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Synthesis of a library of benzoindolizines using poly(ethylene glycol) as soluble support

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Abstract—A library of benzoindolizines (pyrrolo [1,5-*a*] quinolines **10** and pyrrolo [1,5-*a*] quinolines **9**) has been synthesized using poly(ethylene glycol) (PEG) as soluble polymer support. The PEG-supported isoquinolinium salt **4** reacted, respectively, with active alkenes **11** using tetrakispyridinecobalt(II) dichromate (TPCD) as oxidant or alkynes **12** to give **10**, of which yields were from moderate to high. By analogy, the reaction of PEG-supported quinolinium salt **3** with **12** was to produce **9**. However, in the presence of TPCD the reaction of **3** with **11** afforded indolizines **8**, which was discovered firstly.

1. Introduction

Indolizine is an important ring system in view of its similarity to indole. Recently many papers have described the application of indolizine derivatives in biology and medicine. They have not only been used as novel potent inhibitor of 15-lipoxyenase,[1] calcium entry blockers,[2] antileishmanial and antiviral agent,[3] histamine H_3 receptor antagonists,[4] but also have shown antimycobacterial activity,[5] antioxidant properties[6] and delayed replicative senescence of human diploid fibroblasts.[7] In addition, (±)-monomorine,[8] new class of fluorescent β-cyclodextrins[9] and di- or tetrahydroxyindolizidine[10] have been synthesized using them by miscellaneous methods.

In principle, there may be three approaches to synthesize indolizine. The most general method is the formation of the five-membered ring moiety in the indolizine framework mainly by intra- or intermolecular condensation,[4] 1,3-dipolar cycloadditions,[11] 1,5-dipolar cyclization.[6,12] Recently some other methods constructing five-membered rings have been reported such as Cu-assisted cycloisomerization of alkynyl imines,[8] electrophilic Baylis–Hillman reaction,[13] one-step gas-phase synthesis,[14] Aza Wolff rearrangement for 4-oxoquinolizine-3-diazonium tetrafluoroborates,[15] cerium(III)-catalyzed cyclization with 1-cyanomethylene tetrahydro-isoquionline,[16] the reaction of 2-formyl-1,4-dihydropyridine derivative with malonitrile[17] or activated methylene reagent.[18] The formation of six-membered rings by electrochemically induced hetero-[4 + 2]-cycloadditon,[19] condensation by $BF_3(OEt_2)$ as catalyst[20] and intramolecular Dieckmann type cyclization[21] may be the second type of approach for which there are only a few examples. The third method is the simultaneous formation of the five-membered and six-membered rings, which is only an example recently.[22] There are many methods introduced, however, the most important methods for the synthesis of indolizine and benzoindolizine derivatives is based on 1,3-dipolar cycloaddition reactions of N-heterocyclic ylides with electron-deficient alkenes and alkynes.

Currently, liquid-phase synthesis using soluble polymers technique greatly attracts the interests of organic chemists in the field of combinatorial chemistry. It has the advantages of conventional liquid-phase synthesis and easy separation purification of the products in solid-phase synthesis. Moreover, the soluble polymer-bound species allow using routine analytical methods (NMR, TLC or IR) to monitor the reaction process and to determine the structures of products attached to polymer support directly. Poly(ethylene glycol) (PEG) is an ideal support and the most widely used polymer for iquid-phase combinatorial synthesis in terms of its controllable solubility in different solvents. Therefore, we have reported that indolizines were synthesized effectively by PEG-supported pyridinium ylide reacted

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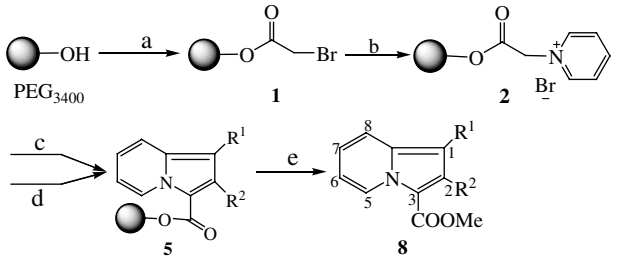


Scheme 1. (a) $BrCH_2COBr$, DIPEA, CH_2Cl_2, 0 °C. (b) Pyridine, rt CH_2Cl_2, overnight. (c) Alkenes **11**, DIPEA, TPCD, DMF, 85-90 °C, 3–4 h. (d) Alkynes **12**, DIPEA, toluene, 90 °C, 3 h. (e) 1% KCN/CH_3OH, rt 24 h.

