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Synthesis of Phenanthridine Derivatives via Photolysis

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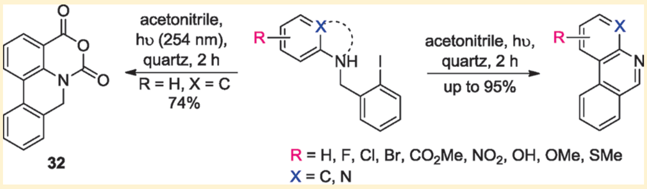
S *Supporting Information*

ABSTRACT: An improved photochemical method for producing the prolifically bioactive phenanthridine system is reported. A wide variety of derivatives were obtained in two steps in yields ranging from 31 to 95%.



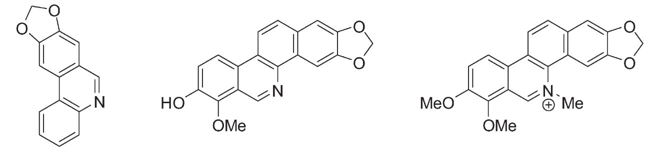
32

Our interest in the phenanthridine core stems from the important role this system plays in a large number of natural products. The diversity of these molecules is large and far reaching from almost completely unsubstituted phenanthridines cores like trispheridine (**1**)[1] to more complex structures like decarine (**2**)[2] or chelerythrine (**3**) (Figure 1).[2] Most of these alkaloids demonstrate expansive biological activity including nematodical, antitumor, antifungal, antibacterial, and cytotoxic activity.[2,3]

Recently, Pierini and Rossi et al.[4] reported a new method for synthesizing phenanthridines from the photolysis of *N*-(*o*-iodobenzyl)arylamines in liquid ammonia (or DMSO) and potassium *tert*-butoxide (*t*-BuOK). In addition to the contribution of Pierini and Rossi, other photochemical approaches to phenanthridines have been reported. Badger and Lewis demonstrated the photochemical cyclization of *N*-benzylideneaniline in concentrated sulfuric acid,[5] whereas Kessar,[6] Park,[7] and Sakurai[8] showed later that halobenzyl arylamines give phenanthridines under basic conditions (NaOH) in water−acetonitrile on photolysis. Moreover, Rodríguez et al. and McBurney et al. irradiated acyloximes and oxime carbonates affording phenanthridines.[9]

Building on limited work in this area and the unfriendly conditions so far required, we report herein a rapid, convenient, and practical photolytic method to access the phenanthridine core in yields ranging from 31 to 95%.

Taking inspiration from the work of Pierini and Rossi,[4a] Kessar,[6] Park,[7] and Sakurai,[8] we identified halogenated anilines (**6**) as a strategic starting point but wanted to avoid the requirement of strong base and undesirable solvents (i.e., DMSO and liquid ammonia). To gain an understanding of why such conditions were required, irradiation experiments with the *N*-alkylated anilines **8**−**20** (Table 1, entries 1−13) were investigated. The method of Romera et al.[10] was found to be superior for the rapid *N*-alkylation of most anilines **4** accommodating numerous functionalities such as a thioester, alkoxyl, halogen, free OH, and nitro groups. An excess of the respective aniline **4** was introduced together with 2-iodobenzyl bromide (**5**) and a catalytic amount of potassium iodide in acetonitrile. The mixture was heated for 15 min in the microwave at 170 °C, and the desired product **6** was obtained, in most cases, in good to excellent yields (Table 1, entries 1−13). Only the nitro derivative gave a yield below 65% (entry 9, Table 1).



Trispheridine (**1**) Decarine (**2**) Chelerythrine (**3**)

Figure 1. Examples for natural products containing a phenanthridine core.

Initial attempts at photolysis were very promising. That is, simple irradiation of **8** (entry 1, Table 1) in anhydrous acetonitrile under argon in a Rayonet photochemical reactor (254 nm) gave the phenanthridine **21** in 85% in under 2 h. This was quite surprising, especially considering previous reports suggest strong base and aprotic solvents are required. This method was found to be quite general, the results of which are shown in Table 1.

Overall, the photochemical cyclization gave products in high yields, especially halides (**26**, **27**), ester (**22**), and nitro groups (**29**) which gave yields in the 95% range. Surprisingly, even the phenol derivative **24** was obtained in 90% yield. Significantly lower yields, 58% and 67%, respectively, were obtained with methoxy (**23**) and methylthio (**25**) substituents. A possible explanation could be that the newly formed products (i.e., **23** and **25**) could be sensitive toward ultraviolet light, facilitating decomposition on further irradiation. The side product phenanthridine (**21**), obtained from the photolysis of the methoxy aniline derivate **10**, somewhat verifies this point (e.g., methoxy radical production or hydrogen atom abstraction leading to deformylation), although **21** was not observed in the case of the

