EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201402837

Diversity-Oriented Synthesis of Calothrixins and Ellipticines

Dattatraya H. Dethe*[a] and Ganesh M. Murhade[b]

Keywords: Natural products / Nitrogen heterocycles / Quinones / Rearrangement / Oxidation

The divergent synthesis of calothrixins and ellipticines has been accomplished by utilising the one-pot formation of *o*-diacylarenes as a key intermediate through rearrangement of *o*-hydroxy ketone monoacyl hydrazones by lead tetraacetate mediated oxidation.

Introduction

In 1959, Goodwin and colleagues reported the isolation and structure determination of ellipticine (**1**) and 9-methoxyellipticine (**2**) 6*H*-pyrido[4,3-*b*]carbazole alkaloids from the leaves of *Ochrosia elliptica Labill* (family Apocynaceae) (Figure 1).[1] The promising antitumor activity of ellipticines prompted several groups to explore the synthesis and pharmacological properties of such compounds.[2] Several ellipticine derivatives (e.g., **2**) have been used in clinical trials.[3] Calothrixin A (**4**) and B (**5**) are two naturally occurring pentacyclic isoquinoline alkaloids that were isolated from cyanobacterium of the genus *Calothrix* in 1999.[4] The discovery of their antimalarial and antiproliferative properties against several cancer cell lines as well as human DNA topoisomerase I poisoning activity has led to an explosion of synthetic,[5] biological, and pharmacological studies.[4,6]

Reactions mediated by lead tetraacetate (LTA) and other metallic acetates with nitrogen-containing derivatives of carbonyl compounds have been the subject of extensive research.[7,8] Kotali et al. have discovered an interesting rearrangement of *o*-hydroxy ketone monoacyl hydrazones by LTA-mediated oxidation, resulting in an unusual replacement of the phenolic hydroxyl group with an acyl substituent to give *o*-diacylbenzene.[7a] The mechanistic studies performed by Kotali and Katritzky showed that this rearrangement occurs through 1,3,4-oxadiazoline and 1,3-dioxane intermediates.[7b] Einhorn et al.[8a] and Dong et al.[8b] also utilised this method for the synthesis of a range of *o*-diacylbenzenes. Although there are various reports on the formation of *o*-diacylbenzenes by LTA-mediated oxidation, as mentioned above,[7] so far this reaction has not been explored with heterocyclic aromatic compounds such as indoles, quinoline, and pyridines. In this article, we report a concise five-step total synthesis of calothrixins B (**5**) and a range of analogues by using LTA-mediated rearrangement of suitable *o*-hydroxy aryl ketone monoacylhydrazone directly into the corresponding quinone as the key step.

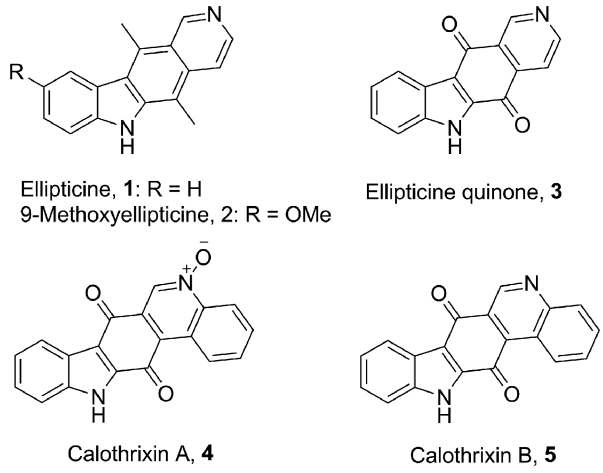


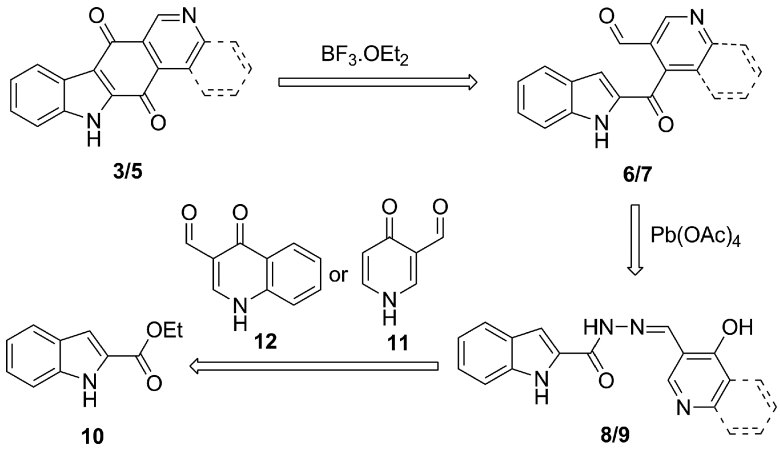
Figure 1. Structures of the natural products.

Results and Discussion

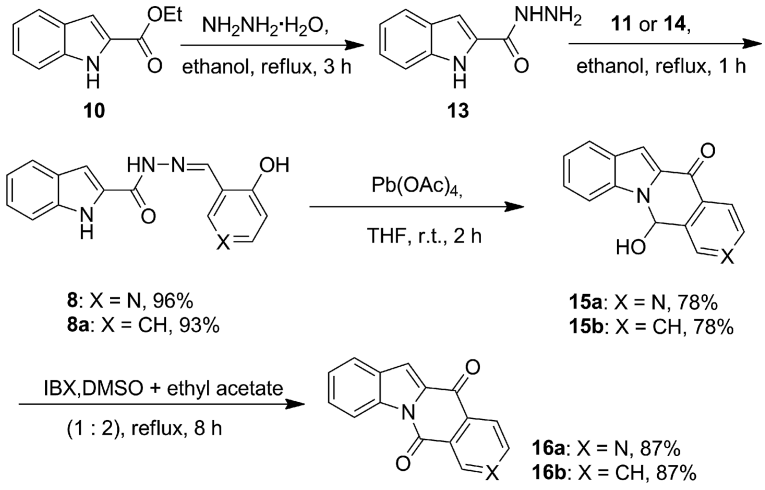
It was envisioned that both ellipticines quinone (**3**) and calothrixin (**5**) could be obtained from key intermediate **6**/**7** by Lewis-acid mediated intramolecular nucleophilic attack of C-3 indole onto aldehyde followed by oxidation (Scheme 1). Compounds **8** (hydrazone derivatives of pyridine) and **9** (hydrazone derivatives of quinoline) could be synthesised by coupling hydrazide derivatives of ethyl 1*H*-indole-2-carboxylate **10** with either pyridine derivative **11** or quinoline derivative **12**, followed by LTA-mediated rearrangement. The latter pyridine and quinoline derivatives **11** and **12** were prepared in two steps by reported procedures.[9] Compound **10**, on treatment with hydrazine

[a] Department of Chemistry, Indian Institute of Technology Kanpur,
Kanpur 208016, India
E-mail: ddethe@iitk.ac.in
http://home.iitk.ac.in/~ddethe/
[b] Department of Chemistry, Indian Institute of Technology Kanpur,
Kanpur 208016, India
E-mail: gmurhade@iitk.ac.in

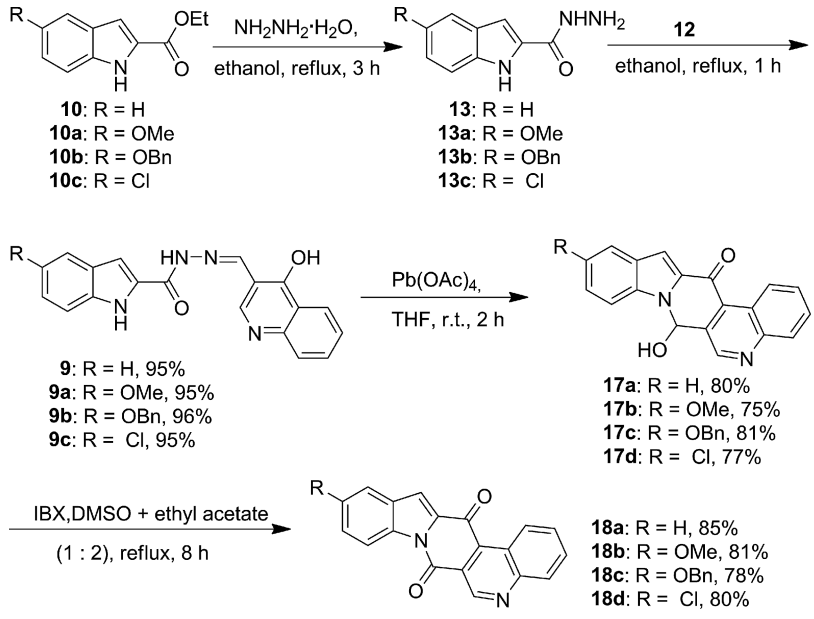
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402837.



Scheme 1. Retrosynthetic analysis of calothrixin and ellipticine quinone.



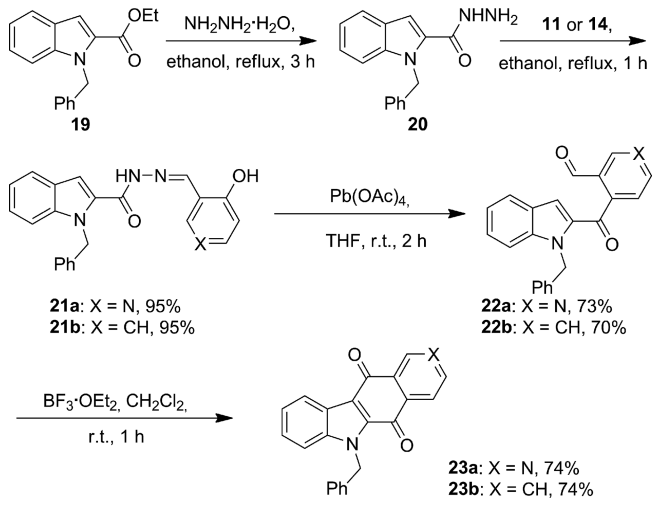
Scheme 2. Formal synthesis of ellipticine and its analogue.



