (ε, 0.227); ^{1}H NMR (DMSO-d_6): δ 2.26 (d, 3H, J = 0.6 Hz, 6-CH_3), 6.31(s, 1H, H-5), 8.52 (s, 1H, H-5′), 10.32 (s, 2H, NH_2), 12.42 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.4 (6-*C*H_3), 94.3 (C-3), 100.9 (C-5), 124.9 (C-5′), 149.3 (C-4′), 161.7 (C-6), 167.6 (C-2′), 169.9 (C-2), 179.3 (C-4), 185.50 (C=S); ESI$^{(+)}$-MS: *m/z* ESI$^{(+)}$-MS: *m/z* 269 [(M + H)$^+$, 100], 291 [(M + Na)$^+$, 55]. Anal. Calcd. for $C_{10}H_8N_2O_3S_2$: C, 44.76; H, 3.01; N, 10.44. Found: C, 44.70; H, 2.95; N, 10.32.

4-Hydroxy-6-methyl-3-(2-(phenyldiazenyl)thiazol-4-yl)-2H-pyran-2-one (11e). This compound was obtained as a red solid with mp 275–277°C; IR (ν, cm^{-1}) 3100–3500, 2980, 1754, 1660, 1448, 1490, 1379, 990, 820, 735; UV (λ_{max}, nm) 344 (ε, 0.227); ^{1}H NMR (DMSO-d_6): δ 2.31(s, 3H, 6-CH_3), 6.09 (s, 1H, H-5), 8.48 (s, 1H, H-5′), 7.58–7.62 (m, 3H, Ph-$H_{ortho\ +\ para}$), 8.01–8.05 (m, Ph-H_{meta}), 13.84 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 20.1 (6-*C*H_3), 94.3 (C-3), 101.5 (C-5), 117.9 (C-5′), 124.1 (Ph-$C_{ortho\ +\ para}$), 129.5 (Ph-C_{meta}), 133.5 (Ph-C_{ipso}), 142.2 (C-4′), 162.2 (C-6), 162.3 (C-2′), 169.0 (C-2), 177.4 (C-4); ESI$^{(+)}$-MS: *m/z* 314 [(M + H)$^+$, 100], 336 [(M + Na)$^+$, 40]. Anal. calcd. for $C_{15}H_{11}N_3O_3S$: C, 57.50; H, 3.54; N, 13.41. Found: C, 57.45; H, 3.43; N, 16.08.

General procedure for the synthesis of 2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione (14a–f). ***Classical heating conditions.*** A solution of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** (0.38 g, 2.3 mmol) and the appropriate benzaldehyde (5 mmol) in a mixture of glacial acetic acid (12 mL) and hydrochloric acid (12 mL) was refluxed, with stirring, for 1 h. After cooling the reaction mixture to room temperature, the obtained solid was collected by filtration and purified by recrystallization from boiling chloroform, yielding 2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-diones (**14a–f**): **14a** (0.28 g, 49%); **14b** (0.37 g, 57%), **14c** (0.34 g, 52%); **14d** (0.44 g, 58%), **14e** (0.35 g, 52%); **14f** (0.31 g, 46%).

Microwave conditions. A solution of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** (0.19 g, 1.15 mmol) and the appropriate benzaldehyde (2.3 mmol) in a mixture of glacial acetic acid (10 mL) and hydrochloric acid (10 mL) was irradiated with microwave radiation (600 W) for a 2–3 min. After cooling the reaction mixture to room temperature, the resulting solid is filtered and recrystallized from chloroform, yielding 2-arylidene-6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-diones (**14a–f**): **14a** (0.16 g, 55%); **14b** (0.20 g, 62%), **14c** (0.19 g, 60%); **14d** (0.24 g, 65%), **14e** (0.20 g, 59%); **14f** (0.18 g, 55%).