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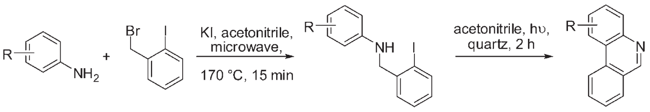
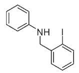
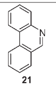
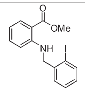
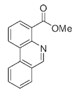
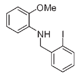
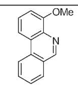
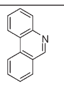
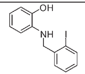
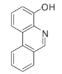
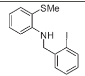
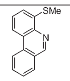
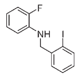
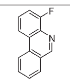
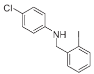
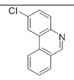
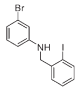
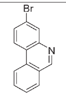
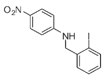
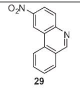
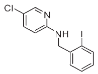
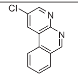
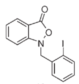
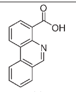
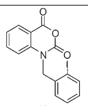
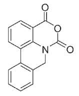
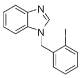
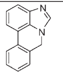
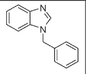
Table 1. Summary of N-Alkylation and Subsequent Photolysis Giving Phenanthridines

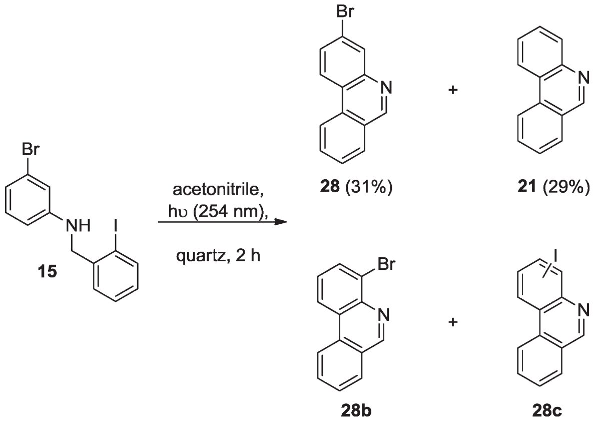


4 5 6 7

Entry	*N*-Alkylation product	Yield	Photolysis product	Yield
1	 8	90%	 21	85%
2	 9	65%	 22	95% (85%)[c]
3	 10	94%	 23  21	**23**: 67% **21**: 5%
4	 11	68%	 24	90%
5	 12	66%	 25	58%
6	 13	86%	 26	95% (82%)[d]
7	 14	71%	 27	95%
8	 15	78%	 28	31% (see Scheme 1)
9	 16	31%	 29	95%
10	 17	82%	 30	55%
11[a]	 18	22%	 31	63%
12[b]	 19	38%	 32	74%
13	 20	64%	 33  33b	**33**: 0% **33b**: 54%

[a] N-Alkylation method: NaH, THF, 0 °C to rt, 3 h. [b] N-Alkylation method: K_2CO_3, DMF, rt, 18 h. [c] Yield of reaction when conducted in air and solvent directly from the supplier. [d] Yield using 100 mg of starting material.

Scheme 1. Product Mixture Obtained from the Photolysis of 15



methylthio aniline derivative **12**. In an attempt to gain further insight into this question, the UV spectra (see the Supporting Information) of the starting anilines (**10**, **12**, **14**, and **16**) and phenanthridine products (**23**, **25**, **27**, and **29**) were compared and showed that all compounds absorb strongly around 254 nm, suggesting additional photochemical transformations are possible post-phenanthridine formation.

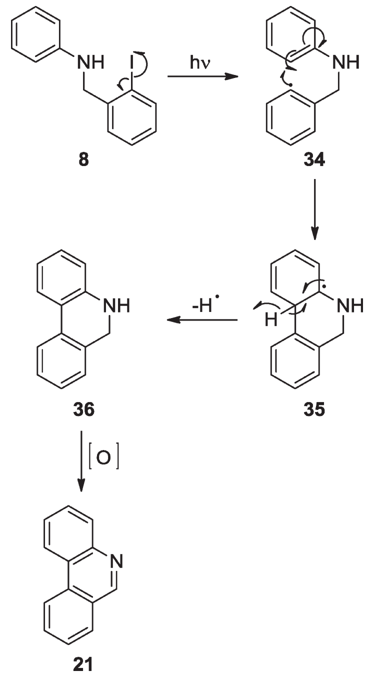
Reaction of compound **15** (entry 8, Table 1) gave a mixture of four products: 4-bromophenanthridine (**28**), 3-bromophenanthridine (**28b**), phenanthridine (**21**), and an iodophenanthridine **28c** (Scheme 1). It was possible to isolate 4-bromophenanthridine (**28**) in 31% yield and phenanthridine (**21**) in 29% yield, but it was not possible to separate 3-bromophenanthridine (**28b**) from the iodo compound **28c**, both of which remain tentatively assigned.

