4-Hydroxy-6-methyl-3-(5-phenyl-2*E*,4*E*-pentadien-1-oyl)-2*H*-pyran-2-one: Synthesis and Reactivity with Amines

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The synthesis and reactivity studies of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,4*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** with nucleophiles are reported. Reactions of **2** with hydrazine derivatives gave new pyrazole-type compounds while the reaction with *ortho*-phenylenediamines yielded 1,5-benzodiazepines. The reaction of **2** with ethylamine implies the 2*H*-pyran-2-one ring opening and the formation of a strong conjugated compound **3**.

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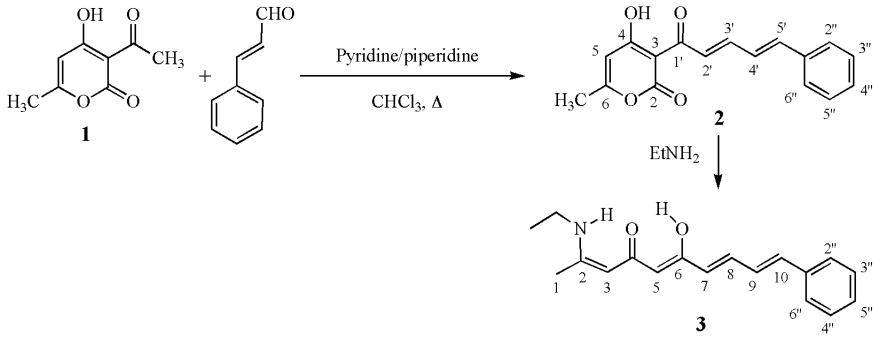
Reactions of aromatic aldehydes with 3-acetyl-4-hydroxy-6-methylpyran-2-one **1** (DHA) and of the obtained compounds [3-(3-aryl-2*E*-propen-1-oyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one] with amines have been the subject of some research groups [1-6]. Following our work on this field, we report here reactions of **1** with cinnamaldehyde and of the obtained product **2** with amines and hydrazine derivatives.

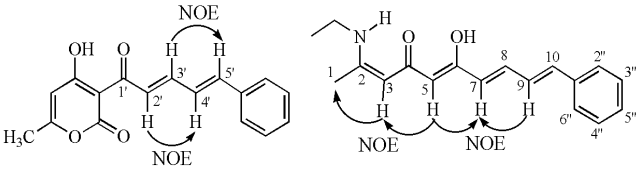
Treatment of DHA **1** with an equimolar amount of cinnamaldehyde in the presence of catalytic amounts of piperidine and pyridine gave 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,4*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** in very good yield (92%). Mass spectrum of **2** indicate that an aldol reaction occurs while the nmr data indicate that an α,β,γ,δ-unsaturated system is present in the molecule. The coupling constant values ($^3J_{H2'\text{-}H3'}$ = 14.8 Hz; $^3J_{H4'\text{-}H5'}$ = 15.2 Hz) allowed us to establish as *trans* the stereochemistry of the two double bonds. However, the stereochemistry of the α,β,γ,δ-unsaturated moiety of **2** was established by NOESY experiments, where a close proximity between H-2' and H-4' and also between H-3' and H-5' have been found (Figure 1), thus allowing us to establish

Scheme 1



as *trans(s-trans)-trans* the stereochemistry of the compounds **2** as shown in Scheme 1 and Figure 1.

Treatment of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,4*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** with an equimolar amount of ethylamine gave a new compound **3**. Its mass spectrum (molecular ion at m/z 283) indicate the incorporation of one ethylamine molecule and a decarboxylation, while the nmr spectra reveals the presence of an α,β,γ,δ-unsaturated system plus two vinylic protons (instead of one in the case of **2**) and one NH proton. Careful analysis of the HSQC spectrum confirm the presence of all these vinylic carbons while the connectivites found in the HMBC spectrum (NH → C-1, CH_2 and C-3; H-3 → C-1, C-2, C-4 and C-5; H-5 → C-3, C-4, C-6 and C-7) supports the structure of compound **3**. The stereochemistry of 2-ethylamino-6-hydroxy-10-phenyl-2*Z*,5*Z*,7*E*,9*E*-decatetraen-4-one **3** was established by the analysis of its NOESY spectrum, which presented NOE cross peaks between H-1 → H-3 → H-5 → H-7 → multiplet of H-8 and H-9 (Figure 1). Since the resonances of H-8 and H-9 appear as a multiplet, it was not possible to either determine their coupling constant or their relative spatial position. However the structure and the full stereochemistry were confirmed by single crystal X-ray analysis (Figure 2) [7,8].



