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Rational design of an efficient one-pot synthesis of 6*H*-pyrrolo[2,3,4-*gh*]perimidines in polyphosphoric acid†

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Several highly efficient one-pot synthetic protocols were developed, enabling polyphosphoric acid-activated nitroalkanes to act as electrophiles in reactions with aminonapthalenes. The featured methods allow for the single step assembly of polyheterocyclic aromatic derivatives of 6*H*-pyrrolo[2,3,4-*gh*] perimidine scaffold in high yields.

Introduction

1*H*-Cyclopenta[*cd*]phenalenes **2** are interesting polycyclic aromatic architectures that can be viewed as derivatives of the acenaphthene system *peri*-anneleated by a benzene ring. These compounds attract the attention of chemists and material scientists due to being the smallest structural units modeling the orbital and physico-chemical properties of fullerenes and defected carbon nanotubes.[1] Along with pyrene (**1**) derivatives, such compounds could be used as fluorescent probes and light-sensing units in various biochemical assays.[2] However, due to a very low solubility in water and significant carcinogenicity, the potential of these structural fragments for cytological and *in vivo* applications could be limited. We pondered if this issue can be addressed by partial replacement of carbon with nitrogen atoms[3] to afford aromatic polyheterocyclic scaffolds with improved solubility, which also are expected to show much lower metabolitic stability. We previously demonstrated several synthetic approaches towards 1,3-diazopyrenes **3**, which we intended as a convenient substitute of the pyrene unit for material science applications.[4,5] We also invested efforts in the development of synthetic approaches towards 6*H*-pyrrolo[2,3,4-*gh*]perimidine scaffold **4**, primarily capitalizing on *peri*-annulations of a pyrrole ring to 1*H*-perimidines (Fig. 1).[6] Furthermore, we recently reported on umpolung-activation of nitroalkanes **6** toward the addition of carbon- and nitrogen-based nucleophiles with polyphosphoric acids (Scheme 1). This chemistry was employed for the installation of amino and carboxamide groups *via* direct C–H functionalization of arenes **5** (Scheme 1, eqn (1))[7] and for efficient preparation of benzoxazoles and benz-imidazoles **11** (Scheme 1, eqn (2)).[8] Herein we wish to report our synthetic studies towards 6*H*-pyrrolo[2,3,4-*gh*] perimidine **4** employing this unusual chemistry.

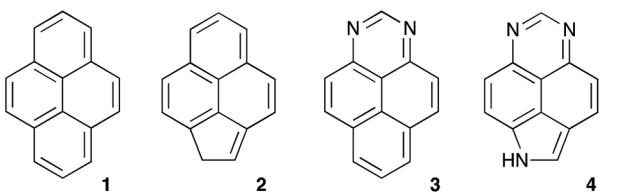
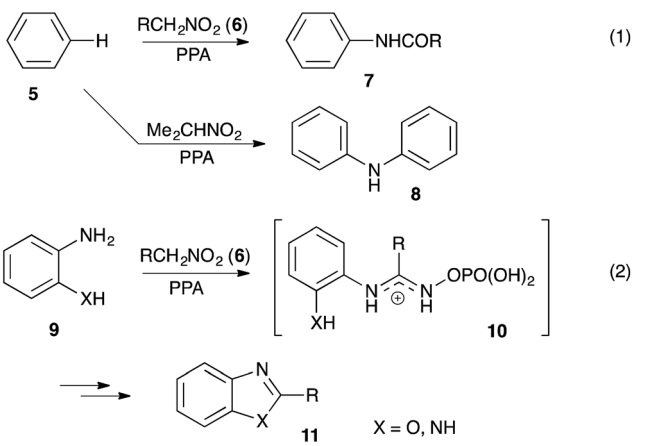


Fig. 1 Condensed aromatic hydrocarbons and their nitrogen analogs.



