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SYNTHESIS OF SOME NEW INOLIZINE AND PYRROLO[1,2-*a*]-QUINOLINE DERIVATIVES *VIA* NITROGEN YLIDES

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Abstract – The pyridinium bromides **2a,b** reacted with dimethyl acetylene-dicarboxylate (DMAD) to give the indolizine derivatives **6a,b**. Bromide salts **2a,b** reacted also with β-nitrostyrene, ethyl acrylate and with acrylamide to give the corresponding indolizine derivatives **8a,b** and **10a-d**. Reaction of the quinolinium salts **12a,b** with DMAD, β-nitrostyrene and with ethyl acrylate as dipolarophiles furnished the corresponding pyrrolo[1,2-*a*]quinoline derivatives **16a,b, 18a,b** and **20a,b,** respectively. Bromide salts **2b** and **22** underwent intramolecular cyclization *via* elimination of water and hydrogen bromide molecules when heated at reflux condition to give the angularly fused indolizine and pyrrolo[1,2-*a*]quinoline structures **21** and **23**, respectively.

INTRODUCTION

Indolizine derivatives have been found to possess a variety of biological activities such as antiinflammatory,[1] antiviral,[2] analgestic,[3] and antitumor[4] activities. In addition, indolizine moiety was found in several naturally occurring alkaloids with important biological activity.[5,6] Coumarin[7] and benzofuran[8,9] derivatives are well-known as highly biologically active compounds. Furthermore, quinolinium salts were found to be potent inhibitors of lymphocyte apoptosis[10] and protein kinase C.[11] The use of heteroaromatic *N*-ylides as 1,3-dipoles has received increasing interest in the synthesis of new condensed heterocyclic structures *via* 3+2 cycloaddition.[12-14] As part of our research interest towards developing new routes for the synthesis of fused heterocyclic systems,[15-17] we conduct here a facile access to some indolizine and pyrrolo[1,2-*a*]quinoline derivatives utilizing some new heteroaromatic *N*-ylides.