2 **3**

Figure 1

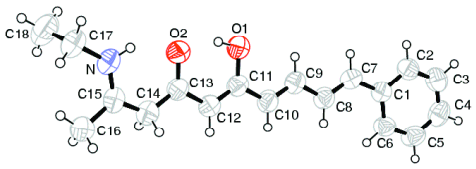


Figure 2

The reactivity of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,4*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** with some binucleophiles was also studied. Reaction of **2** with hydrazine gave 5-(2-hydrazino-6-phenyl-3*E*,5*E*-hexadien)-3-methyl-1*H*-pyrazole **4**. From the ^{1}H nmr spectrum of **4** one can identify an α,β,γ,δ-unsaturated system (δ 6.46, 6.68, 6.90 and 6.64 ppm, respectively), a methylene group ($\delta_{H\text{-}1'}$ 3.77 ppm) and a typical H-4 (δ_H 5.91 ppm) of a 3,5-disubstituted pyrazole. The coupling constants values ($^3J_{H3'\text{-}H4'}$ = 15.5 Hz; $^3J_{H4'\text{-}H5'}$ = 10.4 Hz; $^3J_{H5'\text{-}H6'}$ = 15.7 Hz) allowed us to establish as *trans* the stereochemistry of the two double bonds. However, the stereochemistry of the all α,β,γ,δ-unsaturated moieties of **4** was established by NOESY experiments, where a close proximity between H-3' and H-5' and also between H-4' and H-6' has been found, thus allowing us to establish as *trans(s-trans)-trans* the stereochemistry of the compound **4** as shown in Scheme 2 and Figure 3. A close proximity between methylenic protons (H-1') and H-3' and H-4' and those of the 3-methyl group were also observed. From the NMR data it is observed only one tautomer of pyrazole **4** (no prototropy was observed), this can probably be due to a week intramolecular hydrogen bond between the NH and the hydrazino group, although the NH resonance it was not observed in the ^{1}H NMR spectrum. The connectivities found in the HMBC spectrum of pyrazole **4** (3-CH_3 → C-3 and C-4; H-4 → C-3 and C-5; H-1' → C-4, C-5 and C-2') allowed the unequivocal assignments of their C-3, C-5 and C-2' resonances and at the same time support the proposed structure. This structure indicates that the reaction of pyran-2-one **2** with hydrazine involves the opening of the pyran-2-one ring followed by decarboxylation, ring closure into pyrazole and also the formation of a hydrazone (Figure 3).

Reaction of pyran-2-one **2** with phenylhydrazine gave only 1-phenyl-2-pyrazoline **5**. The resonances of the two non-equivalent methylene protons (H-4' at δ 3.51 and 3.95 ppm), the methynic proton (H-5' at δ 4.79 ppm) and that of the C-3' carbon (δ 150.6 ppm) confirm the presence of the 2-pyrazoline ring in structure **5**. The signal at δ 13.34 ppm was assigned to the hydroxylic proton (4-OH) and indicates an intramolecular hydrogen bond with the nitrogen N-2 of the pyrazoline ring. The assignment of the other proton and carbon resonances were based on the 2D nmr (COSY, HSQC, HMBC and NOESY) spectra of 2-pyrazoline **5** and also on the data described for compound **2**. Since the reaction of **2** with phenylhydrazine was carried out in a neutral medium, the mechanism of the reaction involves the formation of a hydrazone (reaction of the primary amine with the carbonyl group) followed by a conjugate addition of the secondary amine to the vinylic system.