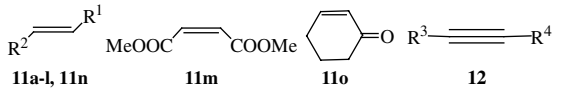


Figure 1.

with active alkenes using TPCD as oxidant and alkynes (Scheme 1).[23]

In an extension of our work on PEG-supported N-heterocyclic ylides, we here reported firstly the synthesis of new benzoindolizines (pyrrolo [1,5-*a*] quinolines **9** and pyrrolo [1,5-*a*] isoquinolines **10**) by 1,3-dipolar cycloaddition of PEG-supported quinolinium and isoquinolinium ylides, respectively, with active alkenes **11** and alkynes **12**. The structures of **11** and **12** were shown in Figure 1.

2. Results and discussion

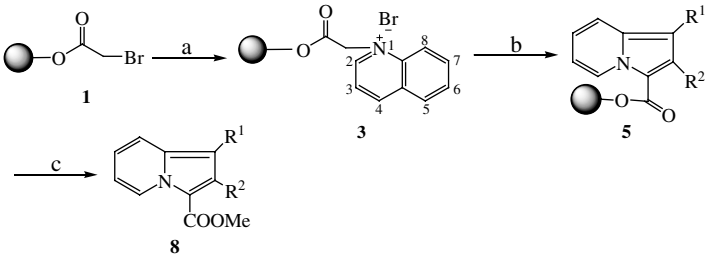
At the beginning, we employed PEG-supported quinolinium ylide derived from quinolinium salt **3**[24] to react with **11** using TPCD (1 equiv) as oxidant and DIPEA (2 equiv) as base at 90 °C; for 3–4 h, which did not get our anticipative pyrrolo [1,5-*a*] quinolines **9** but indolizines **8** (except that the reaction of **3** with **11l** afforded the product **8l** and **9l** from ^{1}H NMR spectra) (Scheme 2). However, Zhang et al.[25] reported that the reaction of quinolinium ylides and, α,β-unsaturated ketones gave pyrrolo [1,5-*a*] quinolines. Under the above reaction condition, some yields of **8** were low. Therefore, optimizing the cycloaddition reaction conditions to obtain better yield, we choose K_2CO_3 to replace DIPEA and prolonged the reaction time, of which yields were improved (Table 1). Whereas, enhancing the reaction temperature did not improve the yields. It was obvious that the yields were less than those of **8a**–**o** synthesized by the reaction of PEG-bound pyridinium salt with **11** in the presence of TPCD. The structure of **8m** which was obtained by this method was confirmed by MS, ^{1}H and ^{13}C NMR, ^{1}H–^{1}H COSY and DEPT spectral data. Because of giving products of indolizines, we considered if the oxidant TPCD was excessive. We tried decreasing TPCD or changing the reaction temperature, but the product were still **8**[26] (except for **11l** which still produce **8l** and **9l**).

Table 1. Synthesis of indolizines **8** from pyridinium ylide and quinolinium ylide with alkenes **11**

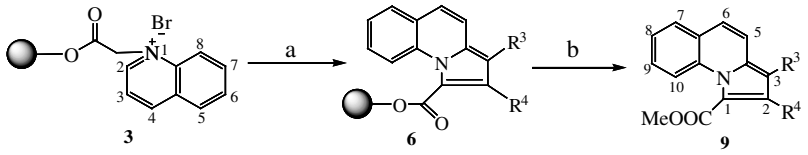
Entry	R^1	R^2	Yield[a] (%)	
8a	COPh	Ph	—	50[c]
8b	COPh	*p*-Tolyl	—	52[c]
8c	COPh	*p*-Anisyl	—	39[c]
8d	COPh	*p*-FPh	—	37[c]
8e	COPh	*p*-ClPh	—	29[c]
8f	COPh	*p*-BrPh	—	31[c]
8g	COPh	*p*-NCPh	—	43[c]
8h	COPh	*p*-O_2 NPh	—	67[c]
8i	COPh	*m*-Furan	—	21[c]
8j	COMe	*m*-Furan	—	25[c]
8k	COMe	Ph	—	30[c]
8l	COOMe	H	—	40[cd]
8m	COOMe	COOMe	75[b]	34[c]
8n	CN	H	82[b]	60[c]
8o	*o*,*m*-Cyclohexone		70[b]	25[c]

[a] Based on the loading capacity of PEG and purified by by column chromatography.
[b] From pyridinium salt **2**, **8a**–**l** see Ref. 23.
[c] From quinolinium salt **3** in the presence of 1 equiv TPCD.
[d] Containing **8l** (main) and **9l**.

