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Synthetic studies of benzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthroline

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Abstract—6,11-Dihydrobenzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthroline-5,8-dione (**6**), which possesses a unique heterocyclic ring system similar to that in plakinidines A–D (**1**–**4**), was synthesized from 2-acetyl-3′-nitrodiphenylamine (**16**) in nine steps.
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1. Introduction

A series of structurally unique pentacyclic aromatic alkaloids have been obtained from marine organisms. In 1990, the isolation and structure elucidation of new cytotoxic alkaloids, plakinidines A (**1**), B (**2**) and C (**3**), from a *Plakortis* sponge were reported.[1] ^{1}H and ^{13}C NMR spectroscopy and X-ray crystallographic analysis revealed that the structure of **1** is 9,10-dihydro-7-(methylamino)-benzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthrolin-8(11*H*)-one. Plakinidines B (**2**) and C (**3**) are the *N*-methyl and 9,10-didehydro derivatives of **1**, respectively. Furthermore, plakinidine D (**4**) was isolated from the ascidian *Didemnum rubeum*.[2] Those alkaloids possess a unique heterocyclic parent ring system, benzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthroline (**5**). In this report, we describe the synthesis of 6,11-dihydrobenzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthroline-5,8-dione (**6**) (Fig. 1).

2. Results and discussion

First, we attempted to prepare **6** via benzo[*b*][1,10]phenanthroline (**12**) (Scheme 1). 2-Acetyl-2′-nitrodiphenylamine[3] (**7**) was heated in sulfuric acid–acetic acid to give 9-methyl-4-nitroacridine (**8**). 4-Amino-9-methylacridine (**9**), which was obtained by the catalytic reduction of **8**, was treated with 5-(methoxymethylene)-2,2-dimethyl-1,3-dioxane-4,6-dione[4] to give Meldrum's acid derivative (**10**).

Nitration of **10** with fuming nitric acid in acetic acid at rt gave the desired nitro compound (**11**) in only 36% yield. Treatment of **10** with copper(II) nitrate[5] in acetic anhydride in the presence of ascorbic acid at 70 °C gave **11** in 79% yield. The structure of **11** was confirmed by ^{1}H NMR measurements. No nuclear Overhauser effect (NOE) was observed between the protons at 2.95 ppm (C_9–CH_3) and all other protons except that at 8.34 ppm (C_8–H).

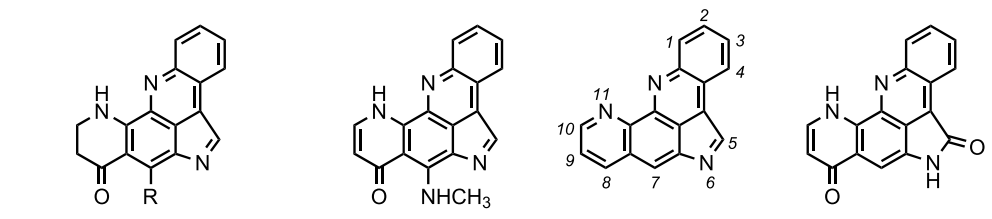

Figure 1.

Keywords: Acridine; Phenanthroline; Nitration; Cyclization.
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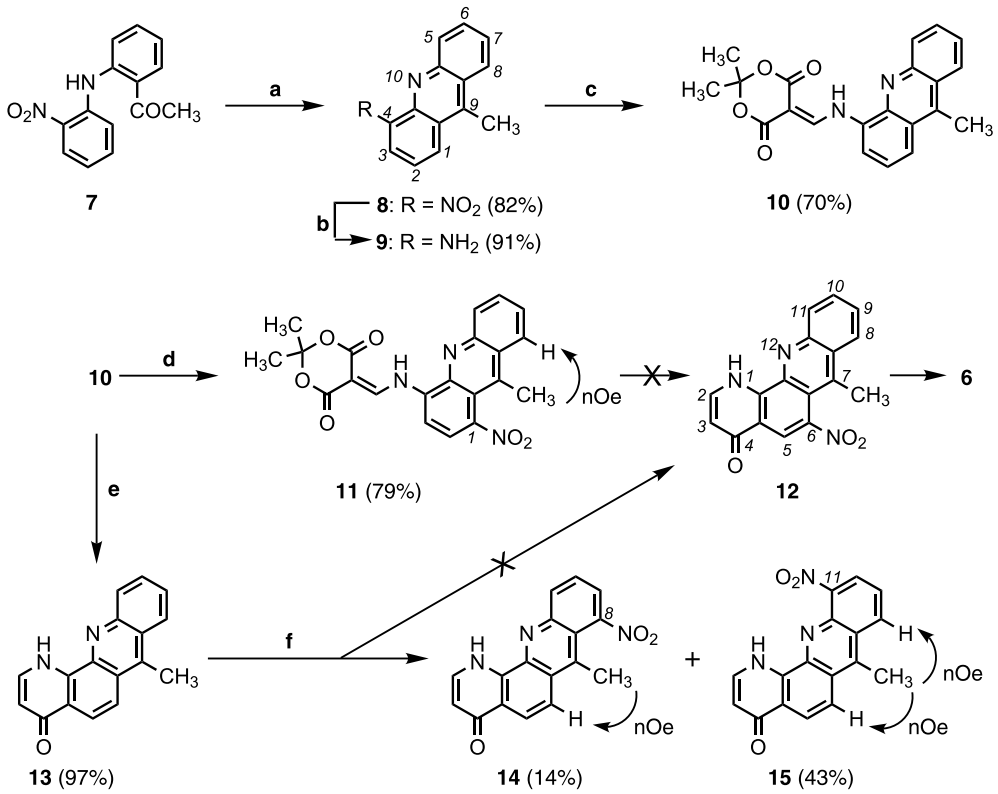