Treatment of pyran-2-one **2** with *o*-phenylenediamines yielded only a single reaction product (Scheme 2). The mass spectra of the obtained compounds **6a-c** revealed the addition of one phenylenediamine molecule and the elimination of a water molecule relatively to the starting material **2**. The nmr spectra of these compounds revealed the presence of one methylene and one methyne groups whereas the chemical shift of the starting material carbonyl group (~δ 192 ppm) was absent and was replaced by another at ~ δ 173 ppm. These data are only compatible with the structure of compounds **6a-c**. In the NOESY spectrum of **6b** NOE cross peaks were observed between signals of NH, H-9' and 8'-CH_3, while in the case of **6c** there was NOE cross peaks between NH and H-9'. These data support the structure of compounds **6** and seems to indicate that the mechanism of

Scheme 2

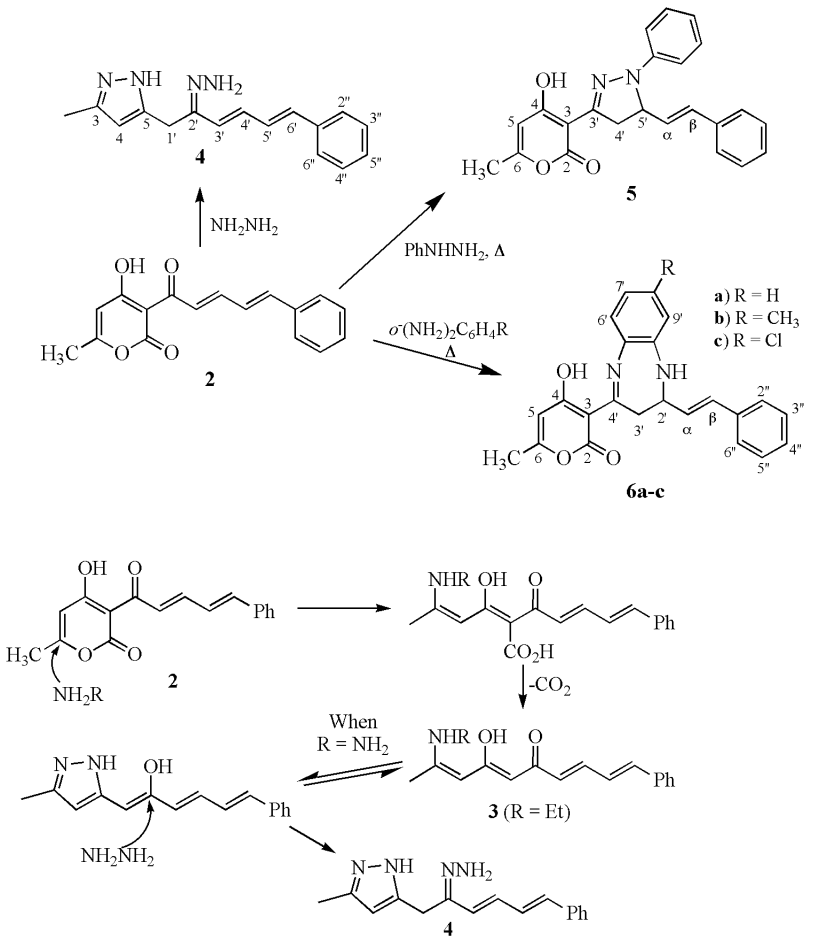


Figure 3

the reaction must involve the attack of the more nucleophilic amine (*para* relative to the substituent of the phenylenediamine) to the carbonyl group of the pyran-2-one **2**, leading to a hydrazone formation, followed by a conjugate addition of the other amine group to the vinylic system.

