2*H*-Pyran-2-one-3-carbothioamide Derivatives: Synthesis and Reaction with Hydrazine Hydrate

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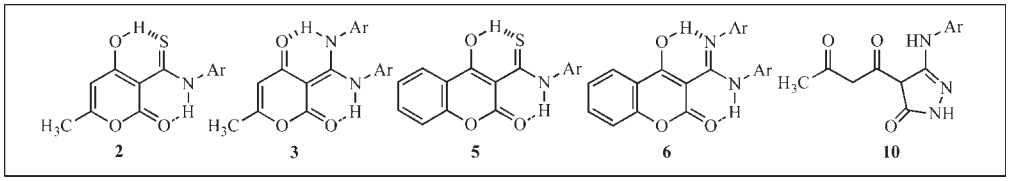

N-Aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothiamides and *N*-aryl-4-hydroxycoumarin-3-carbothiamides were synthesized by the reaction of arylisothiocyanates with 4-hydroxy-6-methylpyran-2-one and 4-hydroxycoumarin, respectively. Novel products 3-[bis(arylamino)methylene]-6-methyl-2*H*,4*H*-pyran-2,4-diones and *N*,*N*′-diaryl-4-hydroxycoumarin-3-carboximidamides have also been obtained in the same reactions. Novel 4-acetoacetyl-3-phenylamino-4,5-dihydro-5*H*-pyrazol-5-ones were synthesized from the reaction of *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothiamides with an excess of hydrazine. The structure of all compounds was established by NMR and mass spectra.

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INTRODUCTION

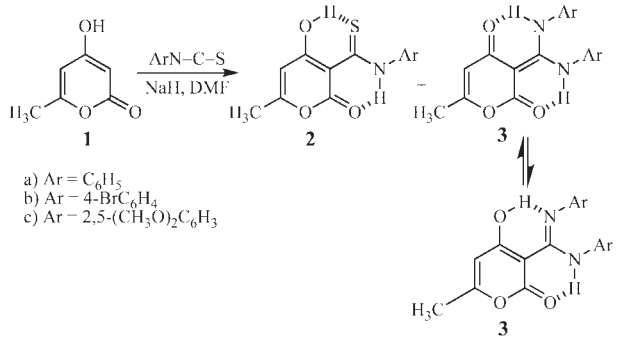
2-Pyrones and coumarins are an important class of heterocyclic compounds presenting important pharmaceutical properties. They have been found in a large number of natural products displaying significant biological activities, and certain synthetic derivatives are biologically active compounds (*e.g.*, potent HIV-1 protease and photosynthetic electron transport inhibitors; presenting sedative, anticonvulsive, anesthetic, and antifungal properties) [1–8]. These important potential applications led to the development of a plethora of synthetic procedures to synthesize pyrone derivatives either by traditional approaches or by transition metal-catalyzed procedures [9–21].

Taking into consideration the referred important biological activities of the 2-pyrones and coumarins and following our studies on the transformations of 4-hydroxy-6-methylpyran-2-one (triacetic acid lactone, TAL) **1** [22] and 4-hydroxycoumarin **4** [23–25], we developed a new synthetic method for *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothioamides **2** and *N*-aryl-4-hydroxycoumarin-3-carbothioamides **5**. In these transformations, novel products 3-[bis(arylamino)methylene]-6-methyl-2*H*,4*H*-pyran-2,4-diones **3** and *N*,*N*′-diaryl-4-hydroxycoumarin-3-carboximidamides **6** have also been obtained. In this communication, the synthesis of novel 4-acetoacetyl-3-arylamino-4,5-dihydro-5*H*-pyrazol-5-ones **10** were also established, by the reaction of *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothioamides **2** with hydrazine hydrate.