Scheme 1

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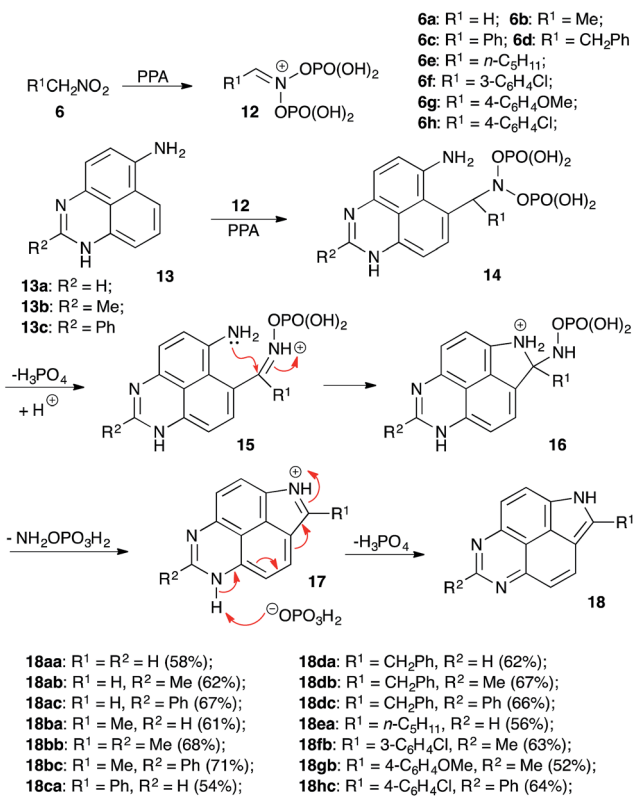
Results and discussion

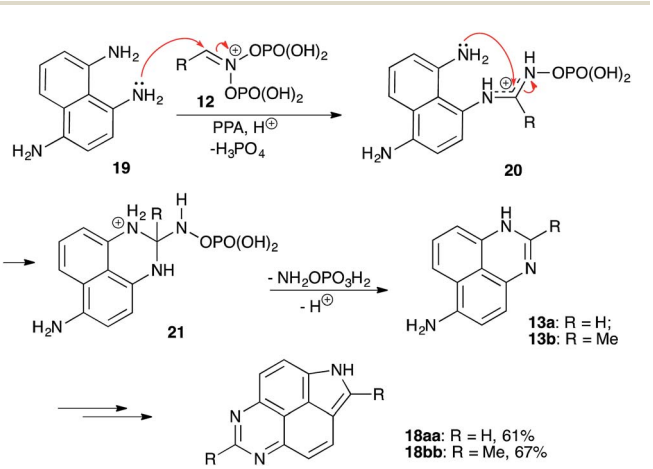
Polyphosphoric acid (PPA) possesses an array of unique physico-chemical properties, which makes it a very attractive ionic liquid-like reaction medium to carry out cascade and one-pot transformations involving acid-catalyzed steps, such as electrophilic aromatic substitution, Schmidt and Beckmann rearrangements, Vilsmeier-type reactions, nucleophilic substitutions, as well as various acid-promoted elimination and condensation processes. Adjusting the content of P_2O_5 in PPA affects both effective acidity and anhydridic activity of this medium, allowing for fine-tuning of the reaction conditions and intelligent design of multi-step processes. Furthermore, an *in situ* phosphorylation of various functional groups can be used as a temporary protection or to modify reactivity, for example, to equip good leaving group or totally alter the function's normal reactivity pattern. Thus, we previously demonstrated[7,8] that normally nucleophilic nitroalkanes **6** can be stabilized by phosphorylation as highly electrophilic *aci*-forms **12** (Scheme 2). We reasoned, that generation of this species in the presence of 6-amino-1*H*-perimidines **13** would trigger an electrophilic attack at C-7 to afford (azanediyl)bis(phosphoric acid) **14**, which after elimination of H_3PO_4 at low pH would provide the protonated form of phosphorylated oxime **15** (Scheme 2). Intramolecular 5-*exo*-trig nucleophilic attack of the aniline function and subsequent elimination of phosphorylated hydroxylamine would provide species **17**, which after deprotonation and rearomatization would yield the desired 6*H*-pyrrolo[2,3,4-*gh*]perimidine **18** (Scheme 3). To test this idea we subjected 6-amino-1*H*-perimidine (**13a**) to the reaction with an excess of nitromethane (**6a**). First, the mixture was stirred in 86% PPA at 80–90 °C, then the reaction was forced to completion at 130–140 °C. The expected 6*H*-pyrrolo[2,3,4-*gh*]perimidine (**18aa**) was formed as the sole product in good preparative yield (Scheme 3). Similarly, nitroethane (**6b**), α-nitrotoluenes (**6c**, **f–h**), 2-phenylnitroethane (**6d**), and 1-nitrohexane (**6e**), were also employed in the reaction with 6-amino-1*H*-perimidines **13b**, **c** substituted at C-2 to afford the corresponding 6*H*-pyrrolo[2,3,4-*gh*]perimidines with different substituents C-2 and C-7 (Scheme 2). Remarkably, these compounds were obtained as sole products and isolated in pure form after aqueous work up followed by recrystallization. Purification by column chromatography was not required.