EXPERIMENTAL

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 deuteriochloroform solutions, on a Bruker DRX 300 spectrometer, operating at 300.13 and 75.47 MHz, respectively; the chemical shifts are expressed in δ (ppm) and coupling constants (*J*) in Hertz (Hz). ^{1}H assignments were made by using 2D COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made using HSQC and HMBC (delays for long-range $J_{C/H}$ coupling constants were optimised for 7Hz) experiments. Electron impact mass spectra were obtained at 70 eV electron impact ionisation using Nermag R 10-10C quadruple mass spectrometer. Infrared spectra were recorded on Magna-IR 550 series II Nicolet apparatus, using potassium bromide pellets. UV spectra were recorded on Cary 50 Scan UV-Visible spectrometer in chloroform solutions

4-Hydroxy-6-methyl-3-(5-phenyl-2*E*,5*E*-pentadien-1-oyl)-2*H*-pyran-2-one (**2**).

A mixture of piperidine (10 drops) and pyridine (10 drops) was added to a solution of 8.4 g of DHA **1** (50.0 mmol) and 6.3 ml of cinnamaldehyde (50.0 mmol) in 50 ml of chloroform. The reaction mixture was refluxed in a steam dark apparatus with stirring for 1 hour. After cooling the solution the solvent was evaporated to dryness and the obtained residue crystallised from ethanol yielding 12.97 g of **2** (92%) as orange crystals, mp 180 °C; ^{1}H nmr (deuteriochloroform): δ 2.26 (d, 3 H, 6-C*H*$_3$, *J* = 0.6 Hz), 5.92 (d, 1 H, H-5, *J* = 0.6 Hz), 7.03 (dd, 1 H, H-5', *J* = 15.2 Hz), 7.04-7.15 (m, 1 H, H-4'), 7.30-7.41 (m, 3 H, H-3'',4'',5''), 7.50 (dd, 2 H, *J* = 1.6 and 7.9 Hz, H-2'',6''), 7.70-7.85 (m, 1 H, H-3'), 7.84 (d, 1 H, H-2', *J* = 14.8 Hz), 18.06 (s, 1 H, O*H*); ^{13}C nmr (deuteriochloroform): δ 20.6 (C-7), 99.3 (C-3), 102.5 (C-5), 126.2 (C-2'), 127.3 (C-4'), 127.5 (C-2'',6''), 128.8 (C-3'',5''), 129.5 (C-4''), 135.9 (C-1''), 143.4 (C-5'), 146.7 (C-3'), 161.2 (C-2), 168.3 (C-6), 183.3 (C-4), 192.2 (C-1'); ms: m/z 282 ($M^{+\bullet}$, 10), 263 (4), 253 (4), 198 (7), 170 (10), 153 (14), 141 (15), 128 (67),

115 (30), 85 (37), 77 (32), 69 (51), 63 (51), 51 (29), 43 (100), 41 (28); ir: (ν, cm^{-1}) 3469, 3422, 3234, 3093, 2999, 1730, 1716, 1615, 1508, 1470, 1383, 1253, 1152, 994, 664; uv: (λ_{max}, nm) 275 (ε, 0.478), 318 (ε, 0.385), 378 (ε, 0.509).

Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.10; H, 4.95.

2-Ethylamino-6-hydroxy-10-phenyl-2*Z*,5*Z*,7*E*,9*E*-decatetraen-4-one (**3**).

