Alkyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates in the Synthesis of Heterocyclic Systems

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Alkyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates **4a,b** were prepared. They react with *C*-nucleophiles such a 2-pyridinylacetonitrile **5** and methyl-2-quinolinylacetate **8**, cyclohexane-1,3-dione **10** and its derivatives **12** and **14**, resorcinol derivative **16**, 2-naphtol **18**, 2-pyranone derivatives **20** and **22**, and 4-hydroxypyridin-2(1*H*)-one **24**, to form substituted amino derivatives of quinolizine **6**, benzo[*c*]quinolizine **9**, tetrahydrobenzopyran-2-one **11**, **13**, **15**, naphto[2,1-*b*]pyran-3-one **19**, pyranopyranones **21**, **23**, and pyrano[3,2-*c*]pyridine **25**.

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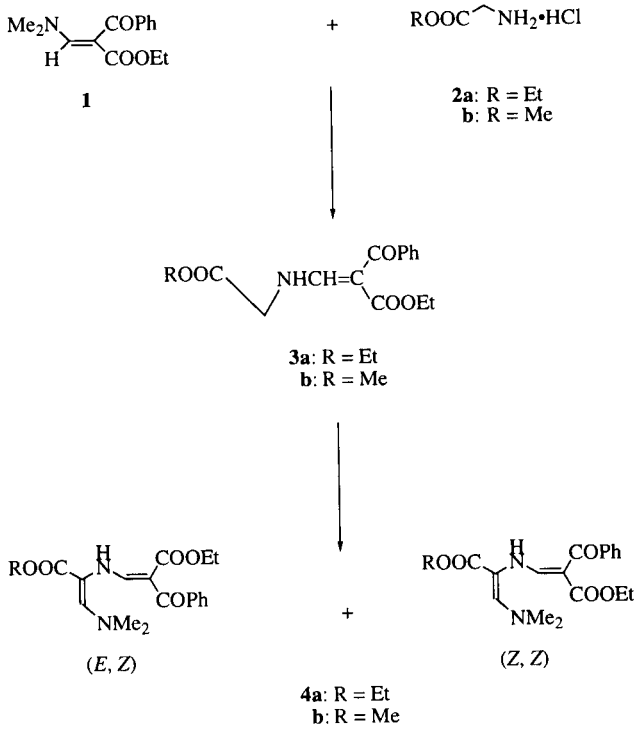
Recently, the synthesis of various derivatives of pyran-2-one and fused pyran-2-one has arisen a great interest, since many of them are nonpeptide HIV proteaze inhibitors [1-8].

In connection with our systematic studies of 2-acyl-3-dimethylaminopropenoates [9-13] and ethyl (*Z*)-2-[2,2-bis(ethoxycarbonyl)vinyl]amino-3-dimethylaminopropenoate [14] as new reagents in the synthesis of heterocyclic systems have been prepared, recently.

Scheme 1



In this communication we report the synthesis of alkyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates **4** and their reactions with *C*-nucleophiles to form a variety of fused heterocyclic systems, many fused pyran-2-ones among others, with substituted amino and other functions at position 3 in the newly formed heterocyclic ring.

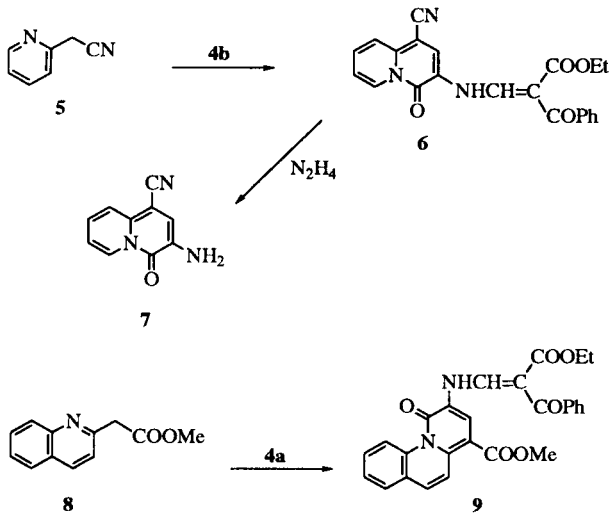
The compounds **4a,b** were prepared from ethyl 2-benzoyl-3-dimethylaminopropenoate (**1**) [15] and glycine ethyl ester hydrochloride (**2a**) or methyl ester **2b** to form *N*-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)glycine ethyl ester (**3a**) [16] or methyl ester **3b**, respectively. The compounds **3a,b** were then treated with *N,N*-dimethylformamide dimethyl acetal to yield ethyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**4a**) and its methyl ester analogue **4b** in 68% and 67% yield, respectively. (Scheme 1)