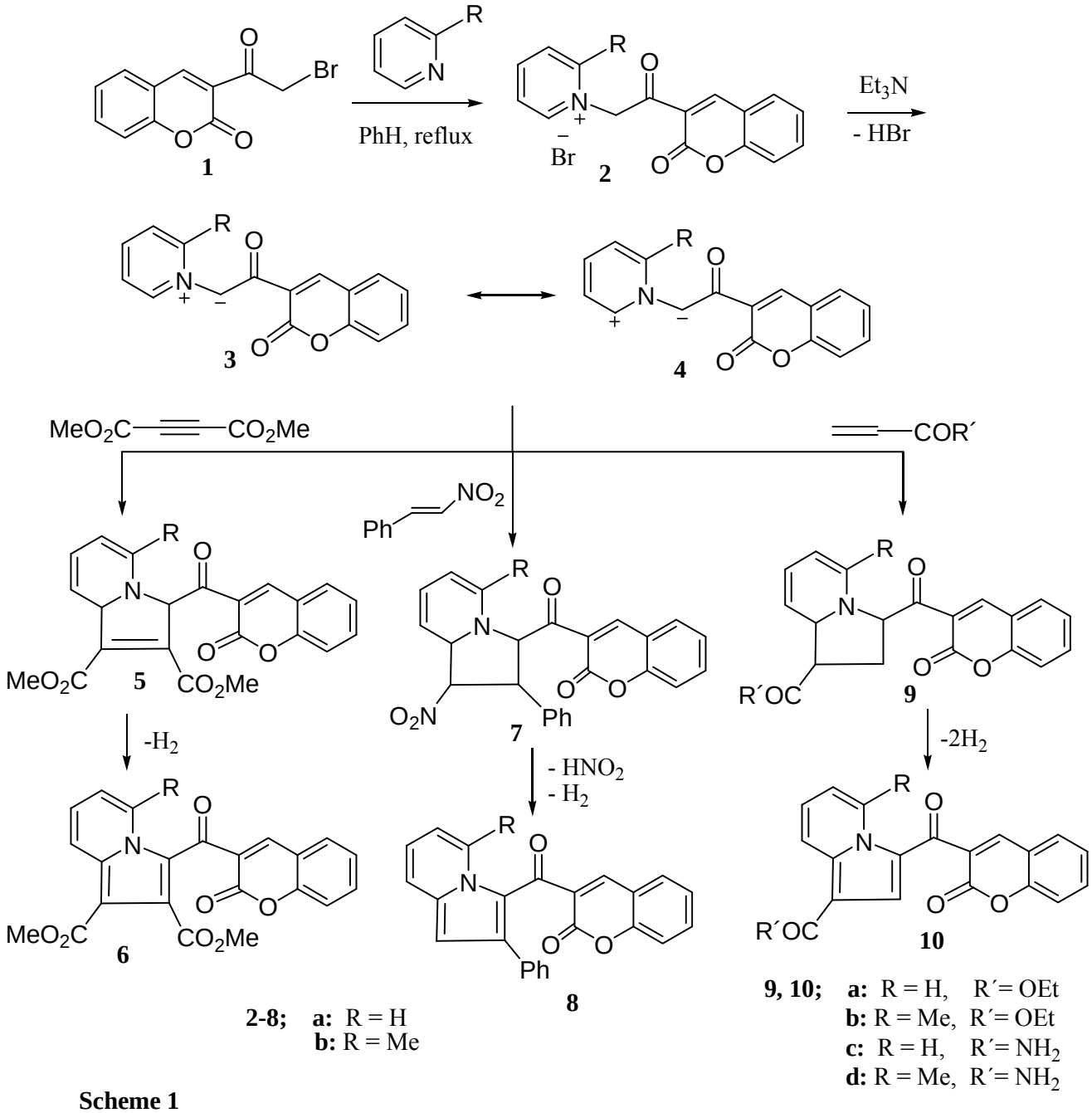
RESULTS AND DISCUSSION

Pyridinium bromides **2a,b** were quantitatively obtained by treatment of 3-(2-bromoacetyl)-*2H*-chromen-2-one **1** with an equivalent amount of pyridine or 2-picoline in dry benzene at refluxing condition. Reaction of the bromide salt **2a** with dimethyl acetylenedicarboxylate (DMAD) in dry benzene at refluxing temperature, in the presence of triethylamine resulted in the formation of a single product as examined by TLC of the crude reaction mixture. Spectroscopic data (MS, IR, ^{1}H and ^{13}C NMR) as well as elemental analysis of the obtained product were in complete agreement with the assigned indolizine structure **6a**, as outlined in Scheme 1. The ^{1}H NMR spectrum of compound **6a** exhibited two singlet peaks at δ 3.56 and 3.85 due to two methyl ester groups in addition to the aromatic multiplets in the region δ 7.36-9.54. Its IR spectrum showed also two characteristic carbonyl absorptions at 1732 and 1695 cm^{-1}. In the same manner, pyridinium bromide **2b** reacted with DMAD under the same reaction conditions to afford the indolizine derivative **6b**, Scheme 1. Formation of the indolizine derivatives **6a,b** is assumed to be formed via 1,3-dipolar cycloaddition of DMAD to the nitrogen ylides **4a,b** [which were formed *in situ* through the reaction of the pyridinium bromides **2a,b** with triethylamine under refluxing benzene] to give the non-isolable intermediates **5a,b** which were consequently oxidized under the reaction conditions to give the indolizine products **6a,b**.

Next, when the pyridinium bromide **2a** was allowed to react with β-nitrostyrene in refluxing benzene, in the presence of triethylamine and manganese dioxide, it afforded only one product. The elemental analyses and spectroscopic data of the latter product established its structure as 3-(2*H*-2-oxo-chromen-3-yl)carbonyl-2-phenylindolizine (**8a**) (Scheme 1). In a similar manner, compound **2a** reacted with ethyl acrylate and with acrylamide under the same reaction conditions as mentioned above, to give the corresponding indolizine structures **10a** and **10c** as shown in Scheme 1. The ^{1}H NMR spectrum of compound **10a** revealed triplet signal at δ 1.34 and a quartet one at 4.33 due to the ethyl-ester protons in addition to an aromatic mutiplet at δ 7.12-9.82. It mass spectrum showed a molecular ion peak at *m/z* 361. The IR spectrum of compound **10a** showed three carbonyl absorption bands at 1666, 1705 and 1752 cm^{-1}.