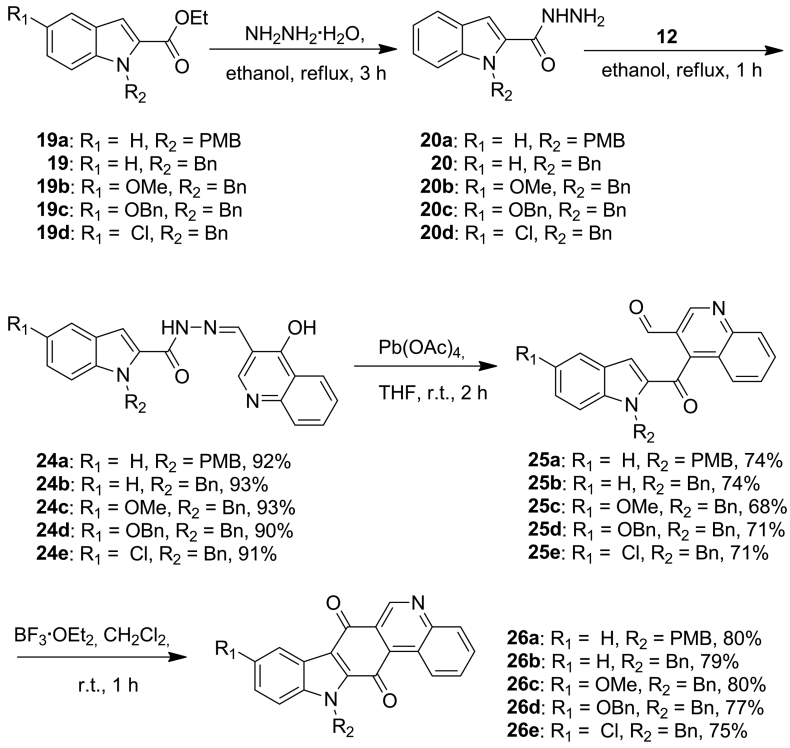
Scheme 3. Synthesis of isocalothrixins and its analogues.

hydrate in ethanol, generated indolyl-hydrazide **13** (Scheme 2), which was used in next step without further purification. Condensation of **13** with **11** afforded hydrazone **8**. To our surprise, LTA-mediated oxidative rearrangement of acyl-hydrazone **8** afforded the keto alcohol **15a** directly. Contrary to our expectation, LTA-mediated rearrangement of compound **8** produced the aldehyde in situ, which, on intramolecular nucleophilic attack of indole nitrogen on aldehyde instead of C-3 of indole, afforded the keto alcohol **15a**. Oxidation of the secondary alcohol by using 2-iodoxybenzoic acid (IBX) afforded isoellipticine quinone **16a** in 87% yield. Conversion of the latter quinone **16a** into ellipticines **1** has already been described,[10] thus this approach constitutes a formal synthesis of ellipticine **1**. The benzene analogue **16b** of isoellipticine quinone was also synthesised by using salicylaldehyde **14** (Scheme 2). Similarly, condensation of various indolyl-hydrazides (**13** and **13a**–**c**) with quinoline derivative **12** followed by LTA-mediated oxidative rearrangement and IBX-mediated oxidation afforded isocalothrixin analogues **18a**–**d** in very good overall yield (Scheme 3).

Considering the observed attack of the indole nitrogen on the aldehyde formed in situ, we decided to protect the indole nitrogen of ethyl 1*H*-indole-2-carboxylate. To this end, reaction of indole **10** with benzyl bromide in the presence of NaH generated the *N*-benzyl protected indole **19**. Compound **19**, on treatment with hydrazine hydrate and heating to reflux with ethanol, generated N-protected indolyl-hydrazide **20**, which was used in next step without further purification. Condensation of **20** with pyridine derivative **11** afforded acyl-hydrazone **21a**. To our delight, LTA-mediated oxidative rearrangement of **21a** afforded key intermediate keto-aldehyde **22a** (Scheme 4). $BF_3{\cdot}OEt_2$ catalysed cyclisation by intramolecular nucleophilic attack of C-3 of indole on aldehyde followed by concomitant oxidation of the alcohol thus directly afforded quinone **23a** in 74% yield. Ellipticines quinone **23a** has previously been transformed into ellipticines **1**,[4,10] thus this reaction completes the second formal total synthesis of ellipticine **1**. It was surprising that in the presence of $BF_3{\cdot}OEt_2$, **22a** generated quinone **23a** directly instead of the corresponding keto alcohol as in the synthesis of isoellipticine quinone **16a** (Scheme 2) by further oxidation of alcohol to ketone. The

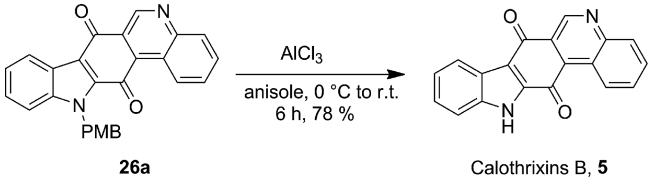


Scheme 4. Synthesis of ellipticine quinone and its analogue.



Scheme 5. Total synthesis of calothrixin B and its analogues.

same strategy was used for the synthesis of benz-ellipticine quinone **23b** from salicylaldehyde **14**. Similarly, condensation of *N*-PMB protected indole derivative **19a** (obtained by reaction of ethyl 1*H*-indole-2-carboxylate **10** with PMB-Cl in the presence of NaH) with quinoline derivative **12**, followed by LTA-mediated oxidative rearrangement, $BF_3{\cdot}OEt_2$-mediated cyclisation, and deprotection of the PMB group, afforded calothrixin B (**5**) in 39.1% overall yield from **10** (Scheme 5 and Scheme 6). A range of analogues of calothrixin (**26a**–**e**) were made by using same strategy, as shown in Scheme 5.



Scheme 6. Synthesis of calothrixin B.

Conclusions

We have demonstrated a novel approach for the synthesis of calothrixin B, ellipticine, and their various analogues in excellent overall yield by using the rearrangement of *o*-hydroxy ketone monoacyl hydrazones induced by lead tetraacetate as a key step.

Experimental Section

General: All reactions were carried out under either a nitrogen or argon atmosphere with anhydrous solvents under anhydrous conditions, unless otherwise mentioned. Anhydrous THF and diethyl ether were distilled from sodium benzophenone, and dichloromethane was distilled from calcium hydride, yields refer to chromatographically pure material, unless otherwise stated.

Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates ($60F_{254}$) using UV light as a visualising agent and an *p*-anisaldehyde or ninhydrine stain, and heat as developing agents. Merck silica gel (particle size 100–200 and 230–400 mesh) was used for flash column chromatography.

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. NMR spectra were recorded with either a Bruker Avance 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz), Bruker Avance 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), Bruker Avance 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz), or JEOL ECX 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz). The following abbreviations were used to explain the multiplicities in the NMR spectra: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of a doublet of a doublet, dm = doublet of a multiplet, m = multiplet, br = broad. Mass spectrometric data were obtained with a WATERS-Q-Tof Premier-ESI-MS.

Preparation of Acylhydrazones 8 and 9. General Procedure A: Indole-2-carbohydrazide was added at room temperature to a solution of the desired aldehyde in ethanol. The reaction mixture was heated to reflux for 30 min, poured on ice, and the resulting solid was filtered and washed with water. The solid was taken into a round-bottomed flask, methanol was added and the mixture was heated to reflux for another 15 min. The solid was filtered again, washed with methanol and dried under vacuum.

(*E*)-*N*′-[(4-Hydroxypyridin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (8): According to General Procedure A, 1*H*-indole-2-carbohydrazide (**13**; 1.1 g, 6.20 mmol) and aldehyde **11** (773 mg, 6.20 mmol) in ethanol (25 mL) were used to furnish product **8** (1.66 mg, 96%) as a light-yellow solid; m.p. 250–255 °C. IR (neat): $\tilde{\nu}_{max}$ = 3444, 2922, 1626, 1542, 1455, 1321, 1270 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 4.64 (br. s, 1 H), 7.06–7.23 (m, 3 H), 7.44 (s, 1 H), 7.66 (s, 1 H), 8.31 (s, 1 H), 8.76 (s, 2 H), 11.90 (s, 1 H), 12.40 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 104.5, 112.5, 115.2, 120.1, 120.7, 122.0, 124.2, 127.0, 129.6, 137.0, 138.5, 140.3, 140.8, 157.7, 171.3 ppm. HRMS: *m*/*z* calcd. for $C_{15}H_{13}N_4O_2$ [M + H]$^+$ 281.1039; found 281.1039.

(*E*)-*N*′-(2-Hydroxybenzylidene)-1*H*-indole-2-carbohydrazide (8a): According to General Procedure A, 1*H*-indole-2-carbohydrazide (**13**; 300 mg, 1.71 mmol) and aldehyde **14** (0.2 mL, 1.71 mmol) in ethanol (10 mL) were used to furnish product **8a** (443 mg, 93%) as a light-yellow solid; m.p. 266 °C; IR (neat): $\tilde{\nu}_{max}$ = 3295, 1653, 1616, 1576, 1537, 1486, 1443, 1346, 1308, 1268, 1239 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.94 (m, 2 H), 7.08 (t, *J* = 7.3 Hz, 1 H), 7.23 (t, *J* = 7.3 Hz, 1 H), 7.28–7.33 (m, 2 H), 7.48 (d, *J* = 7.8 Hz, 1 H), 7.59 (d, *J* = 7.3 Hz, 1 H), 7.69 (d, *J* = 7.8 Hz, 1 H), 8.66 (s, 1 H), 11.19 (s, 1 H), 11.85 (s, 1 H), 12.15 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 103.8, 112.5, 116.4, 118.9, 119.4, 120.1, 121.9, 124.0, 127.0, 129.2, 129.7, 131.4, 136.9, 147.2, 157.3, 157.4 ppm. HRMS: *m*/*z* calcd. for $C_{16}H_{14}N_3O_2$ [M + H]$^+$ 280.1086; found 280.1082.

(*E*)-*N*′-[(4-Hydroxyquinolin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (9): According to General Procedure A, 1*H*-indole-2-carbohydrazide (**13**; 500 mg, 2.85 mmol) and aldehyde **12** (494 mg, 2.85 mmol) in ethanol (15 mL) were used to furnish product **9** (893 mg, 95%) as a light-yellow solid; m.p. 296–298 °C. IR (neat): $\tilde{\nu}_{max}$ = 3230, 3055, 1620, 1575, 1520, 1557, 1475, 1359, 1316, 1214 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.06 (m, 1 H), 7.21 (m, 1 H), 7.35 (s, 1 H), 7.40–7.47 (m, 2 H), 7.66–7.71 (m, 3 H), 8.21 (d, *J* = 7.9 Hz, 1 H), 8.54 (s, 1 H), 8.82 (s, 1 H), 11.76 (s, 1 H), 11.82 (s, 1 H), 12.39 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 103.3, 112.7, 113.8, 119.0, 119.9, 121.7, 123.7, 124.3, 125.2, 125.7, 127.1, 130.2, 132.2, 136.8, 137.0, 139.3, 143.2, 157.3, 175.0 ppm. HRMS: *m*/*z* calcd. for $C_{19}H_{15}N_4O_2$ [M + H]$^+$ 331.1195; found 331.1198.