A solution of 2.82 g of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,5*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** (10 mmol) and ethylamine (10 mmol) in 40 ml of ethanol was refluxed with stirring for 4 hours. After solvent evaporation and recrystallisation in ethanol, 2.29 g of 2-ethylamino-6-hydroxy-10-phenyl-2*Z*,5*Z*,7*E*,9*E*-decatetraen-4-one **3** have been obtained as coloured crystals (80.9%), mp 162°C; ^{1}H nmr (dimethylsulfoxide-d_6): δ 1.16 (t, 3 H, NCH_2CH_3, *J* = 7.2 Hz), 2.00 (s, 3 H, H-1), 3.28-3.34 (m, 2 H, NCH_2CH_3), 4.83 (s, 1 H, H-3), 5.31 (s, 1 H, H-5), 6.15 (d, 1 H, H-7, *J* = 14.0 Hz), 6.88 (d, 1 H, H-10, *J* = 14.7 Hz), 7.03-7.10 (m, 2 H, H-8 and H-9), 7.28 (t, 1 H, H-4', *J* = 7.3 Hz), 7.37 (t, 2 H, H-3',5', *J* = 7.3 Hz), 7.52 (d, 2 H, H-2',6', *J* = 7.3 Hz), 10.22 (t, 1 H, N*H*, *J* = 5.7 Hz), 15.14 (s, 1 H, 6-O*H*); ^{13}C nmr (dimethylsulfoxide-d_6): δ 15.2 (NCH_2CH_3), 18.8 (C-1), 37.6 (CH_2), 94.5 (C-3), 102.6 (C-5), 126.8 (C-2',6'), 127.5 (C-7), 127.9 (C-9), 128.3 (C-4'), 128.8 (C-3',5'), 134.4 (C-8), 136.3 (C-10), 136.6 (C-1'), 164.6 (C-2), 166.3 (C-6), 188.6 (C-4); ms: m/z 283 ($M^{+\bullet}$, 7), 213 (5), 192 (8), 164 (10), 141 (6), 128 (20), 112 (100), 94 (10), 84 (12), 85 (28), 77 (7), 70 (27), 55 (8), 42 (45); ir: (ν, cm^{-1}) 3455, 3400, 29779, 1599, 1547, 1515, 1420, 1303, 997, 809, 756, 691, 668; uv: (λ_{max}, nm) 345 (ε, 1.33), 414 (ε, 0.625).

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 75.95; H, 7.40, N, 4.89.

Synthesis of 5-(2-Hydrazino-6-phenyl-3*E*,5*E*-hexadien)-3-methyl-1*H*-pyrazole (**4**).

A solution of 2.82 g of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,5*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** (10 mmol) and hydrazine hydrate (10 mmol) in 25 ml of ethanol was stirred for 24 hours and then heated at reflux for 5 min. After cooling to room temperature the obtained solid was collected by filtration, washed with 10 ml of acetone and recrystallised from ethanol; 918 mg of 5-(2-hydrazino-6-phenyl-3*E*,5*E*-hexadien)-3-methylpyrazole **4** were obtained (38.4%), mp 140 °C; ^{1}H nmr (deuteriochloroform): δ 2.27 (s, 3 H, 3-CH_3), 3.77 (s, 2 H, H-1'), 5.91 (s, 1 H, H-4), 6.46 (d, 1 H, H-3', *J* = 15.5 Hz), 6.68 (dd, 1 H, H-4', *J* = 10.4 and 15.5 Hz), 6.64 (d, 1 H, H-6', *J* = 15.7 Hz), 6.90 (dd, 1 H, H-5', *J* = 10.4 and 15.7 Hz), 7.22 (t, 1 H, H-4", *J* = 7.4 Hz), 7.32 (t, 2 H, H-3",5", *J* = 7.4 Hz), 7.41 (d, 2 H, H-2",6", *J* = 7.4 Hz); ^{13}C nmr (deuteriochloroform): δ 11.3 (3-CH_3), 23.8 (C-1'), 103.7 (C-4), 126.4 (C-2",6"), 127.7 (C-4"), 128.7 (C-3",5"), 129.0 (C-5'), 130.4 (C-4'), 133.2 (C-3'), 133.4 (C-6'), 137.1 (C-1"), 141.4 (C-3), 147.1 (C-5), 149.1 (C-2'); ms: m/z 266 ($M^{+\bullet}$, 35), 250 (20), 189 (80), 171 (40), 163 (32), 154 (73), 144 (13), 128 (73), 115 (77), 102 (25), 95 (100), 91 (45), 83 (96), 77 (72), 65 (52), 51 (53), 42 (72); ir: (ν, cm^{-1}) 3000-3200, 3500, 1650, 1579, 1444, 1305, 1257, 1070, 993, 755, 748, 690; uv: (λ_{max}, nm) 329(ε, 1.618).

Anal. Calcd. for $C_{16}H_{18}N_4$: C, 72.15; H, 6.81; N, 21.04. Found: C, 72.00; H, 6.75; N, 20.95.