Next, we decided to investigate the possibility of generating 6-amino-1*H*-perimidines species **13** *in situ*. It was anticipated that generation of phosphorylated *aci*-form **12** in the presence of naphthalene-1,4,5-triamine (**19**) would induce nucleophilic attack by one of the amino-groups affording phosphorylated iminamide **20** (shown in protonated from in Scheme 3). The later would undergo a 6-*exo*-trig cyclization involving a second amino group in the *peri*-position and provide cyclic methanetriamine intermediate **21**. Subsequent acid-mediated elimination of phosphorylated hydroxylamine is expected to provide 6-amino-1*H*-perimidine **13** (Scheme 3), which should react further according to the mechanism, depicted in Scheme 2, ultimately yielding the target 6*H*-pyrrolo[2,3,4-*gh*]perimidines **18**. Gratifyingly, this multistep cascade transformation proceeded as planned. Reactions of **19** with excess (3.1 equiv.) nitromethane (**6a**) or nitroethane (**6b**) afforded products **18aa** and **18bb**, respectively, in good yields (Scheme 3).

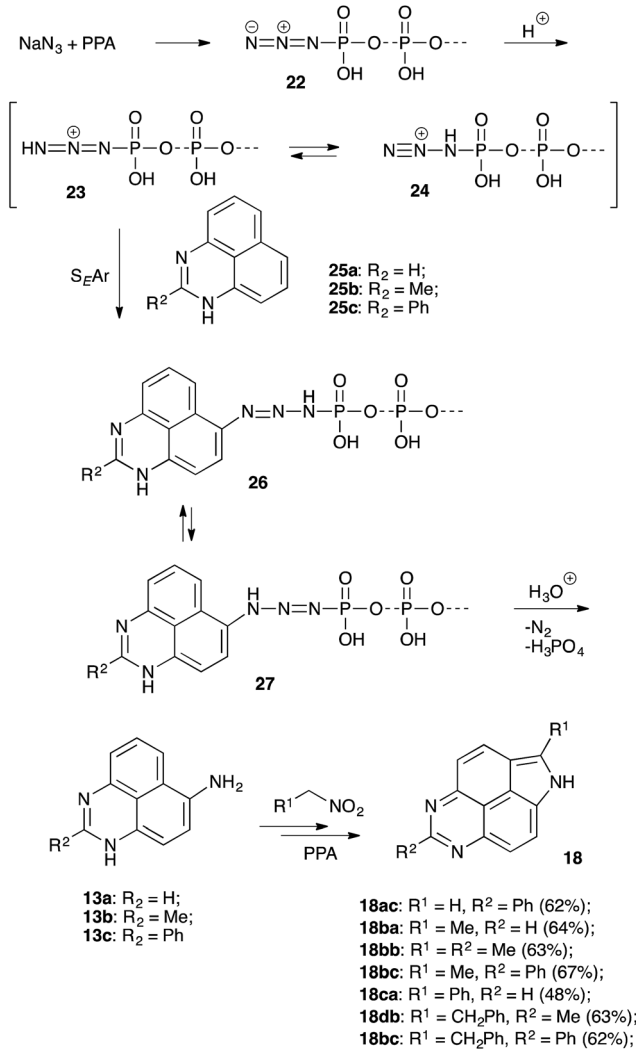
We also envisioned an alternative method for the *in situ* generation of key intermediate **13** employing a PPA-assisted Schmidt reaction of perimidines **25** in the presence of sodium azide. It is believed, that hydrazoic acid generated under these reaction conditions, reacts with PPA to form phospharazidic acid **22**, which after protonation provides phosphonotriazynium ion **24**, that exists in equilibrium with tautomer **23**