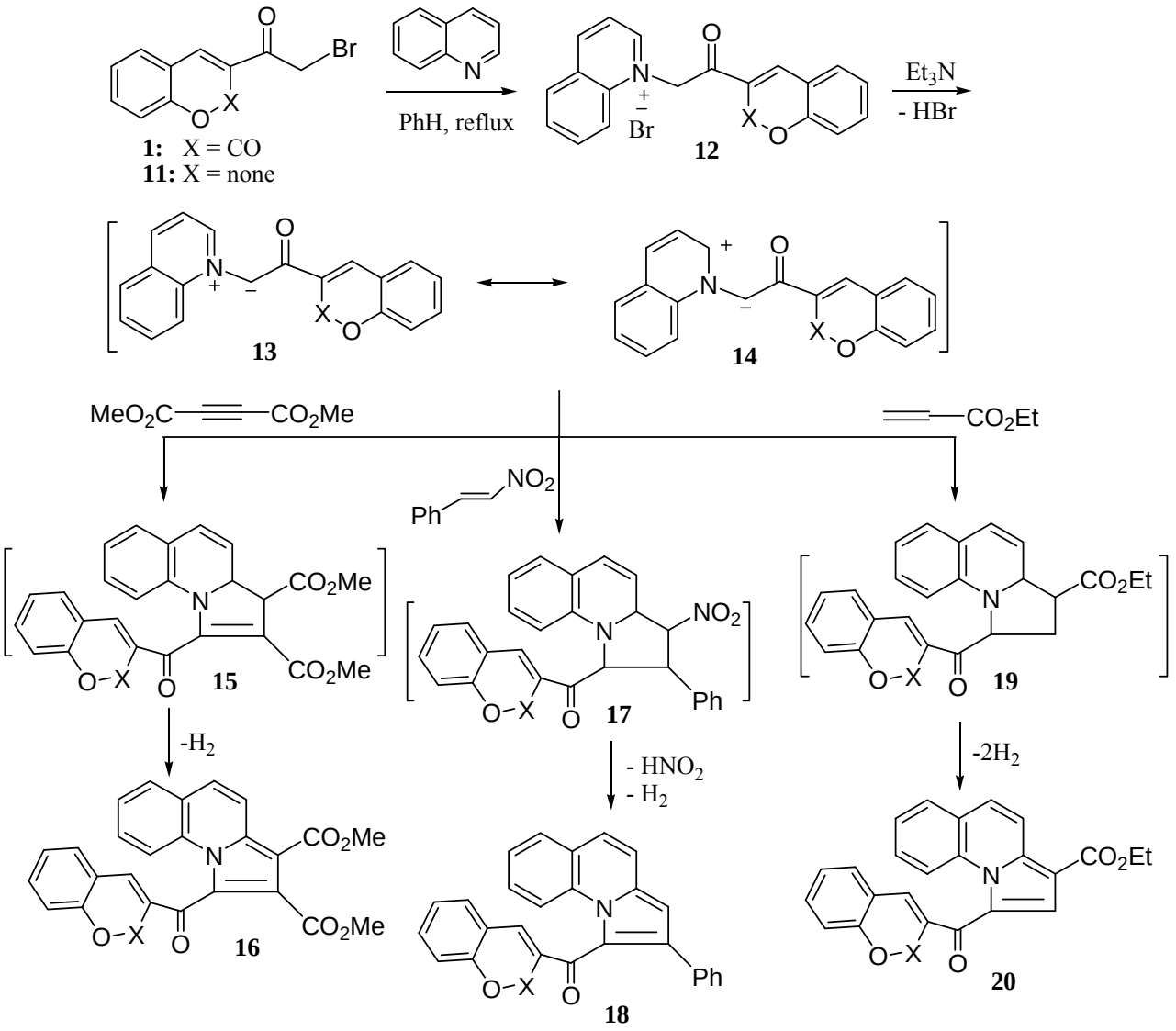
The 2-picolinium ylide **3b,** from its bromide salt **2b**, reacted in a similar fashion with β-nitrostyrene, ethyl acrylate and with acrylamide under the same reaction conditions above, to give the corresponding indolizine derivatives **8b**, **10b**, and **10d**, respectively as shown in Scheme 1. The above reactions are assumed to proceed via a reaction sequence of [3+2] cycloaddition of the *N*-ylide with the alkene and subsequent elimination of nitrous acid and hydrogen molecules (in case of the formation of **8a** and **8b**) or two hydrogen molecules (in case of the formation of **10a-d**) under the reaction conditions (Scheme 1).

The proposed mechanism is similar to analogous examples reported in literature.[18,19]



Scheme 1

Similarly, treatment of 3-(2-bromoacetyl)-2*H*-chromen-2-one **1** or 2-(2-bromoacetyl)benzofuran **11** with quinoline in dry benzene at refluxing temperature gave the corresponding quinolinium bromides **12a,b**. Reaction of the bromide salts **12a,b** with DMAD in dry benzene at refluxing temperature, in the presence of triethylamine, resulted in the formation the annulated dimethyl pyrrolo[1,2-*a*]quinoline-2,3-dicarboxylates **16a,b,** respectively, as shown in Scheme 2. Spectroscopic data as well as elemental analyses of the obtained products were in complete agreement with the assigned structures **16a,b**.



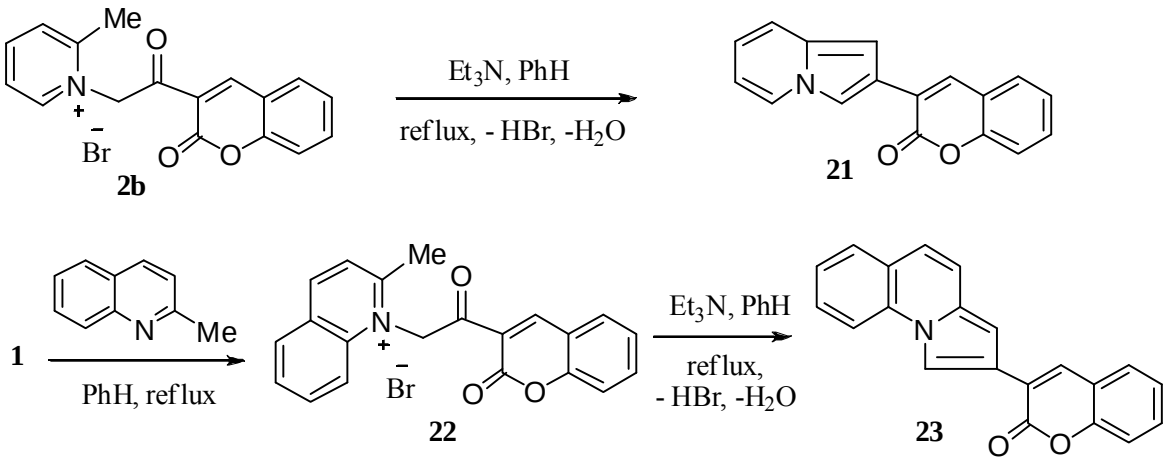
Scheme 2

12-20; a: X = CO
b: X= none

Reaction of the quinolinium bromides **12a,b** with β-nitrostyrene as dipolarophile in refluxing benzene, in the presence of triethylamine and manganese dioxide, furnished the corresponding 2-phenylpyrrolo[1,2-*a*]quinoline derivatives **18a,b** (Scheme 2). In a similar manner, quinolinium bromides **12a,b** reacted with ethyl acrylate under the same reaction conditions that mentioned above to give the corresponding ethyl pyrrolo[1,2-*a*]quinoline-3-carboxylates **20a,b** as shown in Scheme 2. Structures of compounds **18a,b** and **20a,b** were deducted from the elemental analyses and spectral data (MS, IR, ^{1}H and ^{13}C NMR) of the corresponding reaction products.