The previous papers[11] reporting indolizine derivatives seldom or did not obtain **9** by 1,3-dipolar cycloaddition reaction of quinolinium ylides. It is difficult to explain the mechanism of the oxidation course. In addition, we employed MnO_2 or CrO_3 to replace TPCD in the reaction of **11m** and found that using CrO_3, no product obtained and the product **9m** was afforded in the presence of MnO_2 (the yield was very low). Therefore, the results implied that quinoline moiety were oxidated to pyridine ring by TPCD in the reaction.



Scheme 2. (a) Quinoline, rt CH_2Cl_2, overnight. (b) Alkenes **11**, 1 equiv K_2CO_3, 1 equiv TPCD, DMF, 90 °C, overnight. (c) 1% KCN/CH_3OH, rt 24 h.



Scheme 3. (a) Alkynes **12**, 1 equiv K_2CO_3, DMF, 90 °C, overnight. (b) 1% KCN/CH_3OH, rt 24 h.

Table 2. Synthesis of pyrrolo [1,5-*a*] quinolines **9** from alkynes **12**

Entry	R^3	R^4	Yield[a] (%)
9l	COOMe	H	51
9m	COOMe	COOMe	55

[a] Based on the loading capacity of PEG and purified by column chromatography.

In succession, treatment of **3** with alkynes **12** using K_2CO_3 as base at 90 °C overnight obtained PEG-bound pyrrolo [1, 5-*a*] quinolines **6** and cleaved, purified by column chromatography to give anticipative pyrrolo [1,5-*a*] quinolines **9**[27] (Scheme 3). The yields were given in Table 2.

The annelation reaction was also extended to PEG-bound isoquinolinium salts **4**[28] derived from isoquinoline (Scheme 4). Treatment of **4**, respectively, with **11** and **12** finally afforded the corresponding products **10**,[29] in moderate to high yields (Tables 3 and 4). In this reaction, the **8** or isomer products did not occur. The structure of **10a**–**o** were confirmed by element analyses, IR, ^1H NMR spectral data (**10c**,**e**,**l**,**n** were given ^{13}C NMR spectra).

In addition we further confirmed the structure of **10c** (Fig. 2) by MS, ^1H–^1H COSY, NOE 1D, ^1H–^{13}C COSY and DEPT spectra data.

3. Conclusion

In conclusion, we have developed a novel and efficient liquid-phase synthesis of pyrrolo [1,5-*a*] quinolines and pyrrolo [1,5-*a*] isoquinolines by a one-pot reaction via 1,3-dipolar cycloaddition by the soluble PEG-supported

Table 3. Synthesis of pyrrolo [1,5-*a*] isoquinolines **10** from alkenes **11**

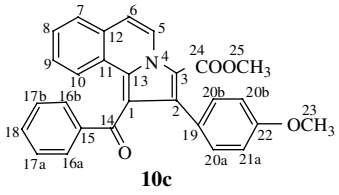
Entry	R^1	R^2	Yield[a] (%)
10a	COPh	Ph	71
10b	COPh	*p*-Tolyl	73
10c	COPh	*p*-Anisyl	84
10d	COPh	*p*-FPh	79
10e	COPh	*p*-ClPh	68
10f	COPh	*p*-BrPh	62
10g	COPh	*p*-NCPh	74
10h	COPh	*p*-O_2 NPh	75
10i	COPh	*m*-Furan	56
10j	COMe	*m*-Furan	50
10k	COMe	Ph	58
10l	COOMe	H	70
10m	COOMe	COOMe	72
10n	CN	H	80
10o	*o*,*m*-cyclohexone		65

[a] Based on the loading capacity of PEG and purified by by column chromatography.