2-Benzylidene-6-methyl-2H-furo[3,2-c]pyran-3,4-dione (14a). This compound was obtained as a yellow solid with mp 219–220°C. IR (ν, cm^{-1}): 1767, 1660, 1590, 1480, 1247, 1040, 895, 760, 700; ^{1}H NMR (DMSO-d_6): δ 2.46 (s, 1H, 6-CH_3), 6.84 (s, 1H, H-7), 7.13 (s, 1H, =CH), 7.50–7.53 (m, 1H, H-4′), 7.70–7.73 (m, 2H, H-3′,5′), 7.81–7.84 (m, 2H, H-2′,6′); ^{13}C NMR (DMSO-d_6): δ 21.2 (6-*C*H_3), 96.8 (C-7), 101.0 (C-9), 126.2 (C-3′,5′), 128.0 (C-4′), 128.9 (C-2′,6′), 130.2 (=CH), 132.5 (C-1′), 155.5 (C-6), 169.3 (C-2), 173.9 (C-4), 188.6 (C-8), 193.0 (C-3); ESI$^{(+)}$-MS: *m/z* 255 [(M + H)$^+$, 100], 277 [(M + Na)$^+$, 60]. Anal. Calcd. for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96. Found: C, 70.93; H, 3.99.

2-(4-Methoxybenzylidene)-6-methyl-2H-furo[3,2-c]pyran-3,4-dione (14b). This compound was obtained as a yellow solid with mp 171–172°C. IR (ν, cm^{-1}): 1767, 1662, 1590, 1480, 1247, 1005, 730, 700; ^{1}H NMR (DMSO-d_6): δ 2.39 (s, 1H, 6-CH_3), 3.84 (s, 3H, OCH_3), 6.74 (s, 1H, H-7), 7.15 (s, 1H, =CH), 7.50–7.53 (m, 2H, H-3′,5′), 7.70–7.73 (m, 2H, H-2′,6′); ^{13}C NMR (DMSO-d_6): δ 21.2 (6-CH_3), 56.1 (O*C*H_3), 96.8 (C-7), 101.0 (C-9), 114.2 (C-3′,5′), 130.2 (=CH), 131.0 (C-1′, C-2′,6′), 154.5 (C-4′), 155.5 (C-6), 169.3 (C-2), 174.0 (C-4), 188.6 (C-8), 193.0 (C-3); ESI$^{(+)}$-MS: *m/z* 285 [(M + H)$^+$, 100], 307 [(M + Na)$^+$, 48)]. Anal. Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.25. Found: C, 67.67; H, 4.30.

2-(4-Chlorobenzylidene)-6-methyl-2H-furo[3,2-c]pyran-3,4-dione (14c). This compound was obtained as a yellow solid with mp 268–269°C. IR (ν, cm^{-1}): 1766, 1660, 1593, 1482, 1247, 1040; ^{1}H NMR (DMSO-d_6): δ 2.43 (d, 3H, J = 0.6 Hz, 6-CH_3), 6.97 (d, 1H, J = 0.6 Hz, H-7), 7.05 (s, 1H, =CH), 7.59 (d, 2H, J = 8.6 Hz, H-3′,5′), 7.94 (d, 2H, J = 8.6 Hz, H-2′,6′); ^{13}C NMR (DMSO-d_6): δ 21.2 (6-*C*H_3), 96.8 (C-7), 101.0 (C-9), 127.2 (C-2′,6′), 128.9 (C-3′,5′), 130.2 (=CH), 133.0 (C-1′, C-4′), 155.5 (C-6), 169.3 (C-2), 174.0 (C-4), 188.6 (C-8), 192.9 (C-3); ESI$^{(+)}$-MS: *m/z* 289 [(M + H)$^+$, ^{35}Cl, 48], 291 [(M + H)$^+$, ^{37}Cl, 14], 311 [(M + Na)$^+$, ^{35}Cl, 100], 313 [(M + Na)$^+$, ^{37}Cl, 30]. Anal. Calcd. for $C_{15}H_9ClO_4$: C, 62.41; H, 3.14. Found: C, 62.38; H, 3.10.