Interestingly, the pyridyl system **17** (entry 10, Table 1) smoothly converted to the azaphenanthridine **30** (55%) but the benzimidazole **20** failed to undergo cyclization, although these systems are electronically different.

Of further intrigue was the cyclization performance of the sensitive heterocylic systems **18** and **19** using these conditions. The heterocycle isoxazolidinone **18** was found to be very unstable and underwent ring-opening giving acid **31** in 63% yield. The isatoic anhydride **19** on the other hand gave the desired product **32** in 74% yield. Lastly, we discovered that (1) photolysis could be performed in air using supplier-grade acetonitrile with only a slight reduction in yield (Table 1, entry 2) and (2) even though photochemical reactions were generally performed on small scale (e.g., 20 mg), when a reaction was performed on larger scale (100 mgs) (i.e., fluoro derivative **13**, entry 6) the yield decreased only slightly.

Mechanistically, Rossi[4] has nicely demonstrated that their systems follow an $S_{RN}1$ single electron transfer (SET) process, induced by strongly basic conditions. In this case, shown in Scheme 2, strongly basic conditions are absent suggesting a preference for a classical photochemical radical cleavage of the carbon−iodine bond (i.e., **8**) leading to cyclization of **34** and removal of a hydrogen atom (i.e., **35**) affording the dehydrophenanthridine **36**. It is possible that **35** could propagate the reaction from SET to starting material **8** followed by elimination of hydrogen iodide. Lastly, iodine (arising from hydrogen iodide) or aerial oxidation on workup affords product (e.g., **21**). Interestingly, Pierini and Rossi[4a] also observed oxidation without

Scheme 2. Proposed Mechanism of the Photolysis



isolation of the dehydro analogue **36**. Furthermore, they observed on occasion dehalogenation, which we also see, but most prominently with **20** (entry 13, Table 1) as **33b** is the sole product. This aspect supports a radical mechanism. Outright radical approaches to this system have been reported by Nakanishi.[11]

In summary, a wide range of substituted phenanthridines were rapidly synthesized in good to excellent yields. Systems containing electron-withdrawing groups were generally obtained in higher yields as compared to systems containing electron-donating groups.

EXPERIMENTAL SECTION

All reactions were performed using dried glassware under a positive pressure of argon unless otherwise stated. All reagents and solvents were dried, distilled, or purified before use according to Perrin and Amarego's *Purification of Laboratory Chemicals*, 5th ed.[12] Tetrahydrofuran was freshly distilled from Na^0/benzophenone. DMF and acetonitrile were freshly distilled from CaH_2. Thin-layer chromatography was performed using E. Merck silica gel 60 F254 precoated plates. Column chromatography was undertaken on silica gel (flash silica gel 230–400 mesh). Other chromatographic methods involved using Celite 545. ^{1}H and ^{13}C NMR spectra were recorded on 400.13 and 100.62 MHz (or 125.76 MHz) spectrometers, respectively. Coupling constants are given in Hz, and chemical shifts are reported in δ values in ppm with the solvent resonance as the internal standard (^{1}H NMR: $CDCl_3$: δ 7.26; ^{13}C NMR: $CDCl_3$: δ 77.0). Data are reported as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, dd = double doublet, dt = double triplet, ddd = double double doublet, m = multiplet), coupling constants (Hz), and integration. High-resolution electrospray ionization (HRESIMS) accurate mass measurements were recorded in positive or negative mode on a quadrupole-time of flight instrument with a ESI source using sodium formate as a reference calibrant. For microwave-assisted reactions the CEM discover microwave was used.

N-Alkylation General Procedure. A mixture of 2-iodobenzyl bromide (1.00 equiv, 0.50 mmol, 149 mg), amine (3.00 equiv, 1.50 mmol), and potassium iodide (0.10 equiv, 0.05 mmol, 8.00 mg) in acetonitrile (1.50 mL) in a sealed vial was heated in a microwave reactor (200W, ramp time 5–10 min) (170 °C, 15 min holdtime). After being cooled to room temperature, the reaction mixture was diluted with dichloromethane (10 mL) and washed with an aqueous saturated sodium bicarbonate solution (10 mL) and brine (10 mL). Then the solution was dried ($MgSO_4$), and the solvent was evaporated. The crude product was purified by flash chromatography.

*N-(2-Iodobenzyl)aniline (**8**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a white solid in 90% yield: R_f = 0.54 (pet. spirit/EtOAc = 5:1); mp = 64–66 °C (lit. mp 1:[13] 66–68 °C, lit. mp 2:[4a,14] 62–64 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.87 (d, J = 7.8 Hz, 1H), 7.40 (dd, J = 7.6 Hz, J = 1.5 Hz, 1H), 7.31 (dt, J = 7.4 Hz, J = 1.0 Hz, 1H), 7.22–7.17 (m, 2H), 6.98 (dt, J = 7.5 Hz, J = 1.6 Hz, 1H), 6.74 (dt, J = 7.3 Hz, J = 0.9 Hz, 1H), 6.62 (dd, J = 8.5 Hz, J = 0.9 Hz, 1H), 4.33 (s, 2H), 4.19 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 147.5, 140.9, 139.4, 129.2, 128.9, 128.7, 128.3, 117.7, 112.9, 98.4, 53.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{13}IN$ 310.0093, found 310.0087.

*Methyl 2-(2-Iodobenzylamino)benzoate (**9**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 40:1), and the product was obtained as a white solid in 65% yield: R_f = 0.20 (pet. spirit/EtOAc = 40:1); mp = 103–106 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.27 (bs, 1H), 7.95 (dd, J = 7.9 Hz, J = 1.6 Hz, 1H), 7.86 (dd, J = 7.9 Hz, J = 1.0 Hz, 1H), 7.34–7.26 (m, 3H), 6.96 (dt, J = 7.7 Hz, J = 1.6 Hz, 1H), 6.65–6.60 (m, 1H), 6.51 (d, J = 8.4 Hz, 1H), 4.43 (d, J = 5.9 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 169.0, 150.5, 140.2, 139.4, 134.6, 131.6, 128.8, 128.3, 128.0, 115.1, 111.7, 110.3, 98.2, 52.1, 51.5; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{15}H_{14}INNaO_2$ 389.9967, found 389.9961.

*N-(2-Iodobenzyl)-2-methoxyaniline (**10**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a white solid in 94% yield: R_f = 0.57 (pet. spirit/EtOAc = 5:1); mp = 59–62 °C (lit.[4a] mp 59–61°C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.87 (dd, J = 7.8 Hz, J = 1.2 Hz, 1H), 7.38 (dd, J = 7.6 Hz, J = 1.6 Hz, 1H), 7.30 (dt, J = 7.5 Hz, J = 1.2 Hz, 1H), 6.97 (dt, J = 7.6 Hz, J = 1.7 Hz, 1H), 6.86–6.81 (m, 2H), 6.70 (dt, J = 7.7 Hz, J = 1.5 Hz, 1H), 6.49 (dd, J = 7.6 Hz, J = 1.4 Hz, 1H), 4.81 (bs, 1H), 4.36 (s, 2H), 4.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 146.7, 141.0, 139.3, 137.5, 128.7, 128.5, 128.3, 121.2, 116.8, 110.2, 109.4, 98.4, 55.4, 52.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{15}INO$ 340.0198, found 340.0193.

*2-(2-Iodobenzylamino)phenol (**11**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a green solid in 68% yield: R_f = 0.26 (pet. spirit/EtOAc = 5:1); mp = 85–87 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.86 (dd, J = 7.8 Hz, J = 1.1 Hz, 1H), 7.38 (dd, J = 7.6 Hz, J = 1.5 Hz, 1H), 7.29 (dt, J = 7.5 Hz, J = 1.1 Hz, 1H), 6.97 (dt, J = 7.6 Hz, J = 1.6 Hz, 1H), 6.81 (t, J = 7.4 Hz, 1H), 6.75 (d,^{J}= 7.4 Hz, 1H), 6.64 (t, J = 7.1 Hz, 1H), 6.56 (d, J = 7.7 Hz, 1H), 4.70 (bs, 1H, OH) 4.34 (s, 2H), 2.65 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.6, 140.9, 139.3, 136.3, 128.8, 128.7, 128.3, 121.5, 118.0, 114.3, 112.7, 98.6, 53.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{13}INO$, 326.0042; found, 326.0036.

*N-(2-Iodobenzyl)-2-(methylthio)aniline (**12**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1) and the product was obtained as a white solid in 66% yield: R_f = 0.47 (pet. spirit/EtOAc = 5:1); mp = 61–64 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.87 (d, J = 7.7 Hz, 1H), 7.44 (dd, J = 7.6 Hz, J = 1.4 Hz, 1H), 7.34–7.28 (m, 2H), 7.17–7.11 (m, 1H), 6.98 (dt, J = 7.5 Hz, J = 2.0 Hz, 1H), 6.68 (dt, J = 7.4 Hz, J = 1.1 Hz, 1H), 6.48 (d, J = 8.1 Hz, 1H), 5.52 (bs, 1H), 4.39 (d, J = 5.8 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.6, 140.6, 139.4, 134.2, 129.5, 128.9, 128.5, 128.4, 119.8, 117.4, 110.4, 98.4, 53.0, 18.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{15}INS$ 355.9970, found 355.9964.