(*E*)-*N*′-[(4-Hydroxyquinolin-3-yl)methylene]-5-methoxy-1*H*-indole-2-carbohydrazide (9a): According to General Procedure A, 5-methoxy-1*H*-indole-2-carbohydrazide (**13a**; 270 mg, 1.31 mmol) and aldehyde **12** (173 mg, 1.31 mmol) in ethanol (10 mL) were used to furnish product **9a** (448 mg, 95%) as a light-yellow solid; m.p. 288–292 °C. IR (neat): $\tilde{\nu}_{max}$ = 3334, 1626, 1558, 1518, 1476, 1446, 1386, 1249 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.78 (s, 3 H), 6.87 (d, *J* = 7.9 Hz, 1 H), 7.13 (s, 1 H), 7.26 (s, 1 H), 7.35 (d, *J* = 8.5 Hz, 1 H), 7.41 (m, 1 H), 7.66–7.71 (m, 2 H), 8.20 (d, *J* = 7.3 Hz, 1 H), 8.53 (s, 1 H), 8.81 (s, 1 H), 11.60 (s, 1 H), 11.17 (s, 1 H), 12.36 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 55.3, 102.1, 103.0, 113.1, 113.9, 115.0, 119.0, 124.3, 125.2, 125.7, 127.4, 130.5, 132.1, 136.9, 139.2, 143.1, 153.8, 157.2, 175.0 ppm. HRMS: *m*/*z* calcd. for $C_{20}H_{17}N_4O_3$ [M + H]$^+$ 361.1301; found 361.1299.

(*E*)-5-(Benzyloxy)-*N*′-[(4-hydroxyquinolin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (9b): According to General Procedure A, 5-(benzyloxy)-1*H*-indole-2-carbohydrazide (**13b**; 354 mg, 1.25 mmol) and aldehyde **12** (217 mg, 1.25 mmol) in ethanol (15 mL) were used

to furnish product **9b** (523 mg, 96%) as a light-yellow solid; m.p. 254 °C. IR (neat): $\tilde{\nu}_{max}$ = 1643, 1569, 1475, 1451, 1261, 1218 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 5.11 (s, 2 H), 6.96 (s, 1 H), 7.24–7.48 (m, 9 H), 7.67 (m, 1 H), 8.20 (s, 1 H), 8.54 (s, 1 H), 8.81 (s, 1 H), 11.62 (s, 1 H), 11.76 (s, 1 H), 12.37 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 69.6, 103.1, 103.7, 113.2, 113.9, 115.5, 119.0, 124.3, 125.2, 125.7, 127.3, 127.7, 128.4, 130.6, 132.2, 136.9, 137.6, 139.3, 143.1, 152.9, 157.2, 175.0 ppm. HRMS: *m*/*z* calcd. for $C_{26}H_{21}N_4O_3$ [M + H]$^+$ 437.1614; found 437.1614.

(*E*)-5-Chloro-*N*′-[(4-hydroxyquinolin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (9c): According to General Procedure A, 5-chloro-1*H*-indole-2-carbohydrazide (**13c**; 310 mg, 1.48 mmol) and aldehyde **12** (256 mg, 1.48 mmol) in ethanol (15 mL) were used to furnish product **9c** (511 mg, 95%) as a light-yellow solid; m.p. 294–296 °C. IR (neat): $\tilde{\nu}_{max}$ = 3384, 3268, 1624, 1578, 1473, 1272 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.21 (m, 1 H), 7.32 (s, 1 H), 7.40–7.47 (m, 2 H), 7.65–7.75 (m, 3 H), 8.20 (m, 1 H), 8.57 (s, 1 H), 8.80 (s, 1 H), 11.92 (s, 1 H), 11.98 (s, 1 H), 12.44 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 103.1, 113.9, 114.1, 119.1, 120.9, 123.9, 124.5, 124.6, 125.4, 125.8, 128.2, 131.8, 132.3, 135.3, 137.3, 139.4, 143.8, 157.2, 175.2 ppm. HRMS: *m*/*z* calcd. for $C_{19}H_{14}ClN_4O_2$ [M + H]$^+$ 365.0805; found 365.0800.

Preparation of Keto Alcohol 15 and 17. General Procedure B: At room temperature, the appropriate hydrazone was dissolved in THF (analytical grade). At 0 °C, lead tetraacetate was gradually added to the solution. The resulting mixture was stirred for 3–4 h at room temp., and the progress of the reaction was monitored by the evolution of nitrogen. The solvent was removed under reduce pressure. Ethyl acetate was added to the residue and the suspension was filtered through Celite. The organic layer was washed with a saturated solution of $NaHCO_3$ then brine, and dried with Na_2SO_4. The solvent was removed under vacuo and the residue was purified on a silica gel column using EtOAc/hexane as eluent to furnish the product.

12-Hydroxyindolo[1,2-*b*][2,7]naphthyridin-5(12*H*)-one (15a): According to General Procedure B, compound **8** (300 mg, 1.07 mmol) and Pb(OAc)$_4$ (474 mg, 1.07 mmol) in THF (15 mL) were used to furnish product **15a** (208 mg, 78%) as a yellow solid; m.p. 180 °C; R_f = 0.40 (EtOAc/hexane, 50:50). IR (neat): $\tilde{\nu}_{max}$ = 3413, 1660, 1532, 1440, 1466, 1290, 1250 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]-DMSO): δ = 7.14 (d, *J* = 9.7 Hz, 1 H), 7.25 (t, *J* = 7.2 Hz, 1 H), 7.37 (d, *J* = 10.0 Hz, 1 H), 7.50 (t, *J* = 8.0 Hz, 1 H), 7.54 (s, 1 H), 7.84 (m, 2 H), 7.98 (d, *J* = 4.9 Hz, 1 H), 8.89 (d, *J* = 4.9 Hz, 1 H), 9.10 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 72.3, 108.2, 112.7, 118.0, 122.0, 123.2, 126.5, 127.2, 131.7, 134.6, 135.3, 137.9, 150.5, 151.1, 175.8 ppm. HRMS: *m*/*z* calcd. for $C_{15}H_{10}N_2O_2$ [M + H]$^+$ 251.0821; found 251.0820.

6-Hydroxyindolo[1,2-*b*]isoquinolin-11(6*H*)-one (15b): According to General Procedure B, compound **8a** (260 mg, 0.98 mmol) and Pb(OAc)$_4$ (434 mg, 0.98 mmol) in THF (10 mL) were used to furnish product **15b** (190 mg, 78%) as a yellow solid; m.p. 132–136 °C; R_f = 0.40 (EtOAc/hexane, 50:50). IR (neat): $\tilde{\nu}_{max}$ = 3275, 1632, 1598, 1530, 1354, 1275, 1197 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.36 (br. s, 1 H), 6.86 (d, *J* = 8.5 Hz, 1 H), 7.25 (m, 1 H), 7.39 (s, 1 H), 7.48 (t, *J* = 7.0 Hz, 1 H), 7.55 (t, *J* = 7.0 Hz, 1 H), 7.70–7.75 (m, 2 H), 7.81 (t, *J* = 8.5 Hz, 2 H), 8.19 (d, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 73.9, 107.2, 112.8, 121.8, 123.1, 125.9, 127.3, 129.1, 129.3, 129.8, 132.2, 134.0, 137.8, 141.3, 176.7 ppm. HRMS: *m*/*z* calcd. for $C_{16}H_{11}NNaO_2$ [M + Na]$^+$ 272.0687; found 272.0680.

7-Hydroxybenzo[*f*]indolo[1,2-*b*][2,7]naphthyridin-14(7*H*)-one (17a): According to General Procedure B, compound **9** (330 mg, 1.00 mmol) and Pb(OAc)$_4$ (443 mg, 1.00 mmol) in THF (15 mL) were used to furnish product **17a** (240 mg, 80%) as a yellow solid; m.p. 172 °C; R_f = 0.30 (EtOAc/hexane, 50:50). IR (neat): $\tilde{\nu}_{max}$ = 3127, 1658, 1570, 1523, 1320, 1241 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 7.19 (d, *J* = 10.1 Hz, 1 H), 7.25 (t, *J* = 7.8 Hz, 1 H), 7.43–7.49 (m, 2 H), 7.51 (s, 1 H), 7.81–7.91 (m, 4 H), 8.17 (d, *J* = 7.8 Hz, 1 H), 9.32 (s, 1 H), 9.62 (d, *J* = 8.3 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 72.5, 108.1, 112.5, 121.9, 122.9, 123.2, 126.3, 126.4, 127.3, 129.1, 129.7, 130.2, 132.9, 134.9, 137.4, 148.2, 151.5, 178.8 ppm. HRMS: *m*/*z* calcd. for $C_{19}H_{13}N_2O_2$ [M + H]$^+$ 301.0977; found 301.0973.

7-Hydroxy-11-methoxybenzo[*f*]indolo[1,2-*b*][2,7]naphthyridin-14(7*H*)-one (17b): According to General Procedure B, compound **9a** (200 mg, 0.55 mmol) and Pb(OAc)$_4$ (246 mg, 0.55 mmol) in THF (10 mL) were used to furnish product **17b** (135 mg, 75%) as a yellow solid; m.p. 170–175 °C; R_f = 0.33 (EtOAc/hexane, 40:60). IR (neat): $\tilde{\nu}_{max}$ = 3169, 2925, 1659, 1537, 1456 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.82 (s, 3 H), 7.16 (m, 2 H), 7.28 (m, 1 H), 7.42 (m, 1 H), 7.76 (d, *J* = 9.2 Hz, 1 H), 7.85 (m, 1 H), 7.91 (m, 1 H), 8.15 (m, 1 H), 9.32 (s, 1 H), 9.65 (d, *J* = 9.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 55.3, 72.5, 102.7, 107.54, 113.5, 118.1, 122.9, 126.5, 127.9, 129.1, 129.7, 129.7, 130.2, 132.8, 133.2, 135.0, 148.2, 151.4, 155.1, 178.5 ppm. HRMS: *m*/*z* calcd. for $C_{20}H_{13}N_2O_3$ [M + H]$^+$ 329.0926; found 329.0922.