Scheme 1. (a) H_2SO_4, CH_3CO_2H, 95–105 °C, 30 min; (b) H_2, 10% Pd–C, $CH_3CO_2C_2H_5$, 20 min; (c) (i) Meldrum's acid, $CH(OCH_3)_3$, reflux, 1 h, (ii) **9**, $CH(OCH_3)_3$, reflux, 20 min; (d) $Cu(NO_3)_2{\cdot}3H_2O$, $(CH_3CO)_2O$, ascorbic acid, 70 °C, 9 h; (e) $(C_6H_5)_2O$, reflux, 15 min; (f) KNO_3, H_2SO_4–fum. H_2SO_4 (4:1), CH_3NO_2, −25 °C, 39 h.

All attempts at the thermal cyclization of **11** to **12** in diphenyl ether[4] at various temperatures met with failure (e.g., 250–260 °C: a complex mixture; 200–210 °C: no reaction).

On the other hand, treatment of **10** at 250–260 °C for 15 min gave the cyclized product (**13**) in quantitative yield. Nitration of **13** with copper(II) nitrate in acetic anhydride in the presence of ascorbic acid at 70 °C gave a complex mixture. Treatment of **13** with potassium nitrate in sulfuric acid–oleum at −25 °C gave 8-nitro- (**14**) and 11-nitrobenzo[*b*][1,10]phenanthrolinone (**15**) in 14 and 43% yields, respectively, but no 6-nitrobenzo[*b*][1,10]-phenanthrolinone (**12**). The structures of **14** and **15** were confirmed by ^{1}H NMR measurements. No NOE was observed between the protons at 2.95 ppm (C_7–CH_3) and all other protons except that at 8.08 ppm (C_6–H) for **14**. In contrast, NOE was observed between (a) the protons at 3.25 ppm (C_7–CH_3) and 8.11 ppm (C_6–H) and (b) the protons at 3.25 ppm (C_7–CH_3) and 8.60 ppm (C_8–H) for **15**.

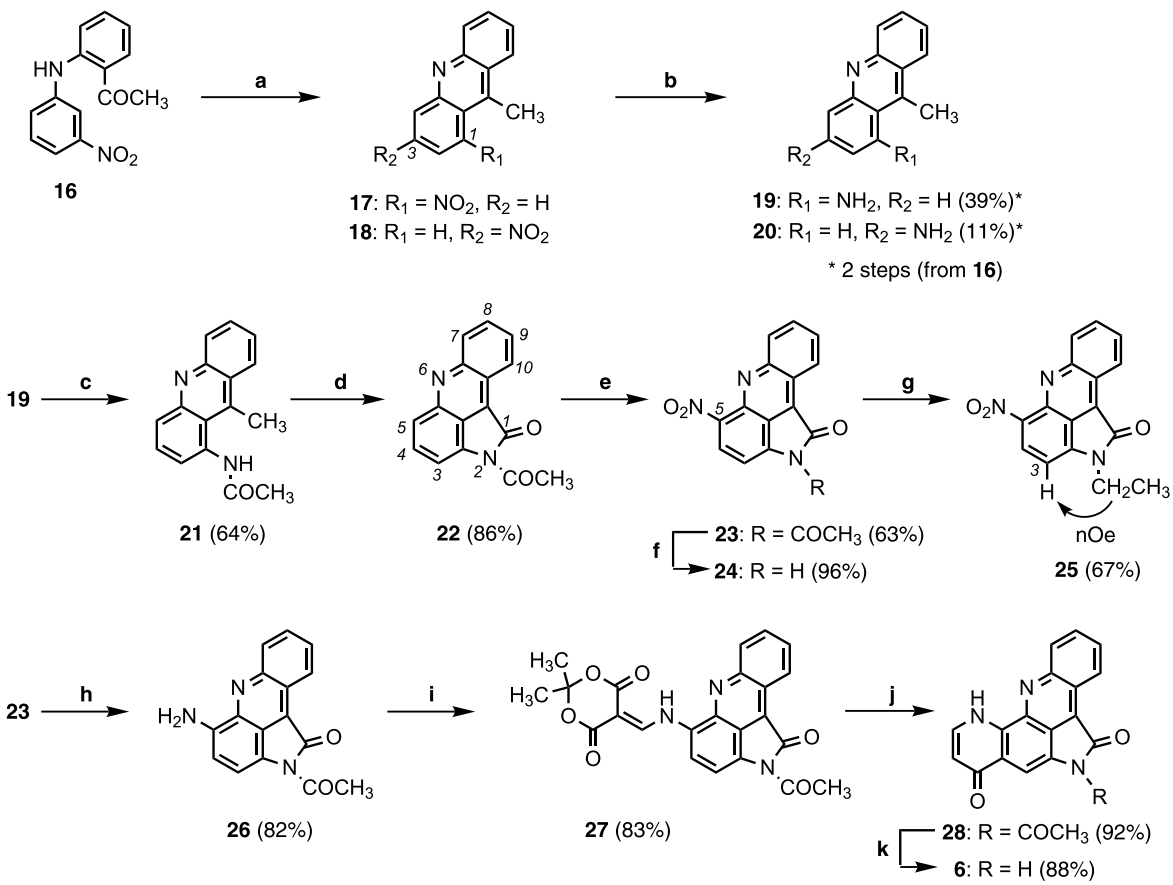
The results demonstrated that it is difficult to prepare **6** via benzo[*b*][1,10]phenanthrolinone (**12**). Thus, we examined another route to **6**, as shown in Scheme 2.