2-Fluoro-N-(2-iodobenzyl)aniline (**13**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 10:1), and the product was obtained as a white solid in 86% yield: R_f = 0.50 (pet. spirit/EtOAc = 10:1); mp =80−83 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 7.86 (d, *J* = 7.7 Hz, 1H), 7.39−7.28 (m, 2H), 7.03−6.91 (m, 3H), 6.68−6.61 (m, 1H), 6.61−6.54 (m, 1H), 4.47 (bs, 1H), 4.37 (s, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 151.5 (d, ^{1}J = 283.4 Hz), 140.4, 139.5, 136.0 (d, *J* = 11.4 Hz), 129.0, 128.5, 128.4, 124.6 (d, *J* = 3.3 Hz), 117.1 (d, *J* = 6.8 Hz), 114.4 (d, *J* = 18.3 Hz), 112.4 (d, *J* = 3.0 Hz), 98.4, 52.7; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{13}H_{12}FIN$ 327.9998, found 327.9993.

4-Chloro-N-(2-iodobenzyl)aniline (**14**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a brown solid in 71% yield: R_f = 0.50 (pet. spirit/EtOAc = 5:1); mp = 57−59 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 7.86 (d, *J* = 7.8 Hz, 1H), 7.36−7.28 (m, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 8.2 Hz, 2H), 4.29 (s, 2H), 4.21 (bs, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 146.1, 140.3, 139.5, 129.0, 128.6, 128.4, 122.3, 114.0, 98.4, 53.2; HRMS (ESI) *m/z* [M +H]$^+$ calcd for $C_{13}H_{12}ClIN$ 343.9703, found 343.9697.

3-Bromo-N-(2-iodobenzyl)aniline (**15**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a yellow oil in 78% yield: R_f = 0.55 (pet. spirit/EtOAc = 5:1); ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 7.87 (dd, *J* = 7.7 Hz, *J* = 1.0 Hz, 1H), 7.36−7.29 (m, 2H), 7.04−6.97 (m, 2H), 6.84 (ddd, *J* = 7.8 Hz, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 6.76 (t, *J* = 2.0 Hz, 1H), 6.50 (ddd, *J* = 8.1 Hz, *J* = 2.3 Hz, *J* = 0.8 Hz, 1H), 4.30 (s, 2H), 4.22 (bs, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 148.8, 140.2, 139.5, 130.5, 129.1, 128.7, 128.4, 123.2, 120.5, 115.5, 111.5, 98.5, 52.9; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{13}H_{12}BrIN$ 387.9198, found 387.9192.

N-(2-Iodobenzyl)-4-nitroaniline (**16**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a yellow solid in 31% yield: R_f = 0.27 (pet. spirit/EtOAc = 5:1); mp = 139−142 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 8.08 (d, *J* = 9.1 Hz, 2H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.35−7.28 (m, 2H), 7.02 (dt, *J* = 7.7 Hz, *J* = 2.1 Hz, 1H), 6.56 (d, *J* = 9.1 Hz, 2H), 4.98 (bs, 1H), 4.43 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 152.5, 139.8, 139.0, 138.6, 129.5, 128.6, 128.5, 126.3, 111.4, 98.4, 52.5 (2 quaternary carbons not detected); HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{13}H_{12}IN_2O_2$ 354.9943, found 354.9938.

5-Chloro-N-(2-iodobenzyl)pyridin-2-amine (**17**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a white solid in 82% yield: R_f = 0.38 (pet. spirit/EtOAc = 5:1); mp = 95−97 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 8.04 (bd, *J* = 2.1 Hz, 1H), 7.84 (dd, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H), 7.38−7.31 (m, 2H), 7.29 (dt, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H), 6.97 (dt, *J* = 7.6 Hz, *J* = 1.7 Hz, 1H), 5.10 (bs, 1H), 4.48 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 156.5, 146.5, 140.5, 139.5, 137.2, 129.1, 128.8, 128.4, 120.1, 107.7, 98.6, 51,1; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{12}H_{11}ClIN_2$ 344.9655, found 344.9650.

1-(2-Iodobenzyl)benzo[c]isoxazol-3(1H)-one (**18**). Isoxazolidinone[15] (181 mg, 1.34 mmol) was dissolved in anhydrous THF (30 mL). The solution was cooled to 0 °C, and washed sodium hydride (38.6 mg, 1.61 mmol) was added in one portion. The solution was stirred at 0 °C for 30 min, and then 2-iodobenzyl bromide (478 mg, 1.61 mmol) was added. The solution was stirred at 0 °C for 1 h, warmed to room temperature, and stirred for a further 2 h. The solution was cooled to 0 °C, and an ice-cooled solution of diethyl ether/water =1/1 (15 mL) was added to the reaction mixture. The resolution was extracted with diethyl ether (3 × 20 mL), washed with brine (10 mL), and dried (MgSO$_4$) and the solvent evaporated under vacuum. The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1). The product was obtained as a white solid in 22% yield: R_f = 0.39 (pet. spirit/EtOAc = 5:1); mp = 142−145 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 7.89 (dd, *J* = 7.9 Hz, *J* = 1.0 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.78−7.65 (m, 1H), 7.57 (dd, *J* = 7.6 Hz, *J* = 1.4 Hz, 1H), 7.38 (dt, *J* = 7.5 Hz, *J* = 1.1 Hz, 1H), 7.31−7.26 (m, 2H), 7.05 (dt, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H), 4.71 (s, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 167.6, 157.0, 139.6, 136.2, 135.1, 130.5, 130.0, 128.5, 125.8, 124.4, 113.1, 112.0, 99.4, 65.0; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{10}INNaO_2$ 373.9654, found 373.9648.