The structures of the compounds **4** were determined by elemental analyses, which give the molecular formula $C_{19}H_{24}N_2O_5$ for the ethyl ester **4a** and $C_{18}H_{22}N_2O_5$ for the methyl ester **4b**. The ^1H nmr spectrum of **4a** shows two triplets in the ratio 1:1, integrating each for three protons, at δ = 0.96 ppm and δ = 1.27 ppm, and two quartets, each integrating for two protons, at δ = 3.99 ppm and 4.17 ppm for two ester groups, a singlet, integrating for six protons, at δ = 3.05 ppm for the dimethylamino group, a multiplet, integrating for six protons, at δ = 7.27-7.49 ppm for the proton attached to the double bond adjacent to the dimethylamino group overlapped with the signals for the phenyl group, and two doublets for CHNH structural element with the coupling constant J_{CHNH} = 13.5 Hz, indicating the trans orientation. The orientation around the double bond, to which both amino groups are attached, was established by NOE, while the orientation around the

other double bond was determined by long range ^{13}C-^{1}H coupling constants, indicating the existence of two isomers, *(E, Z)* and *(Z, Z)* in the ratio 5:3 in hexadeuteriodimethylsulfoxide solution, while in deuteriochloroform solution the *(E, Z)* isomer is present in over 95% [17].

The ^{1}H nmr spectrum of **4b** shows two triplets, integrating for three protons, at δ = 0.87 ppm and δ = 0.89 ppm