2-Picolinium bromide **2b** when heated at reflux in dry benzene and in the presence of triethylamine, furnished a single product as examined by TLC. Elemental analyses and mass spectrum of the reaction product established its molecular formula as $C_{17}H_{11}NO_2$. Spectroscopic data of the reaction product were

in complete agreement with the assigned 3-(indolizin-2-yl)-2*H*-chromen-2-one structure **21**, as outlined in Scheme 3. Furthermore, treatment of 3-(2-bromoacetyl)-2*H*-chromen-2-one **1** with 2-methylquinoline in dry benzene at refluxing temperature gave the corresponding 2-methylquinolinium bromide **22** which underwent intramolecular cyclization *via* elimination of water and hydrogen bromide molecules to give the angularly fused 2-(2*H*-2-oxo-chromen-3-yl)pyrrolo[1,2-*a*]quinoline **23** (Scheme 3). The IR spectrum of compound **23** showed only one carbonyl absorption at 1704 cm^{-1} and its ^1H NMR spectrum was free of aliphatic protons and showed only peaks due to aromatic ones. Its mass spectrum showed a peak at *m/z* 311 due to the molecular ion.



Scheme 3

EXPERIMENTAL

All melting points were measured on a Gallenkamp melting point apparatus. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP 3300 and Shimadzu FT IR 8101 PC infrared spectrophotometers. The NMR spectra were recorded on a Varian Mercury VX-300 NMR spectrometer. ^1H spectra were run at 300 MHz and ^{13}C spectra were run at 75.46 MHz in deuterated chloroform ($CDCl_3$) or dimethyl sulfoxide (DMSO-d_6). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 e.V. Elemental analyses were carried out at the Microanalytical Center of Cairo University, Giza, Egypt. 3-(2-Bromoacetyl)-2*H*-chromen-2-one (**1**)[20,21] and 2-(2-bromoacetyl)benzofuran (**11**)[22] were prepared according to the reported literature.

Preparation of the pyridinium and quinolinium salts 2a,b, 12a,b and 22

To a solution of 3-(2-bromoacetyl)-2*H*-chromen-2-one **1** or 2-(2-bromoacetyl)benzofuran **11** (5 mmol) in dry benzene (50 mL) was add the appropriate nitrogen-heterocycle (pyridine, 2-picoline, quinoline or

2-methylquinoline) (5 mmol). The mixture was refluxed for 30 min then left to cool. The solid product was filtered off, washed with Et_2O / benzene and dried to afford the pyridinium bromide salts **2a,b, 12a,b** and **22,** respectively.

2a: Yield (85%), mp > 300 °C; IR (KBr) ν 1729, 1691 (2 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 6.32 (s, 2H, CH_2), 7.44-7.53 (m, 3H, Ar-H), 7.75-8.28 (m, 4H, Ar-H), 8.86-8.97 (m, 2H, Ar-H), 9.01 (s, 1H, Ar-H). *Anal.* Calcd for $C_{16}H_{12}BrNO_3$: C, 55.51; H, 3.49; N, 4.05. Found: C, 55.85; H, 3.65; N, 4.20%.

2b: Yield (86%), mp 221-223 °C; IR (KBr) ν 1727, 1686 (2 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.71 (s, 3H, CH_3), 6.30 (s, 2H, CH_2), 7.47-7.59 (m, 2H, Ar-H), 7.83-7.89 (m, 1H, Ar-H), 8.06-8.17 (m, 3H, Ar-H), 8.58-8.63 (m, 1H, Ar-H), 8.93 (s, 1H, Ar-H), 8.96 (s, 1H, Ar-H). *Anal.* Calcd for $C_{17}H_{14}BrNO_3$: C, 56.69; H, 3.92; N, 3.89. Found: C, 56.25; H, 3.90; N, 3.99%.

12a: Yield (72%), mp 216-218 °C; IR (KBr) ν 1735, 1722 (2 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 5.89 (s, 2H, CH_2), 7.20-7.89 (m, 6H, Ar-H), 8.04-9.01 (m, 6H, Ar-H). *Anal.* Calcd for $C_{20}H_{14}BrNO_3$: C, 60.62; H, 3.56; N, 3.53. Found: C, 60.25; H, 3.69; N, 3.30%.