(*E*)-4-Hydroxy-6-methyl-3-(1-phenyl-5-styryl-4,5-dihydropyrazol-3-yl)-2*H*-pyran-2-one (**5**).

A solution of 2.82 g of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,5*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** (10 mmol) and phenylhydrazine (10 mmol) in 40 ml of ethanol was refluxed with stirring for 4 hours. After solvent evaporation and recrystallisation in ethanol, 3.05 g of (*E*)-4-hydroxy-6-methyl-3-(1-phenyl-5-styryl-4,5-dihydropyrazol-3-yl)-2*H*-pyran-2-one **5** (82%) was obtained, mp 146 °C; ^{1}H nmr (deuteriochloroform): δ 2.26 (s, 3 H, 6-CH_3), 3.51 (dd, 1 H, *J* = 7.4 and 18.8 Hz, H-4'), 3.95 (dd, 1 H, *J* = 11.6 and 18.8 Hz, H-4'), 4.79 (dt, 1 H, *J* = 7.4 and 11.6 Hz, H-5'), 6.03 (s, 1 H, H-5), 6.27 (dd, 1 H, *J* = 7.4 and 15.9 Hz, H-α), 6.63 (d, 1 H, *J* = 15.9 Hz, H-β), 6.89 (t, 1 H, *J* = 7.3 Hz, H-4"), 7.06 (d, 2 H, *J* = 7.9 Hz, H-2",6"), 7.21-7.37 (m, 7 H, H-3",5" and N-Ph), 13.34 (s, 1 H, 4-O*H*); ^{13}C nmr (deuteriochloroform): δ 20.2 (CH_3-6), 43.4 (C-4'), 62.0 (C-5'), 94.8 (C-3), 101.1 (C-5), 113.6 (C-2',6 of N-Ph), 120.2 (C-4 of N-Ph), 126.5 (C-2",6"), 127.9 (C-α), 128.4 (C-4), 128.6 (C-3",5"), 129.2 (C-3,5 of N-Ph), 132.0 (C-β), 136.0 (C-1"), 144.5 (C-1 of N-Ph), 150.6 (C-3'), 162.5 (C-2), 163.2 (C-6), 170.5 (C-4); ms: m/z 372 ($M^{+\bullet}$, 100), 329 (5), 280 (14), 269 (65), 237 (7), 211 (8), 196 (10), 185 (19), 167 (11), 153 (11), 141 (7), 128 (26), 115 (21), 91 (26), 85 (21), 77 (47), 64 (12), 51 (16), 43 (43); ir: (ν, cm^{-1}) 3500, 3350, 3100, 2700, 1720, 1650, 1579, 1495, 1444, 1289, 1128, 986, 741, 690; uv: (λ_{max}, nm) 368 (ε, 0.340).

Anal. Calcd. for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 73.95; H, 5.37; N, 7.50.

General Procedure for the Synthesis of (*E*)-4-Hydroxy-6-methyl-3-(2-styryl-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-pyran-2-ones (**6**).

A solution of 2.82 g of 4-hydroxy-6-methyl-3-(5-phenyl-2*E*,5*E*-pentadien-1-oyl)-2*H*-pyran-2-one **2** (10 mmol) and the appropriate *ortho*-phenylenediamine (10 mmol) in 40 ml of xylene was refluxed with stirring for 5 hours. After solvent evaporation and recrystallisation in ethanol compounds **6a-c** were obtained.

(*E*)-4-Hydroxy-6-methyl-3-(2-styryl-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-pyran-2-one (**6a**).