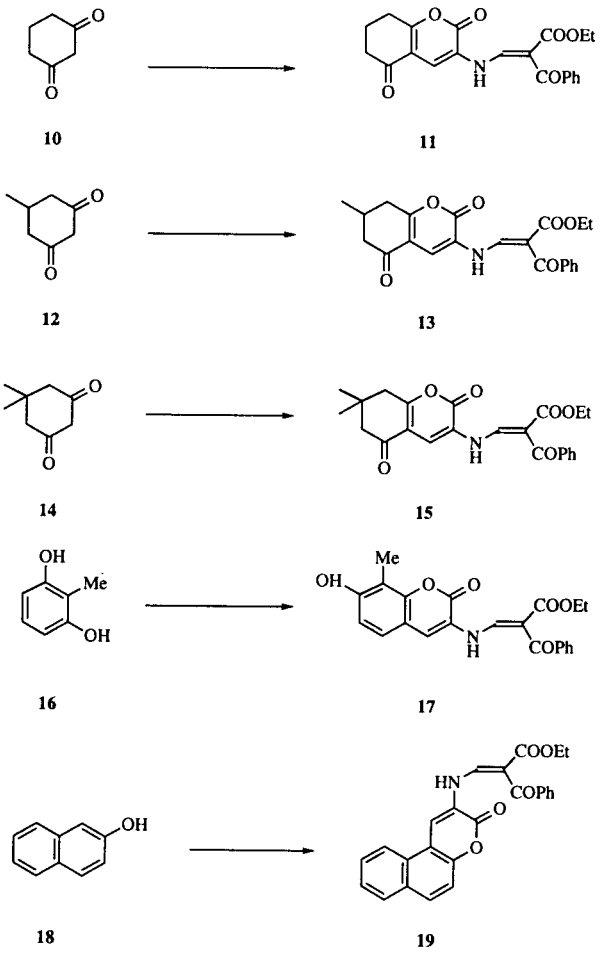
Scheme 2



for the ethyl ester group, and two quartets, integrating for two protons, at δ = 3.85 ppm and δ = 3.95 ppm, a singlet, integrating for six protons, at δ = 3.02 ppm for dimethylamino group, a singlet, integrating for three protons, at δ = 3.61 ppm for the methyl ester group, a multiplet, integrating for six protons, at δ = 7.30-7.50 ppm for the proton attached to the double bond adjacent to the dimethylamino group, overlapped with the signals for the phenyl group, and two doublets, integrating for one proton, at δ = 7.42 ppm and δ = 7.79 ppm for C*H*NH and two doublets, integrating for one proton, at δ = 9.51 ppm and δ = 10.72 ppm for CHN*H* group, with the coupling constant J_{CHNH} = 14.0 Hz.

Compounds **4** react with various *C*-nucleophiles, having an active or potentially active methylene group. For this purpose, the heterocyclic compounds with activated methylene group attached at α-position in respect to the ring nitrogen atom, such as 2-pyridinylacetonitrile (**5**) and methyl 2-quinolinylacetate (**8**), the compounds with an active methylene group incorporated into the cyclic system, such as cyclohexane-1,3-dione (**10**) and its 5-methyl **12** and 5,5-dimethyl derivative **14**, the compounds with a potentially active methylene group, such as aromatic hydroxy compounds 2,4-dihydroxytoluene (**16**), 2-hydroxynaphtalene (**18**), and heterocyclic hydroxy compounds 4-hydroxy-6-methyl-2*H*-pyran-2-one (**20**), 4-hydroxy-2*H*-1-benzopyran-2-one (**22**) and 4-hydroxypyridin-2(1*H*)-one (**24**) were selected. The reactions were

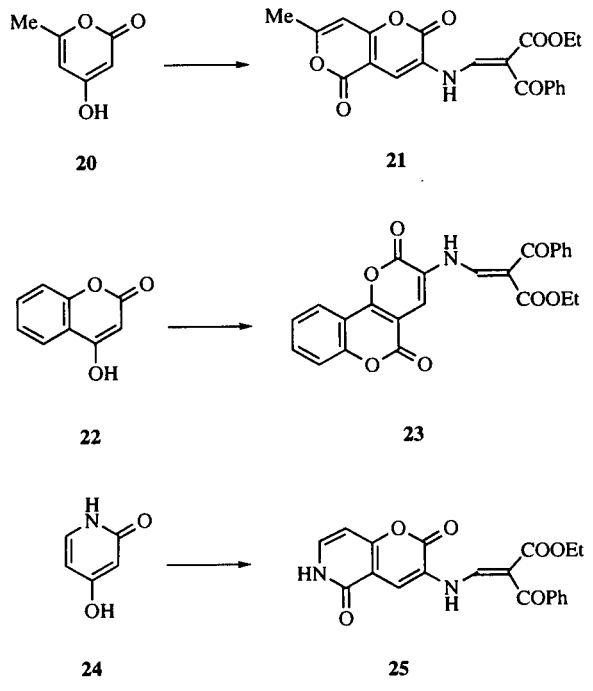
Scheme 3



carried out in glacial acetic acid at room temperature or in the cases of less reactive substrates at reflux temperature for several hours. Under these conditions the dimethylamino group, attached to the ethenyl part of the reagent, was exchanged with *C*-nucleophiles to form the corresponding intermediates, which were further cyclized without isolation.

In this manner, the compounds with an exocyclic active methylene group **5** and **8** were converted into 4*H*-quinolizin-4-one derivative (**6**) and 1*H*-benzo[*c*]quinolizin-4-one derivative **9** in 84% and 28% yield, respectively (Scheme 2). The compounds with an endocyclic methylene group **10**, **12** and **14**, gave 5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-ones **11**, **13**, and **15**, in 71-80% yield, substituted phenols **16** and **18** the corresponding 2*H*-1-benzopyran-2-one **17** and 3*H*-naphto[2,1-*b*]pyran-3-one **19**, in low yields, pyranones **20** and **22** the corresponding 2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione and 2*H*,5*H*-pyrano[4,3-*b*][1]benzopyran-2,5-dione **23** derivative in 73% and 68% yield, respectively, and pyridinone **24** 2*H*-pyrano[3,2-*c*]pyridine-2,5-dione **25** in 51% yield. (Schemes 3 and 4).