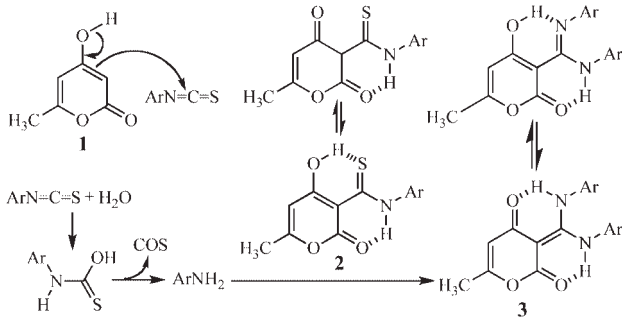
RESULTS AND DISCUSSION

Treatment of 4-hydroxy-6-methylpyran-2-one **1** with arylisothiocyanates in the presence of sodium hydride in DMF for 15 h led to the formation of a solid after the addition of water to the reaction mixture. The aqueous layer was acidified with hydrochloric acid (pH = 4–5), and after vigorous stirring at room temperature for 1.5 h, it led to the formation of a new solid. The elemental analysis and the mass spectra of the first solid indicated the absence of sulfur in the structure and that two molecules of arylisothiocyanates reacted with **1**. In the case of compound **3a**, apart from the molecular ion at *m*/*z* 320 ($C_{19}H_{16}N_2O_3$), its mass spectrum presents peaks corresponding to the loss of Ph—NH_2 and Ph—NH and intense peaks at *m*/*z* 85 and 65 corresponding to the characteristic fragments from cleavage of the 2-pyrone ring. These data suggest the formation of 3-(bis-phenylaminomethylene)-6-methyl-2*H*,4*H*-pyran-2,4-dione **3a**. This structure was also supported by its ^{1}H NMR spectrum, which presents four signals as singlets at δ 2.23, 5.73, 12.00, and 14.18 ppm because of the 6-Me, H-5, and two N*H* proton resonances, respectively. The ^{13}C NMR spectrum of **3a** presents two signals for the resonance of each carbon of the pyrandione moiety: C-3 (δ 85.2 and 104.4 ppm), C-5 (δ 105.8 and 108.4 ppm), C-6 (δ 140.3 and 163.4 ppm), C-4 (δ 178.8 ppm assigned to C—OH; δ 186.2 ppm assigned to C=O), and C-1′ [δ 168.9 ppm assigned to =C(NHAr)$_2$; δ 182.5 ppm

Scheme 1



Scheme 2



assigned to —C(NHAr)=NAr and the signals of the aromatic carbon. The appearance of this type of double ^{13}C NMR spectra is due to the presence of two tautomeric forms of compound **3a** (Scheme 1). All the spectroscopic features of **3b** and **3c** are similar to those described for **3a**, except for the resonances of the aromatic moieties and for the corresponding *m/z* values; confirming the generality of the reaction for other substituted arylisothiocyanates (Scheme 1).

The elemental analysis and the mass spectrum of the second solid are consistent with the structure of *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothiamides **2a–c**, bearing sulfur and nitrogen atoms in the structure. The ^1H NMR spectra of **2a–c** present four singlets at δ 2.29–2.30, 6.36–6.38, 12.70–12.92, and 14.90–15.89 ppm because of the resonance of 6-Me, H-5, NH, and OH, respectively. The ^{13}C NMR spectra of **2a–c** present signals characteristics of the carbothiamoyl group at δ 187.5–189.6 ppm. The mass spectra of **2a–c** present peaks corresponding to the molecular ion followed by the peaks corresponding to the loss of Ar—NH_2 and Ar—NH and intense peaks at *m/z* 85 and 65 corresponding to the characteristic fragments from cleavage of the 2-pyrone ring.

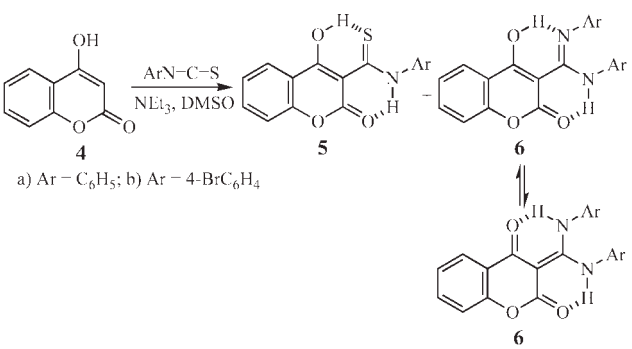
Surprisingly, to the best of our knowledge, 3-[bis(arylamino)methylene]-6-methyl-2*H*,4*H*-pyran-2,4-diones **3a–c** or related compounds have never been described in the literature; however, Bruno et al. have studied an analogous reaction of 5,6-dihydro-4-hydroxy-6-methyl-2*H*-pyran-2-one with arylisothiocyanates under the same experimental conditions and have isolated only 5,6-dihydro derivatives of compounds **2a–c** [26]. The formation of compounds **3a–c** would be explained through the formation of unstable intermediates thiocarbamic acid derivatives from arylisothiocyanates, which yields aniline derivatives after a decarboxylation-type reaction [27] that react with the already formed *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothioamides **2a–c** affording **3a–c** (Scheme 2). The yield of **3a** was considerably dependent on the amount of phenylisothiocyanate; using one molar equivalent 4-hydroxy-6-methyl-*N*-phenyl-2*H*-pyran-2-one-3-carbothioamide **2a** was the major product (75%), while using two molar equivalent led to the formation of 3-[bis(phenylamino)methylene]-6-methyl-2*H*,4*H*-pyran-2,4-dione **3a** as the major product (90%). This condensation was attempted in DMSO as solvent and in the presence of triethylamine giving rise to the expected products **2a** and **3a** in 45 and 55% yield, respectively.