This compound was obtained as white powder (75%, ethanol), mp 167 °C; ^{1}H nmr (deuteriochloroform): δ 2.14 (d, 3 H, *J* = 0.8 Hz, 6-CH_3), 3.12 (dd, 1 H, *J* = 9.4 and 12.5 Hz, H-3'), 3.89 (s br, 1 H, N*H*), 3.97 (dd, 1 H, *J* = 3.6 and 12.5 Hz, H-3'), 4.87-4.94 (m, 1 H, H-2'), 5.75 (d, 1 H, *J* = 0.8 Hz, H-5), 6.35 (dd, 1 H, *J* = 7.37 and 15.7 Hz, H-α), 6.66 (d, 1 H, *J* = 15.7 Hz, H-β), 6.92 (dd, 1 H, *J* = 1.18 and 7.87 Hz, H-9'), 6.81 (ddd, 1 H, *J* = 1.3, 7.0 and 7.8 Hz, H-7'), 7.14-7.18 (d, 2 H, H-6' and H-8'), 7.23-7.38 (m, 5 H, H-2",3",4",5",6"); ^{13}C nmr (deuteriochloroform): δ 19.9 (C-7), 35.0 (C-3'), 67.0 (C-2'), 96.6 (C-3), 107.4 (C-5), 121.8 (C-9'), 121.9 (C-7'), 124.6 (C-6'), 126.6 (C-2",6"), 127.1 (C-5a'), 127.9 (C-4"), 128.4 (C-7'), 128.6 (C-3",5"), 130.0 (C-α), 130.7 (C-β), 136.1 (C-1"), 139.8 (C-9a'), 163.2 (C-6), 163.7 (C-2), 173.0 (C-4'), 184.7 (C-4); ms: m/z 372 ($M^{+\bullet}$, 96), 355 (4), 329 (3), 287 (13), 255 (100), 242 (65), 221 (14), 211 (9), 183 (6), 169 (10), 158 (15), 143 (7), 130 (17), 119 (23), 103 (10), 91 (8), 77 (10), 65 (12), 51 (5), 43 (21); ir: (ν, cm^{-1}) 3450, 3330, 2910, 2853, 2422, 1810, 1730, 1681, 1604, 1566, 1469, 1385, 1308, 1154, 947; uv: (λ_{max}, nm) 321(ε, 0.312), 371 (ε, 0.375).

Anal. Calcd. for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 73.83; H, 5.30; N, 7.46.

(*E*)-4-Hydroxy-6-methyl-3-(8-methyl-2-styryl-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-2*H*-pyran-2-one (**6b**).

This compound was obtained as white powder (62.3%, ethanol), mp 180 °C; ^{1}H nmr (deuteriochloroform): δ 2.14 (s, 3 H, 6-C*H*$_3$), 2.32 (s, 3 H, 8'-C*H*$_3$), 3.10 (dd, 1 H, *J* = 9.5 and 12.4 Hz, H-3'), 3.82 (s br, 1 H, N*H*), 3.96 (dd, 1 H, *J* = 3.8 and 12.4 Hz, H-3'), 4.83-4.91 (m, 1 H, H-2'), 5.75 (s, 1 H, H-5), 6.34 (dd, 1 H, *J* = 7.4 and 15.7 Hz, H-α), 6.65 (d, 1 H, *J* = 15.7 Hz, H-β), 6.72 (s br, 1 H, H-9'), 6.81 (dd, 1 H, *J* = 1.2 and 8.0 Hz, H-7'), 7.04 (d, 1 H, *J* = 8.0 Hz, H-6'), 7.23-7.37 (m, 5 H, H-2",3",4",5",6"); ^{13}C nmr (deuteriochloroform): δ 19.9 (C-7), 21.0 (8'-*C*H$_3$), 35.0 (C-3'), 66.8 (C-2'), 96.5 (C-3), 107.4 (C-5), 122.1 (C-9'), 122.8 (C-7'), 124.4 (C-6'), 124.5 (C-5a'), 126.6 (C-2",6"), 127.9 (C-4"), 128.6 (C-3",5"), 130.1 (C-α), 130.7 (C-β), 136.2 (C-1"), 138.7 (C-9a'), 139.6 (C-8'), 163.0 (C-6), 163.2 (C-2), 172.6 (C-4'), 184.6 (C-4); ms: m/z 386 (M$^{+\bullet}$, 100), 301 (10), 269 (87), 256 (94), 235 (14), 225 (7), 185(7), 172 (20), 157 (6), 146 (11), 133 (30), 115 (17), 91 (7), 77 (14), 65 (5), 43 (20); ir: (ν, cm^{-1}) 3368, 2918, 1801, 1720, 1658, 1658, 1604, 1566, 1466, 1385, 1303, 1224, 1154, 1044, 947; uv: (λ$_{max}$, nm) 282 (ε, 0.776), 304 (ε, 0.651).