Scheme 4



The structures of all new compounds were determined by ^{1}H nmr spectra and elemental analyses for C, H, and N.

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on a Bruker Avance 300 DPX spectrometer with TMS as the internal standard, ir spectra on a Perkin-Elmer 1310 instrument, mass spectra on an Autospeck Q spectrometer and microanalyses for C, H and N on a Perkin-Elmer Analyser 2400.

The following compounds were prepared according to the procedures described in the literature: ethyl 2-benzoyl-3-dimethylaminopropenoate (**1**) [15] and *N*-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)glycine ethyl ester (**3a**) [16].

The Synthesis of *N*-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)-glycine Methyl Ester (**3b**).

The mixture of ethyl 2-benzoyl-3-dimethylaminopropenoate (**1**) (0.247 g, 1 mmole) and glycine methyl ester hydrochloride (0.126 g, 1 mmole) in ethanol (3 ml) was heated under reflux for 1.5 hours. After the volatile components were evaporated *in vacuo,* the solid product was recrystallized from a mixture of ethanol and water to give **3b** in 89% yield, mp 96-97°; ^{1}H nmr (DMSO-d_6): δ 0.82 and 0.89 (3H, 2t, CH_2CH_3), 3.70 (3H, s, $COOCH_3$), 3.88 and 3.92 (2H, 2q, CH_2CH_3), 4.31 and 4.34 (2H, 2d, CH_2NH), 7.36-7.49 (5H, m, COPh), 7.83 and 8.06 (1H, 2d, CHNH), 9.09-9.13 and 10.20-10.25 (1H, 2 br m, CHN*H*), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 14.4 Hz, $J_{CH_2\text{-}NH}$ = 6.1 Hz.

Anal. Calcd. for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.76; H, 5.90; N. 4.83.

The Synthesis of Alkyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates (**4**).

General Procedure:

To a solution of *N*-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)-glicyne alkyl ester (**3**) (1 mmole) in *N,N*-dimethylformamide (2 ml) *N,N*-dimethylformamide dimethyl acetal (2 mmoles) was added and the mixture was heated in an oil bath at 90° for 3 hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and ether as a solvent). After the reaction was completed, the volatile components were evaporated *in vacuo.* The oily residue was dissolved in methylene chloride (30 ml) and the solution was extracted with water (3 times, 10 ml each time). The organic layer was dried over anhydrous sodium sulphate and evaporated *in vacuo.* To the oily residue diisopropyl ether was added and, after cooling, the solid product crystallized and was collected by filtration and recrystallized from ether.

The following compounds were prepared in this manner:

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**4a**).

This compound was prepared from **3a** (0.305 g, 1 mmole) in 68% yield, mp 78-79°, ^{1}H nmr (deuteriochloroform): δ 0.96 and 1.27 (2 x 3H, 2t, 2 x CH_2CH_3), 3.05 (6H, s, NMe_2), 3.99 and 4.17 (2 x 2H, 2q, 2 x CH_2CH_3), 7.27-7.49 (6H, m, COPh, CHNMe$_2$), 8.01 (1H, d, CHNH), 11.12 (1H, d, CHN*H*), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz.

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71; N, 7.77. Found: C, 63.71; H, 6.90; N, 7.69.

Methyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**4b**).

This compound was prepared from **3b** (0.291 g, 1 mmole) in 67% yield, mp 105-106°; ^{1}H nmr (DMSO-d_6): δ 0.87 and 0.89 (3H, 2t, CH_2CH_3), 3.02 (6H, s, NMe_2), 3.61 (3H, s, $COOCH_3$), 3.85 and 3.95 (2H, 2q, CH_2CH_3), 7.30-7.50 (6H, m, COPh, CHNMe$_2$), 7.42 and 7.79 (1H, 2d, CHNH), 9.51 and 10.72 (1H, 2d, CHN*H*), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 14.0 Hz.