1-(2-Iodobenzyl)-1H-benzo[d][1,3]oxazine-2,4-dione (**19**). Isatoic anhydride (109 mg, 0.67 mmol) was dissolved in DMF (7.0 mL), and 2-iodobenzyl bromide (200 mg, 0.67 mmol) and K$_2$CO$_3$ (111 mg, 0.80 mmol) were added. The mixture was stirred at room temperature for 18 h. Then water (10 mL) was added to the solution. The solution was extracted with dichloromethane (3 × 20 mL), washed with water (3 × 10 mL), and dried (MgSO$_4$) and the solvent evaporated under vacuum. The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1). The product was obtained as a white solid in 38% yield: R_f = 0.24 (pet. spirit/EtOAc = 5:1); mp =194−196 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 8.19 (dd, *J* = 7.9 Hz, *J* = 1.3 Hz, 1H), 7.92 (dd, *J* = 7.9 Hz, *J* = 1.1 Hz, 1H), 7.66−7.62 (m, 1H), 7.32−7.24 (m, 2H), 7.05−6.99 (m, 1H), 6.94 (d, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 5.26 (s, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 158.1, 148.2, 141.0, 139.9, 137.4, 135.4, 130.8, 129.6, 128.8, 126.0, 124.3, 114.8, 111.7, 97.0, 53.8; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for $C_{15}H_{10}INNaO_3$ 401.9603, found 401.9598.

1-(2-Iodobenzyl)-1H-benzo[d]imidazole (**20**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 1:1), and the product was obtained as a yellow solid in 64% yield: R_f = 0.29 (pet. spirit/EtOAc = 1:1); mp = 119−121 °C (lit.[16] mp = 102−104 °C); ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 7.94 (s, 1H), 7.91 (dd, *J* = 7.9 Hz, *J* = 1.1 Hz, 1H), 7.87−7.84 (m, 1H), 7.32−7.25 (m, 3H), 7.22 (dt, *J* = 7.5 Hz, *J* = 1.1 Hz, 1H), 7.01 (dt, *J* = 7.8 Hz, *J* = 1.6 Hz, 1H), 6.73 (d, *J* = 7.7 Hz, 1H), 5.35 (s, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 143.8, 143.3, 139.8, 137.5, 133.8, 129.8, 128.8, 127.9, 123.2, 122.4, 120.5, 109.9, 97.6, 53.5; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}IN_2$ 335.0045, found 335.0040.

Cyclization General Procedure. N-Alkylated material (20 mg) was dissolved in anhydrous acetonitrile in a quartz flask. The mixture was irradiated [irradiation conditions: Rayonet photochemical reactor using 254 nm lamps (16 lamps)] under an argon atmosphere for 2 h. The solvent was evaporated, and the crude product was purified by flash chromatography. Most compounds were isolated as white or yellow solids but turned brown after a short time on exposure to the atmosphere.

Phenanthridine (**21**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a yellow solid in 85% yield: R_f = 0.29 (pet. spirit/EtOAc = 5:1); mp = 104−106 °C (lit.[17] mp 104−105 °C); ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 9.30 (s, 1H), 8.63 (d, *J* = 8.3 Hz, 1H), 8.59 (dd, *J* = 8.0 Hz, *J* = 1.3 Hz, 1H), 8.20 (dd, *J* = 8.1 Hz, *J* = 1.3 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.90−7.85 (m, 1H), 7.78−7.68 (m, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 153.5, 144.3, 132.5, 131.0, 130.0, 128.8, 128.7, 127.5, 127.1, 126.3, 124.1, 122.2, 121.6; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{13}H_{10}N$ 180.0813, found 180.0808.