To confirm the formation mechanism of **3a–c**, we have reacted **2a** with one equivalent of aniline in DMF for 2 h at room temperature and **3a** was obtained in good yield (90%).

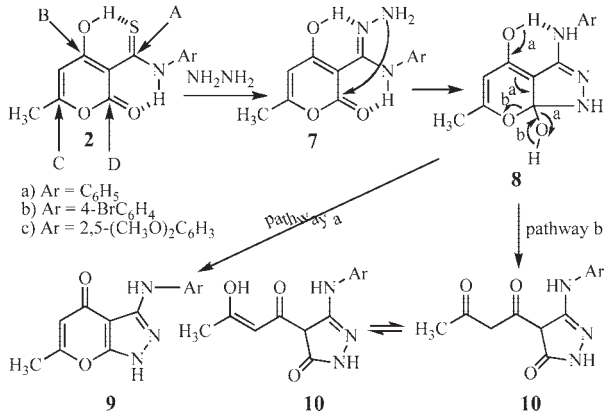
The condensation of 4-hydroxycoumarin **4** with arylisothiocyanates, using DMSO as solvent, gave the corresponding *N*-aryl-4-hydroxycoumarin-3-carbothioamides **5a,b** and also *N,N′*-diaryl-4-hydroxycoumarin-3-carboximidamides **6a,b** (Scheme 3). The ^1H NMR spectra of **5a,b** show two singlets at δ 13.34–13.35 and 17.45–17.60 ppm because of the resonance of NH and OH groups, whereas the ^{13}C NMR spectra show a characteristic carbothiamoyl signal at δ 188.4–189.1 ppm.

The IR spectrum of **6a** presented strong peaks at 1636–1617 and 3479–3407 cm^{-1}, which were attributed to the carbonyl (C=O) and —OH groups on the coumarin ring, respectively. The mass spectra of compounds **6a,b** indicated that the coumarin ring was conserved, with peaks being observed corresponding to the fragmentation of the coumarin ring at *m/z* 134, 143, and 117 [28,29]. From their ^1H NMR spectra, it is possible to observe the presence of signals corresponding to the resonances of two

Scheme 3



Scheme 4



exchangeable protons at δ 13.30–13.35 and 17.46–17.54 ppm, then assigned to the NH and OH groups, respectively. The ^{13}C NMR spectra showed that compound **6a,b** exist as a mixture of two tautomers (Scheme 3).

The next step of our work considered the reaction of compounds **2a–c** with hydrazine hydrate. These compounds **2a–c** have four (A, B, C, D) susceptible centers of nucleophilic attack, three of them into the pyrone ring, and a single molecule of hydrazine would therefore be liable to give a wide range of products (Scheme 4). Compounds **2a–c** reacted with hydrazine hydrate under reflux in a (1:1) mixture of ethanol/acetic acid and yielded only a single isolated solid as the reaction product. Elemental analysis and mass spectra showed that only one molecule of hydrazine had reacted, and the mass spectra also indicated the presence of fragments corresponding to an acetoacetyl group, with peaks at *m/z* 85, 56, and 43. This structure was also supported by the ^1H NMR spectra of **10a–c**, which present five singlets characteristics of a tautomeric equilibrium of acetoacetyl groups at δ 2.06–2.07, 2.32–2.33, 4.30–4.40, 6.11–6.13, and 16.30–16.70 ppm. These signals are assigned to the proton resonances of CH_3 (keto-enol form), CH_3 (β-diketone), CH_2 (β-diketone), CH, and OH (keto-enol form), respectively. We also observed two other singlets at δ 7.90–8.62 and 13.00–13.15 ppm, which were assigned to the NH-pyrazolone and NH—Ar groups, respectively. This condensation reaction allowed us to synthesize novel aminopyrazole derivatives in good yields (95–98%).