Scheme 2



Scheme 3

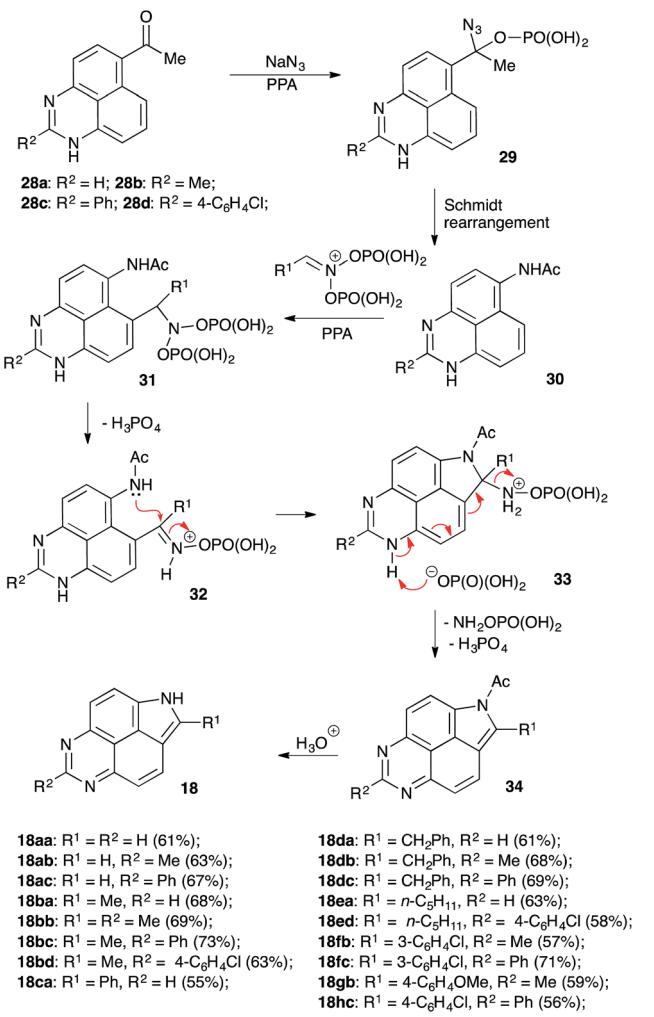


Scheme 4

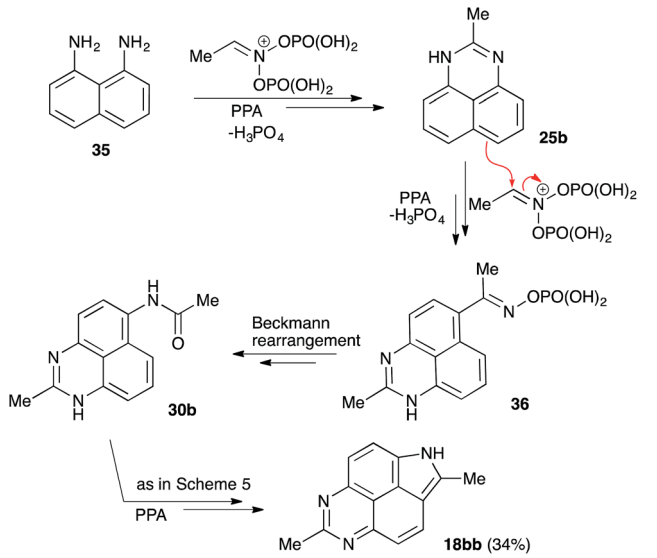
(Scheme 4). Species **24** can be viewed as the stabilized form of *N*-amino-diazonium, and it's reactivity reminds that of diazonium salts.[9] In particular, it can participate in efficient S_EAr-reaction with electron-rich aromatic compounds, such as perimidines **25** to afford the corresponding (aryltriaz-1-en-1-yl)phosphonic acids **26** (existing in equilibrium with tautomeric form **27**). Acid-mediated decomposition of these species, accompanied with a evolution of nitrogen gas would afford intermediate 6-aminopiperidine **13**, that can be consumed in a subsequent one-pot reaction with an appropriate nitroalkane. We were pleased to discover, that this process design was viable, and the corresponding 6*H*-pyrrolo[2,3,4-*gh*]perimidines **18** were produced in very good yield (Scheme 4).