2-Acetyl-3′-nitrodiphenylamine[6] (**16**) was heated in sulfuric acid–acetic acid to afford 9-methyl-1-nitroacridine (**17**) and 9-methyl-3-nitroacridine (**18**). As the separation of the isomeric mixture (**17** and **18**, approximately 2:1 ratio) was difficult (it was possible only by column chromatography using a large amount of silica gel), the mixture was reduced with tin(II) chloride in hydrochloric acid to give 1-aminoacridine (**19**) and 3-aminoacridine (**20**) in 39 and 11% yields from **16**, respectively.

Oxidation of **21**, which was obtained by acetylation of **19**, with selenium dioxide[7] gave a cyclized product, pyrrolo[2,3,4-*kl*]acridine (**22**) in 86% yield. Nitration of **22** with potassium nitrate in sulfuric acid at 0–5 °C afforded 5-nitropyrrolo[2,3,4-*kl*]acridine (**23**), the structure of which was confirmed by ^{1}H NMR measurement of the *N*-ethyl compound (**25**) that was obtained from **23** in two steps. NOE was observed between the protons at 4.07 ppm (CH_2CH_3) and 6.93 ppm (C_3–H).

Amine **26**, which was obtained by reducing **23** with sodium hydrosulfite in aqueous tetrahydrofuran, was treated with 5-(methoxymethylene)-2,2-dimethyl-1,3-dioxane-4,6-dione to give Meldrum's acid derivative (**27**). Thermal cyclization of **27** in diphenyl ether followed by deacetylation with aqueous sulfuric acid furnished 6,11-dihydrobenzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthroline-5,8-dione (**6**) in 81% yield (from **27**).

Thus, the compound (**6**) possessing a unique pentacyclic ring system was synthesized from 2-acetyl-3′-nitrodiphenylamine (**16**) in nine steps. The synthetic studies of plakinidine C (**3**) are in progress.



Scheme 2. (a) H_2SO_4, CH_3CO_2H, 110–120 °C, 20 min; (b) $SnCl_2{\cdot}2H_2O$, HCl, 70–80 °C, 3 h; (c) $(CH_3CO)_2O$, rt, 14 h; (d) SeO_2, dioxane, 70–75 °C, 1 h; (e) KNO_3, H_2SO_4, 0–5 °C, 1 h; (f) 10% H_2SO_4, dioxane, 80 °C, 30 min; (g) C_2H_5I, K_2CO_3, acetone, reflux, 1 h; (h) $Na_2S_2O_4$, THF–H_2O, rt, 1 h; (i) (i) Meldrum's acid, $CH(OCH_3)_3$, reflux, 1 h, (ii) **26**, $CH(OCH_3)_3$, reflux, 30 min; (j) $(C_6H_5)_2O$, reflux, 10 min; (k) 20% H_2SO_4, dioxane, 90 °C, 20 min.

3. Experimental

3.1. General

All melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. ^{1}H NMR spectra were measured in $CDCl_3$ (unless otherwise specified) at 270.05 MHz with a JEOL JNM-EX 270 spectrometer and chemical shifts were recorded in δ values relative to an internal standard, tetramethylsilane. Mass spectra were recorded on a JMS-DX 302 mass spectrometer. Elemental analyses were carried out on a Perkin–Elmer Model 240B elemental analyzer. All reactions were run with magnetic stirring. Anhydrous sodium sulfate was used for drying organic solvent extracts, and the solvent was removed initially with a rotary evaporator and finally under high vacuum. Column (or flash) chromatography was performed with E. Merck silica gel 60 (230–400 mesh).

3.1.1. 9-Methyl-4-nitroacridine (8). A solution of 2-acetyl-2′-nitrodiphenylamine (**7**, 0.152 g, 0.59 mmol) and sulfuric acid (0.6 mL) in acetic acid (7.5 mL) was heated at 95–105 °C for 30 min. After cooling, the reaction mixture was diluted with water (30 mL) and basified with aqueous ammonia. The precipitated yellow crystals were collected by filtration, dried, and chromatographed (ethyl acetate–hexane 1:4–1:2) to give **8** (0.116 g, 82%) as a yellow solid. Mp 154–156 °C (ethyl acetate–hexane). MS *m*/*z* (%): 238 (M^+, 100), 192 (39), 180 (24). High-resolution MS Calcd for $C_{14}H_{10}N_2O_2$: 238.0742. Found: 238.0741. Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.75; H, 4.28; N, 11.51. ^{1}H NMR δ: 3.19 (3H, s, CH_3), 7.59 (1H, dd, J=8.9, 7.3 Hz, C_2–H), 7.63–7.88 (2H, m, C_6–H, C_7–H), 8.05 (1H, dd, J=7.3, 1.3 Hz, C_3–H), 8.22–8.32 (2H, m, C_5–H, C_8–H), 8.48 (1H, dd, J=8.9, 1.3 Hz, C_1–H).