An explanation for the formation of pyrazole derivatives **10a–c** considered the hydrazine attack to the thioamide group (center A) of compounds **2a–c** leading to the carboximidamides **7a–c**. An intramolecular nucleophilic attack of the amine group from the amide moiety to the lactone carbonyl carbon (center D) gave rise to intermediates **8a–c**, which can follow two possible pathways (a and b). However, the isolation of pyrazole-type compounds **10a–c** led us to conclude that **8a–c** underwent the opening of the pyran ring by pathway b.

EXPERIMENTAL

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 Bruker Avance 300 (300.13 MHz for ^1H and 75.47 MHz for ^{13}C) and Nujeol GSX 270 WB (270.00 MHz for ^1H and 67.5 MHz for ^{13}C) spectrometers. 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 DEPT-135, HSQC, and HMBC (delays for one bond and long-range *J* C/H couplings were optimized for 145 and 7 Hz, respectively) experiments. Mass spectra are obtained with ESI(+) and GC-MS. 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].

General procedure for the synthesis of *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothioamides (2a–c) and 3-[bis(arylamino)methylene]-6-methyl-2*H*,4*H*-pyran-2,4-diones (3a–c). A solution of arylisothiocyanates (21 mmol) dissolved in 5 mL of DMF was added to a stirred solution of 2.52 g (20 mmol) of 4-hydroxy-6-methylpyran-2-one **1** and 0.576 g (24 mmol) of NaH 20% in mineral oil in 10 mL of DMF, under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 15 h. After this period, 50 mL of cold water was added to the reaction mixture, and the precipitate thus formed was collected by filtration and washed several times with a (1:1) mixture of diethyl ether:light petroleum. The solid was in each case recrystallized from isopropyl alcohol giving 3-[bis-(arylamino)methylene]-6-methyl-2*H*,4*H*-pyran-2,4-diones **3a–c**: **3a**, 1.92 g (30%); **3b**, 1.92 g (20%); **3c**, 3.08 (35%).

The aqueous layer was acidified with HCl 1*N* (pH = 4–5). After vigorous stirring at room temperature for 1.5 h, the precipitate thus formed was collected by filtration and washed several times with diethyl ether. The solid was in each case recrystallized from methanol giving *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothioamides **2a–c**: **2a**, 3.13 g (60%); **2b**, 5.10 g (75%); **2c**, 2.57 g (40%).

4-Hydroxy-6-methyl-N-phenyl-2H-pyran-2-one-3-carbothioamide (2a). This compound was obtained as yellow powder, mp 189–190°C; ^1H NMR ($CDCl_3$): δ 2.30 (s, 3H, C*H*$_3$), 6.37 (s, 1H, H-5), 7.31 (t, 1H, *J* = 7.5 Hz, ArH), 7.43 (t, 2H, *J* = 7.50 Hz, ArH), 7.53 (d, 2H, *J* = 7.5 Hz, ArH), 12.92 (s, 1H, N*H*), 15.89 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 19.1, 97.6, 102.6, 124.8, 127.0, 128.6, 137.1, 162.8, 165.3, 175.7, 187.5; ms (EI): *m/z* 263 (6, ^{34}S), 262 [28, $(M+H)^+$], 261 ($M^{+\cdot}$, 100, ^{32}S), 260 (77), 228 (87), 93 (42), 77 (40), 85 (32), 69 (12). *Anal*. Calcd. for $C_{13}H_{11}NO_3S$ (261.30): C, 59.76; H, 4.24; N, 5.36. Found: C, 60.07; H, 4.60; N, 5.59.