Next, we decided to elaborate on the one-pot preparation of target heteroaromatic tetracycles starting from readily available 6-acylperimidines. It was expected, that initial nucleophilic addition of the azide across C=O bond would provide *O*-phosphorylated 1-azidoalcohol **29**, which should undergo facile Schmidt rearrangement to provide acetamide **30**. The subsequent addition of nitroethane **6** and *in situ* generation of electrophilic *aci* form **12** would invoke alkylation of **30** at C-7 to yield intermediate **31**, which, after elimination of H_3PO_4 would provide phosphorylated oxime **32** (shown in Scheme 5 in protonated form). We reasoned, that the acetamide group in **32** could be further involved in nucleophilic 5-*exo*-trig cyclization affording tetracyclic intermediate **33**, which after elimination of *O*-phosphoryl hydroxylamine would yield *N*-acetylpyrroloperimidine **34**. Aqueous work up accompanied with hydrolytic cleavage of *N*-acetyl moiety would finally afford the target material **18**. This process design worked smoothly, as shown by a series of one-pot reactions involving 6-acylperimidines **28a–d** and nitroalkanes **6a–h**, which led to formation of the corresponding pyrroloperimidines in good yields (Scheme 5).

Finally, we investigated the possibility to develop a multistep cascade transformation involving an even more affordable starting material, 1,8-naphthalenediamine (**28**). It was anticipated that in the presence of *aci*-form, generated upon phosphorylation of nitroethane (**6b**), two amino groups would be used to assemble a heterocyclic ring of perimidine **25b** (Scheme 6). This process would involve a two-fold nucleophilic attack by nitrogen atoms and it's mechanism would be identical



Scheme 5



Scheme 6

to the one previously described in Scheme 3. We also expected that the excess of *aci*-form would serve as an electrophile in the subsequent acetamidation reaction, that should be directed to C-6 of perimidine.[7] This reaction involves an initial alkylation of the activated heteroaromatic compound to form phosphorylated ketoxim **29**, which upon heating in PPA should undergo Beckmann rearrangement to afford acetanilide **30b** (Scheme 6). The following transformation would proceed according to the mechanism outlined in Scheme 5 to afford the pyrroloperimidine core. We tested this transformation on a single example, and were thrilled to find that compound **18bb** was formed as sole isolable product, albeit in somewhat marginal yield (Scheme 5).

Conclusions

We have designed a series one-pot and cascade transformations involving an unusual electrophilic behavior of polyphosphoric acid-activated nitroalkanes. These processes involved PPA-mediated Schmidt and Beckmann rearrangements, reactions of direct electrophilic amination with azides and acetamidation with nitroalkanes, and *N*-Nef reaction. For the first time these steps are arranged in multi-step one-pot processes of increased complexity. The versatility of PPA as an "intelligent" reaction media was showcased.

Experimental part

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-III spectrometer (400 or 100 MHz, respectively) equipped with BBO probe in DMSO-d_6, using TMS as internal standard. High-resolution mass spectra were registered with a Bruker Maxis spectrometer (electrospray ionization, in MeCN solution, using HCO_2Na–HCO_2H for calibration). Melting points were measured with a Stuart smp30 apparatus. All reactions were performed in oven-dried 5 mL Erlenmeyer flasks open to the atmosphere, employing overhead stirring. Reaction progress and purity of isolated compounds were controlled by TLC on Silufol UV-254 plates. Compounds **6f–h**,[10] **13a–c**,[7c,11] and **28a–c**,[12] were prepared according to the literature procedures. All other reagents and solvents were purchased from commercial vendors and used as received.