Anal. Calcd. for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.29; H, 5.66; N, 7.17.

(*E*)-3-(8-Chloro-2-vinyl-2,3-dihydro-1*H*-1,5-benzodiazepin-4-yl)-4-hydroxy-6-methyl-2*H*-pyran-2-one (**6c**).

This compound was obtained as white powder (54.3%, ethanol), mp 169 °C; ^{1}H nmr (deuteriochloroform): δ 2.13 (s, 3 H, 6-C*H*$_3$), 3.18 (dd, 1 H, *J* = 9.6 and 12.2 Hz, H-3'), 3.94 (dd, 1 H, *J* = 3.8 and 12.2 Hz, H-3'), 4.05 (s br, 1 H, N*H*), 4.83-4.89 (m, 1 H, H-2'), 5.75 (s, 1 H, H-5), 6.31 (dd, 1 H, *J* = 7.2 and 15.7 Hz, H-α), 6.64 (d, 1 H, *J* = 15.7 Hz, H-β), 6.92 (s br, 1 H, H-9'), 6.93 (d, 1 H, *J* = 7.7 Hz, H-7'), 7.04 (d, 1 H, *J* = 7.7 Hz, H-6'), 7.24-7.37 (m, 5 H, H-2",3",4",5",6"); ^{13}C nmr (deuteriochloroform): δ 19.9 (C-7), 34.8 (C-3'), 66.2 (C-2'), 96.7 (C-3), 107.3 (C-5), 121.0 (C-9'), 121.6 (C-7'), 125.6 (C-6'), 125.2 (C-5a'), 126.6 (C-2",6"), 128.0 (C-4"), 128.6 (C-3",5"), 129.8 (C-α), 131.0 (C-β), 135.8 (C-1"), 135.9 (C-8'), 140.8 (C-9a'), 163.0 (C-6), 163.2 (C-2), 172.8 (C-4'), 184.7 (C-4); ms: m/z 406 (M$^{+\bullet}$, 20), 289 (22), 276 (20), 264 (11), 253 (13), 170 (27), 154 (39), 142 (20), 128 (90), 115 (54), 102 (17), 91 (20), 85 (44), 77 (35), 69 (32), 51 (30), 43 (100); ir: (ν ,cm^{-1}) 3362, 3098, 2918, 1875, 1720, 1656, 1604, 1508, 1469, 1385, 1250, 1154, 1070, 993; uv: (λ$_{max}$, nm) 380 (ε, 0.768).

Anal. Calcd. for $C_{23}H_{19}ClN_2O_3$: C, 67.90; H, 4.71; N, 6.89. Found: C, 67.65; H, 4.60; N, 6.76.

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[7] Crystal data for $C_{18}H_{22}NO_2$ (**3**) M = 284.37 Monoclinic, space group $P2_1/c$, a = 8.4377(2); b = 7.8352(2); c = 24.5483(8); β = 91.997(2); V = 1621.93(8)^3; Z = 4; Dx = 1.165g.cm^{-3}; μ(MoK$_\alpha$) = 0.075 mm^{-1}, F(000) = 612. Data: 6013 collected reflections and 3163 unique reflections [I>2σ(I)] were measured on an Enraf Nonius Kappa CCD with Mo-Kα radiation (graphite monochromator) using ω-scans at 293(2) K. The structure was solved by direct methods and the least-squares refinement of the structure was performed by using the program SHELXL97. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares based on F^2. All the hydrogen atoms were placed in corresponding calculated positions except the hydrogen atoms bonded to nitrogen and oxygen atoms which were located from a difference Fourier map and were refined. Refinement converged satisfactorily to give R = 0.074 and wR =0.203.

[8] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nº CCDC-210679. Copies of the data can be obtained free of charge on application to CCDC, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: Int. +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk.