Synthesis of Some New Furocoumarins and their Usage in Peptide Synthesis

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1,5-Benzodiazepin-2-ones (**3a – d**) were obtained from ω-carbethoxy visnaginone or ω-carbethoxy khellinone and substituted 1,2-phenylenediamines. Reactions of active nitriles such as malononitrile and ethyl cyanoacetate with substituted 6-dimethylaminomethylene furocoumarins (**4a,b**) are described. Additionally, reaction of substituted 6-dimethylaminomethylene furocoumarins with different amino acids gave furochromen-6-ylidenemethyl amino acids (**7 – 9**). Compound **7** was coupled with glycine ethyl ester to form amino acetic acid ethyl ester (**10**).

Key words: Furocoumarins, Enaminones, Amino Acids

Introduction

A number of investigations have been carried out on the condensation of 4-hydroxycoumarin with amines. For example, 4-aminocoumarines have been synthesized by condensation of primary and secondary amines [1, 2], while the condensation of 4-hydroxycoumarin with aliphatic, cyclic and aromatic 1,2-diamines gave diazepine derivatives [3, 4].

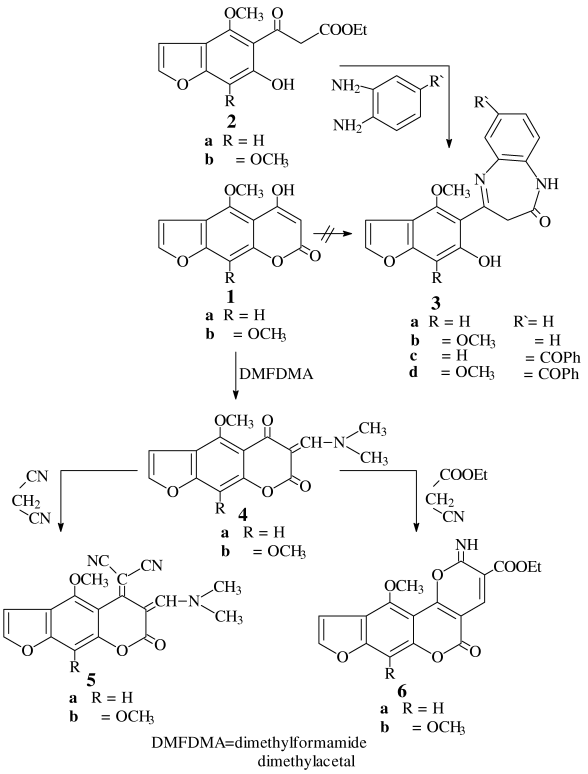
In the course of our research on the synthesis of new heterocyclic compounds of potential biological interest from 5-hydroxyfurocoumarin [5, 6] and in an attempt to obtain benzodiazepines of potential therapeutic [7 – 10], we decided to synthesize some benzodiazepines derived from 5-hydroxybergapten (**1a**) and 5-hydroxyisopimpinellin (**1b**) which are derived from the naturally occurring furochromones visnagin and khellin, respectively [11, 12].

Results and Discussion

In the first instance, we heated 1,2-phenylenediamine or 4-benzoyl-1,2-phenylenediamine with 5-hydroxybergapten (**1a**) and 5-hydroxyisopimpinellin (**1b**) in boiling toluene or ethanol. Nucleophilic attack of the diamine was expected to take place on either the 5- or 7-positions of the coumarin ring, which by internal cyclisation produce the same 1,5-benzodiazepine-2-one derivatives. Unfortunately, no reaction occurred.

Our alternative method starts with ω-carbethoxy visnaginone **2a** [5] and ω-carbethoxy khellinone **2b** [12] which were condensed smoothly with 1,2-phenylenediamine or 4-benzoyl-1,2-phenylenediamine to yield 1,5-benzodiazepine-2-one derivatives **3a – d**. Their IR spectra showed the absence of an ester group and revealed absorption bands at 3400 – 3200 cm^{-1} for (OH, NH) and 1700 – 1680 cm^{-1} (CO). The ^{13}C NMR spectrum of compound **3d** showed signals at $\delta = 42.54$ ppm (CH_2), 61.23 ppm (OMe), 165.13 ppm (C=N), 169.32 ppm (CONH), 195.34 ppm (COPh). Moreover, the mass spectra of compounds **3a** and **3d** showed a molecular ion peak at $m/z = 322$ and 456, respectively.

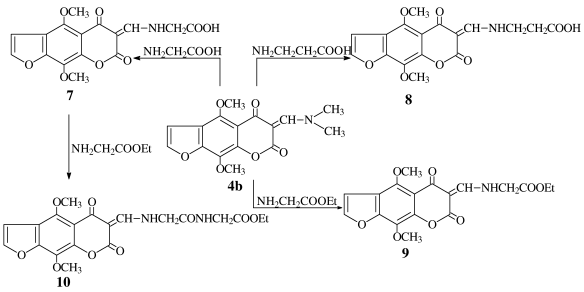
Previously, we reported a new and simple synthetic method for preparing hitherto unknown 4-methoxy (**4a**) and 4,9-dimethoxy-6-dimethylaminomethylene-5-oxo-5*H*-furo [3,2-g] coumarin (**4b**) [5]. The availability of compounds **4a** and **4b** encouraged us to synthesize some new furocoumarin derivatives *via* the reaction of compounds **4a** and **4b** with some active nitriles such as malononitrile and ethyl cyanoacetate. Reaction of compounds **4a** and **4b** with malononitrile gave 6,7-dihydro-furo[3,2-g]chromen-5-ylidene) malononitriles (**5a,b**) in good yield without ring closure. All analytical and spectral data supported the suggested structures. Their IR spectra of **5a** and **5b** showed absorption band at 2208 – 2207 cm^{-1} (CN). The ^1H NMR spectra showed a dimethylamino signal at $\delta = 3.35$ ppm (-$N(CH_3)_2$). The 2D H-H COSY of compound **5b** showed a correlation between 2-H at $\delta = 7.98$ ppm and 3-H at 7.11 ppm of the furan



Scheme 1.

ring. Additionally, the mass spectrum of compound **5b** showed a molecular ion peak at $m/z = 365$. The reaction of compounds **4a** and **4b** with ethyl cyanoacetate yielded 11-methoxy (**6a**) and 7,11-dimethoxy-3-carbethoxy-2-imino-2*H*-furo [3,2-g] pyrano [3,2-c] coumarin (**6b**) in moderate yields *via* elimination of the dimethylaminomethylene group followed by ring closure (Scheme 1). Assignments of structures **6a, b** were established on the basis of elemental analysis, IR, ^{1}H NMR, 2D NMR and mass spectra. The IR spectra showed absorption band at 1740 – 1734 cm^{-1} (COOEt). The ^{1}H NMR of compounds **6a** and **6b** showed ethyl signals at their expected locations at $\delta = 1.30$, 1.40 ppm (CH_3), 4.20, 4.40 ppm (CH_2), and a signal at $\delta = 11.25$, 11.40 ppm (br. s, NH), respectively. The ethyl ester signals of compound **6b** also were observed by 2D H-H COSY at $\delta = 1.40$ ppm (CH_3), 4.40 ppm (CH_2) and also the correlation between two protons of furan ring was observed. Moreover, the mass spectrum of compound **6b** showed a molecular ion peak at $m/z = 385$.

As a further extension to our work, we describe the use of substituted 6-dimethylaminomethylene furo-



Scheme 2.

coumarin derivatives in the peptide synthesis. Reaction with nucleophiles always proceeds by substitution of the dimethylamino group as the first step and then, when possible, further cyclization takes place [13 – 16].

We selected compound **4b** for reaction with some amino acids. Substitution of the dimethylamino group with the amino acids glycine, β-alanine and glycine ethyl ester proceeded smoothly in glacial acetic acid at 80 °C giving [(furo[3,2-*g*]chromen-6-ylidenemethyl)-amino]-acetic acid (**7**), 3-[(furo[3,2-*g*]chromen-6-ylidenemethyl)-amino]-propionic acid (**8**), [(furo[3,2-*g*]chromen-6-ylidenemethyl)-amino]-acetic acid ethyl ester (**9**). The ^{1}H NMR spectra of compounds **7 – 9** showed the absence of the dimethylamino group and revealed a signal at $\delta = 11.58 - 11.70$ ppm (br. s, NH).

Coupling of compound **7** with glycine ethyl ester by using *N,N*-dicyclohexylcarbodiimide in dichloromethane gave {2-[(furo[3,2-*g*]chromen-6-ylidenemethyl)-amino]-acetylamino}-acetic acid ethyl ester (**10**) in moderate yield (Scheme 2).

Experimental Section

Melting points are uncorrected. Elemental analyses were carried out in the Microanalytical Unit of the Faculty of Science, Cairo University. IR spectra were recorded on a Mattson 5000 FTIR spectrometer. ^{1}H NMR spectra were taken on a Jeol-Ex-270 MHz and Varian-Vx-300 MHz NMR spectrometer using TMS as an internal standard with ($\delta =$ 0 ppm). ^{13}C{^{1}H}NMR spectra were taken on a Varian-Vx-75 MHz NMR spectrometer using TMS as an internal standard with ($\delta = 0$ ppm). Mass spectra were determined on a GC-MS.QP-100 (Schimadzu, Japan).

*1,5-Benzodiazepin-2-ones (**3a – d**)*

A mixture of ω-carbethoxy visnaginone **2a** or ω-carbethoxy khellinone **2b** (0.01 mol) and 1,2-phenylenediamine or 3,4-diaminobenzophenone (0.01 mol)

in dry toluene (25 ml) was refluxed for 3 h. The precipitate which formed while hot or on cooling to room temperature was washed with ether and recrystallized from ethanol to give **3a – d**.

*4-(6-Hydroxy-4-methoxy-benzofuran-5-yl)-1,3-dihydro-benzo[b][1,5]diazepin-2-one (**3a**)*

Pale yellow crystals, yield 80%, m.p. 234 – 235 °C. – IR: ν = 3400 – 3200 (OH, NH), 1680 (CO), 1616 cm^{-1} (C=N). – ^{1}H NMR (270 MHz, DMSO): δ = 3.55 (s, 2H, CH_2), 4.00 (s, 3H, OCH_3), 6.70 (s, 1H, 7-H), 7.10 (d, 1H, $J_{2,3}$ = 2.3 Hz, 3-H), 7.20 – 7.40 (m, 4H, Ar-H), 7.85 (d, 1H, $J_{2,3}$ = 2.3 Hz, 2-H), 10.50 (s, 1H, NH), 11.85 (s, 1H, OH). – ^{13}C{^{1}H}NMR (75 MHz, DMSO): δ = 42.39 (CH_2), 60.92 (OCH_3), 93.26 (C-7), 103.82 (C-5), 107.92 (C-3a), 109.51(C-3), 122.63 (benzodiazepine C-9), 123.22 (benzodiazepine C-6), 126.57 (benzodiazepine C-7), 127.86 (benzodiazepine C-8), 135.35 (benzodiazepine C-9a), 144.21 (benzodiazepine C-5a), 151.13 (C-2), 153.69 (C-6), 155.23 (C-4), 159.72 (C-7a), 165.12 (benzodiazepine C-4) ,169.36 (CONH). – MS: M$^+$ at m/z = 322. – $C_{18}H_{14}N_2O_4$ (322.31): calcd. C 67.07, H 4.38, N 8.69; found C 67.20, H 4.50, N 8.60.

*4-(6-Hydroxy-4,7-dimethoxy-benzofuran-5-yl)-1,3-dihydro-benzo[b][1,5]diazepin-2-one (**3b**)*

Pale yellow crystals, yield 82%, m.p. 219 – 220 °C. – IR: ν = 3400 – 3200 (OH, NH), 1684 (CO), 1612 cm^{-1} (C=N). – ^{1}H NMR (270 MHz, DMSO): δ = 3.55 (s, 2H, CH_2), 3.90 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.15 (d, 1H, $J_{2,3}$ = 2.3 Hz, 3-H), 7.20 – 7.40 (m, 4H, Ar-H), 7.90 (d, 1H, $J_{2,3}$ = 2.3 Hz, 2-H), 10.55 (s, 1H, NH), 11.90 (br. s, 1H, OH). – ^{13}C{^{1}H}NMR (75 MHz, DMSO): δ = 42.42 (CH_2), 61.12 (2 OCH_3), 105.22 (C-5), 109.67 (C-3), 111.23 (C-3a), 122.61 (benzodiazepine C-9), 123.39 (benzodiazepine C-6), 126.62 (C-7), 127.34 (benzodiazepine C-7), 127.98 (benzodiazepine C-8), 135.38 (benzodiazepine C-9a), 139.21 (C-6), 144.30 (benzodiazepine C-5a), 150.24 (C-4), 151.22 (C-2, C-7a), 165.23 (benzodiazepine C-4) ,169.42 (CONH).– $C_{19}H_{16}N_2O_5$ (352.34): calcd. C 64.77, H 4.58, N 7.95; found C 64.90, H 4.70, N 8.00.

*7-Benzoyl-4-(6-hydroxy-4-methoxy-benzofuran-5-yl)-1,3-dihydrobenzo[b][1,5]diazepin-2-one (**3c**)*

Yellow crystals, yield 83%, m.p. 245 – 246 °C. – IR: ν = 3400 – 3200(OH, NH), 1700(CO), 1615 cm^{-1} (C=N). – ^{1}H NMR (270 MHz, DMSO): δ = 3.55 (s, 2H, CH_2), 4.00 (s, 3H, OCH_3), 6.70 (s, 1H, 7-H), 7.00 (d, 1H, $J_{2,3}$ = 2.3 Hz, 3-H), 7.20 – 7.60 (m, 8H, Ar-H), 7.80 (d, 1H, $J_{2,3}$ = 2.3 Hz, 2-H), 10.60 (s, 1H, NH), 11.40 (br. s, 1H, OH). – ^{13}C{^{1}H}NMR (75 MHz, DMSO): δ = 42.45 (CH_2), 60.95 (OCH_3), 93.31 (C-7), 103.96 (C-5), 107.85 (C-3a), 109.62 (C-3), 122.32 (benzodiazepine C-9), 126.78 (benzodiazepine C-6), 128.57 (phenyl C-3,5, benzodiazepine C-8), 130.06 (phenyl C-2,4,6), 132.87 (benzodiazepine C-7), 136.08 (phenyl C-1), 137.16 (benzodiazepine C-9a), 143.66 (benzodiazepine C-5a), 151.31 (C-2), 153.35 (C-6), 155.36 (C-4), 159.92 (C-7a), 165.07 (benzodiazepine C-4), 169.03 (CONH), 195.15 (COPh). – $C_{25}H_{18}N_2O_5$ (426.42): calcd. C 70.41, H 4.25, N 6.57; found C 70.60, H 4.40, N 6.70.

*7-Benzoyl-4-(6-hydroxy-4,7-dimethoxy-benzofuran-5-yl)-1,3-dihydrobenzo[b][1,5]-diazepin-2-one (**3d**)*

Yellow crystals, yield 85%, m.p. 225 – 226 °C. IR: ν = 3400 – 3200 (OH, NH), 1697(CO), 1613 cm^{-1} (C=N). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 2H, CH_2), 4.00 (s, 3H, OCH_3), 4.20 (s, 3H, OCH_3), 6.90 (d, 1H, $J_{2,3}$ = 2.3 Hz, 3-H), 7.00 – 7.60 (m, 8H, Ar-H), 7.70 (d, 1H, $J_{2,3}$ = 2.3 Hz, 2-H), 9.00 (s, 1H, NH), 13.60 (br. s, 1H, OH). – ^{13}C{^{1}H}NMR (75 MHz, $CDCl_3$): δ = 42.54 (CH_2), 61.23 (2 OCH_3), 105.63 (C-5), 109.71(C-3), 111.43 (C-3a), 123.81 (benzodiazepine C-9), 126.84 (benzodiazepine C-6), 127.94 (C-7), 128.61(phenyl C-3,5, benzodiazepine C-8), 130.11 (phenyl C-2,4,6), 132.94 (benzodiazepine C-7), 136.14 (phenyl C-1), 137.22 (benzodiazepine C-9a), 139.35 (C-6), 143.73 (benzodiazepine C-5a), 150.12 (C-4), 151.40 (C-2, C-7a), 165.13 (benzodiazepine C-4), 169.32 (CONH), 195.34 (COPh). – MS: M$^+$ at m/z = 456. – $C_{26}H_{20}N_2O_6$ (456.45): calcd. C 68.41, H 4.42, N 6.14; found C 68.50, H 4.50, N 6.20.

*2-(4-Methoxy (**5a**) and 4,9-dimethoxy-6-dimethylaminome-thylene-7-oxo-6,7-dihydro-furo[3,2-g]chromen-5-ylidene) malononitrile (**5b**)*

A mixture of compound **4a** or **4b** (0.01 mol) and malononitrile (0.01 mol) in absolute ethanol (25 ml) was refluxed for 3 h. The precipitate which formed after cooling, collected, filtered off and crystallized from ethanol to give **5a** and **5b**.

5a: Yellow crystals, yield 82%, m.p. 259 – 260 °C.– IR: ν = 2965, 2850 (CH),2208 (CN), 1684 cm^{-1} (CO). – ^{1}H NMR (270 MHz, DMSO): δ = 3.35 (s, 6H, 2CH_3), 4.00 (s, 3H, OCH_3), 7.20(s, 1H, 9-H), 7.50 (d, 1H, $J_{2,3}$ = 2.3 Hz, 3-H), 7.72 (s, 1H, C=CHN(CH_3)$_2$), 8.00 (d, 1H, $J_{2,3}$ = 2.3 Hz, 2-H). –^{13}C{^{1}H}NMR (75 MHz, DMSO): δ = 42.76 (2CH_3), 61.55 (OCH_3), 73.25 (=C-($CN)_2$), 98.85 (C-9), 109.11 (C-3), 110.11 (C-4a), 110.51(C-6), 111.25 (C-3a), 118.61 (2CN), 150.89 (C-2), 151.68 (C-8a), 152.42 (=CH-N-), 154.33 (C-4), 157.25 (C-9a), 163.11 (C=O), 175.82 (C-5).– $C_{18}H_{13}N_3O_4$ (335.31): calcd. C 64.47, H 3.91, N 12.53; found C 64.60, H 4.00, N 12.60

5b: Yellow crystals, yield 85%, m.p. 198 – 200 °C. – IR: ν = 2946, 2838 (CH), 2207(CN), 1682 cm^{-1} (CO). – ^{1}H NMR (300MHz, DMSO): δ = 3.35 (s, 6H, 2CH_3), 3.89 (s,

3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.11 (d, 1H, $J_{2,3} = 2.3$ Hz, 3-H), 7.72 (s, 1H, C=CHN$(CH_3)_2$), 7.98 (d, 1H, $J_{2,3} = 2.3$ Hz, 2-H). – $^{13}C\{^1H\}$NMR (75 MHz, DMSO): $\delta = 42.82$ ($2CH_3$), 61.52 ($2OCH_3$), 73.32 (=C-$(CN)_2$), 109.37 (C-3), 110.21 (C-4a), 110.85 (C-6), 112.30 (C-3a), 118.83 (2CN), 132.50 (C-9), 134.25 (C-8a), 144.23 (C-9a), 150.98 (C-2), 151.42 (C-4), 152.62 (=CH-N-), 163.23 (C=O), 175.89 (C-5). – MS: M^+ at $m/z = 365$. – $C_{19}H_{15}N_3O_5$ (365.34): calcd. C 62.46, H 4.14, N 11.50; found C 62.60, H 4.20, N 11.40.

*11-Methoxy (**6a**) and 7,11-dimethoxy-3-carbethoxy-2-imino-2H-furo[3,2-g]pyrano[3,2-c]coumarin (**6b**)*

A mixture of compound **4a** or **4b** (0.01 mol) and ethyl cyanoacetate (0.01 mol) in absolute ethanol (25 ml) was refluxed for 3 h. The precipitate which formed after cooling, collected, filtered off and crystallized from ethanol to give **6a** and **6b**.

6a: Yellow crystals, yield 70%, m.p. 254 – 256 °C. – IR: $\nu = 311$(NH), 1734 (COOEt), 1662 (CO), 1619 cm^{-1} (C=N). – ^{1}H NMR (300 MHz, DMSO): $\delta = 1.30$ (t, 3H, CH_3), 4.00 (s, 3H, OCH_3), 4.20 (q, 2H, CH_2), 7.00 (s, 1H, 7-H), 7.15 (d, 1H, $J_{2,3} = 2.3$ Hz, 10-H), 7.90 (d, 1H, $J_{2,3} = 2.3$ Hz, 9-H), 8.50 (s, 1H, 4-H), 11.25 (br. s, 1H, NH). –$^{13}C\{^1H\}$NMR (75 MHz, DMSO): $\delta = 13.24$ (CH_3), 58.59 (CH_2), 60.94 (OCH_3), 96.42 (C-4a), 98.65 (C-7), 109.26 (C-10), 110.21 (C-11a), 111.12 (C-10a), 117.91 (C-3), 140.71(C-4), 150.91 (C-9), 151.73 (C-6a), 153.90 (C-11), 156.96 (C-7a), 163.32 (C=O), 166.82 (C-4b), 167.52 (C=O). – C_{18} $H_{13}NO_7$ (355.30): calcd. C 60.85, H 3.69, N 3.94; found C 60.70, H 3.80, N 4.00.

6b: Yellow crystals, yield 75%, m.p. 249 – 250 °C. – IR: $\nu = 3307$ (NH), 1740 (COOEt), 1667 (CO), 1620 cm^{-1} (C=N). – ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.40$ (t, 3H, CH_3), 4.19 (s, 3H, OCH_3), 4.30 (s, 3H, OCH_3), 4.40 (q, 2H, CH_2), 7.00 (d, 1H, $J_{2,3} = 2.3$ Hz, 10-H), 7.70 (d, 1H, $J_{2,3} = 2.3$ Hz, 9-H), 8.87 (s, 1H, 4-H) 11.40 (br. s, 1H, NH). –$^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): $\delta = 13.29$ (CH_3), 58.68 (CH_2), 60.98 ($2OCH_3$), 96.45 (C-4a), 109.42 (C-10), 110.27 (C-11a), 112.25 (C-10a), 117.94 (C-3), 132.62 (C-7), 134.25 (C-6a), 140.84 (C-4), 144.75 (C-7a), 150.95 (C-9), 151.82(C-11), 163.37 (C=O), 166.89 (C-4b), 167.64 (C=O). – MS: M^+ at $m/z = 385$. – $C_{19}H_{15}NO_8$ (385.32): calcd. C 59.22, H 3.92, N 3.63; found C 59.10, H 3.80, N 3.70.

*[(4,9-Dimethoxy-5,7-dioxo-5H-furo[3,2-g]chromen-6-yl-idenemethyl)-amino]acids (**7, 8**)*

A mixture of compound **4b** (3.17 g, 0.01 mol), glacial acetic acid (20 ml) and amino acids (0.01 mol) was stirred at 80 °C for 2 h, cooled and solvent evaporated *in vacuo*. Water (50 ml) was added to the residue, triturated and left at room temperature. The precipitate that formed was filtered off, dried and crystallized from ethanol to give **7** and **8**.

*[(4,9-Dimethoxy-5,7-dioxo-5H-furo[3,2-g]chromen-6-yl-idenemethyl)-amino]-acetic acid (**7**)*

Pale yellow crystals, yield 72%, m.p. 241 – 242 °C. – IR: $\nu = 3162$ (NH), 2988 (CH), 1711, 1640 cm^{-1} (CO). – ^{1}H NMR (300 MHz, DMSO): $\delta = 3.90$ (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.42 (d, 2H, CH_2), 7.14 (d, 1H, $J_{2,3} = 2.3$ Hz, 3-H), 8.00 (d, 1H, $J_{2,3} = 2.3$ Hz, 2-H), 8.48 (d, 1H, C=CH), 11.58 (br. s, 1H, NH). – $^{13}C\{^1H\}$NMR (75 MHz, DMSO): $\delta = 56.72$ (CH_2), 60.95 ($2OCH_3$), 109.25 (C-3), 110.52 (C-4a, C-6), 113.23 (C-3a), 133.21 (C-9), 136.35 (C-8a), 150.90 (C-2), 151.42 (C-9a), 152.35 (C-4), 160.11(=CH-NH), 163.28, 175.11, 185.82 (all C=O). – $C_{16}H_{13}NO_8$ (347.28): calcd. C 55.34, H 3.77, N 4.03 ; found C 55.20, H 3.90, N 4.10.

*3-[(4,9-Dimethoxy-5,7-dioxo-5H-furo[3,2-g]chromen-6-yl-idenemethyl)-amino]-propionic acid (**8**)*

Colorless crystals, yield 70%, m.p. 236 – 237 °C. IR: $\nu = 3196$ (NH), 2979 (CH), 1713, 1636 cm^{-1} (CO). – ^{1}H NMR (300 MHz, DMSO): $\delta = 2.55$ (m, 4H, $2CH_2$), 3.90 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.16 (d, 1H, $J_{2,3} = 2.3$ Hz, 3-H), 8.00 (d, 1H, $J_{2,3} = 2.3$ Hz, 2-H), 8.40 (d, 1H, C=CH), 11.70 (br. s, 1H, NH). – $^{13}C\{^1H\}$NMR (75 MHz, DMSO): $\delta = 40.22$, 46.62 ($2CH_2$), 61.11 ($2OCH_3$), 109.30 (C-3), 110.57 (C-4a, C-6), 113.35 (C-3a), 133.37 (C-9), 136.25 (C-8a), 150.70 (C-2), 151.35 (C-9a), 152.24 (C-4), 160.12(=CH-NH), 163.25, 176.14, 185.65 (all C=O). – $C_{17}H_{15}NO_8$ (361.30): calcd. C 56.51, H 4.18, N 3.88; found C 56.40, H 4.30, N 4.00.

*[(4,9-Dimethoxy-5,7-dioxo-5H-furo[3,2-g]chromen-6-yl-idenemethyl)-amino]-acetic acid ethyl ester (**9**)*

A mixture of **4b** (3.17 g, 0.01 mol), glacial acetic acid (20 ml) and glycine ethyl ester hydrochloride (1.40 g, 0.01 mol) was refluxed for 2 h, cooled and solvent evaporated *in vacuo* and the residue crystallized from ethanol. The precipitate was collected by filtration to give **9**: Yellow crystals, yield 75%, m.p. 224 – 225 °C. – IR: $\nu = 3142$ (NH), 2984 (CH), 1711 (COOEt), 1636 cm^{-1} (CO). – ^{1}H NMR (300 MHz, DMSO): $\delta = 1.24$ (t, 3H, CH_3), 3.97 (s, 3H, OCH_3), 4.17 (s, 3H, OCH_3), 4.20 (q, 2H, CH_2), 4.50 (d, 2H, CH_2), 7.15 (d, 1H, $J_{2,3} = 2.3$ Hz, 3-H), 8.00 (d, 1H, $J_{2,3} = 2.3$ Hz, 2-H), 8.41 (d, 1H, C=CH), 11.59 (br. s, 1H, NH). – $^{13}C\{^1H\}$NMR (75 MHz, DMSO): $\delta = 13.12$ (CH_3), 54.28, 58.85 ($2CH_2$), 61.13 ($2OCH_3$), 109.27 (C-3), 110.65 (C-4a, C-6), 113.27 (C-3a), 133.11 (C-9), 136.38 (C-8a), 150.92 (C-2), 151.47 (C-9a), 152.38 (C-4), 160.17(=CH-NH), 163.28, 170.32, 185.86 (all C=O). – $C_{18}H_{17}NO_8$ (375.33): calcd. C 57.60, H 4.56, N 3.73; found C 57.70, H 4.40, N 3.60.

{2-[(4,9-Dimethoxy-5,7-dioxo-5H-furo[3,2-g]chromen-6-yl-idenemethyl)-amino]-acetylamino} acetic acid ethyl ester ***(10)***

A mixture of compound **7** (3.47 g, 0.01 mol), dichloromethane (40 ml) and glycine ethyl ester hydrochloride (1.40 g, 0.01 mol) was stirred at 0 °C for five minutes, then 4-methylmorpholine (1.00 ml) and after five minutes *N*,*N*-dicyclohexylcarbodiimide (2.06 g, 0.01 mol) was added. The mixture was stirred at 0 °C for 1 h. *N*,*N*-dicyclohexylurea, which precipitated, was filtered off, washed with 10 ml of dichloromethane and the filterate was washed first with dilute hydrochloric acid (40 ml, 1%), then with aqueous sodium bicarbonate (40 ml, 5%) and finally with water (40 ml), dried over anhydrous sodium sulphate, filtered and the solvent evaporated *in vacuo* and the residue was solidified using petroleum ether. The solid was filtered off, dried and crystallized from ethanol to give **10**: Pale yellow crystals, yield 65%, m.p. 176 – 177 °C. – IR: $\nu = 3197$, 3148 (NH), 2984, 2945 (CH), 1711 (COOEt), 1636 cm^{-1} (CO). – ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.30$ (t, 3H, CH_3), 4.00 (s, 3H, OCH_3), 4.16 (s, 3H, OCH_3), 4.20 – 4.32 (m, 6H, $2CH_2NH$, CH_2), 6.97 (d, 1H, $J_{2,3} = 2.3$ Hz, 3-H), 7.58 (d, 1H, $J_{2,3} = 2.3$ Hz, 2-H), 8.30 (d, 1H, C=CH), 10.20 (br. s, 1H, NH), 12.00 (br. s, 1H, NH). – $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): $\delta = 13.32$ (CH_3), 47.77, 54.32, 58.93 (all CH_2), 61.11 ($2OCH_3$), 109.23 (C-3), 110.68 (C-4a, C-6), 113.31 (C-3a), 133.12 (C-9), 136.43 (C-8a), 150.90 (C-2), 151.44 (C-9a), 152.53 (C-4), 160.18 (=CH-NH), 163.43, 170.50, 170.75, 186.21 (all C=O).– MS: M^+ at $m/z = 432$. – $C_{20}H_{20}N_2O_9$ (432.38): calcd. C 55.56, H 4.66, N 6.48; found C 55.70, H 4.80, N 6.60.

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