Anal. Calcd. for $C_{18}H_{22}N_2O_5$: C, 62.42; H, 6.40; N, 8.09. Found: C, 62.12; H, 6.32; N, 8.09.

The Synthesis of 4*H*-Quinolizin-4-one Derivatives **6**, **7** and **9**.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-1-cyano-4*H*-quinolizin-4-one (**6**).

To a solution of **4b** (0.346 g, 1 mmole) in glacial acetic acid (3 ml) 2-pyridinylacetonitrile (**5**) (0.118 g, 1 mmole) was added and the mixture was stirred at room temperature for 5 hours. The precipitate was collected by filtration and washed with ethanol to give **6** in 84% yield, mp 190-192°; ^{1}H nmr (DMSO-d_6): δ 0.90 and 0.97 (3H, 2t, CH_2CH_3), 3.99 and 4.03 (2H, 2q, CH_2CH_3), 7.43-7.96 (8H, m, COPh, H_7, H_8, H_9), 8.48 and 8.73 (1H, 2d, CHNH), 8.59 and 8.70 (1H, 2s, H_2), 9.11 (1H, dd, H_6), 11.03 and 12.15 (1H, 2d, CHN*H*), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 14.0 Hz, $J_{H6,H7}$ = 10.0 Hz, $J_{H6\ H8}$ = 7.4 Hz.

Anal. Calcd. for $C_{22}H_{17}N_3O_4$: C, 68.22; H, 4.46; N, 10.93. Found: C, 68 04; H, 4.16; N, 10.96.

3-Amino-1-cyano-4*H*-quinolizin-4-one (**7**).

To a suspension of 3-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-1-cyano-4*H*-quinolizin-4-one (**6**) (0.384 g, 1 mmole) in ethanol (3 ml) hydrazine hydrate (99%, 0.2 ml) was added and the mixture was heated under reflux for 15 minutes. The solvent was evaporated *in vacuo*, the crude product was suspended in ethanol and collected by filtration and washed with ethanol to give **7** in 92% yield, mp 190-192°; ^{1}H nmr (deuteriochloroform): δ 4.41 (s, 2H, NH_2), 7.01 (ddd, 1H, H_7), 7.19 (s, 1H, H_2), 7.28 (ddd, 1H, H_8), 7.80 (dd, 1H, H_9), 8.96 (dd, 1H, H_6), $J_{H6,H7}$ = 7.5 Hz, $J_{H8,H9}$ = 9.1 Hz, $J_{H6,H8}$ = 1.0 Hz.

Anal. Calcd. for $C_{10}H_7N_3O$: C, 64.84; H, 3.81; N, 22.69. Found: C, 64.75; H, 3.72; N, 22.64.

2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-4-methoxycarbonyl-1*H*-benzo[*c*]quinolizine (**9**).

To a solution of **4a** (0.360 g, 1 mmole) in glacial acetic acid (5 ml) methyl 2-quinolinylacetate (**8**) (0.201 g, 1 mmole) was added and the mixture was heated in an oil bath at 80° for 1 hour. The solvent was evaporated *in vacuo*. After cooling, methanol was added, the precipitate was collected by filtration and washed with methanol to give **9** in 28% yield, mp 215-217°; ^{1}H nmr (deuteriochloroform): δ 1.24 (3H, t, CH_2CH_3), 3.88 (3H, s, $COOCH_3$), 4.29 (2H, q, CH_2CH_3), 7.14-8.52 (12H, m, COPh, 7H, H_3, H_5, H_6, H_7, H_8, H_9, H_{10}), 8.50 (1H, d, CHNH), 12.55 (1H, br s, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 10.0 Hz.

Anal. Calcd. for $C_{27}H_{22}N_2O_6$: C, 68.93; H, 4.71; N, 5.95. Found: C, 69.03; H, 4.43; N, 5.84.

The Synthesis of Fused 2*H*-Pyran-2-ones **11**, **13**, **15**, **17**, **19**, **21**, **23**, **25**.