N-(4-Bromophenyl)-4-hydroxy-6-methyl-2H-pyran-2-one-3-carbothioamide (2b). This compound was obtained as yellow powder, mp 190–191°C; ^1H NMR (DMSO-d_6): δ 2.29 (s, 3H, C*H*$_3$), 6.38 (s, 1H, H-5), 7.58 (d, 2H, *J* = 8.0 Hz, ArH), 7.63 (d, 2H, *J* = 8.0 Hz, ArH), 12.70 (s, 1H, N*H*), 15.30 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 20.0, 99.7, 102.9, 120.0, 128.0, 132.7, 137.4, 163.2, 166.0, 174.8, 188.7; ms (ESI+): *m/z* 364 [7, $(M+Na)^+$, ^{81}Br, ^{32}S), 362 [9, $(M+Na)^+$, ^{79}Br, ^{32}S], 342

[80, $(M+H)^+$, ^{81}Br, ^{32}S], 340 [100, $(M+H)^+$, ^{79}Br, ^{32}S]. *Anal*. Calcd. for $C_{13}H_{10}BrNO_3S$ (340.19): C, 45.90; H, 2.96; N, 4.11. Found: C, 45.95; H, 3.01; N, 4.16.

***N*-(2,5-Dimethoxyphenyl)-4-hydroxy-6-methyl-2H-pyran-2-one-3-carbothioamide (2c).** This compound was obtained as yellow powder, mp 169–170°C; ^1H NMR (DMSO-d_6): δ 2.28 (s, 3H CH_3), 3.80 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.36 (s, 1H, H-5), 7.60 (d, 1H, J = 7.3 Hz, ArH), 7.70 (d, 1H, J = 7.3 Hz, ArH), 8.10 (s, 1H, ArH), 12.70 (s, 1H, N*H*), 14.90 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 20.3, 58.0, 60.0, 100.9, 102.7, 125.8, 127.0, 129.6, 131.2, 131.5, 131.8, 162.9, 165.9, 174.0, 189.6; ms (EI): *m/z* 321 (M^{+-}, 45), 233 (100), 221 (5), 189 (8), 125 (8), 116 (10), 85 (20), 69 (55). *Anal*. Calcd. for $C_{15}H_{15}NO_5S$ (321.40): C, 56.06; H, 4.70; N, 4.36. Found: C, 55.95; H, 4.57; N, 4.36.

***3*-[Bis(phenylamino)methylene]-6-methyl-2H,4H-pyran-2,4-dione (3a).** This compound was obtained as yellow powder, mp 147–148°C; ^1H NMR ($CDCl_3$): δ 2.23 (s, 3H, CH_3), 5.73 (s, 1H, H-5), 6.70–6.86 (m, 5H, ArH), 7.14–7.28 (m, 5H, ArH), 12.00 (s, 1H, N*H*) 14.18 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 19.1, 19.5, 85.2, 104.4, 105.8, 108.4, 117.4, 119.8, 123.4, 126.8, 128.2, 129.3, 140.3, 142.1, 144.8, 161.0, 163.4, 168.9, 178.8, 182.5, 186.2; IR: ν (cm^{-1}) 3478, 3209, 3031, 1636, 1550, 1448, 1342, 927, 759, 696; ms (EI): *m/z* 320 (M^{+-}, 18), 227 (14), 194 (38), 93 (100), 85 (4), 69 (17). *Anal*. Calcd. for $C_{19}H_{16}N_2O_3$ (320.34): C, 71.24; H, 5.03; N, 8.74. Found: C, 71.79; H, 5.13; N, 8.72.

***3*-[Bis(4-bromophenylamino)methylene]-6-methyl-2H,4H-pyran-2,4-dione (3b).** This compound was obtained as yellow powder, mp 159–160°C; ^1H NMR (DMSO-d_6): δ 2.27 (s, 3H, CH_3), 5.93 (s, 1H, H-5), 7.43 (d, J = 8.0 Hz, 2H, ArH), 7.49 (d, J = 8.1 Hz, 2H, ArH), 7.55 (d, J = 8.1 Hz, 2H, ArH), 7.62 (d, J = 8.0 Hz, 2H, ArH), 13.20 (s, 1H, N*H*), 14.3 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.6, 20.0, 88.9, 103.3, 108.0, 117.1, 119.9, 126.1, 131.8, 132.3, 135.6, 137.6, 158.7, 162.3, 165.7, 166.3, 174.9, 182.9, 188.8; ms (ESI+): *m/z* 503 [5, $(M+Na)^+$, 2 × ^{81}Br], 501 [9, $(M+Na)^+$, ^{81}Br, ^{79}Br), 499 [4, $(M+Na)^+$, 2 × ^{79}Br], 481 [50, $(M+H)^+$, 2 × ^{81}Br], 479 [100, $(M+H)^+$, ^{81}Br, ^{79}Br], 477 [52, $(M+H)^+$, 2 × ^{79}Br]. *Anal*. Calcd. for $C_{19}H_{14}Br_2N_2O_3$ (478.13): C, 47.73; H, 2.95; N, 5.86. Found: C, 47.78; H, 2.96; N, 5.88.

***3*-[Bis(2,5-dimethoxyphenylamino)methylene]-6-methyl-2H, 4H-pyran-2,4-dione (3c).** This compound was obtained as white powder, mp 186–187°C; ^1H NMR (DMSO-d_6): δ 2.24 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.25 (s, 1H, H-5), 7.40 (d, J = 7.2 Hz, 1H, ArH), 7.58 (d, J = 7.2 Hz, 1H, ArH), 7.60 (s, 1H, ArH), 7.67 (d, J = 8.2 Hz, 1H, ArH), 7.70 (d, J = 8.2 Hz, 1H, ArH), 8.12 (s, 1H, ArH), 13.20 (s, 1H, N*H*), 14.20 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6): δ 19.6, 19.9, 56.6, 88.9, 100.8, 103.3, 124.3, 125.5, 125.6, 126.5, 126.9, 130.8, 131.1, 131.3, 138.8, 139.8, 140.0, 147.0, 149.0, 162.9, 164.0, 165.0, 174.9, 180.0, 189.9; ms (EI): *m/z* 440 (20), 368 (14), 358 (29), 253 (9), 233 (69), 207 (100), 85 (12), 69 (20). *Anal*. Calcd. for $C_{23}H_{24}N_2O_7$ (440.45): C, 60.52; H, H 5.30; N, 6.14. Found: C, 61.07; H, 5.61; N, 6.39.

General procedure for the synthesis of *N*-aryl-4-hydroxycoumarin-3-carbothioamides (5a,b) and *N*,*N*′-diaryl-4-hydroxycoumarin-3-carboximidamides (6a,b). Aryliso-thiocyanates (15 mmol) was added to a stirred solution of 0.81 g (5 mmol) of 4-hydroxycoumarin **4** and 0.8 mL (5 mmol) of triethylamine dissolved in 10 mL of DMSO. The reaction mixture was stirred at room temperature for 15 h. After the addition of 50 mL of cold water, the precipitate thus formed was filtered and washed several times with a (1:1) mixture of diethyl ether:light petroleum. The solid was in each case recrystallized from isopropyl alcohol giving *N*,*N*′-diaryl-4-hydroxycoumarin-3-carboximidamides **6a,b**: **6a**, 979.0 mg (55%); **6b**, 1.15 g (45%).

The aqueous layer was acidified with HCl 1*N* (pH = 4–5). After vigorous stirring at room temperature for 1.5 h, the precipitate thus formed was collected by filtration and washed several times with diethyl ether. The solid was in each case recrystallized from isopropyl alcohol giving *N*-aryl-4-hydroxycoumarin-3-carbothioamides **5a,b**: **5a**, 445.5 mg (30%); **5b**, 659.8 mg (35%).

***4*-Hydroxy-*N*-phenylcoumarin-3-carbothioamide (5a).** This compound was obtained as yellow powder, mp 145–146°C; ^1H NMR ($CDCl_3$): δ 6.88–7.54 (m, 5H, ArH), 7.68–8.17 (m, 4H, ArH), 13.35 (s, 1H, N*H*), 17.60 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 98.2, 117.0, 124.1, 125.4, 126.2, 128.1, 128.9, 129.5, 135.7, 137.7, 152.5, 163.6, 175.1 (C—OH), 189.1 (C=S), ms (ESI+): *m/z* 320 [100, $(M+Na)^+$], 298 [45, $(M+H)^+$]. *Anal*. Calcd. for $C_{16}H_{11}NO_3S$ (297.33): C, 64.63; H, 3.73; N, 4.71. Found: C, 64.68; H, 3.71; N, 4.71.

***N*-(4-Bromophenyl)-4-hydroxycoumarin-3-carbothioamide (5b).** This compound was obtained as yellow powder, mp 270–271°C; ^1H NMR ($CDCl_3$): δ 6.75 (d, 2H, J = 9.8 Hz, ArH), 7.17 (d, 2H, J = 9.8 Hz, ArH), 7.31 (t, 1H, J = 9.0 Hz, ArH), 7.37 (d, 1H, J = 9.0 Hz, ArH), 7.69 (t, 1H, J = 9.0 Hz, ArH), 8.12 (d, 1H, J = 9.0 Hz, ArH), 13.34 (s, 1H, N*H*), 17.45 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 97.3, 116.0, 123.7, 125.3, 126.8, 131.2, 131.7, 134.7, 135.7, 136.0, 151.5, 162.7, 179.4 (C—OH), 188.4 (C=S); ms (ESI+): *m/z* 400 [26, $(M+Na)^+$, ^{81}Br], 398 [29, $(M+Na)^+$, ^{79}Br], 378 [96, $(M+H)^+$, ^{81}Br], 376 [100, $(M+H)^+$, ^{79}Br]. *Anal*. Calcd. for $C_{16}H_{10}BrNO_3S$ (376.23): C, 51.08; H, 2.68; N, 3.72. Found: C, 51.39; H, 3.04; N, 3.95.

***4*-Hydroxy-*N*,*N*′-diphenylcoumarin-3-carboximidamide (6a).** This compound was obtained as white powder, mp 179–180°C; ^1H NMR ($CDCl_3$): δ 6.82–7.68 (m, 10 H, ArH), 8.05–8.10 (m, 4H, ArH), 13.30 (s, 1H, N*H*), 17.54 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 89.3, 97.7, 116.2, 116.5, 120.7, 123.6, 124.0, 124.9, 125.7, 125.8, 127.6, 128.4, 129.0, 135.2, 136.0, 137.2, 152.0, 152.6, 158.7, 163.0, 165.9, 174.6, 179.6, 188.6; IR: ν (cm^{-1}) 3479, 3407, 3235, 1617, 1381, 1048, 754; ms (ESI+): *m/z* 379 [80, $(M+Na)^+$], 357 [100, $(M+H)^+$]. *Anal*. Calcd. for $C_{22}H_{16}N_2O_3$ (356.34): C, 74.15; H, 4.53; N, 7.86. Found: C, 73.60; H, 4.52; N, 7.88.

***N*,*N*′-Di(4-bromophenyl)-4-hydroxycoumarin-3-carboximidamide (6b).** This compound was obtained as white powder, mp 235–236°C; ^1H NMR ($CDCl_3$): δ 6.74 (d, 2H, J = 9.6 Hz, ArH), 7.17 (d, 2H, J = 8.7 Hz, ArH), 7.28 (d, 1H, J = 9.3 Hz, ArH), 7.31 (d, 2H, J = 8.7 Hz, ArH), 7.37 (t, 1H, J = 9.3 Hz, ArH), 7.55 (d, 2H, J = 9.6 Hz, ArH), 7.69 (t, 1H, J = 9.3 Hz, ArH), 8.12 (d, 1H, J = 9.3 Hz, ArH), 13.35 (s, 1H, N*H*), 17.46 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 89.4, 97.4, 116.1, 122.2, 123.8, 124.5, 124.7, 126.9, 131.3, 135.7, 149.2, 151.6, 158.7, 162.7, 166.0, 174.3, 180.2, 189.5; ms (EI): *m/z* 512 (40), 449 (9), 447 (10), 359 (18), 357 (20), 216 (15), 215 (100), 214 (15), 213 (99), 183 (3.9), 181 (4), 158 (2.5), 156 (3), 155 (25), 143 (2), 134 (50), 117 (2), 107 (9), 76 (8). *Anal*.

Calcd. for $C_{22}H_{14}Br_2N_2O_3$ (514.17): C, 51.39; H, 2.74; N, 5.45. Found: C, 51.64; H, 2.80; N, 5.51.

General procedure for the synthesis of 4-acetoacetyl-3-arylamino-4,5-dihydro-5*H*-pyrazol-5-ones (10a–c). Acetic acid (10 mL) and 5 mL ethanol were added to a mixture of *N*-aryl-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-carbothioamides **2a–c** (10 mmol) and 5 mL (0.1 mol) of hydrazine hydrate. The reaction mixture was refluxed for 5 h and poured into crushed ice, and then the solid was collected by filtration, washed with water, and with a (1:1) mixture of water:ethanol. The solid was in each case recrystallized from A (1:1) mixture of ethanol:acetone giving 4-acetoacetyl-3-arylamino-4,5-dihydro-5*H*-pyrazol-5-ones **10a–c** (which are in equilibrium with the corresponding enolic form): **10a**, 2.47 g (95%); **10b**, 3.21 g (95%); **10c**, 3.13 g (98%).