2-(4-Bromobenzylidene)-6-methyl-2H-furo[3,2-c]pyran-3,4-dione (14d). This compound was obtained as a yellow solid

with mp 240–241°C. IR (ν, cm^{-1}): 1767, 1661, 1592, 1481, 1247, 1040, 990, 820, 735; ^{1}H NMR (DMSO-d_6): δ 2.43 (d, 3H, J = 0.6 Hz, 6-CH_3), 6.97 (d, 1H, J = 0.6 Hz, H-7), 7.02 (s, 1H, =CH), 7.86 (d, 2H, J = 8.6 Hz, H-3′,5′), 7.72 (d, 2H, J = 8.6 Hz, H-2′,6′); ^{13}C NMR (DMSO-d_6): δ 21.3 (6-CH_3), 96.7 (C-7), 101.0 (C-9), 127.1 (C-2′,6′), 128.9 (C-3′,5′), 130.2 (=CH), 133.0 (C-1′, C-4′), 155.6 (C-6), 169.2 (C-2), 173.9 (C-4), 188.5 (C-8), 192.9 (C-3); ESI$^{(+)}$-MS: m/z 333 [$(M + H)^+$, ^{79}Br, 100], 335 [$(M + H)^+$, ^{81}Br, 98], 355 [$(M + Na)^+$, ^{79}Br, 40], 357 [$(M + Na)^+$, ^{81}Br, 38]. Anal. Calcd. for $C_{15}H_9BrO_4$: C, 54.08; H, 2.72. Found: C, 54.00; H, 2.82.

6-Methyl-2-(4-nitrobenzylidene)-2H-furo[3,2-c]pyran-3,4-dione (14e). This compound was obtained as a yellow solid with mp 220–222°C. IR (ν, cm^{-1}) 1766, 1660, 1592, 1480, 1247, 1040, 1000, 950, 885, 840, 780, 750, 705; ^{1}H NMR (DMSO-d_6): δ 2.43 (d, 3H, J = 0.6 Hz, 6-CH_3), 6.97 (d, 1H, J = 0.6 Hz, H-7), 7.05 (s, 1H, =CH), 7.59 (d, 2H, J = 8.6 Hz, H-2′,6′), 7.94 (d, 2H, J = 8.6 Hz, H-3′,5′); ^{13}C NMR (DMSO-d_6): δ 21.3 (6-*C*H_3), 96.8 (C-7), 101.0 (C-9), 123.9 (C-3′,5′), 127.1 (C-2′,6′), 130.2 (=CH), 139.5 (C-1′), 142.9 (C-4′), 155.6 (C-6), 169.3 (C-2), 173.9 (C-4), 188.6 (C-8), 192.9 (C-3); ESI$^{(+)}$-MS: m/z 300 [$(M + H)^+$, 45], (M^++H, 45), 322 [$(M + Na)^+$, 100]. Anal. Calcd. for $C_{15}H_9NO_6$: C, 60.21; H, 3.03; N, 4.68. Found: C, 60.17; H, 3.00; N, 4.60.

6-Methyl-2-(2-nitrobenzylidene)-2H-furo[3,2-c]pyran-3,4-dione (14f). This compound was obtained as a yellow solid with mp 280–281°C. IR (ν, cm^{-1}): 1766, 1660, 1591, 1480, 1248, 1040, 950, 885, 780, 750; ^{1}H NMR (DMSO-d_6): δ 2.43 (s, 3H, 6-CH_3), 6.92 (s, 1H, H-7), 7.27 (s, 1H, =CH), 7.73–7.76 (m, 1H, H-5′), 7.89-7.91 (m, 1H, H-4′), 8.03–8.05 (m, 1H, H-6′), 8.17–8.20 (m, 1H, H-3′); ^{13}C NMR (DMSO-d_6): δ 21.2 (6-*C*H_3), 96.8 (C-7), 100.9 (C-9), 127.3 (C-3′), 127.4 (C-6′), 128.5 (C-4′), 130.2 (=CH), 131.1 (C-1′), 132.9 (C-5′), 146.2 (C-2′), 155.6 (C-6), 169.3 (C-2), 173.9 (C-4), 188.6 (C-8), 192.9 (C-3); ESI$^{(+)}$-MS: m/z 300 [$(M + H)^+$, 100], 323 [$(M + H)^+$, 48]. Anal. Calcd. for $C_{15}H_9NO_6$: C, 60.21; H, 3.03; N, 4.68. Found: C, 60.19; H, 3.01; N, 4.62.