12b: Yield (65%), mp 222-224 °C; IR (KBr) ν 1678 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 5.60 (s, 2H, CH_2), 7.34-7.57 (m, 3H, Ar-H), 7.69-8.13 (m, 5H, Ar-H), 8.23 -8.69 (m, 2H, Ar-H), 9.07 (s, 1H, Ar-H), 9.29 (s, 1H, Ar-H). *Anal.* Calcd for $C_{19}H_{14}BrNO_2$: C, 61.97; H, 3.83; N, 3.80. Found: C, 61.25; H, 3.69; N, 3.24%.

22: Yield (85%), mp 160-162 °C; IR (KBr) ν 1727, 1686 (2 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.32 (s, 3H, CH_3), 5.73 (s, 2H, CH_2), 7.22-7.95 (m, 6H), 8.10-8.52 (m, 4H), 8.61 (s, 1H). *Anal.* Calcd for $C_{21}H_{16}BrNO_3$: C, 61.48; H, 3.93; N, 3.41. Found: C, 61.25; H, 3.69; N, 3.30%.

Synthesis of the Indolizine 6a,b and Pyrrolo[1,2-*a*]quinoline Derivatives 16a,b

To a mixture of the appropriate pyridinium **2a,b** or quinolinium **12a,b** bromides (2 mmol) and dimethyl acetylenedicarboxylate (DMAD) (0.57 g, 4 mmol) in dry benzene (30 mL), triethylamine (0.4 mL) was added and the reaction mixture was refluxed 2~3 h, then left to cool to rt. The triethylamine hydrobromide was removed by filtration and the filtrate was evaporated under vacuum. The residue was triturated with MeOH where a yellow-colored precipitate was formed that was filtered off, washed with MeOH, dried. Recrystallization from DMF/EtOH afforded the corresponding indolizine **6a,b** or pyrrolo[1,2-*a*]quinoline **16a,b** derivatives.

Dimethyl 3-(2*H*-2-oxo-chromen-3-yl)carbonylindolizine-1,2-dicarboxylate (6a): Yield (75%), mp 231-232 °C; IR (KBr) ν 1730, 1702, 1669 (3 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.21 (s, 3H, $COOCH_3$), 3.86 (s, 3H, $COOCH_3$), 7.36-7.53 (m, 3H, Ar-H), 7.73-7.81 (m, 3H, Ar-H), 8.32 (s, 1H, Ar-H), 8.34-8.37 (m, 1H, Ar-H), 9.81 (d, 1H, Ar-H, *J* = 6.9 Hz); ^{13}C NMR (DMSO-d_6) δ: 51.8, 52.4, 103.7, 109.3, 116.1, 116.4, 117.6, 119.3, 125.1, 125.7, 128.2, 129.4, 130.3, 132.3, 133.6, 137.7, 143.1, 153.6, 157.3, 162.2, 165, 178.9; MS *m/z* (%): 405 (M^+, 100), 374 (33.6), 346 (26.8), 330 (34.4), 202 (16.5), 173 (13.1), 143 (16.5), 89 (15.5). *Anal.* Calcd for $C_{22}H_{15}NO_7$: C, 65.19; H, 3.73; N, 3.46. Found: C, 65.43; H, 3.62; N, 3.14%.

Dimethyl 5-methyl-3-(2*H*-2-oxo-chromen-3-yl)carbonylindolizine-1,2-dicarboxylate (6b): Yield (65%), mp 192-194 °C; IR (KBr) ν 1733, 1690, 1635 (3 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.09 (s, 3H, picoline-CH_3), 3.36 (s, 3H, $COOCH_3$), 3.83 (s, 3H, $COOCH_3$), 7.2 (d, 1H, Ar-H, *J* = 7.2 Hz), 7.45-7.52 (m, 2H, Ar-H), 7.63-7.85 (m, 3H, Ar-H), 8.27 (d, 1H, Ar-H, *J* = 7.8 Hz), 8.71 (s, 1H, Ar-H); ^{13}C NMR (DMSO-d_6) δ: 51.6, 52.3, 102, 116.4, 116.8, 117.7, 117.9, 120.6, 123.1, 124.9, 125.2, 128.7, 129.9, 130.2, 134.7, 138.8, 139.1, 147.9, 154.3, 157.1, 162.4, 165.3, 178.8; MS *m/z* (%): 419 (M^+, 100), 387 (53.9), 359 (57.6), 344 (29.5), 301 (35.4), 246 (66.8), 216 (33.2), 173 (68.5), 129 (29.5), 89 (24.6). *Anal.* Calcd for $C_{23}H_{17}NO_7$: C, 65.87; H, 4.09; N, 3.34. Found: C, 66.05; H, 4.12; N, 3.03%.