11-(Benzyloxy)-7-hydroxybenzo[*f*]indolo[1,2-*b*][2,7]naphthyridin-14(7*H*)-one (17c): According to General Procedure B, compound **9b** (200 mg, 0.458 mmol) and Pb(OAc)$_4$ (202 mg, 0.458 mmol) in THF (10 mL) were used to furnish product **17c** (150 mg, 81%) as a yellow solid; m.p. 178 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 3429, 2923, 1653, 1450, 1354, 1205, 1025 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.16 (s, 2 H), 7.15 (d, *J* = 10 Hz, 1 H), 7.24 (dd, *J* = 2.5, 9.1 Hz, 1 H), 7.32–7.45 (m, 6 H), 7.50 (m, 2 H), 7.77 (d, *J* = 9.1 Hz, 1 H), 7.83–7.92 (m, 2 H), 8.18 (dd, *J* = 1.4, 8.4 Hz, 1 H), 9.31 (s, 1 H), 9.64 (dd, *J* = 1.2, 8.4 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 69.6, 72.5, 104.3, 107.5, 113.6, 118.5, 122.9, 126.5, 127.7, 127.8, 127.9, 128.5, 129.1, 129.7, 129.7, 130.2, 133.0, 133.3, 135.0, 137.2, 148.2, 151.4, 154.1, 178.5 ppm. HRMS: *m*/*z* calcd. for $C_{26}H_{19}N_2O_3$ [M + H]$^+$ 407.1396; found 407.1393.

11-Chloro-7-hydroxybenzo[*f*]indolo[1,2-*b*][2,7]naphthyridin-14(7*H*)-one (17d): According to General Procedure B, compound **9c** (300 mg, 0.824 mmol) and Pb(OAc)$_4$ (365 mg, 0.824 mmol) in THF (15 mL) were used to furnish product **17d** (212 mg, 77%) as a yellow solid; m.p. 185 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 3113, 2848, 1660, 1524, 1524, 1444, 1427, 1355, 1316, 1273, 1175 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.18 (m, 1 H), 7.45–7.52 (m, 3 H), 7.82–7.91 (m, 4 H), 8.17 (d, *J* = 7.9 Hz, 1 H), 9.30 (s, 1 H), 9.58 (d, *J* = 8.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 72.6, 107.2, 114.2, 122.1, 122.7, 126.3, 126.3, 126.4, 128.2, 128.8, 129.7, 129.8, 130.2, 133.9, 134.8, 135.6, 148.1, 151.3, 178.7 ppm. HRMS: *m*/*z* calcd. for $C_{19}H_{12}ClN_2O_2$ [M + H]$^+$ 335.0587; found 335.0580.

Oxidation of Alcohol 16 and 18. General Procedure C: Compound was dissolved in a mixture of ethyl acetate and DMSO (2:1) and IBX was added. The reaction mixture was heated to reflux for 8 h. After completion of reaction, aq. $NaHCO_3$ was added and the mixture was extracted with ethyl acetate (3 × 15 mL). The organic extract was washed with brine and dried with Na_2SO_4. Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc/hexane as eluent furnished the product.

Indolo[1,2-*b*][2,7]naphthyridine-5,12-dione (16a): According to General Procedure C, compound **15a** (25 mg, 0.10 mmol), IBX

(74 mg, 0.30 mmol) and a mixture of EtOAc (4 mL) and DMSO (2 mL) were used to furnish product **16a** (21 mg, 87%) as a yellow solid; m.p. 190 °C; R_f = 0.34 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1651, 1477, 1050, 1004 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 7.44 (t, J = 7.9 Hz, 1 H), 7.67 (d, J = 7.9 Hz, 1 H), 7.83 (s, 1 H), 7.90 (d, J = 7.9 Hz, 1 H), 8.02 (d, J = 4.9 Hz, 1 H), 8.51 (d, J = 8.2 Hz, 1 H), 9.14 (d, J = 4.9 Hz, 1 H), 9.48 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 116.4, 116.4, 118.3, 124.2, 124.8, 125.4, 128.3, 130.1, 133.7, 136.4, 138.9, 150.1, 155.3, 158.5, 174.8 ppm. HRMS: m/z calcd. for $C_{15}H_9N_2O_2$ $[M + H]^+$ 249.0664; found 249.0666.

Indolo[1,2-*b*]isoquinoline-6,11-dione (16b): According to General Procedure C, compound **15b** (40 mg, 0.16 mmol), IBX (119 mg, 0.48 mmol) and a mixture of EtOAc (4 mL) and DMSO (2 mL) were used to furnish product **16b** (34 mg, 87%) as a yellow solid; m.p. 140–144 °C; R_f = 0.34 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1688, 1662, 1552, 1444, 1372, 1247 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.38 (t, J = 7.2 Hz, 1 H), 7.59 (t, J = 7.2 Hz, 1 H), 7.66 (s, 1 H), 7.75 (d, J = 7.9 Hz, 1 H), 7.80–7.86 (m, 2 H), 8.30 (m, 1 H), 8.44 (m, 1 H), 8.63 (d, J = 8.3 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 116.5, 117.2, 123.7, 125.3, 126.9, 128.6, 129.3, 129.8, 131.2, 133.5, 134.1, 134.4, 137.2, 159.2, 175.6 ppm. HRMS: m/z calcd. for $C_{16}H_{10}NO_2$ $[M + H]^+$ 248.0712; found 248.0719.

Benzo[*f*]indolo[1,2-*b*][2,7]naphthyridine-7,14-dione (18a): According to General Procedure C, compound **17a** (74 mg, 0.24 mmol), IBX (183 mg, 0.73 mmol) and a mixture of EtOAc (9 mL) and DMSO (3 mL) were used to furnish product **18a** (60 mg, 85%) as a yellow solid; m.p. 249 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1698, 1656, 1573, 1419, 1382, 1235 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37 (t, J = 7.1 Hz, 1 H), 7.60 (t, J = 7.1 Hz, 1 H), 7.67 (s, 1 H), 7.73 (d, J = 7.8 Hz, 1 H), 7.81 (t, J = 8.5 Hz, 1 H), 7.91 (t, J = 8.5 Hz, 1 H), 8.23 (d, J = 8.5 Hz, 1 H), 8.56 (d, J = 8.5 Hz, 1 H), 9.70 (d, J = 8.7 Hz, 1 H), 9.91 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 117.1, 117.9, 122.6, 123.3, 123.9, 125.7, 127.8, 128.6, 130.3, 130.5, 130.7, 132.4, 133.8, 134.0, 136.7, 149.5, 151.7, 158.3, 177.6 ppm. HRMS: m/z calcd. for $C_{19}H_{11}N_2O_2$ $[M + H]^+$ 299.0821; found 299.0825.

11-Methoxybenzo[*f*]indolo[1,2-*b*][2,7]naphthyridine-7,14-dione (18b): According to General Procedure C, compound **17b** (98 mg, 0.29 mmol), IBX (220 mg, 0.89 mmol) and a mixture of EtOAc (8 mL) and DMSO (2 mL) were used to furnish product **18b** (77 mg, 81%) as a red solid; m.p. 206 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1689, 1650, 1570, 1477, 1240 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.90 (s, 3 H), 7.16 (m, 1 H), 7.23 (m, 1 H), 7.63 (s, 1 H), 7.83 (m, 1 H), 7.93 (m, 1 H), 8.25 (d, J = 8.5 Hz, 1 H), 8.47 (d, J = 9.2 Hz, 1 H), 9.73 (d, J = 8.5 Hz, 1 H), 9.92 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.7, 105.1, 117.6, 118.0, 120.2, 122.7, 123.4, 127.8, 129.7, 130.3, 130.7, 131.6, 132.4, 134.0, 149.4, 151.8, 157.8 ppm. HRMS: m/z calcd. for $C_{20}H_{13}N_2O_3$ $[M + H]^+$ 329.0926; found 329.0928.

11-(Benzyloxy)benzo[*f*]indolo[1,2-*b*][2,7]naphthyridine-7,14-dione (18c): According to General Procedure C, compound **17c** (190 mg, 0.46 mmol), IBX (348 mg, 1.40 mmol) and a mixture of EtOAc (10 mL) and DMSO (5 mL) were used to furnish product **18c** (145 mg, 78%) as a red solid; m.p. 230–235 °C; R_f = 0.30 (EtOAc/hexane, 30:70). IR (neat): $\tilde{\nu}_{max}$ = 1686, 1654, 1573, 1539, 1442, 1460, 1392, 1255 cm^{-1}. ^1H NMR [500 MHz, $CDCl_3$ + TFA (10:1)]: δ = 4.94 (dd, J = 11.5, 25.8 Hz, 2 H), 6.87 (s, 1 H), 7.21–7.31 (m, 6 H), 8.00 (t, J = 8.0 Hz, 1 H), 8.25 (t, J = 8.0 Hz, 1 H), 8.54 (d, J = 8.6 Hz, 1 H), 8.69 (d, J = 9.2 Hz, 1 H), 9.71 (d, J = 8.6 Hz, 1 H), 10.16 (s, 1 H) ppm. ^{13}C NMR [125 MHz, $CDCl_3$ + TFA (10:1)]: δ = 70.7, 105.4, 111.0, 113.3, 115.6, 117.8, 119.0, 122.6, 123.5, 125.3, 127.3, 128.4, 128.6, 129.1, 129.8, 130.2, 131.0, 134.0, 135.7, 137.5, 139.9, 141.2, 145.1, 154.8, 158.1, 173.9 ppm. HRMS: m/z calcd. for $C_{26}H_{17}N_2O_3$ $[M + H]^+$ 405.1239; found 405.1238.

11-Chlorobenzo[*f*]indolo[1,2-*b*][2,7]naphthyridine-7,14-dione (18d): According to General Procedure C, compound **17d** (100 mg, 0.29 mmol), IBX (222 mg, 0.89 mmol) and a mixture of EtOAc (8 mL) and DMSO (2 mL) were used to furnish product **18d** (77 mg, 80%) as a light-orange solid; m.p. 249 °C; R_f = 0.33 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 2923, 1691, 1654, 1541, 1419, 1385, 1322, 1280, 1177 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.56 (dd, J = 2.3, 9.2 Hz, 1 H), 7.62 (s, 1 H), 7.73 (d, J = 1.7 Hz, 1 H), 7.82–7.86 (m, 1 H), 7.92–7.96 (m, 1 H), 8.25 (d, J = 7.4 Hz, 1 H), 8.52 (d, J = 9.2 Hz, 1 H), 9.69 (d, J = 9.7 Hz, 1 H), 9.91 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 116.4, 118.2, 122.6, 123.0, 123.3, 127.8, 129.8, 130.3, 130.6, 130.9, 131.4, 132.0, 132.7, 133.9, 134.9, 149.4, 151.8, 158.3, 177.6 ppm. HRMS: m/z calcd. for $C_{19}H_{10}ClN_2O_3$ $[M + H]^+$ 333.0431; found 333.0432.