3.1.2. 4-Amino-9-methylacridine (9). Nitroacridine **8** (126 mg, 0.53 mmol) in ethyl acetate (40 mL) containing 10% palladium on carbon (70 mg) was catalytically hydrogenated at 1 atm for 20 min. The catalyst was filtered off and the filtrate was evaporated. The residue was chromatographed (ethyl acetate–hexane, 1:1) to give **9** (100 mg, 91%) as an orange solid. Mp 92–94 °C (hexane). MS *m*/*z* (%): 208 (M^+, 100). High-resolution MS Calcd for $C_{14}H_{12}N_2$: 208.1000. Found: 208.0996. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45. Found: C, 81.07; H, 5.95; N, 13.43. ^{1}H NMR δ: 3.08 (3H, s, CH_3), 5.1–5.5 (2H, br, NH_2), 6.94 (1H, dd, J=7.3, 1.0 Hz, C_3–H), 7.36 (1H, dd, J=8.9, 7.3 Hz, C_2–H), 7.53 (1H, ddd, J=7.6, 6.6, 1.3 Hz, C_6–H or C_7–H), 7.57 (1H, dd, J=8.9, 1.0 Hz, C_1–H), 7.71 (1H, ddd, J=8.6, 6.6, 1.3 Hz, C_7–H or C_6–H), 8.15–8.25 (2H, m, C_5–H, C_8–H).

3.1.3. 5-[[(9-Methylacridin-4-yl)amino]methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (10). After Meldrum's acid (64 mg, 0.44 mmol) in trimethyl orthoformate (7 mL) was refluxed for 1 h, a solution of **9** (50 mg, 0.24 mmol) in trimethyl orthoformate (4 mL) was added. The resulting

solution was refluxed for 20 min and then evaporated. The residue was chromatographed ($CHCl_3$–hexane, 1:5) to give **10** (61 mg, 70%) as a yellow solid. Mp 240–242 °C (CH_2Cl_2–ether). MS *m/z* (%): 362 (M^+, 27), 304 (94), 276 (59), 232 (100), 231 (65). High-resolution MS Calcd for $C_{21}H_{18}N_2O_4$: 362.1266. Found: 362.1263. Anal. Calcd for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73. Found: C, 69.29; H, 5.10; N, 7.59. ^{1}H NMR δ: 1.81 (6H, s, $C(CH_3)_2$), 3.15 (3H, s, C_9–CH_3), 7.58 (1H, dd, *J*=8.9, 7.3 Hz, C_2–H), 7.63 (1H, ddd, *J*=7.9, 6.6, 1.3 Hz, C_7–H), 7.71 (1H, dd, *J*=7.3, 1.0 Hz, C_3–H), 7.82 (1H, ddd, *J*=8.6, 6.6, 1.3 Hz, C_6–H), 8.11 (1H, dd, *J*=8.9, 1.0 Hz, C_1–H), 8.27 (1H, d, *J*=7.9 Hz, C_8–H), 8.36 (1H, d, *J*=8.6 Hz, C_5–H), 8.98 (1H, d, *J*=14.9 Hz, CH=), 13.30 (1H, d, *J*=14.9 Hz, NH).

3.1.4. 5-[[(9-Methyl-1-nitroacridin-4-yl)amino]methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (11). (a) Fuming nitric acid (2.5 mL) was added dropwise to **10** (30 mg, 0.083 mmol) in acetic acid (7.5 mL). The resulting mixture was stirred for 5 h, diluted with water (75 mL), and extracted with $CHCl_3$ (3×40 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$) to give **11** (12 mg, 36%) as a yellow solid. Mp >250 °C. MS *m/z* (%): 407 (M^+, 17), 349 (100), 304 (90), 276 (35), 232 (72), 231 (49). High-resolution MS Calcd for $C_{21}H_{17}N_3O_6$: 407.1117. Found: 407.1113. ^{1}H NMR δ: 1.82 (6H, s, $C(CH_3)_2$), 2.95 (3H, s, CH_3), 7.59 (1H, d, *J*=8.3 Hz, C_3–H), 7.74 (1H, ddd, *J*=8.6, 7.9, 1.3 Hz, C_6–H), 7.92 (1H, dd, *J*=8.6, 7.9, 1.3 Hz, C_7–H), 8.01 (1H, d, *J*=8.3 Hz, C_2–H), 8.34 (1H, d, *J*=8.6 Hz, C_8–H), 8.40 (1H, d, *J*=8.6 Hz, C_5–H), 8.96 (1H, d, *J*=14.5 Hz, CH=), 13.38 (1H, d, *J*=14.5 Hz, NH).

(b) Copper(II) nitrate trihydrate (406 mg, 1.7 mmol) was added in portions over 7 h to a heated (70 °C) solution of **10** (300 mg, 0.83 mmol) in acetic anhydride (20 mL) containing ascorbic acid (42 mg) under argon atmosphere. The reaction mixture was heated at 70 °C for 2 h under argon atmosphere, cooled, diluted with water (200 mL), stirred at 25 °C for 30 min, and extracted with ethyl acetate (3×150 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$–hexane 1:5) to give **11** (266 mg, 79%).

3.1.5. 7-Methylbenzo[*b*][1,10]phenanthrolin-4(1*H*)-one (13). A mixture of **10** (30 mg, 0.083 mmol) and diphenyl ether (20 mL) was refluxed for 15 min under argon atmosphere. The mixture was cooled and diluted with petroleum ether (40 mL). After 16 h, the precipitated yellow crystals of **13** were collected by filtration and washed with petroleum ether. Yield 21 mg (97%). Mp 285–288 °C ($CHCl_3$–ether). MS *m/z* (%): 260 (M^+, 100), 232 (63). High-resolution MS Calcd for $C_{17}H_{12}N_2O$: 260.0950. Found: 260.0954. ^{1}H NMR δ: 3.03 (3H, s, CH_3), 6.63 (1H, d, *J*=7.3 Hz, C_3–H), 7.67 (1H, ddd, *J*=8.6, 7.3, 1.3 Hz, C_9–H), 7.84 (1H, ddd, *J*=8.6, 7.3, 1.3 Hz, C_{10}–H), 7.88 (1H, d, *J*=9.6 Hz, C_6–H), 7.92 (1H, d, *J*=7.3 Hz, C_2–H), 8.17 (1H, d, *J*=9.6 Hz, C_5–H), 8.20 (1H, d, *J*=8.6 Hz, C_{11}–H), 8.26 (1H, d, *J*=8.6 Hz, C_8–H), 10.80 (1H, brs, NH).

3.1.6. Nitration of 13. A suspension of **13** (131 mg, 0.50 mmol) in nitromethane (3 mL) was added in portions over 15 min to a cooled (−25 °C) solution of potassium nitrate (43.8 mg, 0.43 mmol) and sulfuric acid–oleum (4:1, 2.5 mL) in nitromethane (2 mL). The reaction mixture was stirred at −25 °C for 35 h. Potassium nitrate (43.8 mg, 0.43 mmol) was added and the entire mixture was stirred at −25 °C for 4 h. The reaction mixture was poured into ice water, basified with aqueous NaOH solution, and extracted with $CHCl_3$ containing 10% methanol (3×100 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$–methanol 100:1–50:1) to give 7-methyl-8-nitrobenzo[*b*][1,10]phenanthrolin-4(1*H*)-one (**14**, 21 mg, 14%) and 7-methyl-11-nitrobenzo[*b*][1,10]phenanthrolin-4(1*H*)-one (**15**, 66 mg, 43%) as a yellow solid.

Compound **14**. Mp 245–250 °C ($CHCl_3$–ether). MS *m/z* (%): 305 (M^+, 100), 288 (66), 259 (33), 231 (24). High-resolution MS Calcd for $C_{17}H_{11}N_3O_3$: 305.0800. Found: 305.0806. ^{1}H NMR ($CDCl_3$–CD_3OD) δ: 2.95 (3H, s, CH_3), 6.76 (1H, d, *J*=7.3 Hz, C_3–H), 7.86 (1H, dd, *J*=8.6, 7.3 Hz, C_{10}–H), 8.01 (1H, dd, *J*=7.3, 1.3 Hz, C_9–H), 8.08 (1H, d, *J*=9.6 Hz, C_6–H), 8.11 (1H, d, *J*=7.3 Hz, C_2–H), 8.34 (1H, d, *J*=9.6 Hz, C_5–H), 8.51 (1H, dd, *J*=8.6, 1.3 Hz, C_{11}–H).

Compound **15**. Mp >250 °C ($CHCl_3$–ether). MS *m/z* (%): 305 (M^+, 100), 277 (19), 259 (27). High-resolution MS Calcd for $C_{17}H_{11}N_3O_3$: 305.0800. Found: 305.0793. ^{1}H NMR ($CDCl_3$–CD_3OD) δ: 3.25 (3H, s, CH_3), 6.84 (1H, d, *J*=7.3 Hz, C_3–H), 7.79 (1H, dd, *J*=8.9, 7.3 Hz, C_9–H), 8.10 (1H, d, *J*=7.3 Hz, C_2–H), 8.11 (1H, d, *J*=9.6 Hz, C_6–H), 8.22 (1H, dd, *J*=7.3, 1.3 Hz, C_{10}–H), 8.37 (1H, d, *J*=9.6 Hz, C_5–H), 8.60 (1H, dd, *J*=8.9, 1.3 Hz, C_8–H).

3.1.7. 9-Methyl-1-nitroacridine (17) and 9-methyl-3-nitroacridine (18). A solution of 2-acetyl-3′-nitrodiphenylamine (**16**, 2.00 g, 7.80 mmol) and sulfuric acid (1.2 mL) in acetic acid (12.0 mL) was heated at 110–120 °C for 20 min. After cooling, the reaction mixture was diluted with water (80 mL), basified with 25–28% aqueous ammonia solution, and extracted with $CHCl_3$ (3×80 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$) to give an isomeric mixture of **17** and **18** (1.48 g, 80%) as a yellow solid, which was used in the next step. A part of the mixture (0.37 g) was chromatographed (benzene) using a large amount (400 g) of silica gel to give **17** (0.24 g) and **18** (0.11 g).