Dimethyl 1-(2*H*-2-oxo-chromen-3-yl)carbonylpyrrolo[1,2-*a*]quinoline-2,3-dicarboxylate (16a): Yield (52%), mp 140-142 °C; IR (KBr) ν 1732, 1726, 1656 (3 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.61 (s, 3H, $COOCH_3$), 3.90 (s, 3H, $COOCH_3$), 7.50-7.88 (m, 6H, Ar-H), 8.42-8.45 (m, 2H, Ar-H), 8.78-8.83 (m, 2H, Ar-H), 9.22 (d, 1H, Ar-H, *J* = 6.9 Hz); ^{13}C NMR (DMSO-d_6) δ: 51.3, 52.5, 115.7, 116.4, 117.3, 117.7, 119.2, 123, 123.9, 124.7, 125, 125.4, 126.3, 127.5, 128.5, 129.4, 129.8, 130.5, 131.9, 133.9, 134.9, 144.3, 148.4, 153.8, 154.4, 164.6; MS *m/z* (%): 455 (M^+, 83), 424 (25.2), 396 (19.2), 380 (15.6), 310 (20.4), 252 (24.8), 193 (14.8), 172 (26.1), 88 (33), 43 (100). *Anal.* Calcd for $C_{26}H_{17}NO_7$: C, 68.57; H, 3.76; N, 3.08. Found: C, 68.25; H, 3.69; N, 3.32%.

Dimethyl 1-(benzofuran-2-yl)carbonylpyrrolo[1,2-*a*]quinoline-2,3-dicarboxylate (16b): Yield (55%), mp 219-221 °C; IR (KBr) ν 1742, 1702, 1653 (3 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.24 (s, 3H, $COOCH_3$), 3.80 (s, 3H, $COOCH_3$), 7.47-7.82 (m, 7H, Ar-H), 8.36-8.69 (m, 3H, Ar-H), 9.61 (s, 1H); MS *m/z* (%): 427 (M^+, 100), 338 (16.2), 282 (13.5), 145 (38.6), 128 (10.3), 57 (6.5). *Anal.* Calcd for $C_{25}H_{17}NO_6$: C, 70.25; H, 4.01; N, 3.28. Found: C, 70.21; H, 4.36; N, 3.64%.

Synthesis of the Indolizine Derivatives 8a,b, 10a-d, 18a,b and 20a,b

To a mixture of the appropriate pyridinium **2a,b** or quinolinium **12a,b** salts (1 mmol) and the appropriate β-nitrostyrene or ethyl acrylate or acrylamide (6 mmol) in benzene (30 mL) in the presence of triethylamine (0.15 mL, 1.5 mmol), manganese dioxide (0.7 g, 8 mmol) was added. The mixture was refluxed for 4h then cooled to rt. The solid salts were removed by filtration, and the filtrate was evaporated under vacuum. The residue was treated with MeOH, and the solid precipitate was filtered off, washed with MeOH and dried. Recrystallization from EtOH/DMF afforded the corresponding indolizine derivatives **8a,b, 10a-d, 18a,b** and **20a,b**, respectively.

3-(2*H*-2-Oxo-chromen-3-yl)carbonyl-2-phenylindolizine (8a): Yield (65%), mp >300 °C; IR (KBr) ν 1721, 1680 (2 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 7.28-7.53 (m, 7H, Ar-H), 7.68-7.83 (m, 5H, Ar-H), 8.05-8.45 (m, 2H, Ar-H), 8.80 (d, 1H, *J* = 6.9 Hz); MS *m/z* (%): 365 (M^+, 65), 306 (20.4), 288 (34.5), 273 (14.6), 203 (13.5), 192 (14.8), 173 (16.2), 149 (20.8), 115 (13.6), 77 (100). *Anal.* Calcd for $C_{24}H_{15}NO_3$: C, 78.89; H, 4.14; N, 3.83. Found: C, 78.95; H, 4.69; N, 3.29%.

5-Methyl-3-(2*H*-2-oxo-chromen-3-yl)carbonyl-2-phenylindolizine (8b): Yield (68%), mp 275-277 °C; IR (KBr) ν 1714, 1652 (2 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 2.45 (s, 3H, picoline-CH_3), 6.68 (s, 1H), 7.49-7.87 (m, 9H, ArH), 8.09-8.27 (m, 4H, ArH); ^{13}C NMR (DMSO-d_6) δ: 17.4, 114.3, 115.4, 116.9, 117.8, 119.7, 124.6, 125.7, 128.2, 128.6, 129.1, 129.7, 131.9, 132.1, 133.4, 134.8, 137.9, 139.1, 142.5, 147.3, 153.4, 164.8, 178.1; MS *m/z* (%): 379 (M^+, 22.6), 309 (56.8), 261 (73.9), 218 (100), 181 (54.5), 171 (43.9), 130 (41.3), 102 (35.2), 77 (45.5), 65 (41.9). *Anal.* Calcd for $C_{25}H_{17}NO_3$: C, 79.14; H, 4.52; N, 3.69. Found: C, 79.00; H, 4.65; N, 3.44%.

Ethyl 3-(2*H*-2-oxo-chromen-3-yl)carbonylindolizine-1-carboxylate (10a): Yield (70%), mp 211-213 °C; IR (KBr) ν 1752, 1705, 1666 (3 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 1.34 (t, 3H, $COOCH_2CH_3$, *J* = 7.2 Hz), 4.33 (q, 2H, $COOCH_2CH_3$, *J* = 7.2 Hz), 7.12-7.18 (m, 2H, Ar-H), 7.29-36 (m, 4H, Ar-H), 7.63-7.69 (m, 1H, Ar-H), 8.31-8.35 (m, 1H, Ar-H), 8.54 (s, 1H, Ar-H),9.81 (d, 1H, Ar-H, *J* = 6.9 Hz); ^{13}C NMR (DMSO-d_6) δ: 14.3, 59.7, 105.7, 116.1, 116.3, 118.8, 121.9, 122.4, 124.3, 127.7, 127.9, 128.4, 128.6, 128.8, 132.1, 134.3, 139.2, 151.2, 162.9, 166.8, 183.8; MS *m/z* (%): 361 (M^+, 35.3), 288 (46.8), 188 (13.6), 173 (100), 146 (18.9), 115 (31.4), 79 (31.6). *Anal.* Calcd for $C_{21}H_{15}NO_5$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.52; H, 4.59; N, 3.54%.