Preparation of Acylhydrazone 21 and 24. General Procedure D: The N-alkylated indole-2-carbohydrazide was added at room temperature to a solution of the desired aldehyde in ethanol. The reaction mixture was heated to reflux for 30 min, poured on ice, and the resulting solid was filtered and washed with water. The solid was taken into a round-bottomed flask, methanol was added, and the mixture was heated to reflux for another 15 min. The solid was filtered again, washed with methanol, and dried under vacuum.

(*E*)-1-Benzyl-*N*′-[(4-hydroxypyridin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (21a): According to General Procedure D, 1-benzyl-1*H*-indole-2-carbohydrazide (**20**; 500 mg, 1.88 mmol) and aldehyde **11** (232 mg, 1.88 mmol) in ethanol (20 mL) were used to furnish product **21a** (660 mg, 95%) as a white solid; m.p. 254–256 °C. IR (neat): $\tilde{\nu}_{max}$ = 3190, 1635, 1522, 1494, 1452, 1215 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 4.62 (br. s, 1 H), 5.90 (s, 2 H), 7.07 (s, 2 H), 7.19–7.29 (m, 6 H), 7.50 (s, 1 H), 7.57 (s, 1 H), 7.74 (s 1 H), 8.42 (s, 1 H), 8.71 (s, 1 H), 8.83 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 47.0, 107.1, 111.3, 112.07, 116.2, 121.0, 122.3, 124.7, 125.9, 126.6, 127.2, 128.6, 129.7, 138.8, 140.1, 141.7, 149.3, 159.8, 173.0 ppm. HRMS: m/z calcd. for $C_{22}H_{19}N_4O_2$ $[M + H]^+$ 371.1508; found 371.1501.

(*E*)-1-Benzyl-*N*′-(2-hydroxybenzylidene)-1*H*-indole-2-carbohydrazide (21b): According to General Procedure D, 1-benzyl-1*H*-indole-2-carbohydrazide (**20**; 500 mg, 1.9 mmol) and aldehyde **14** (0.2 mL, 1.9 mmol) in ethanol (15 mL) were used to furnish product **21b** (666 mg, 95%) as a white solid; m.p. 180–182 °C. IR (neat): $\tilde{\nu}_{max}$ = 3217, 1646, 1543, 1488, 1451, 1350, 1274, 1207 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.81 (s, 2 H), 6.90 (t, J = 7.3 Hz, 1 H), 7.00 (d, J = 8.2 Hz, 1 H), 7.09 (d, J = 7.4 Hz, 3 H), 7.15–7.27 (m, 5 H), 7.31 (t, J = 8.2 Hz, 1 H), 7.37 (d, J = 8.2 Hz, 1 H), 7.69 (d, J = 7.9 Hz, 1 H), 8.27 (br. s, 1 H), 9.25 (br. s, 1 H), 10.88 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 47.9, 111.0, 117.3, 119.3, 121.2, 122.2, 125.2, 126.1, 126.4, 127.3, 128.6, 130.9, 132.0, 137.9, 139.2, 147.8, 154.5, 158.2, 161.5 ppm. HRMS: m/z calcd. for $C_{23}H_{20}N_3O_2$ $[M + H]^+$ 370.1556; found 370.1551.

(*E*)-*N*′-[(4-Hydroxyquinolin-3-yl)methylene]-1-(4-methoxybenzyl)-1*H*-indole-2-carbohydrazide (24a): According to General Procedure D, 1-(4-methoxybenzyl)-1*H*-indole-2-carbohydrazide (**20a**; 1 g, 3.38 mmol) and aldehyde **12** (586 mg, 3.38 mmol) in ethanol (25 mL) were used to furnish product **24a** (1.39 g, 92%) as a light-yellow solid; m.p. 305–310 °C. IR (neat): $\tilde{\nu}_{max}$ = 3406, 1614, 1554, 1473, 1313, 1248 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 3.63 (s, 3 H), 5.78 (s, 2 H), 6.78 (d, J = 8.6 Hz, 2 H), 7.04–7.10 (m, 2 H), 7.22 (m, 1 H), 7.31 (s, 1 H), 7.37 (m, 1 H), 7.54–7.69 (m, 5 H),

8.15 (d, J = 8.02 Hz, 1 H), 8.47 (s, 1 H), 8.74 (s, 1 H), 11.86 (s, 1 H), 12.36 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 46.2, 55.0, 106.1, 111.1, 113.8, 118.9, 120.4, 121.8, 124.0, 124.2, 125.2, 125.6, 125.8, 128.0, 130.2, 130.6, 132.1, 132.2, 136.9, 138.3, 139.2, 143.5, 155.7, 158.0, 158.3, 174.9 ppm. HRMS: m/z calcd. for $C_{27}H_{23}N_4O_3$ [M + Na]$^+$ 451.1770; found 451.1778.

(*E*)-1-Benzyl-*N*′-[(4-hydroxyquinolin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (24b): According to General Procedure D, 1-benzyl-1*H*-indole-2-carbohydrazide (**20**; 150 mg, 0.86 mmol) and aldehyde **12** (230 mg, 0.86 mmol) in ethanol (10 mL) were used to furnish product **24b** (335 mg, 93%) as a light-yellow solid; m.p. 288 °C. IR (neat): $\tilde{\nu}_{max}$ = 3406, 2922, 1630, 1517, 1477, 1451, 1222, 1106 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 5.90 (s, 2 H), 7.08–7.15 (m, 4 H), 7.19–7.27 (m, 4 H), 7.40 (s, 2 H), 7.56 (m, 1 H), 7.65 (m, 1 H), 7.71 (m, 2 H), 8.19 (d, J = 7.9 Hz, 1 H), 8.50 (s, 1 H), 8.77 (s, 1 H), 11.92 (s, 1 H), 12.37 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 46.9, 106.3, 111.1, 113.9, 119.0, 120.6, 122.0, 124.2, 124.4, 125.3, 125.7, 125.9, 126.5, 127.0, 128.5, 130.3, 132.2, 137.0, 138.4, 138.8, 139.3, 143.6, 158.0, 175.0 ppm. HRMS: m/z calcd. for $C_{26}H_{20}N_4NaO_2$ [M + Na]$^+$ 443.1484; found 443.1483.

(*E*)-1-Benzyl-*N*′-[(4-hydroxyquinolin-3-yl)methylene]-5-methoxy-1*H*-indole-2-carbohydrazide (24c): According to General Procedure D, 1-benzyl-5-methoxy-1*H*-indole-2-carbohydrazide (**20b**; 285 mg, 0.96 mmol) and aldehyde **12** (167 mg, 0.96 mmol) in ethanol (15 mL) were used to furnish product **24c** (401 mg, 93%) as a white solid; m.p. 285 °C. IR (neat): $\tilde{\nu}_{max}$ = 3450, 1641, 1552, 1474, 1451, 1230, 1165 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.78 (s, 3 H), 5.86 (s, 2 H), 6.91 (t, J = 7.9 Hz, 1 H), 7.06 (m, 2 H), 7.23 (m, 5 H), 7.44 (m, 2 H), 7.66 (m, 2 H), 8.20 (d, J = 7.49 Hz, 1 H), 8.49 (s, 1 H), 8.77 (s, 1 H), 11.85 (s, 1 H), 12.34 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 46.9, 55.4, 102.5, 105.8, 112.0, 113.9, 115.1, 119.0, 124.3, 125.2, 125.7, 126.2, 126.4, 127.0, 128.4, 130.4, 132.1, 133.1, 133.7, 136.9, 138.9, 139.2, 143.4, 154.3, 157.9, 174.9 ppm. HRMS: m/z calcd. for $C_{27}H_{23}N_4O_3$ [M + H]$^+$ 451.1770; found 451.1778.

(*E*)-1-Benzyl-5-(benzyloxy)-*N*′-[(4-hydroxyquinolin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (24d): According to General Procedure D, 1-benzyl-5-(benzyloxy)-1*H*-indole-2-carbohydrazide (**20c**; 200 mg, 0.53 mmol) and aldehyde **12** (93 mg, 0.53 mmol) in ethanol (15 mL) were used to furnish product **24d** (251 mg, 90%) as a white solid; m.p. 286–290 °C. IR (neat): $\tilde{\nu}_{max}$ = 3227, 1643, 1569, 1475, 1451, 1278 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 5.12 (s, 2 H), 5.86 (s, 2 H), 7.00 (d, J = 8.6 Hz, 1 H), 7.00 (d, J = 7.4 Hz, 2 H), 7.19 (m, 1 H), 7.25 (m, 5 H), 7.32 (t, J = 6.87 Hz, 1 H), 7.39 (m, 3 H), 7.47 (m, 3 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.71 (t, J = 6.87 Hz, 1 H), 8.19 (d, J = 7.45 Hz, 1 H), 8.49 (s, 1 H), 8.76 (s, 1 H), 11.87 (s, 1 H), 12.4 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]-DMSO): δ = 46.9, 69.8, 104.0, 105.8, 112.0, 113.8, 115.6, 119.0, 124.3, 125.2, 125.7, 126.1, 126.4, 126.9, 127.6, 128.4, 130.5, 132.1, 133.8, 136.9, 137.5, 138.8, 139.2, 143.4, 153.3, 174.9 ppm. HRMS: m/z calcd. for $C_{33}H_{27}N_4O_3$ [M + H]$^+$ 527.2083; found 527.2082.

(*E*)-1-Benzyl-5-chloro-*N*′-[(4-hydroxyquinolin-3-yl)methylene]-1*H*-indole-2-carbohydrazide (24e): According to General Procedure D, 1-benzyl-5-chloro-1*H*-indole-2-carbohydrazide (**20d**; 250 mg, 0.83 mmol) and aldehyde **12** (143 mg, 0.83 mmol) in ethanol (12 mL) were used to furnish product **24e** (342 mg, 91%) as a white solid; m.p. 284–285 °C. IR (neat): $\tilde{\nu}_{max}$ = 3139, 3040, 1644, 1557, 1475, 1458, 1258 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 5.90 (s, 2 H), 7.70 (d, J = 7.3 Hz, 2 H), 7.18–7.28 (m, 4 H), 7.35 (s, 1 H), 7.41 (t, J = 6.9 Hz, 1 H), 7.60–7.72 (m, 3 H), 7.82 (s, 1 H), 8.18 (d, J = 6.87 Hz, 1 H), 8.49 (s, 1 H), 8.77 (s, 1 H), 11.97 (s, 1 H), 12.36 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 47.0, 105.6, 112.8, 113.7, 119.0, 121.0, 124.2, 124.3, 125.1, 125.2, 125.7, 126.4, 126.9, 127.1, 128.5, 131.7, 132.2, 136.7, 137.0, 138.4, 139.2, 143.9, 157.5, 174.9 ppm. HRMS: m/z $C_{26}H_{19}ClN_4NaO_2$ [M + Na]$^+$ 477.1094; found 477.1098.

Preparation of Keto-aldehyde 22 and 25. General Procedure E: At room temperature, the appropriate hydrazone was dissolved in THF (analytical grade). At 0 °C, lead tetraacetate was gradually added to the solution. The resulting mixture was stirred for 3–4 h at room temp. and the progress of the reaction was monitored by the evolution of nitrogen. The solvent was removed under reduce pressure. Ethyl acetate was added to the residue and the suspension was filtered through Celite. The organic layer was washed with a saturated solution of $NaHCO_3$ then brine, and dried with Na_2SO_4. The solvent was removed under vacuo and the residue was purified on a silica gel column using EtOAc/hexane as eluent to furnish the product.

4-(1-Benzyl-1*H*-indole-2-carbonyl)nicotinaldehyde (22a): According to General Procedure E, compound **21a** (400 mg, 1.08 mmol) and $Pb(OAc)_4$ (478 mg, 1.08 mmol) in THF (15 mL) were used to furnish **22a** (268 mg, 73%) as a light-orange solid; m.p. 225–230 °C; R_f = 0.40 (EtOAc/hexane, 50:50). IR (neat): $\tilde{\nu}_{max}$ = 1701, 1647, 1510, 1496, 1456, 1403, 1259 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.96 (s, 2 H), 6.78 (s, 1 H), 7.14–7.30 (m, 7 H), 7.36–7.47 (m, 3 H), 7.61 (d, J = 8.3 Hz, 1 H), 8.91 (d, J = 4.9 Hz, 1 H), 9.18 (s, 1 H), 9.97 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.4, 111.1, 117.7, 121.7, 122.3, 123.5, 126.0, 126.5, 127.4, 127.7, 128.7, 128.8, 133.6, 137.7, 141.0, 148.4, 151.4, 154.0, 185.6, 189.2 ppm. HRMS: m/z calcd. for $C_{22}H_{17}N_2O_2$ [M + H]$^+$ 341.1290; found 341.1291.

2-(1-Benzyl-1*H*-indole-2-carbonyl)benzaldehyde (22b): According to General Procedure E, compound **21b** (490 mg, 1.32 mmol) and $Pb(OAc)_4$ (584 mg, 1.32 mmol) in THF (15 mL) were used to furnish **22b** (313 mg, 70%) as a yellow solid; m.p. 134 °C; R_f = 0.25 (EtOAc/hexane, 10:90). IR (neat): $\tilde{\nu}_{max}$ = 1698, 1650, 1512, 1453, 1204 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.01 (s, 2 H), 6.85 (s, 1 H), 7.16–7.25 (m, 4 H), 7.31 (m, 2 H), 7.39 (m, 1 H), 7.45 (m, 1 H), 7.64 (m, 2 H), 7.67 (m, 2 H), 8.03 (m, 1 H), 9.97 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.2, 111.0, 117.3, 121.3, 123.3, 126.0, 126.5, 127.0, 127.3, 128.6, 129.0, 129.1, 130.5, 133.0, 135.0, 135.2, 138.0, 140.6, 142.4, 188.1, 190.4 ppm. HRMS: m/z calcd. for $C_{23}H_{17}NNaO_2$ [M + Na]$^+$ 362.1157; found 362.1150.

4-[1-(4-Methoxybenzyl)-1*H*-indole-2-carbonyl]quinoline-3-carbaldehyde (25a): According to General Procedure E, compound **24a** (1 g, 2.20 mmol) and $Pb(OAc)_4$ (974 mg, 2.20 mmol) in THF (25 mL) were used to furnish **25a** (683 mg, 74%) as a red solid; m.p. 190–192 °C; R_f = 0.33 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1697, 1647, 1512, 1477, 1456, 1403, 1248 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 6.02 (s, 2 H), 6.86 (s, 1 H), 6.88 (d, J = 8.5 Hz, 2 H), 7.14 (t, J = 7.3 Hz, 1 H), 7.19 (d, J = 8.9 Hz, 2 H), 7.42–7.49 (m, 2 H), 7.53 (t, J = 8.5 Hz, 3 H), 7.85 (m, 1 H), 8.23 (d, J = 8.2 Hz, 1 H), 9.45 (s, 1 H), 10.06 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.0, 55.3, 111.1, 114.1, 118.4, 121.7, 123.6, 124.5, 126.2, 126.8, 127.9, 128.2, 128.4, 130.0, 132.7, 134.7, 141.1, 149.0, 149.1, 150.3, 159.1, 186.3, 189.1 ppm. HRMS: m/z calcd. for $C_{27}H_{21}N_2O_3$ [M + H]$^+$ 421.1552; found 421.1556.

4-(1-Benzyl-1*H*-indole-2-carbonyl)quinoline-3-carbaldehyde (25b): According to General Procedure E, compound **24b** (180 mg, 0.43 mmol) and $Pb(OAc)_4$ (190 mg, 0.43 mmol) in THF (10 mL) were used to furnish **25b** (124 mg, 74%) as a red solid; m.p. 142 °C; R_f = 0.40 (EtOAc/hexane, 40:60). IR (neat): $\tilde{\nu}_{max}$ = 1695, 1643, 1562, 1511, 1452, 1247 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.11 (s, 2 H), 6.69 (s, 1 H), 7.15 (t, J = 7.7 Hz, 1 H), 7.23 (m, 2 H),

7.29–7.37 (m, 3 H), 7.41–7.57 (m, 5 H), 7.85 (t, J = 7.7 Hz, 1 H), 8.23 (d, J = 8.3 Hz, 1 H), 9.45 (s, 1 H), 10.06 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.5, 111.0, 118.3, 121.7, 123.5, 124.5, 124.5, 126.1, 126.6, 126.7, 127.5, 127.9, 128.4, 128.7, 129.8, 132.7, 134.6, 137.8, 141.1, 148.9, 149.0, 150.2, 186.2, 188.9 ppm. HRMS: m/z calcd. for $C_{26}H_{19}N_2O_2$ $[M + H]^+$ 391.1447; found 391.1457.

4-(1-Benzyl-5-methoxy-1*H*-indole-2-carbonyl)quinoline-3-carbaldehyde (25c): According to General Procedure E, compound **24c** (170 mg, 0.37 mmol) and $Pb(OAc)_4$ (167 mg, 0.37 mmol) in THF (10 mL) were used to furnish **25c** (105 mg, 68%) as a dark-red solid; m.p. 200–202 °C; R_f = 0.2 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1697, 1643, 1572, 1517, 1454, 1244, 1211 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H), 6.06 (s, 2 H), 6.57 (s, 1 H), 6.87 (d, J = 2.2 Hz, 1 H), 7.11 (dd, J = 2.2, 9.3 Hz, 1 H), 7.19 (d, J = 6.8 Hz, 2 H), 7.30–7.41 (m, 4 H), 7.48 (t, J = 7.3 Hz, 1 H), 7.56 (d, J = 7.8 Hz, 1 H), 7.85 (t, J = 7.1 Hz, 1 H), 8.22 (d, J = 8.5 Hz, 1 H), 9.44 (s, 1 H), 10.05 (s, 1 H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$): δ = 48.7, 55.6, 102.4, 112.2, 117.6, 120.4, 124.5, 124.5, 126.4, 126.6, 126.8, 127.6, 128.4, 128.8, 129.9, 132.7, 134.8, 136.9, 137.9, 148.8, 149.3, 150.3, 155.2, 185.8, 189.0 ppm. HRMS: m/z calcd. for $C_{27}H_{21}N_2O_3$ $[M + H]^+$ 421.1552; found 421.1559.

4-[1-Benzyl-5-(benzyloxy)-1*H*-indole-2-carbonyl]quinoline-3-carbaldehyde (25d): According to General Procedure E, compound **24d** (180 mg, 0.34 mmol) and $Pb(OAc)_4$ (150 mg, 0.34 mmol) in THF (10 mL) were used to furnish product **25d** (119 mg, 71%) as a red solid; m.p. 140–142 °C; R_f = 0.33 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1698, 1628, 1573, 1495, 1453, 1242 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.01 (s, 2 H), 6.06 (s, 2 H), 6.55 (s, 1 H), 6.93 (m, 1 H), 7.19 (m, 3 H), 7.29–7.42 (m, 9 H), 7.48 (m, 1 H), 7.55 (m, 1 H), 7.85 (m, 1 H), 8.22 (d, J = 8.0 Hz, 1 H), 9.43 (s, 1 H), 10.05 (s, 1 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 48.6, 70.4, 104.0, 112.1, 117.6, 120.8, 124.5, 124.5, 126.4, 126.6, 127.3, 127.6, 127.9, 128.4, 128.5, 128.7, 129.8, 132.7, 134.8, 136.8, 137.9, 148.8, 149.2, 150.2, 154.3, 185.8, 189.0 ppm. HRMS: m/z calcd. for $C_{33}H_{25}N_2O_3$ $[M + H]^+$ 497.1865; found 497.1866.

4-(1-Benzyl-5-chloro-1*H*-indole-2-carbonyl)quinoline-3-carbaldehyde (25e): According to General Procedure E, compound **24e** (230 mg, 0.50 mmol) and $Pb(OAc)_4$ (221 mg, 0.50 mmol) in THF (10 mL) were used to furnish **25e** (150 mg, 71%) as a red solid; m.p. 136–140 °C; R_f = 0.25 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1697, 1648, 1562, 1508, 1452, 1403, 1246 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.08 (s, 2 H), 6.56 (s, 1 H), 7.20 (d, J = 6.9 Hz, 2 H), 7.31–7.38 (m, 5 H),7.47–7.54 (m, 3 H), 7.86 (m, 1 H), 8.24 (d, J = 8.7 Hz, 1 H), 9.44 (s, 1 H), 10.07 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 48.7, 112.3, 116.6, 122.5, 124.5, 126.6, 126.8, 127.3, 127.7, 128.3, 128.6, 128.8, 130.0, 132.9, 135.4, 137.4, 139.2, 148.4, 149.4, 150.3, 188.6, 189.0 ppm. HRMS: m/z calcd. for $C_{26}H_{18}ClN_2O_2$ $[M + H]^+$ 425.1057; found 425.1051.

Cyclisation Reaction for the Preparation of 23 and 26. General Procedure F: Under an inert atmosphere of argon, to a stirred solution of keto-aldehyde in CH_2Cl_2, $BF_3{\cdot}OEt_2$ (1 equiv.) was added at 0 °C and the mixture was stirred for 1 h at room temp. The progress of the reaction was monitored by TLC and, upon completion, the reaction was quenched by the addition of sodium bisulfate. The mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with brine and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified on silica gel column chromatography using EtOAc/hexane as eluent to furnish the product.

6-Benzyl-5*H*-pyrido[4,3-*b*]carbazole-5,11(6*H*)-dione (23a): According to General Procedure F, compound **22a** (45 mg, 0.132 mmol) and $BF_3{\cdot}OEt_2$ (0.032 mL, 0.264 mmol) in CH_2Cl_2 (7 mL) were used to furnish **23a** (33 mg, 74%) as a light-orange solid; m.p. 252 °C; R_f = 0.33 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1654, 1511, 1260, 1207 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.99 (s, 2 H), 7.19 (d, J = 6.7 Hz, 2 H), 7.26–7.31 (m, 3 H), 7.42–7.47 (m, 1 H), 7.49 (m, 2 H), 7.93 (d, J = 4.8 Hz, 1 H), 8.51 (d, J = 7.9 Hz, 1 H), 9.03 (d, J = 4.6 Hz, 1 H), 9.46 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.6, 111.7, 118.7, 119.6, 123.9, 124.3, 125.3, 126.7, 128.0, 128.5, 129.0, 136.2, 139.1, 140.3, 148.5, 155.0, 177.8, 180.8 ppm. HRMS: m/z calcd. for $C_{22}H_{15}N_2O_2$ $[M + H]^+$ 339.1134; found 339.1130.

5-Benzyl-5*H*-benzo[*b*]carbazole-6,11-dione (23b): According to General Procedure F, compound **22b** (40 mg, 0.117 mmol) and $BF_3{\cdot}OEt_2$ (0.029 mL, 0.235 mmol) in CH_2Cl_2 (7 mL) were used to furnish **23b** (31 mg, 74%) as a yellow solid; m.p. 130–132 °C; R_f = 0.33 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1652, 1596, 1516, 1466, 1340, 1303 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.98 (s, 2 H), 7.17–7.30 (m, 5 H), 7.37–7.45 (m, 3 H), 7.66 (t, J = 7.3 Hz, 1 H), 7.71 (t, J = 7.3 Hz, 1 H), 8.13 (d, J = 7.3 Hz, 1 H), 8.21 (d, J = 7.8 Hz, 1 H), 8.48 (d, J = 7.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.4, 111.4, 119.3, 123.9, 124.0, 124.6, 126.2, 126.5, 126.6, 127.6, 127.7, 128.8, 132.8, 133.5, 133.8, 134.0, 134.7, 136.5, 139.7, 178.9, 181.2 ppm. HRMS: m/z calcd. for $C_{23}H_{16}NO_2$ $[M + H]^+$ 362.1157; found 362.1150.

12-(4-Methoxybenzyl)-7*H*-indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (26a): According to General Procedure F, compound **25a** (200 mg, 0.476 mmol) and $BF_3{\cdot}OEt_2$ (0.116 mL, 0.952 mmol) in CH_2Cl_2 (15 mL) were used to furnish **26a** (159 mg, 80%) as a red solid; m.p. 243 °C; R_f = 0.33 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1650, 1609, 1512, 1497, 1512, 1238 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.74 (s, 3 H), 5.91 (s, 2 H), 6.82 (d, J = 8.2 Hz, 2 H), 7.19 (d, J = 8.2 Hz, 2 H), 7.38–7.49 (m, 3 H), 7.73 (t, J = 7.3 Hz, 1 H), 7.81 (t, J = 7.3 Hz, 1 H), 8.17 (d, J = 8.2 Hz, 1 H), 8.43 (d, J = 8.2 Hz, 1 H), 9.55 (d, J = 8.5 Hz, 1 H), 9.77 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.0, 55.2, 111.6, 114.2, 117.6, 123.1, 123.3, 123.9, 124.5, 125.1, 127.7, 127.9, 128.1, 128.3, 130.1, 130.3, 131.4, 133.3, 135.1, 140.0, 147.9, 152.1, 159.2, 181.0, 182.0 ppm. HRMS: m/z calcd. for $C_{27}H_{19}N_2O_3$ $[M + H]^+$ 419.1396; found 419.1396.

12-Benzyl-7*H*-indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (26b): According to General Procedure F, compound **25b** (107 mg, 0.278 mmol) and $BF_3{\cdot}OEt_2$ (0.068 mL, 0.556 mmol) in CH_2Cl_2 (10 mL) were used to furnish **26b** (85 mg, 79%) as a red solid; m.p. 230 °C; R_f = 0.25 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1653, 1525, 1495, 1454, 1241 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.00 (s, 2 H), 7.22 (m, 2 H), 7.27–7.32 (m, 3 H), 7.40–7.47 (m, 3 H), 7.72 (m, 1 H), 7.82 (m, 1 H), 8.18 (d, J = 8.3 Hz, 1 H), 8.45 (d, J = 8.3 Hz, 1 H), 9.53 (d, J = 8.3 Hz, 1 H), 9.78 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.5, 111.6, 117.7, 123.1, 123.3, 123.9, 124.5, 125.2, 126.6, 127.7, 127.9, 128.0, 128.9, 130.1, 130.3, 131.4, 133.3, 135.1, 136.2, 140.1, 147.9, 152.2, 181.0, 182.0 ppm. HRMS: m/z calcd. for $C_{26}H_{17}N_2O_2$ $[M + H]^+$ 389.1290; found 389.1290.

12-Benzyl-9-methoxy-7*H*-indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (26c): According to General Procedure F, compound **25c** (53 mg, 0.126 mmol) and $BF_3{\cdot}OEt_2$ (0.031 mL, 0.25 mmol) in CH_2Cl_2 (7 mL) were used to furnish **26c** (42 mg, 80%) as a red solid; m.p. 218–220 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1648, 1614, 1496, 1517, 1474, 1237 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.92 (s, 3 H), 5.96 (s, 2 H), 7.05 (d, J = 8.5 Hz, 1 H), 7.20 (m, 2 H), 7.24–7.31 (m, 4 H), 7.24–7.31 (m, 4 H), 7.71 (m, 1 H), 7.80 (m, 2 H), 8.17 (d, J = 8.5 Hz, 1 H), 9.55

(d, J = 8.5 Hz, 1 H), 9.76 (s, 1 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 48.7, 55.8, 102.8, 112.7, 117.1, 120.3, 123.3, 124.3, 124.7, 126.6, 127.9, 127.9, 128.9, 130.0, 130.1, 131.5, 133.7, 134.8, 135.5, 136.1, 147.5, 158.3, 168.4, 180.7, 181.3 ppm. HRMS: *m*/*z* calcd. for $C_{27}H_{19}N_2O_3$ $[M + H]^+$ 419.1396; found 419.1392.

12-Benzyl-9-(benzyloxy)-7*H*-indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (26d): According to General Procedure F, compound **25d** (48 mg, 0.096 mmol) and $BF_3{\cdot}OEt_2$ (0.023 mL, 0.193 mmol) in CH_2Cl_2 (10 mL) were used to furnish **26d** (36 mg, 77%) as a red solid; m.p. 226 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 1654, 1524, 1496, 1461, 1240 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.19 (s, 2 H), 5.98 (s, 2 H), 7.16–7.22 (m, 3 H), 7.28–7.34 (m, 3 H), 7.36 (d, J = 9.2 Hz, 2 H), 7.43 (t, J = 7.4 Hz, 2 H), 7.52 (d, J = 7.4 Hz, 2 H), 7.73 (m, 1 H), 7.82 (m, 1 H), 7.94 (d, J = 2.2 Hz, 1 H), 8.19 (d, J = 8.5 Hz, 1 H), 9.57 (d, J = 9.2 Hz, 1 H), 9.79 (s, 1 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 48.8, 70.6, 104.2, 112.9, 120.7, 123.3, 124.4, 124.7, 126.7, 127.8, 128.0, 128.2, 128.7, 129.0, 130.1, 130.4, 131.5, 133.6, 134.6, 135.7, 136.3, 136.7, 148.0, 152.2, 153.2, 157.5, 166.4, 168.7, 180.7, 181.7 ppm. HRMS: *m*/*z* calcd. for $C_{33}H_{23}N_2O_3$ $[M + H]^+$ 495.1709; found 495.1704.

12-Benzyl-9-chloro-7*H*-indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (26e): According to General Procedure F, compound **25e** (50 mg, 0.118 mmol) and $BF_3{\cdot}OEt_2$ (0.029 mL, 0.236 mmol) in CH_2Cl_2 (10 mL) were used to furnish **26e** (37 mg, 75%) as an orange solid; m.p. 243 °C; R_f = 0.40 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 2921, 1742, 1656, 1523, 1455, 1343, 1236 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.97 (s, 2 H), 7.18 (m, 2 H), 7.27–7.33 (m, 4 H), 7.37 (m, 2 H), 7.72 (m, 1 H), 7.82 (m, 1 H), 8.41 (s, 1 H), 9.50 (d, J = 8.5 Hz, 1 H), 9.76 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 48.7, 112.8, 116.9, 123.0, 123.1, 124.0, 124.2, 126.5, 127.6, 128.1, 128.6, 129.0, 130.3, 131.2, 131.6, 133.2, 135.7, 135.8, 138.3, 147.7, 152.1, 180.6, 181.8 ppm. HRMS: *m*/*z* calcd. for $C_{26}H_{16}ClN_2O_2$ $[M + H]^+$ 423.0900; found 423.0902.

7*H*-Indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (5): A solution of **26a** (72 mg, 0.172 mmol) in anhydrous anisole (3 mL) was added dropwise to a stirred suspension of $AlCl_3$ (114 mg, 0.861 mmol) in anhydrous anisole (2 mL) at 0 °C, and the resulting reaction mixture was stirred at room temp. for 6 h. After the addition of water, the mixture was extracted with ethyl acetate and the combined organic layers were washed with 5% aqueous $NaHCO_3$ and brine successively, then dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give an oil, which was purified by a silica gel column using EtOAc/hexane as eluent to furnished the product **5** (34 mg, 78%) as a red solid; m.p. 170–175 °C; R_f = 0.30 (EtOAc/hexane, 20:80). IR (neat): $\tilde{\nu}_{max}$ = 3428, 1651, 1050, 1026 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.40 (t, J = 7.4 Hz, 1 H), 7.48 (t, J = 7.4 Hz, 1 H), 7.61 (t, J = 8.0 Hz, 1 H), 7.89 (t, J = 8.0 Hz, 1 H), 7.96 (t, J = 8.0 Hz, 1 H), 8.17 (d, J = 8.0 Hz, 2 H), 9.57 (d, J = 8.6 Hz, 1 H), 9.61 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 114.1, 115.7, 122.5, 122.8, 123.5, 124.5, 125.0, 127.3, 130.0, 130.4, 131.7, 132.7, 138.1, 138.6, 147.7, 151.4, 180.5, 181.0 ppm. HRMS: *m*/*z* calcd. for $C_{19}H_{11}N_2O_2$ $[M + H]^+$ 299.0821; found 299.0824.