Compound **17**. Mp 174–176 °C ($CHCl_3$–hexane) [lit.[6] mp 175–176 °C]. ^{1}H NMR δ: 2.93 (3H, s, CH_3), 7.66 (1H, ddd, *J*=8.6, 6.6, 1.3 Hz), 7.72 (1H, dd, *J*=8.6, 7.3 Hz), 7.80–7.90 (2H, m), 8.23 (1H, d, *J*=8.9 Hz), 8.30 (1H, d, *J*=8.9 Hz), 8.39 (1H, dd, *J*=8.6, 1.3 Hz).

Compound **18**. Mp 198–201 °C ($CHCl_3$–hexane) [lit.[6] mp 198–200 °C]. ^{1}H NMR δ: 3.20 (3H, s, CH_3), 7.68 (1H, ddd, *J*=8.6, 6.6, 1.3 Hz), 7.87 (1H, ddd, *J*=8.6, 6.6, 1.3 Hz), 8.25–8.35 (3H, m), 8.42 (1H, d, *J*=8.9 Hz, C_1–H), 9.16 (1H, d, *J*=2.0 Hz, C_4–H).

3.1.8. 1-Amino-9-methylacridine (19) and 3-amino-9-methylacridine (20). An isomeric mixture of nitroacridines (**17** and **18**, 400 mg, 1.68 mmol), hydrochloric acid (8 mL), tin(II) chloride dihydrate (800 mg, 3.54 mmol) was heated

at 70–80 °C for 3 h. After cooling, the reaction mixture was basified with 5% aqueous NaOH solution and extracted with $CHCl_3$ (6×40 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed; elution with ethyl acetate–$CHCl_3$ (1:9–1:4) gave **19** (172 mg, 49%) and further elution with $CHCl_3$–methanol (9:1–4:1) gave **20** (48 mg, 14%) as a solid with a low melting point, respectively.

Compound **19**. ^{1}H NMR δ: 3.42 (3H, s, CH_3), 4.39 (2H, br, NH_2), 6.72 (1H, d, J=7.3 Hz), 7.4–7.6 (2H, m), 7.66 (1H, d, J=8.6 Hz), 7.73 (1H, dd, J=8.6, 7.6 Hz), 8.13 (1H, d, J=8.6 Hz), 8.22 (1H, dd, J=8.6 Hz).

Compound **20**. ^{1}H NMR δ: 3.05 (3H, s, CH_3), 4.29 (2H, br, NH_2), 7.05 (1H, dd, J=9.2, 2.3 Hz, C_2–H), 7.29 (1H, d, J=2.3 Hz, C_4–H), 7.4–7.7 (2H, m), 8.09 (1H, d, J=9.2 Hz, C_1–H), 8.12 (1H, d, J=8.6 Hz), 8.17 (1H, d, J=8.6 Hz).

3.1.9. 1-Acetylamino-9-methylacridine (21). A solution of **19** (140 mg, 0.67 mmol) in acetic anhydride (2.0 mL) was stirred for 14 h. The reaction mixture was diluted with ice water (20 mL), basified with 10% KOH solution, and extracted with $CHCl_3$ (3×20 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$–methanol 97:3) to give **21** (108 mg, 64%) as a yellow solid. Mp 218–220 °C ($CHCl_3$–ether). MS *m*/*z* (%): 250 (M^+, 65), 208 (100). High-resolution MS Calcd for $C_{16}H_{14}N_2O$: 250.1106. Found: 250.1106. ^{1}H NMR δ: 2.33 (3H, s, $COCH_3$), 3.27 (3H, s, C_9–CH_3), 7.5–7.9 (4H, m), 8.0–8.4 (3H, m).

3.1.10. 2-Acetylpyrrolo[2,3,4-*kl*]acridin-1(2*H*)-one (22). A suspension of **21** (100 mg, 0.40 mmol) and SeO_2 (100 mg, 0.90 mmol) in dioxane (20 mL) was heated at 70–75 °C for 1 h. The reaction mixture was evaporated and the residue was chromatographed ($CHCl_3$) to give **22** (90 mg, 86%) as an orange solid. Mp 226–227 °C ($CHCl_3$–ether). MS *m*/*z* (%): 262 (M^+, 24), 220 (100). High-resolution MS Calcd for $C_{16}H_{10}N_2O_2$: 262.0742. Found: 262.0736. Anal. Calcd for $C_{16}H_{10}N_2O_2$: C, 73.27; H, 3.84; N, 10.68. Found: 73.18; H, 4.19; N, 10.33. ^{1}H NMR δ: 2.88 (3H, s, CH_3), 7.84 (1H, dd, J=8.9, 6.9 Hz, C_4–H), 7.86 (1H, ddd, J=8.3, 6.9, 1.3 Hz, C_9–H), 7.96 (1H, ddd, J=8.6, 6.9, 1.6 Hz, C_8–H), 8.03 (1H, d, J=8.9 Hz, C_5–H), 8.16 (1H, d, J=6.9 Hz, C_3–H), 8.46 (1H, dd, J=8.6, 1.3 Hz, C_7–H), 8.90 (1H, dd, J=8.3, 1.6 Hz, C_{10}–H).

3.1.11. 2-Acetyl-5-nitropyrrolo[2,3,4-*kl*]acridin-1(2*H*)-one (23). Potassium nitrate (20.2 mg, 0.20 mmol) was added to an ice-cooled solution of **22** (26.2 mg, 0.10 mmol) in sulfuric acid (2.0 mL). The reaction mixture was stirred at 0–5 °C for 1 h, diluted with ice water, neutralized with $NaHCO_3$, and extracted with $CHCl_3$ (3×20 mL). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$) to give **23** (19.3 mg, 63%) as a yellow solid. Mp 237–239 °C (ethyl acetate–hexane). MS *m*/*z* (%): 307 (M^+, 54), 265 (100), 235 (31). High-resolution MS Calcd for $C_{16}H_9N_3O_4$: 307.0593. Found: 307.0596. ^{1}H NMR δ: 2.90 (3H, s, CH_3), 7.96 (1H, ddd, J=8.3, 6.9, 1.3 Hz, C_9–H), 8.06 (1H, ddd, J=8.9, 6.9, 1.3 Hz, C_8–H), 8.25 (1H, d, J=7.9 Hz, C_3–H), 8.60 (1H, dd, J=8.9, 1.3 Hz, C_7–H), 8.65 (1H, d, J=7.9 Hz, C_4–H), 8.93 (1H, dd, J=8.3, 1.3 Hz, C_{10}–H).

3.1.12. 5-Nitropyrrolo[2,3,4-*kl*]acridin-1(2*H*)-one (24). A solution of **23** (15.4 mg, 0.05 mmol) and 10% H_2SO_4 (0.5 mL) in dioxane (2.5 mL) was heated at 80 °C for 30 min. After cooling, the reaction mixture was diluted with water (15 mL) and neutralized with $NaHCO_3$. The precipitated orange crystals of **24** were collected by filtration and washed with water. Yield 12.7 mg (96%). Mp >250 °C. MS *m*/*z* (%): 265 (M^+, 100), 235 (33). High-resolution MS Calcd for $C_{14}H_7N_3O_3$: 265.0487. Found: 265.0486. ^{1}H NMR ($CDCl_3$–CD_3OD) δ: 6.98 (1H, d, J=7.6 Hz, C_3–H), 7.87 (1H, ddd, J=8.3, 6.9, 1.3 Hz, C_9–H), 8.00 (1H, ddd, J=8.3, 6.9, 1.3 Hz, C_8–H), 8.58 (1H, ddd, J=8.3, 1.3, 0.7 Hz, C_7–H), 8.63 (1H, d, J=7.6 Hz, C_4–H), 8.86 (1H, ddd, J=8.3, 1.3, 0.7 Hz, C_{10}–H).

3.1.13. 2-Ethyl-5-nitropyrrolo[2,3,4-*kl*]acridin-1(2*H*)-one (25). A mixture of **24** (10.6 mg, 0.04 mmol), potassium carbonate (11.1 mg, 0.08 mmol), and ethyl iodide (63 mg, 0.4 mmol) in dry acetone (5 mL) was refluxed for 1 h. The reaction mixture was cooled and filtered. The filtrate was evaporated and the residue was chromatographed ($CHCl_3$) to give **25** (7.9 mg, 67%) as a yellow solid. Mp 253–257 °C (ethyl acetate–ether). MS *m*/*z* (%): 293 (M^+, 100), 278 (29), 263 (40). High-resolution MS Calcd for $C_{16}H_{11}N_3O_3$: 293.0800. Found: 293.0794. ^{1}H NMR δ: 1.46 (3H, t, J=7.3 Hz, CH_2CH_3), 4.07 (2H, q, J=7 Hz, CH_2CH_3), 6.93 (1H, d, J=7.6 Hz, C_3–H), 7.87 (1H, ddd, J=7.9, 6.9, 1.3 Hz, C_9–H), 7.99 (1H, ddd, J=8.6, 6.9, 1.3 Hz, C_8–H), 8.55 (1H, dd, J=8.6, 1.3 Hz, C_7–H), 8.65 (1H, d, J=7.6 Hz, C_4–H), 8.86 (1H, dd, J=7.9, 1.3 Hz, C_{10}–H).

3.1.14. 2-Acetyl-5-aminopyrrolo[2,3,4-*kl*]acridin-1(2*H*)-one (26). A mixture of **23** (30.7 mg, 0.10 mmol) in THF (15 mL) and sodium hydrosulfite (122 mg, 0.70 mmol) in water (3.0 mL) was stirred for 1 h. After evaporation of THF, the reaction mixture was diluted with water and extracted with $CHCl_3$ (3×20 mL). The extract was washed with water, dried, and evaporated to give **26** (22.6 mg, 82%) as a pale purple solid. MS *m*/*z* (%): 277 (M^+, 40), 235 (100). High-resolution MS Calcd for $C_{16}H_{11}N_3O_2$: 277.0851. Found: 277.0851. ^{1}H NMR δ: 1.55 (2H, br, NH_2), 2.85 (3H, s, CH_3), 6.82 (1H, d, J=7.6 Hz, C_4–H), 7.86 (1H, ddd, J=8.3, 6.9, 1.3 Hz, C_9–H), 7.93 (1H, ddd, J=8.6, 6.9, 1.3 Hz, C_8–H), 7.96 (1H, d, J=7.6 Hz, C_3–H), 8.53 (1H, ddd, J=8.6, 1.3, 0.7 Hz, C_7–H), 8.92 (1H, ddd, J=8.3, 1.3, 0.7 Hz, C_{10}–H).