4-Acetoacetyl-3-phenylamino-4,5-dihydro-5H-pyrazol-5-one (10a). This compound was obtained as green powder, mp 179–180°C; ^{1}H NMR ($CDCl_3$): δ 2.06 (s, C*H*$_3$-enol), 2.32 (s, C*H*$_3$-dione), 3.90 (s, 1H, H-4), 4.40 (s, C*H*$_2$-dione), 6.11 (s, C*H*-enol), 7.31–7.53 (m, 5H, ArH), 8.60 (s, 1H, N*H*), 13.15 (s, 1H, N*H*), 16.70 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 20.7, 64.0, 97.2, 104.0, 126.0, 127.6, 129.6, 137.3, 164.2, 164.5, 177.9, 188.3; ms (EI): *m/z* 260 [100, $(M+H)^+$], 228 (80), 217 (9), 203 (7), 175 (20), 93 (67), 77 (47), 85 (50), 56 (14), 43 (20). *Anal*. Calcd. for $C_{13}H_{13}N_3O_3$ (259.26): C, 60.23; H, 5.02; N, 16.22. Found: C, 60.73; H, 5.38; N, 16.45.

4-Acetoacetyl-3-(4-bromophenylamino)-4,5-dihydro-5H-pyrazol-5-one (10b). This compound was obtained as green powder, mp 200–202°C; ^{1}H NMR ($CDCl_3$): δ 2.07 (s, C*H*$_3$-enol), 2.32 (s, C*H*$_3$-dione), 3.91 (s, 1H, H-4), 4.40 (s, C*H*$_2$-dione), 6.11 (s, C*H*-enol), 7.40 (d, 2H, $J = 9.1$ Hz, ArH), 7.56 (d, 2H, $J = 9.1$ Hz, ArH), 8.62 (s, 1H, N*H*), 13.15 (s, 1H, N*H*), 16.50 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 20.1, 65.0, 97.3, 104.0, 121.0, 127.3, 132.2, 136.3, 164.1, 164.7, 178.0, 188.6; ms (ESI+): *m/z* 362 [96, $(M+Na)^+$, ^{81}Br], 360 [100, $(M+Na)^+$, ^{79}Br], 340 [45, $(M+H)^+$, ^{81}Br], 338 [50, $(M+H)^+$, ^{79}Br]. *Anal*. Calcd. for $C_{13}H_{12}BrN_3O_3$ (338.16): C, 46.29; H, 3.56; N, 12.46. Found: C, 45.74; H, 3.20; N, 12.23.

4-Acetoacetyl-3-(2,5-dimethoxyphenylamino)-4,5-dihydro-5H-pyrazol-5-one (10c). This compound was obtained as green powder, mp 186–187°C; ^{1}H NMR ($CDCl_3$): δ 2.07 (s, C*H*$_3$-enol), 2.33 (s, C*H*$_3$-dione), 3.86 (s, 1H, H-4), 3.93 (s, 3H, OC*H*$_3$), 3.95 (s, 3H, OC*H*$_3$), 4.30 (s, C*H*$_2$-dione), 6.13 (s, C*H*-enol), 7.37 (d, 1H, $J = 8.9$ Hz, ArH), 7.49 (d, 1H, $J = 8.9$ Hz, ArH), 7.70 (s, 1H, ArH), 7.90 (s, 1H, N*H*), 13.00 (s, 1H, N*H*), 16.40 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$): δ 20.1, 54.0, 58.0, 65.0, 104.0, 122.7, 125.2, 127.5, 131.3, 132.9, 136.6, 164.1, 164.9, 178.0, 188.0; ms (ESI+): *m/z* 342 [100, $(M+Na)^+$], 320 [33, $(M+H)^+$]. *Anal*. Calcd. for $C_{15}H_{17}N_3O_5$ (319.31): C, 56.43; H, 5.33; N, 13.16. Found: C, 56.98; H, 5.34; N, 13.70.

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