Supporting Information (see footnote on the first page of this article): Experimental details as well as ^{1}H and ^{13}C NMR spectra of all the compounds reported in this article.

Acknowledgments

G. M. thanks the Council of Scientific and Industrial Research (CSIR), New Delhi, for the award of a research fellowship. Financial support from the Indian Institute of Technology Kanpur is gratefully acknowledged.

[1] S. Goodwin, A. F. Smith, E. C. Horning, *J. Am. Chem. Soc.* **1959**, *81*, 1903.

[2] a) A. W. Schmidt, K. R. Reddy, H.-J. Knölker, *Chem. Rev.* **2012**, *112*, 3193; b) C. M. Miller, F. O. McCarthy, *RSC Adv.* **2012**, *2*, 8883; c) Mal, B. K. Senapati, P. Pahari, *Synlett* **2005**, 994; d) H.-J. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303; e) H.-J. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303; f) M. Álvarez, J. A. Joule, in: *The Alkaloids* (Ed.: G. A. Cordell), Academic Press, New York, **2001**, vol. 57, p. 235; g) Y. Miki, H. Hachiken, N. Yanase, *Org. Biomol. Chem.* **2001**, 2213; h) M. Ishikura, A. Hino, T. Yaginuma, I. Agata, N. Katagiri, *Tetrahedron* **2000**, *56*, 193; a valuable review of references to earlier syntheses is included. Recent references include: i) M. Alvarez, J. A. Joule, in: *The Chemistry of Heterocyclic Compounds* (Ed.: J. E. Saxton), Wiley, Chichester, UK, **1994**, p. 261; j) G. W. Gribble, *Advances in Heterocyclic Natural Product Synthesis* (Ed.: W. H. Pearson), JAI Press, Greenwich, CT, **1990**, vol. 1, p. 43; k) G. W. Gribble, in: *The Alkaloids* (Ed.: A. Brossi), Academic Press, San Diego, CA, **1990**, p. 239; l) V. K. Kansal, P. Potier, *Tetrahedron* **1986**, *42*, 2389; m) M. J. E. Hewlins, M. A. Oliveira-Campos, P. V. R. Shannon, *Synthesis* **1984**, 289; n) M. Sainsbury, *Synthesis* **1977**, 437.

[3] a) M. Ohashi, T. Oki, *Expert Opin. Ther. Pat.* **1996**, *6*, 1285; b) J. G. Rouesse, C. T. Le, P. Caille, J. M. Mondesir, H. Sancho-Garnier, F. May-Levin, M. Spielmann, J. R. De, J. L. Amiel, *Cancer Treat. Rep.* **1985**, *69*, 707; c) C. N. Paoletti, P. Le, P. D.-X. Juret, H. H. Garnier, J. L. Amiel, J. Rouesse, *Recent Results Cancer Res.* **1980**, *74*, 107.

[4] R. W. Rickards, J. M. Rothschild, A. C. Willis, N. M. de Chazal, J. Kirk, K. Kirk, K. J. Saliba, G. D. Smith, *Tetrahedron* **1999**, *55*, 13513.

[5] a) B. M. Ramalingam, V. Saravanan, A. K. Mohanakrishanan, *Org. Lett.* **2013**, *15*, 3726; b) N. Ramkumar, R. J. Nagarajan, *Org. Chem.* **2013**, *78*, 2802; c) S. M. Bhosale, R. L. Gawade, V. G. Puranik, R. S. Kusurkar, *Tetrahedron Lett.* **2012**, *53*, 2894; d) K. Matsumoto, T. Choshi, M. Hourai, Y. Zamami, K. Sasaki, T. Abe, M. Ishikura, N. Hatae, N. Iwamura, S. Tohyama, J. Nobuhiro, S. Hibino, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 4762; e) T. Abe, T. Ikeda, T. Choshi, S. Hibino, N. Hatae, E. Toyata, R. Yanada, M. Ishikura, *Eur. J. Org. Chem.* **2012**, 5018; f) C. S. McEelean, J. Sperry, A. Makke, C. J. Moody, *Tetrahedron Lett.* **2012**, *53*, 2894; g) T. Abe, T. Ikeda, R. Yanada, M. Ishikura, *Org. Lett.* **2011**, *13*, 3356; h) S. Tohyama, T. Choshi, K. Matsumoto, A. Yamabuki, Y. Hieda, J. Nobuhiro, S. Hibino, *Heterocycles* **2010**, *82*, 397; i) T. Choshi, S. Hibino, *Heterocycles* **2009**, *77*, 85; j) P. H. Bernardo, C. L. L. Cahi, M. L. Guen, G. D. Smith, P. Waring, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 82; k) C. S. P. McErlean, J. Sperry, A. J. Blake, C. J. Moody, *Tetrahedron* **2007**, *63*, 10963; l) D. Sissouma, L. Maingot, S. Collet, A. Guingant, *J. Org. Chem.* **2006**, *71*, 8434; m) M.-L. Bennasar, T. Roca, F. Ferrando, *Org. Lett.* **2006**, *8*, 561; n) A. Yamabuki, H. Fujinawa, T. Choshi, S. Tohyama, K. Matsumoto, K. Ohmura, J. Nobuhiro, S. Hibino, *Tetrahedron Lett.* **2006**, *47*, 5859; o) S. Tohyama, T. Choshi, K. Matsumoto, A. Yamabuki, K. Ikegata, J. Nobuhiro, S. Hibino, *Tetrahedron Lett.* **2005**, *46*, 5263; p) D. Sissouma, S. Collet, A. Guingant, *Synlett* **2004**, 2612; q) P. H. Bernardo, C. L. L. Chai, *J. Org. Chem.* **2003**, *68*, 8906; r) P. H. Bernardo, C. L. L. Chai, J. A. Elix, *Tetrahedron Lett.* **2002**, *43*, 2939; s) Kelly, Y. Zhao, M. Cavero, M. Torneiro, *Org. Lett.* **2000**, *2*, 3735.

[6] a) K. Matsumoto, T. Choshi, M. Hourai, Y. Zamami, K. Sasaki, T. Abe, M. Ishikura, N. Hatae, N. Iwamura, S. Tohyama, J. Nobuhiro, S. Hibino, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 4762; b) Q. A. Khan, J. Lu, S. M. Hecht, *J. Nat. Prod.* **2009**, *72*, 438; c) P. H. Bernardo, C. L. L. Chai, M. Le Guen, G. D. Smith, P. Waring, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 82; d) P. H. Bernardo, C. L. L. Chai, G. A. Heath, P. J. Mahon, G. D.

Smith, P. Waring, B. A. Wilkes, *J. Med. Chem.* **2004**, *47*, 4958.

[7] a) A. Kotali, P. G. Tsoungas, *Tetrahedron Lett.* **1987**, *28*, 4321; b) A. R. Katritzky, P. A. Harris, A. J. Kotali, *J. Org. Chem.* **1991**, *56*, 5049; c) A. R. Katritzky, A. Kotali, *Tetrahedron Lett.* **1990**, *31*, 6790; d) A. Kotali, I. S. Lafazanis, P. A. Harris, *Tetrahedron Lett.* **2007**, *48*, 7181; e) A. Kotali, P. A. Harris, *Org. Prep. Proced. Int.* **2003**, *35*, 583; f) A. Kotali, *Curr. Org. Chem.* **2002**, *6*, 965; g) A. Kotali, M. Papapetrou, V. Dimos, *Org. Prep. Proced. Int.* **1998**, *30*, 159; h) A. Kotali, *Tetrahedron Lett.* **1994**, *35*, 6753; i) A. Kotali, U. Glaveri, E. Pavlidou, P. G. Tsoungas, *Synthesis* **1990**, 1172; for similar reactions using phenyliodosodiacetate, see: j) A. Kotali, A. Koulidis, H.-M. Wang, L.-C. Chen, *Org. Prep. Proced. Int.* **1996**, *28*, 622; k) R. M. Moriarty, B. A. Berglund, M. S. C. Rao, *Synthesis* **1992**, 318.

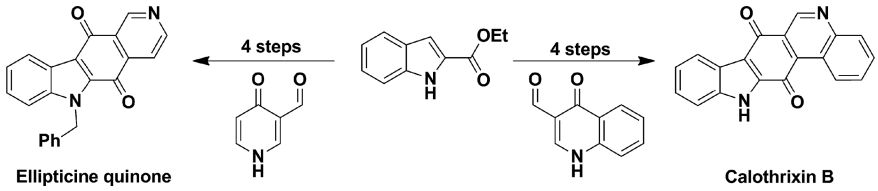
[8] a) H. T. P. Diem, K. Byoungmoo, V. M. Dong, *J. Am. Chem. Soc.* **2009**, *131*, 15608; b) J. Jacq, C. Einhorn, J. Einhorn, *Org. Lett.* **2008**, *10*, 3757.

[9] a) S. G. Raquel, R. Seixas, A. M. S. Silva, I. Alkorta, J. Elguero, *Monatsh. Chem.* **2011**, *142*, 731; b) F. Marsais, F. Trécourt, P. Bréant, G. Quéguiner, *J. Heterocycl. Chem.* **1988**, *25*, 81.

[10] a) M.-L. Bennasar, T. Roca, F. Ferrando, *J. Org. Chem.* **2005**, *70*, 9077; b) H.-J. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303, and references cited therein; c) Y. Miki, Y. Tada, K. Matsushita, *Heterocycles* **1998**, *48*, 1593; d) Y. Yokoyama, N. Okuyama, S. Iwadate, T. Momoi, Y. Murakami, *J. Chem. Soc. Perkin Trans. 1* **1990**, 1319; e) D. M. Kecha, G. W. Gribble, *J. Org. Chem.* **1985**, *50*, 5451; f) G. W. Gribble, M. G. Saulnier, M. P. Sibi, J. A. Obaza-Nutaitis, *J. Org. Chem.* **1984**, *49*, 4518; g) M. Watanabe, V. Snieckus, *J. Am. Chem. Soc.* **1980**, *102*, 1457.

Received: June 29, 2014
Published Online: ■

EurJOC European Journal of Organic Chemistry



The divergent synthesis of calothrixins and ellipticines has been accomplished by utilising the one-pot formation of *o*-diacylarenes as a key intermediate through rearrangement of *o*-hydroxy ketone monoacyl hydrazones by lead tetraacetate mediated oxidation.

Keywords: Natural products / Nitrogen heterocycles / Quinones / Rearrangement / Oxidation