Ethyl 5-methyl-3-(2*H*-2-oxo-chromen-3-yl)carbonylindolizine-1-carboxylate (10b): Yield (70%), mp 158-160 °C; IR (KBr) ν 1728, 1692, 1637 (3 C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 1.17 (t, 3H, $COOCH_2CH_3$, *J* = 7.5 Hz), 2.48 (s, 3H, picoline-CH_3), 3.80 (q, 2H, $COOCH_2CH_3$, *J* = 7.5 Hz), 6.30 (s, 1H,

Ar-H), 7.47-7.83 (m, 3H, Ar-H), 8.16-8.27 (m, 3H, Ar-H), 8.71 (m, 1H, Ar-H), 8.94 (s, 1H, Ar-H); MS *m/z* (%): 375 (M^+, 14.2), 348 (30.3), 298 (100), 202 (20), 173 (16.7), 145 (12.1), 129 (6.8), 93 (15.1), 77 (11.2). *Anal.* Calcd for $C_{22}H_{17}NO_5$: C, 70.39; H, 4.56; N, 3.73. Found: C, 70.29; H, 4.69; N, 3.35%.

3-(2*H*-2-Oxo-chromen-3-yl)carbonylindolizine-1-carboxamide (10c): Yield (82%), mp 250-252 °C; IR (KBr) ν 3213, 3139 (NH2), 1732, 1693 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 7.47-7.59 (m, 4H, Ar-H), 7.82-7.86 (m, 1H, Ar-H), 8.07-8.28 (m, 3H, Ar-H), 8.69-8.96 (m, 4H, Ar-H and NH_2); MS *m/z* (%): 332 (M^+, 10.2), 288 (31.6), 173 (56.4), 159 (11.9), 144 (12.8), 130 (17.5), 115 (8.9), 89 (27.3), 78 (14.9), 52 (100). *Anal.* Calcd for $C_{19}H_{12}N_2O_4$: C, 68.67; H, 3.64; N, 8.43%. Found: C, 68.21; H, 3.29; N, 8.24%.

5-Methyl-3-(2*H*-2-oxo-chromen-3-yl)carbonylindolizine-1-carboxamide (10d): Yield (76%), mp 196-198 °C; IR (KBr) ν 1605, 1709 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 2.51 (s, 3H, picoline-CH_3), 6.52-6.78 (m, 2H, Ar-H), 6.97 (s, 1H, Ar-H), 7.36-7.46 (m, 3H, Ar-H), 7.56-7.80 (m, 2H, Ar-H), 8.31 (br.s, 2H, NH_2), 8.51 (s, 1H, Ar-H); MS *m/z* (%): 346 (M^+, 3.27), 172 (76), 144 (88.2), 132 (100), 117 (72), 90 (84.2), 73 (84.2). *Anal.* Calcd for $C_{20}H_{14}N_2O_4$: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.55; H, 3.99; N, 8.24%.

1-(2*H*-2-Oxo-chromen-3-yl)carbonyl-2-phenylpyrrolo[1,2-*a*]quinoline (18a): Yield (62%), mp 249-251 °C; IR (KBr) ν 1702, 1675 (2 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 7.48-7.55 (m, 11H, Ar-H), 7.83-7.87 (m, 3H, Ar-H), 8.14-8.23 (m, 3H, Ar-H); ^{13}C NMR (DMSO-d_6) δ: 115.2, 116.6, 117.8, 118.2, 120.8, 120.9, 121.8, 123.7, 126.3, 127.7, 128.5, 128.9, 129.1, 129.7, 130.2, 131.9, 132.4, 133.8, 134.6, 137.9, 139.2, 141.3, 145.3, 156.9, 161.8, 175.2; MS *m/z* (%): 415 (M^+, 13.2), 346 (6.1), 245 (2.3), 191 (6.9), 149 (13.4), 115 (8.1), 102 (30.4), 77 (77.4), 65 (21.5), 40 (100). *Anal.* Calcd for $C_{28}H_{17}NO_3$: C, 80.95; H, 4.12; N, 3.37. Found: C, 80.25; H, 4.69; N, 3.35%.

1-(Benzofuran-2-yl)carbonyl-2-phenylpyrrolo[1,2-*a*]quinoline (18b): Yield (62%), mp 176-178 °C; IR (KBr) ν 1652 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 7.15-7.47 (m, 7H, Ar-H), 7.50-7.61 (m, 5H, Ar-H), 8.10-8.35 (m, 3H, Ar-H), 8.88-8.98 (m, 2H, Ar-H); MS *m/z* (%): 387 (M^+, 100), 358 (53), 241 (50.2), 145 (39.1), 89 (46.1). *Anal.* Calcd for $C_{27}H_{17}NO_2$: C, 83.70; H, 4.42; N, 3.62. Found: C, 83.35; H, 4.59; N, 3.34%.