Methyl Phenanthridine-4-carboxylate (**22**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 2:1), and the product was obtained as a yellow oil in 95% yield: R_f = 0.21 (pet. spirit/EtOAc = 2:1); ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 9.40 (s, 1H), 8.71 (dd, *J* = 8.3 Hz, *J* = 1.2 Hz, 1H), 8.61 (d, *J* = 8.3 Hz, 1H), 8.08 (d, *J* = 7.9 Hz, 1H), 7.99 (dd, *J* = 7.3 Hz, *J* = 1.3 Hz, 1H), 7.92−7.87 (m, 1H), 7.78−7.73 (m, 1H), 7.73−7.68 (m, 1H), 4.08 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ = 168.9, 154.4, 141.6, 132.5, 132.1, 131.4, 128.9, 128.8, 128.0, 126.2, 126.1, 125.1, 124.4, 121.9, 52.7; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{15}H_{12}NO_2$ 238.0868, found 238.0863.

4-Methoxyphenanthridine (**23**). The crude product was purified by flash chromatography (pet. spirit/EtOAc = 1:1), and the product was obtained as a yellow solid in 67% yield: R_f = 0.15 (pet. spirit/EtOAc = 1:1); mp =75−78 °C (lit.[18] mp 73−77 °C); ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 9.32 (s, 1H), 8.60 (d, *J* = 8.3 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.07 (d, J = 7.9 Hz, 1H), 7.89−7.84 (m, 1H), 7.75−7.70 (m, 1H), 7.62 (t, J = 8.1 Hz, 1H), 7.18 (d, J = 7.9 Hz, 1H), 4.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 156.0, 152.1, 135.4, 132.4, 130.9, 128.7, 127.6, 127.3, 126.5, 125.3, 122.3, 114.0, 108.2, 56.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{12}NO$ 210.0919, found 210.0913.

*Phenanthridin-4-ol (**24**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 1:1), and the product was obtained as a yellow solid in 90% yield: R_f = 0.69 (pet. spirit/EtOAc = 1:1); mp = 179−183 °C (lit.[19] mp 188−189 °(C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.15 (s, 1H), 8.58 (d, J = 8.3 Hz, 1H), 8.07 (d, J = 7.4 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 7.90−7.85 (m, 1H), 7.75−7.70 (m, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 153.0, 150.9, 133.4, 132.7, 131.2, 128.9, 128.1, 127.6, 126.8, 124.5, 122.4, 112.7, 110.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{13}H_{10}NO$ 196.0762, found 196.0757.

*4-(Methylthio)phenanthridine (**25**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a yellow solid in 58% yield: R_f = 0.38 (pet. spirit/EtOAc = 5:1); mp = 169−173 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.32 (s, 1H), 8.60 (d, J = 8.3 Hz, 1H), 8.33 (dd, J = 8.2 Hz, J = 1.0 Hz, 1H), 8.08 (d, J = 7.9 Hz, 1H), 7.90−7.85 (m, 1H), 7.75−7.70 (m, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.46 (dd, J = 7.6 Hz, J = 0.8 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 152.1, 141.2, 140.6, 132.5, 131.0, 128.8, 127.6, 127.1, 126.5, 124.0, 122.4, 122.3, 117.9, 14.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{12}NS$ 226.0690, found 226.0685.

*4-Fluorophenanthridine (**26**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a yellow solid in 95% yield: R_f = 0.19 (pet. spirit/EtOAc = 5:1); mp =94−98 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.33 (s, 1H), 8.59 (d, J = 8.2 Hz, 1H), 8.35 (d, J = 8.3 Hz, 1H), 8.09 (d, J = 7.9 Hz, 1H), 7.92−7.87 (m, 1H), 7.78−7.74 (m, 1H), 7.62 (dt, J_{HH} = 8.1 Hz, J_{HF} = 5.2 Hz, 1H), 7.46 (ddd, J_{HF} = 10.2 Hz, J_{HH} = 7.9 Hz, J_{HH} = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 158.7 (d, ^1J = 255.0 Hz), 153.7 (d, J = 1.7 Hz), 134.0 (d, ^2J = 10.6 Hz), 131.9 (d, J = 2.8 Hz), 131.5, 129.0, 128.1, 127.0 (d, J = 8.4 Hz), 126.5, 126.1, 122.2, 117.8 (d, J = 4.2 Hz), 113.6 (d, ^2J = 19.8 Hz); HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_8FNaN$ 220.0538, found 220.0533.

*2-Chlorophenanthridine (**27**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 2:1), and the product was obtained as a yellow solid in 95% yield: R_f = 0.39 (pet. spirit/EtOAc = 2:1); mp = 154−157 °C (lit.[19] 155−156°C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.26 (s, 1H), 8.53−8.50 (m, 2H), 8.12 (d, J = 8.7 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.91−7.86 (m, 1H), 7.78−7.73 (m, 1H), 7.68 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 153.6, 142.6, 133.1, 131.5, 131.4, 131.4, 129.2, 128.8, 128.2, 126.4, 125.2, 121.9, 121.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{13}H_8ClN$ 214.0424, found 214.0418.