3.1.15. 5-[[(2-Acetyl-1-oxo-1,2-dihydropyrrolo[2,3,4-*kl*]acridin-5-yl)amino]methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (27). After Meldrum's acid (23.1 mg, 0.16 mmol) in trimethyl orthoformate (4 mL) was refluxed for 1 h, a solution of **26** (22.4 mg, 0.08 mmol) in trimethyl orthoformate (2 mL) was added. The resulting solution was refluxed for 30 min and then evaporated. The residue was washed with ether (20 mL) to give **27** (29.0 mg, 83%) as a red solid. Mp 213–215 °C (decomp.) (ethyl acetate–ether). MS *m*/*z* (%): 431 (M^+, 29), 373 (23), 329 (53), 301 (78), 287 (62), 259 (100). High-resolution MS Calcd for $C_{23}H_{17}N_3O_6$: 431.1117. Found: 431.1115. Anal. Calcd for $C_{23}H_{17}N_3O_6$: C, 64.04; H, 3.97; N, 9.74. Found: 63.78; H, 3.91; N, 9.65.

^{1}H NMR δ: 1.82 (6H, s, $C(CH_3)_2$), 2.88 (3H, s, $COCH_3$), 7.65 (1H, d, J=7.9 Hz, C_4–H), 7.93 (1H, ddd, J=8.6, 6.9, 1.7 Hz, C_9–H), 8.02 (1H, ddd, J=8.6, 6.9, 1.7 Hz, C_8–H), 8.16 (1H, d, J=7.9 Hz, C_3–H), 8.59 (1H, dd, J=8.6, 1.7 Hz, C_7–H), 8.92 (1H, dd, J=8.6, 1.7 Hz, C_{10}–H), 9.16 (1H, d, J=14.5 Hz, CH═), 12.57 (1H, d, J=14.5 Hz, NH).

3.1.16. 6-Acetyl-6,11-dihydrobenzo[*b*]pyrrolo[4,3,2-*de*][1,10]phenanthroline-5,8-dione (28). A mixture of **27** (25.9 mg, 0.06 mmol) and diphenyl ether (3 mL) was refluxed for 10 min under argon atmosphere. The reaction mixture was cooled and diluted with ether (10 mL). After 1 h, the precipitated yellow crystals of **28** were collected by filtration and washed with ether. Yield 18.1 mg (92%). Mp >250 °C. MS *m*/*z* (%): 329 (M^+, 43), 287 (100), 259 (29). High-resolution MS Calcd for $C_{19}H_{11}N_3O_3$: 329.0800. Found: 329.0800. ^{1}H NMR ($CDCl_3$–CF_3CO_2D) δ: 2.99 (3H, s, $COCH_3$), 7.78 (1H, d, J=6.6 Hz, C_9–H), 8.1–8.3 (2H, m, C_2–H, C_3–H), 8.60 (1H, dd, J=7.6, 1.7 Hz, C_1–H or C_4–H), 8.79 (1H, s, C_7–H), 8.85 (1H, d, J=6.6 Hz, C_{10}–H), 9.03 (1H, dd, J=7.9, 1.7 Hz, C_4–H or C_1–H).

3.1.17. 6,11-Dihydrobenzo[*b*]pyrrolo[4,3,2-*de*][1,10]-phenanthroline-5,8-dione (6). A mixture of **28** (16.5 mg, 0.05 mmol) and 20% H_2SO_4 (0.2 mL) in dioxane (7.5 mL) was heated at 90 °C for 20 min. After cooling, the reaction mixture was diluted with water (20 mL) and neutralized with $NaHCO_3$. The precipitated crystals of **6** were collected by filtration, washed with water and ether, and dried. Yield 12.7 mg (88%). Mp >250 °C. MS *m*/*z* (%): 287 (M^+, 100), 259 (46). High-resolution MS Calcd for $C_{17}H_9N_3O_2$: 287.0695. Found: 287.0696. ^{1}H NMR (DMSO-d_6) δ: 6.40 (1H, d, J=7.3 Hz, C_9–H), 7.50 (1H, s, C_7–H), 7.93 (1H, dd, J=7.3, 6.9 Hz, C_{10}–H), 8.02 (1H, ddd, J=7.9, 6.9, 1.3 Hz, C_3–H), 8.12 (1H, ddd, J=8.3, 6.9, 1.3 Hz, C_2–H), 8.56 (1H, dd, J=8.3, 1.3 Hz, C_1–H), 8.83 (1H, dd, J=7.9, 1.3 Hz, C_4–H), 11.24 (1H, s, N_6–H), 12.82 (1H, d, J=6.9 Hz, N_{11}–H).

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