Table 4. Synthesis of pyrrolo [1,5-*a*] isoquinolines **10** from alkynes **12**

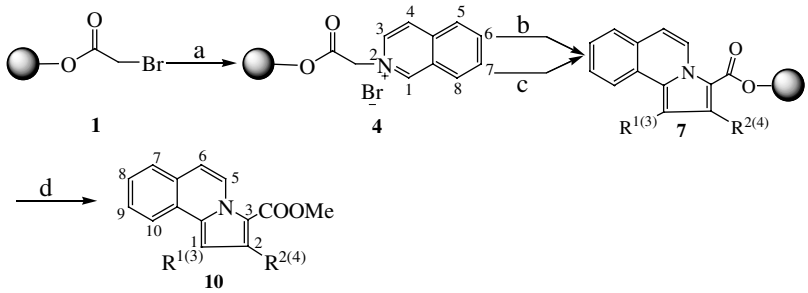
Entry	R^3	R^4	Yield[a] (%)
10l	COOMe	H	79
10m	COOMe	COOMe	82

[a] Based on the loading capacity of PEG and purified by column chromatography.



10c

Figure 2.



Scheme 4. (a) Isoquinoline, rt CH_2Cl_2. (b) Alkenes **11**, 1 equiv DIPEA, 1 equiv TPCD, DMF, 90 °C, 3–4 h. (c) Alkynes **12**, DIPEA, toluene, 90 °C, 3 h. (d) 1% KCN/CH_3OH, rt 24 h.

salts. Furthermore, firstly we discovered that PEG-supported quinolinium salt reacted with active alkenes in the presence of oxidant TPCD afforded indolizines, but not pyrrolo [1,5-*a*] quinolines.

4. Experimental

4.1. General preparation of PEG-supported salts 3 or 4

To a solution of PEG_{3400} (8 g, 4.71 mmol OH) and DIPEA (1.6 mL, 9.42 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise a solution of bromoacetyl bromide (0.8 mL, 9.42 mmol) in dry CH_2Cl_2 (2 mL) at 0 °C and stirred at rt overnight. The mixture was washed with water to remove ammonium bromide, dried with over $MgSO_4$ and concentrated. After precipitation with cold Et_2O, washing with cold Et_2O and drying under vacuum, a white solid **1** was obtained. Into a solution of **1** in dry CH_2Cl_2 (20 mL) was added quinoline or isoquinoline (1.82 g, 14.13 mmol) and stirred at rt for 18 h. After precipitation from cold Et_2O, the suspension was filtered and washed with cold Et_2O to give solid **3** (95%) and **4** (97%), respectively. TLC (EtOAc–petroleum ether, 1:4) showed that the solid is free from any low molecular reactants and by-products.

4.2. Typical procedure for preparation of 8 or 10 from 11

A solution of **3** or **4** (2 g, 0.51 mmol), **11** (3.06 mmol), TPCD (0.62 g, 1.02 mmol) and K_2CO_3 (0.28 g, 2.04 mmol) or DIPEA (0.35 mL, 2.04 mmol) in DMF (30 mL) was stirred at 80–90 °C for overnight or 3–4 h. After the solvent was evaporated under vacuum, the residue was added CH_2Cl_2 (50 mL) and filtered. The filtrate was washed with water to remove ammonium bromide, dried with over $MgSO_4$, filtered, concentrated and precipitated with cold Et_2O to give **5** or **7**. Product **5** or **7** was treated with a 1% solution of KCN in CH_3OH (30 mL) and stirred at rt overnight, evaporated CH_3OH and precipitated with cold Et_2O to give the crude products, which were purified by column chromatography on silica gel (EtOAc–petroleum ether, 1:4–1:2) to afford the pure **8** or **10**.

4.3. Typical procedure for preparation of 9 or 10 from 12

A solution of **3** or **4** (2 g, 0.51 mmol), **12** (3.06 mmol) and K_2CO_3 (0.28 g, 2.04 mmol) or DIPEA (0.35 mL, 2.04 mmol) in toluene was stirred at 90 °C for overnight or 3 h. After solvent was removed, the residue was dissolved in CH_2Cl_2 (50 mL) washed, dried, filtered, concentrated, precipitated and cleaved by using the procedure described above for **8** and **10**. The crude product was purified by column chromatography on silica gel (EtOAc–petroleum ether, 1:3–1:2) to afford pure **9** or **10**.