General Procedure:

To a solution of **4a** or **4b** (1 mmole) in glacial acetic acid (4 ml) a compound with activated methylene group **10**, **12**, **14**, **16**, **18**, **20**, **22**, **24** (1 mmole) was added and a mixture was heated in an oil bath at reflux temperature for several hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and ether as a solvent). After the reaction was completed, the volatile components were evaporated *in vacuo*. To the oily residue water and ethanol were added. The precipitate, deposited after cooling, was collected by filtration and recrystallized from an appropriate solvent.

The following compounds were prepared in this manner:

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (**11**).

This compound was prepared from **4b** (0.364 g) and cyclohexane-1,3-dione (**10**) (0.112 g), by heating for 2 hours, to give **11** in 71% yield, mp 123-125° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 0.98 (3H, t, CH_2CH_3), 2.19 (2H, m, 7-CH_2), 2.58 and 2.89 (2 x 2H, 2t, 6-CH_2, 8-CH_2), 4.11 (2H, q, CH_2CH_3), 7.38-7.69 (6H, m, COPh, H_4), 8.03 and 8.37 (1H, 2d, CHNH), 10.78 and 11.61 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz.

Anal. Calcd. for $C_{21}H_{19}NO_6$: C, 66.14; H, 5.02; N, 3.67. Found: C, 65.76; H, 4.97; N, 3.74.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-7-methyl-5-oxo-5,6,7,8- tetrahydro-2*H*-1-benzopyran-2-one (**13**).

This compound was prepared from **4b** (0.346 g) and 5-methylcyclohexane-1,3-dione (**12**) (0.126 g), by heating for 2 hours, to give **13** in 80% yield, mp 148-149° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 0.98 (3H, t, CH_2CH_3), 1.19 (3H, d, 7-CH_3), 2.22-2.94 (5H, m, 6-CH_2, 8-CH_2, H_7), 4.10 (2H, q, CH_2CH_3), 7.38-7.69 (6H, m, COPh, H_4), 8.03 and 8.32 (1H, 2d, CHNH), 10.77 and 11.60 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz, J_{CH_3CH} = 6.4 Hz.

Anal. Calcd. for $C_{22}H_{21}NO_6$: C, 66.83; H, 5.35; N, 3.54. Found: C, 66.50; H, 5.45; N, 3.59.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (**15**).

This compound was prepared from **4b** (0.346 g) and 5,5-dimethylcyclohexane-1,3-dione (**14**) (0.140 g), by heating for 2 hours, to give **15** in 74% yield, mp 150-152° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 0.98 (3H, t, CH_2CH_3), 1.16 (6H, s, 7,7-CH_3), 2.44 and 2.75 (2 x 2H, 2s, 6-CH_2, 8-CH_2), 4.11 (2H, q, CH_2CH_3), 7.40-7.70 (6H, m, COPh, H_4), 8.03 and 8.35 (1H, 2d, CHNH), 10.78 and 11.61 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz.

Anal. Calcd. for $C_{23}H_{23}NO_6$: C, 67.47; H, 5.66; N, 3.42. Found: C, 67.42; H, 5.67; N, 3.41.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-7-hydroxy-8-methyl-2*H*-1-benzopyran-2-one (**17**).

This compound was prepared from **4b** (0.346 g) and 2,6-dihydroxytoluene (**16**) (0.124 g), by heating for 6 hours, to give **17** in 14% yield, mp 236-238° (from ethanol), ms: m/z = 393 (M^+); ^{1}H nmr (DMSO-d_6): δ 0.87 and 0.94 (3H, 2t, CH_2CH_3), 2.19 (3H, s, Ar-CH_3), 3.98 and 4.01 (2H, 2q, CH_2CH_3), 6.90 and 6.92 (1H, 2d, H_6), 7.33-7.65 (6H, m, COPh, H_5), 8.09 and 8.20 (1H, 2s, H_4), 8.29 and 8.54 (1H, 2d, CHNH), 10.37 (1H, br s, OH), 10.70 and 11.76 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz, $J_{H5,H6}$ = 7.3 Hz.