Ethyl 1-(2*H*-2-oxo-chromen-3-yl)carbonypyrrolo[1,2-*a*]quinoline-3-carboxylate (20a): Yield (66%), mp 163-165 °C; IR (KBr) ν 1730, 1702, 1655 (3 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.30 (t, 3H, $COOCH_2CH_3$, J = 6.9 Hz), 4.33 (q, 2H, $COOCH_2CH_3$, J = 6.9 Hz), 7.14-7.45 (m, 7H, Ar-H), 7.66 (d, 2H,

Ar-H, *J* = 8.4 Hz), 8.05 (d, 2H, Ar-H, *J* = 8.4 Hz), 8.38 (s, 1H, Ar-H); MS *m/z* (%): 411 (M^+, 15.6), 336 (30.4), 283 (26.6), 238 (3.5), 214 (8.3), 172 (18.1), 165 (4.4), 143 (6.8), 130 (30.8), 77 (100). *Anal.* Calcd for $C_{25}H_{17}NO_5$: C, 72.99; H, 4.16; N, 3.40. Found: C, 72.25; H, 4.69; N, 3.30%.

Ethyl 1-(benzofuran-2-yl)carbonylpyrrolo[1,2-*a*]quinoline-3-carboxylate (20b): Yield (72%), mp 207-209 °C; IR (KBr) ν 1697, 1647 (2 C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.17 (t, 3H, $COOCH_2CH_3$, *J* = 6.9 Hz), 4.07 (q, 2H, $COOCH_2CH_3$, *J* = 6.9 Hz), 6.27 (m, 1H, Ar-H), 6.72 (d, 1H, Ar-H, *J* = 8.1 Hz), 7.03 (m, 1H, Ar-H), 7.31-7.49 (m, 5H, Ar-H), 7.62-7.94 (m, 3H, Ar-H), 8.24 (s, 1H, Ar-H); ^{13}C NMR (DMSO-d_6) δ: 14.6, 58.1, 89.4, 111.5, 112.4, 112.6, 115.3, 116.8, 117.3, 121, 121.8, 123.9, 124.3, 126.6, 128.2, 129.2, 131.2, 135.6, 138.3, 148.9, 151.3, 155.6, 164.6, 184.6; MS *m/z* (%): 383 (M^+, 68.6), 338 (42.1), 281 (32.5), 240 (67), 167 (100), 89 (36.9). *Anal.* Calcd for $C_{24}H_{17}NO_4$: C, 75.19; H, 4.47; N, 3.65. Found: C, 75.25; H, 4.69; N, 3.24%.

Synthesis of 2-(2*H*-2-oxo-chromen-3-yl)indolizine 21 and 2-(2*H*-2-oxo-chromen-3-yl)pyrrolo-[1,2-*a*]quinoline 23

To a solution of the appropriate 2-picolinium **2b** or 2-methylquinolinium bromide **22** (1 mmol) in dry benzene (20 mL), triethylamine (0.2 mL) was added and the reaction mixture was refluxed 4 h then left to cool to rt. The triethylamine-hydrobromide salt was removed by filtration and the filtrate was evaporated under vacuum. The residue was triturated with MeOH and the solid product was filtered off, washed with MeOH and dried. Recrystallization from the proper solvent afforded the indolizine **21** or pyrrolo[1,2-*a*]quinoline **23** derivatives, respectively.

3-(Indolizin-2-yl)-2*H*-chromen-2-one (21): Yield (52%), mp 203-205 °C; IR (KBr) ν 1708 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.52-6.74 (m, 2H, Ar-H), 6.96 (s, 1H, Ar-H), 7.36-7.79 (m, 5H, Ar-H), 8.30 (s, 1H, Ar-H), 8.51 (s, 1H, Ar-H); MS *m/z* (%): 261 (M^+, 100), 233 (55.8), 204 (36.7), 130 (7.3), 102 (10.1), 63 (6.4), 50 (11.9). *Anal.* Calcd for $C_{17}H_{11}NO_2$: C, 78.15; H, 4.24; N, 5.36. Found: C, 78.25; H, 4.61; N, 5.22%.

2-(2*H*-2-Oxo-chromen-3-yl)pyrrolo[1,2-*a*]quinoline (23): Yield (55%), mp 229-231 °C; IR (KBr) ν 1704 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.50-6.73 (m, 4H, Ar-H), 7.06-7.09 (m, 2H, Ar-H), 7.24-7.41 (m, 5H, Ar-H), 7.83 (s, 1H, Ar-H), 8.20 (d, 1H, Ar-H, *J* = 8.4 Hz); MS *m/z* (%): 311 (M^+, 10.6), 309 (83.5), 294 (100), 184 (11.3), 165 (17.2), 147 (16.5), 131 (17.1), 109 (17.6), 77 (37.3), 67 (39.0). *Anal.* Calcd for $C_{21}H_{13}NO_2$: C, 81.01; H, 4.21; N, 4.50. Found: C, 81.25; H, 4.69; N, 4.30%.

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