Acknowledgements

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24. PEG-quinolinium salt **3**: IR (KBr): 2884, 1750, 1476, 1280, 1114, 843 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 10.47 (d, 1H, J = 6.0 Hz, H-2), 9.10 (d, 1H, J = 8.4 Hz, H-4), 8.57 (d, 1H, J = 8.4 Hz, H-8), 8.30 (d, 1H, J = 8.4 Hz, H-5), 8.19 (t, 1H, J = 7.8 Hz, H-7), 8.01 (t, 1H, J = 7.8 Hz, H-6) 7.92 (t, 1H, J = 7.6 Hz, H-3), 6.55 (s, 2H, –CH_2CO–), 3.89–3.48 (m, 4n H, –$O(CH_2\ CH_2O)_n$–).
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26. **8a**–**m**: ^1H NMR (600 MHz, $CDCl_3$) see Ref. 23. **8m**: ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.28, 163.26, 160.34, 137.73, 130.47, 127.83, 126.76, 119.82, 115.42, 111.70, 115.42, 111.70, 102.89, 52.88, 51.96, 51.62. MS (ESI) (*m*/*z*): 260 (100), 292 (81) $[M + H]^+$, 314 (59) $[M + 23]^+$, 330 (11) $[M + 39]^+$. **8n**: IR (KBr): 2217, 1694, 1520, 1491, 1445, 763 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.53 (d, 1H, J = 7.2 Hz, H-5), 7.782–7.766 (sd, 2H, H-8, H-2), 7.37 (t, 1H, J = 7.8, 8.4 Hz, H-7), 7.06 (t, 1H, J = 7.2, 6.6 Hz, H-6), 3.94 (s, 3H, COOMe). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 60.71, 140.58, 128.24, 125.88, 124.78, 117.63, 115.36, 115.12, 115.00, 83.85, 51.67. Anal. Calcd for $C_{11}H_8N_2O_2$: C, 63.44; H, 7.74; N, 13.45. Found: C, 63.45; H, 4.00; N, 13.47. **8o**: IR (KBr): 2948, 1688, 1649, 1510, 1438, 780 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.61 (d, 1H, J = 7.8 Hz, H-5), 8.45 (d, 1H, J = 7.2 Hz, H-8), 7.41 (t, 1H, J = 7.8, 7.2 Hz, H-7), 7.05 (t, 1H, J = 6.6 Hz, H-6), 3.95 (s, 3H, COOMe), 3.21 (t, 2H, J = 6.3 Hz, $COCH_2$), 2.62 (t, 2H, J = 6.3 Hz, CH_2), 2.16 (m, 2H, CH_2). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.10; H, 5.35; N, 5.77.
27. Pyrrolo [1,5-*a*] quinolines **9**: **9l**: IR (KBr): 1704, 1615, 1551, 1432, 1081, 813, 754 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.43 (d, 1H, J = 9.0 Hz, Ar-H), 8.31 (d, 1H, J = 9.6 Hz, Ar-H), 7.99 (s, 1H, H-2), 7.80 (d, 1H, J = 7.2 Hz, Ar-H), 7.63 (t, 1H, J = 9.6 Hz, Ar-H), 7.50 (t, 1H, J = 7.50 Hz, Ar-H), 3.98 (s, 3H, COOMe), 3.93 (s, 3H, COOMe). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.46, 162.17, 139.45, 134.55, 133.34, 128.61, 128.33, 127.87, 126.57, 125.36, 125.15, 119.98, 117.64, 107.10, 52.11, 51.32. Anal. Calcd for $C_{16}H_{13}NO_4$: C, 71.90; H, 4.90; N, 5.24. Found: C, 71.87; H, 4.96; N, 5.18. **9m**: IR (KBr): 1706, 1612, 1546, 1482, 1448, 814, 757, 742 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) and ^1H–^1H COSY: δ = 8.25 (d, 1H, J = 9.6 Hz, H-5), 