*3-Bromophenanthridine (**28**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1). A product mixture of four compounds was obtained. Pure **28** could be isolated as a yellow solid in 31% yield: R_f = 0.35 (pet. spirit/EtOAc = 5:1); mp = 206−209 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.29 (s, 1H), 8.58 (d, J = 8.1 Hz, 1H), 8.44 (d, J = 8.6 Hz, 1H), 8.36 (d, J = 2.0 Hz, 1H), 8.07 (d, J = 7.4 Hz, 1H), 7.91−7.87 (m, 1H), 7.78 (dd, J = 8.7 Hz, J = 2.0 Hz, 1H), 7.77−7.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 153.6, 143.4 ($C_{quart.}$, bs, quadrupole), 132.6, 132.5, 131.4, 131.0, 129.5, 128.3, 125.8, 123.8, 123.1, 123.0, 121.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{13}H_9BrN$ 257.9918, found 257.9913.

*2-Nitrophenanthridine (**29**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 2:1), and the product was obtained as a yellow solid in 95% yield: R_f = 0.29 (pet. spirit/EtOAc = 2:1); mp = 259−262 °C (lit.[20] mp = 263 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.52 (s, 1H), 9.52 (bs, 1H), 8.72 (d, J = 8.2 Hz, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.36 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 7.7 Hz, 1H), 8.02 (t, J = 7.7 Hz, 1H), 7.87 (t, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 156.4, 146.2, 146.2, 133.0, 132.7, 130.9, 129.8, 129.3, 126.3, 124.3, 122.8, 122.3, 119.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{13}H_9N_2O_2$ 225.0664, found 225.0659.

*2-Chlorobenzo[c][1,8]naphthyridine (**30**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 1:1), and the product was obtained as a yellow solid in 55% yield: R_f = 0.22 (pet. spirit/EtOAc = 1:1); mp = 234−236 °C (lit.[21] mp 231−233 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.51 (s, 1H), 9.00 (d, J = 2.5 Hz, 1H), 8.87 (d, J = 2.5 Hz, 1H), 8.54 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.98−7.93 (m, 1H), 7.86−7.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 157.2, 151.9, 150.3, 131.8, 131.7, 130.4, 130.0, 129.1, 129.0, 126.5, 122.1, 119.6; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{12}H_7ClNaN_2$ 237.0195, found 237.0190.

*Phenanthridine-4-carboxylic Acid (**31**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 1:1), and the product was obtained as a white solid in 63% yield: R_f = 0.31 (pet. spirit/EtOAc = 1:1); mp = 238−241 °C (lit.[22] mp 242−243°C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.32 (s, 1H), 8.85 (dd, J = 8.3 Hz, J = 1.3 Hz, 1H), 8.81 (dd, J = 7.5 Hz, J = 1.3 Hz, 1H), 8.70 (d, J = 8.3 Hz, 1H), 8.20 (d, J = 7.9 Hz, 1H), 8.07−8.02 (m, 1H), 7.92−7.84 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 167.5, 152.0, 141.4, 133.5, 133.1, 132.8, 129.8, 128.7, 127.7, 127.2, 125.5, 125.3, 124.4, 122.3; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_9NNaO_2$ 246.0531, found 246.0525.

*4H-[1,3]Oxazino[5,4,3-de]phenanthridine-4,6(8H)-dione (**32**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 5:1), and the product was obtained as a white solid in 74% yield: R_f = 0.18 (pet. spirit/EtOAc = 5:1); mp = 245−249 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.17 (dd, J = 7.8 Hz, J = 1.3 Hz, 1H), 8.04 (dd, J = 7.9 Hz, J = 1.4 Hz, 1H), 7.82−7.79 (m, 1H), 7.45−7.36 (m, 2H), 7.32 (t, J = 7.7 Hz, 1H), 7.28−7.25 (m, 1H), 5.22 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 158.0, 147.3, 137.3, 130.0, 129.7, 129.6, 128.8, 128.2, 127.0, 126.9, 124.4, 122.7, 122.3, 111.5, 46.6; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{15}H_9NNaO_3$ 274.0480, found 274.0475.

*1-Benzyl-1H-benzo[d]imidazole (**33b**).* The crude product was purified by flash chromatography (pet. spirit/EtOAc = 1:1), and the product was obtained as a yellow solid in 54% yield: R_f = 0.13 (pet. spirit/EtOAc = 1:1); mp =114−116 °C (lit.[23] mp 115−116°C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.17 (s, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.38−7.28 (m, 6 H), 7.23−7.20 (m, 2H), 5.40 (s, 2H); HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{13}N_2$ 209.1079, found 209.1073.

■ ASSOCIATED CONTENT

S Supporting Information. ^{1}H and ^{13}C NMR spectra and UV spectra of compounds **10**, **12**, **14**, **16**, **23**, **25**, **27**, and **29**. This material is available free of charge via the Internet at http://pubs.acs.org.

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