General procedure for the synthesis of 6-(2-arylprop-1-enyl)-2*H*-furo[3,2-*c*]pyran-3,4-dione (15a,b). ***Classical heating conditions.*** A solution of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** (0.19 g, 1.15 mmol) and appropriate acetophenone (2.3 mmol) in a mixture of glacial acetic acid (12 mL) and hydrochloric acid (12 mL) was refluxed, with stirring, for 3 h. After cooling the reaction mixture to room temperature, the obtained solid was collected by filtration and purified from boiling chloroform, yielding 6-(2-arylprop-1-enyl)-2*H*-furo[3,2-*c*]pyran-3,4-diones (**15a**,**b**): **15a** (0.12 g, 39%); **15b** (0.17 g, 43%).

Microwave conditions. A solution of 6-methyl-2*H*-furo[3,2-*c*]pyran-3,4-dione **8** (0.19 g, 1.15 mmol) and appropriate acetophenone (2.3 mmol) in a mixture of glacial acetic acid (10 mL) and hydrochloric acid (10 mL) was irradiated with microwave radiation (700 W) for a 2–3 min. After cooling the reaction mixture to room temperature, the obtained solid was collected by filtration and purified from boiling chloroform, yielding (*E*)-6-(2-arylprop-1-enyl)-2*H*-furo[3,2-*c*]pyran-3,4-diones (**15a**,**b**): **15a** (0.17 g, 56%); **15b** (0.22 g, 57%).

6-(2-Phenylprop-1-enyl)-2H-furo[3,2-c]pyran-3,4-dione (15a). This compound was obtained as a yellow solid with mp 192–193°C. IR (ν, cm^{-1}): 1740, 1640, 1565, 1440, 1450, 1219, 1132, 895, 760, 700; ^{1}H NMR (DMSO-d_6): δ 2.36 (s, 3H, CH_3), 4.92 (s, 2H, H-2), 6.70 (s, 1H, H-7), 7.41–7.49 (m, 4H, =CH, H-3′,4′,5′), 7.62–7.65 (m, 2H, H-2′,6′); ^{13}C NMR (DMSO-d_6): δ 20.9 (*C*H_3), 77.1 (C-2), 96.8 (C-7), 99.4 (C-9), 127.9 (=CH), 128.5 (C-2′,6′), 128.8 (C-4′), 129.5 (C-3′,5′), 132.5 (C-1′), 137.0 (=C), 155.5 (C-6), 173.9 (C-4), 188.6 (C-8), 192.9 (C-3); ESI$^{(+)}$-MS: m/z 269 [$(M + H)^+$, 100], 291 [$(M + Na)^+$, 65]. Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51. Found: C, 71.70; H, 4.56.

6-(2-Bromophenylprop-1-enyl)-2H-furo[3,2-c]pyran-3,4-dione (15b). This compound was obtained as a yellow solid with mp 188–190°C. IR (ν, cm^{-1}): 1740, 1640, 1566, 1441, 1449, 1219, 1132, 990, 820, 735; ^{1}H NMR (DMSO-d_6): δ 2.39 (s, 3H, CH_3), 5.39 (s, 2H, H-2), 6.84 (s, 1H, H-7), 7.51-7.55 (m, 3H, =CH, H-2′,6′), 7.70–7.72 (m, 2H, H-3′,5′);^{13}C NMR (DMSO-d_6): δ 20.7 (*C*H_3), 77.1 (C-2), 96.8 (C-7), 100.9 (C-9), 128.0 (=CH), 128.3 (C-4′), 128.8 (C-2′,6′), 129.33 (C-3′,5′), 133.1 (C-1′), 135.9 (=C), 155.1 (C-6), 173.1 (C-4), 188.6 (C-8), 193.0 (C-3); ESI$^{(+)}$-MS: m/z 347 [$(M + H)^+$, ^{79}Br, 100], 349 [$(M + H)^+$, ^{79}Br, 98], 371 [$(M + Na)^+$, ^{79}Br, 58], 369 [$(M + H)^+$, ^{81}Br, 60]. Anal. Calcd. for $C_{16}H_{11}BrO_4$: C, 55.36; H, 3.19. Found: C, 56.28; H, 3.12.

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