8.10 (d, 1H, J = 9.0 Hz, H-10), 7.80 (d, 1H, J = 7.2 Hz, H-7), 7.65–7.60 (m, 2H, H-6, H-9), 7.52 (t, 1H, J = 7.5 Hz, H-8), 4.00 (s, 3H, COOMe), 3.97 (s, 3H, COOMe), 3.92 (s, 3H, COOMe). ^{13}C NMR (150 Hz, $CDCl_3$): δ = 166.16, 163.34, 161.20, 137.86, 132.76, 130.99, 128.85, 128.66, 128.61, 125.86, 125.33, 119.52, 117.64, 117.59, 105.18, 52.85, 52.52, 51.81. Anal. Calcd for $C_{18}H_{15}NO_6$: C, 63.34; H, 4.43; N, 4.10. Found: C, 63.38; H, 4.40; N, 4.17.
28. PEG-isoquinolinium salt **4**: IR (KBr): 2884, 1750, 1467, 1113, 947, 842 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 10.87 (s, 1H, H-1), 8.77 (d, 1H, J = 5.4 Hz, H-3), 8.63 (d, 1H, J = 8.4 Hz, H-8), 8.40 (d, 1H, J = 6.0 Hz, H-4), 8.23 (d, 1H, J = 7.8 Hz, H-5), 8.18 (t, 1H, J = 7.5 Hz, H-6), 7.99 (t, 1H, J = 7.5 Hz, H-7), 6.28 (s, 2H, –CH_2CO–), 3.77–3.52 (m, 4n H, –$O(CH_2CH_2O)_n$–).
29. Pyrrolo [1,5-*a*] isoquinolines **10**: **10a**: IR (KBr): 1693, 1658, 1598, 796, 732, 669 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.41 (d, 1H, J = 7.8 Hz, Ar-H), 7.95 (d, 1H, J = 8.4 Hz, Ar-H), 7.74 (d, 2H, J = 7.2 Hz, Ar-H), 7.70 (d, 1H, J = 9.0 Hz, Ar-H), 7.48(t, 1H, J = 7.5 Hz, Ar-H), 7.41 (t, 1H, J = 7.2 Hz, Ar-H), 7.34 (t, 1H, J = 7.8 Hz, Ar-H), 7.26–7.13 (m, 8H, Ar-H), 3.67 (s, 3H, COOMe). Anal. Calcd for $C_{27}H_{19}NO_3$: C, 79.98; H, 4.72; N, 3.45. Found: C, 80.05; H, 4.81; N, 3.50. **10b**: IR (KBr): 1690, 1661, 1520, 1435, 796, 735, 691 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.39 (d, 1H, J = 7.8 Hz, Ar-H), 7.90 (d, 1H, J = 7.8 Hz, Ar-H), 7.76 (d, 2H, J = 7.2 Hz, Ar-H), 7.69 (d, 1H, J = 7.8 Hz, Ar-H), 7.46–7.10 (m, 8H, Ar-H), 6.96 (d, 2H, J = 7.8 Hz, Ar-H), 3.67 (s, 3H, COOMe), 2.25 (s, 3H, Me). Anal. Calcd for $C_{28}H_{21}NO_3$: C, 80.17; H, 5.05; N, 3.34. Found: C, 80.11; H, 4.97; N, 3.35. **10c**: IR (KBr): 1690, 1659, 1522, 1435, 796, 737, 691 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.40 (d, 1H, J = 7.2 Hz, H-5), 7.92 (d, 1H, J = 8.4 Hz, H-10), 7.75 (d, 2H, J = 7.8 Hz, H-16a, 16b), 7.69 (d, 1H, J = 7.8 Hz, H-7), 7.45 (t, 1H, J = 7.5 Hz, H-3), 7.40 (t, 1H, J = 7.2 Hz, H-11), 7.31 (t, 1H, J = 7.8 Hz, H-9), 7.25 (t, 2H, J = 7.5 Hz, H-17a, 17b), 7.14 (d, 2H, J = 8.0 Hz, H-20a, 20b), 7.12 (d, 1H, J = 7.2 Hz, H-6), 6.70 (d, 2H, J = 8.4, H-21a, 21b), 3.74 (s, 3H, COOMe), 3.68 (s, 3H, OMe). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.35 (C-14), 162.23 (C-24), 158.64 (C-23), 138.40 (C-15), 135.61 (C-2), 133.14 (C-18), 131.41 (C-13), 131.36 (C-20a, b), 129.74 (C-16a, b), 129.03 (C-12), 128.25 (C-17a, b), 127.93 (C-9), 127.68 (C-8), 126.96 (C-7), 126.27 (C-19), 124.71 (C-10), 124.65 (C-5), 123.98 (C-3), 118.34 (C-6), 113.36 (C-1), 112.68 (C-21a, b), 55.04, (C-23) 51.04 (C-25). MS (ESI) (*m*/*z*): 404 (15), 436 (100) $[M + H]^+$, 458 (46) $[M + 23]^+$, 474 (6) $[M + 39]^+$. Anal. Calcd for $C_{28}H_{21}NO_4$: C, 77.23; H, 4.86; N, 3.22. Found: C, 77.36; H, 4.82; N, 3.29. **10d**: IR (KBr): 1692, 1657, 1521, 1436, 797, 736, 691 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.41 (d, 1H,J = 7.2 Hz, Ar-H), 7.94 (d, 1H, J = 7.8 Hz, Ar-H), 7.74–7.70 (m, 3H, Ar-H), 7.49–7.17 (m, 9H, Ar-H), 6.86 (t, 1H, J = 8.4 Hz, Ar-H) 3.66 (s, 3H, COOMe). MS (ESI) (*m*/*z*): 288 (94), 316 (43), 392 (12), 424 (100) $[M + H]^+$, 446 (48) $[M + 23]^+$. Anal. Calcd for $C_{27}H_{18}NFO_3$: C, 76.59; H, 4.28; N, 3.31. Found: C, 76.46; H, 4.12; N, 3.38. **10e**: IR (KBr): 1693, 1657, 1512, 1436, 794, 739, 709 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.40 (d, 1H, J = 7.8 Hz, Ar-H), 7.91 (d, 1H, J = 8.4 Hz, Ar-H), 7.73 (d, 2H, J = 7.2 Hz, Ar-H), 7.70 (d, 1H, J = 7.8 Hz, Ar-H), 7.49–7.13 (m, 11H, Ar-H), 3.66 (s, 3H, COOMe). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 195.81, 161.93, 138.34, 134.45, 133.38, 133.13, 131.81(2 C), 131.58, 130.35 (2 C), 129.70, 129.07, 128.41, 128.14, 127.84, 127.05, 124.73, 124.61, 123.92, 121.50, 118.20, 114.13, 113.39, 51.12. Anal. Calcd for $C_{27}H_{18}NClO_3$: C, 73.72; H, 4.12; N, 3.18. Found: C, 73.78; H, 4.20; N, 3.24. **10f**: IR (KBr): 1693, 1656, 1509, 1436, 795, 735, 692 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.40 (d, 1H, 7.8 Hz, Ar-H), 7.90 (d, 1H, J = 8.4 Hz, Ar-H), 7.73 (d, 2H, J = 7.2 Hz, Ar-H), 7.68 (d, 1H, J = 7.8 Hz, Ar-H), 7.49–7.26 (m, 7H, Ar-H), 7.17 (d, 1H, J = 7.2 Hz, Ar-H), 7.09 (d, 2H, J = 8.4 Hz, Ar-H), 3.67 (s, 1H, COOMe). Anal. Calcd for $C_{27}H_{18}NBrO_3$: C, 66.95; H, 3.75; N, 2.18. Found: C: 66.99; H, 3.62; N, 2.10. **10g**: IR (KBr): 2227, 1695, 1657, 1516, 1436, 797, 732, 692 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.41 (d, 1H, J = 7.2 Hz, Ar-H), 7.91 (d, 1H, 8.4 Hz, Ar-H), 7.73–7.71 (m, 3H, Ar-H), 7.52–7.45 (m, 4H, Ar-H), 7.37–7.33 (m, 6H, Ar-H), 7.28 (t, 1H, J = 7.8 Hz, Ar-H), 7.21 (d, 1H, J = 7.8 Hz, Ar-H), 3.65 (s, 3H, COOMe). Anal. Calcd for $C_{28}H_{18}N_2O_3$: C, 78.13; H, 4.21; N, 6.51. Found: C, 78.20; H, 4.17; N, 6.61. **10h**: IR (KBr): 1696, 1517, 1344, 797, 732, 697 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.39 (d, 1H, J = 7.8 Hz, Ar-H), 8.02 (d, 1H, J = 9.0 Hz, Ar-H), 7.71–7.23 (m, 12H, Ar-H), 7.19 (d, 1H, J = 7.8 Hz, Ar-H), 3.467 (s, 3H, COOMe). Anal. Calcd for $C_{27}H_{18}N_2O_5$: C, 71.99; H, 4.03;

N, 6.22. Found: C, 71.96; H, 4.13; N, 6.15.**10i**: IR (KBr): 1694, 1662, 1527, 1450, 1360, 794, 731, 691 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.32 (d, 1H, J = 7.8 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 7.81 (d, 2H, J = 7.2 Hz, Ar-H), 7.66 (d, 1H, J = 7.8 Hz, Ar-H), 7.48–7.29 (m, 5H, Ar-H,), 7.18 (t, 1H, J = 1.2 Hz, furan-H), 7.12 (d, 1H, J = 7.8 Hz, Ar-H), 6.45 (d, 1H, J = 3.0 Hz, furan-H), 6.41 (m, 1H, furan-H), 3.84 (s, 3H, COOMe). Anal. Calcd for $C_{25}H_{17}NO_4$: C, 75.94; H, 4.33; N, 3.54. Found: C, 75.99; H, 4.29; N, 3.55. **10j**: IR (KBr): 1697, 1673, 1511, 1453, 801, 742, 597 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.29 (t, 1H, J = 8.1 Hz, Ar-H), 8.45 (d, 1H, J = 7.8 Hz, Ar-H), 7.67 (t, 1H, J = 6.0 Hz, Ar-H), 7.58–7.51 (m, 3H, Ar-H, furan-H), 7.12 (t, 1H, J = 6.6 Hz, Ar-H), 6.64 (d, 1H, J = 3.0 Hz, furan-H), 6.55 (m, 1H, furan-H), 3.83 (s, 3H, COOMe), 2.23 (s, 3H, COMe). Anal. Calcd for $C_{20}H_{15}NO_4C$, 72.06; H, 4.54; N, 4.20. Found: C, 72.01; H, 4.53; N, 4.12. **10k**: IR (KBr): 1691, 1506, 1436, 796, 711, 667 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.33 (d, 1H, J = 7.8 Hz, Ar-H), 8.41 (d, 1H, J = 8.4 Hz, Ar-H), 7.68 (d, 1H, J = 8.4 Hz, Ar-H), 7.53–7.33 (m, 7H, Ar-H), 7.12 (d, 1H, J = 7.2 Hz, Ar-H), 3.60 (s, 3H, COOMe), 2.04 (s, 3H, COMe). Anal. Calcd for $C_{22}H_{17}NO_3C$, 76.95; H, 4.99; N, 4.08. Found: C, 76.89; H, 4.87; N, 4.11. **10l**: IR (KBr): 1693, 1533, 1430, 798, 758 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.83 (d, 1H, J = 7.8 Hz, Ar-H), 9.38 (d, 1H, J = 7.8 Hz, Ar-H), 8.05 (s, 1H, H-2), 7.74–7.62 (m, 3H, Ar-H), 7.20 (d, 1H, J = 7.8 Hz, Ar-H), 3.95 (s, 3H, COOMe), 3.94 (s, 3H, COOMe). ^{13}C NMR (150 MHz, $CDCl_3$): 165.11, 165.38, 136.01, 129.63, 128.87, 127.75, 127.71, 126.67, 125.36, 124.87, 124.23, 115.59, 115.03, 109.21, 51.73, 51.56. Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.89; H, 4.61; N, 4.91. **10m**: IR (KBr): 1740, 1705, 1532, 1439, 803 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.46 (m, 1H, Ar-H), 9.36 (d, 1H, J = 7.8 Hz, Ar-H), 7.74–7.62 (m, 3H, Ar-H), 7.3 (d, 1H, J = 7.8 Hz, Ar-H), 3.98 (s, 3H, COOMe), 3.93 (s, 3H, COOMe), 3.93 (s, 3H, COOMe). Anal. Calcd for $C_{18}H_{15}NO_6$: C, 63.34; H, 4.43; N, 4.10. Found: C, 63.35; H, 4.30; N, 4.15. **10n**: IR (KBr): 2215, 1702, 1702, 1535, 1418, 794, 740, 688 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 9.32 (d, 1H, J = 7.8 Hz, H-5), 8.96 (d, 1H, J = 8.4 Hz, H-10), 7.80–7.27 (m, 3H, H-7, 8, 9), 7.24 (d, 1H, J = 7.8 Hz, H-6), 3.96 (s, 3H, COOMe). ^{13}C NMR (150 MHz, $CDCl_3$): 160.66, 137.03, 129.52, 128.91, 128.69, 127.19, 124.40, 124.30, 123.85, 123.68, 117.24, 116.90, 115.24, 85.18, 51.84. Anal. Calcd for $C_{15}H_{10}NO_2$: C, 67.26; H, 4.27; N, 5.93. Found: C, 67.30; H, 4.28; N, 5.93. **10o**: IR (KBr): 2941, 1689, 1654, 1525, 1436, 806, 747 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 10.23 (m, 1H, Ar-H), 9.51 (d, 1H, J = 7.2 Hz, Ar-H), 7.74–7.65 (m, 3H, Ar-H), 7.25 (d, 1H, J = 7.8 Hz, Ar-H), 3.98 (s, 3H, COOMe), 3.27 (t, 1H, J = 6.3 Hz, CH_2), 2.73 (t, 1H, J = 6.3 Hz, CH_2), 2.19 (m, 1H, CH_2). Anal. Calcd for $C_{18}H_{15}NO_3C$, 73.71; H, 5.15; N, 4.78. Found: C, 73.73; H, 5.12; N, 4.78.