Anal. Calcd. for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87; N, 3.56. Found: C, 66.53; H, 4.76; N, 3.63.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3*H*-naphto[2,1-*b*]pyran-3-one (**19**).

This compound was prepared from **4b** (0.346 g) and 2-naphthol (**18**) (0.144 g), by heating for 7 hours, to give **19** in 12% yield, mp 213-215° (from a mixture of 2-propanol and water); ^{1}H nmr (deuteriochloroform): δ 0.99 (3H, t, CH_2CH_3), 4.09 and 4.14 (2H, 2q, CH_2CH_3), 7.40-8.26 (12H, m, COPh, 7H-Ar), 8.30 and 8.61 (1H, 2d, CHNH), 11.04 and 11.83 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.4Hz.

Anal. Calcd. for $C_{25}H_{19}NO_5$: C, 72.63; H, 4.63; N, 3.39. Found: C, 72.26; H, 4.53; N, 3.48.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione (**21**).

This compound was prepared from **4a** (0.360 g) and 4-hydroxy-6-methyl-2*H*-pyran-2-one (**20**) (0.126 g), by heating for 1 hour, to give **21** in 73% yield, mp 198-199° (from ethanol); ^{1}H nmr (DMSO-d_6): δ 0.92 and 0.97 (3H, 2t, CH_2CH_3), 2.33 (3H, 2s, Het-CH_3), 3.99 and 4.04 (2H, 2q, CH_2CH_3), 6.69 and 6.71 (1H, 2s, H_8), 7.41-7.68 (5H, m, COPh), 7.87 and 8.00 (1H, 2s, H_4), 8.35 and 8.60 (1H, 2d, CHNH), 10.65 and 11.62 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz.

Anal. Calcd. for $C_{21}H_{17}NO_7$: C, 63.80; H, 4.33; N, 3.54. Found: C, 63.71; H, 4.18; N, 3.61.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran-2,5-dione (**23**).

This compound was prepared from **4a** (0.360 g) and 4-hydroxy-2*H*-1-benzopyran-2-one (**22**) (0.162 g), by heating for 1.5 hours, to give **23** in 68% yield, mp 177-180° (from a mixture of ethanol and DMF); ms: m/z = 431 (M^+); ^{1}H nmr (DMSO-d_6): δ 0.93 and 0.98 (3H, 2t, CH_2CH_3), 4.01 and 4.07 (2H, 2q, CH_2CH_3), 7.41-8.13 (10H, m, COPh, H_4, H_7, H_8, H_9, H_{10}), 8.42 and 8.69 (1H, 2d, CHNH), 10.76 and 11.65 (1H, 2d, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz.

Anal. Calcd. for $C_{24}H_{17}NO_7$: C, 66.82; H, 3.97; N, 3.25. Found: C, 65.57; H, 3.76; N, 3.66.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridine-2,5-dione (**25**).

This compound was prepared from **4a** (0.360 g) and 4-hydroxypyridin-2(1*H*)-one (**24**) (0.111 g), by heating for 2 hours, to give **25** in 51% yield, mp 259-262° (from a mixture of ethanol and DMF); ^{1}H nmr (DMSO-d_6): δ 0.92 and 0.97 (3H, 2t, CH_2CH_3), 4.00 and 4.05 (2H, 2q, CH_2CH_3), 6.31 and 6.41 (1H, 2d, H_8), 7.43-7.61 (6H, m, COPh, H_7), 7.88 and 8.01 (1H, 2s, H_4), 8.33 and 8.55 (1H, 2d, CHNH), 10.66 and 11.83 (1H, 2d, CHNH), 11.98 (1H, br s, OH or NH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.5 Hz, $J_{H7,H8}$ = 7.2 Hz.

Anal. Calcd. for $C_{20}H_{16}N_2O_6$: C, 63.16; H, 4.24; N, 7.36. Found: C, 62.93; H, 4.01; N, 7.31.

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[17] A detailed nmr study of this and related compounds will be published elsewhere.