Preparation of 2-(4-chlorophenyl)-6-(7)-acetylperimedine (28d)

Anhydrous aluminum chloride (1.33 g, 10.0 mmol) and acetyl chloride (85 μL, 94 mg, 1.2 mmol) were vigorously stirred in dry dichloromethane (20 mL) for 30 min at room temperature. 2-(4-Chloro)phenylperimidine (279 mg, 1.0 mmol) was added by portions over 15 min, and the stirring was continued for 30 min. The formed solution was poured into cold water (20 mL) and dichloromethane was removed in vacuum. Solid precipitate was filtered off and re-crystallized from ethanol to afford the titled compound as carrot-orange crystals. Yield 295 mg (0.92 mmol, 92%), mp 236–238 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.57 (3H, s, CH_3), 6.75 (1H, d, J = 8.1 Hz, H-4(9)), 6.97 (1H, d, J = 7.2 Hz, H-9(4)), 7.47 (1H, dd, J = 8.7, 7.2 Hz, H-8(5)), 7.67 (2H, d, J = 8.6 Hz, Ar (H-3,5)), 8.09 (3H, m, H-5(8), Ar (H-2,6)), 8.56 (1H, d, J = 8.7 Hz, H-7(6)), 11.39 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 28.6, 106.2, 111.4, 118.8, 121.2, 123.6, 127.7, 128.6 (2C), 129.1 (2C), 130.9, 132.6, 136.0, 136.5, 140.6, 145.4, 151.8, 197.5; FT-IR (NaCl, cm^{-1}): 3320 (NH), 2390, 1650 (CO), 1551, 1455, 1250, 820; HRMS (TOF-ES): calcd for $C_{19}H_{14}ClN_2O$ (M + H), 321.0789, found 321.0784 (1.6 ppm).

General procedure for preparation of pyrrolo[2,3,4-*gh*] perimidines from 6-aminoperimidines (method A)

A mixture of 6-aminoperimidine **13** (1.00 mmol), nitroalkane **6** (2.10 mmol), and 86% PPA (3–4 g) was vigorously stirred for 1 h at 80–90 °C, then heated to 130–140 °C, and stirred for additional 3 h. The reaction mixture was poured out into stirred cold water (30 mL), and the mixture was basified with aqueous ammonia to pH 8. Formed precipitate was filtered off, the supernatant solution was extracted with toluene (3 × 50 mL). The precipitate was also extracted for 5 h with toluene (100 mL) in Soxhlet apparatus. Combined organic extracts were evaporated and the residual solid was re-crystallized.

General procedure for preparation of pyrrolo[2,3,4-*gh*] perimidines from 1,4,8-naphthalenetriamine (method B)

A mixture of 1,4,8-triaminonaphthalene **19** (0.173 g, 1.00 mmol), nitroalkane **6** (3.10 mmol), and 86% PPA (3–4 g) was vigorously stirred for 3 h at 80–90 °C, then heated to 130–140 °C, and stirred for additional 3 h. Aqueous work up, isolation and purification of products is carried out in the manner described for the method **A**.

General procedure for preparation of pyrrolo[2,3,4-*gh*] perimidines from perimidines (method C)

A mixture of perimidine **25** (1.00 mmol), sodium azide (0.195 g, 3.00 mmol), 86% PPA (3–4 g) was vigorously stirred for 4 h; the reaction progress was monitored by TLC. Then nitroalkane **6**

(4.00 mmol) was added, the temperature was raised to 110–120 °C and the stirring was continued for additional 5 h. Aqueous work up, isolation and purification of products is carried out in the manner described for the method **A**.

General procedure for preparation of pyrrolo[2,3,4-*gh*] perimidines from 6-acetylperimidines (method D)

A mixture of 6-acetylperimidine **28** (1.00 mmol), sodium azide (0.070 g, 1.07 mmol) in 86% PPA (2–3 g) was vigorously stirred for 1 h at 55–60 °C. Then nitroalkane **6** was added (2.00 mmol), and the temperature was increased to 110–120 °C (90–100 °C for reactions with nitromethane) and the stirring was continued for additional 3 h. Aqueous work up, isolation and purification of products is carried out in the manner described for the method **A**.

Preparation of 2,7-dimethylpyrrolo[2,3,4-*gh*]perimidine from 1,8-diaminonaphthalene (method E)

A mixture of 1,8-diaminonaphthalene (**35**) (0.158 g, 1.00 mmol), nitroalkane **6** (2.10 mmol), and 86% PPA (2–3 g) was vigorously stirred for 3 h at 90–100; the reaction progress was monitored by TLC, eluting with EtOAc/EtOH mixture, 1 : 1. Then, the temperature was increased to 140–150 °C and the stirring was continued for additional 3 h. Aqueous work up, isolation and purification of products is carried out in the manner described for the method **A**.

6*H*-Pyrrolo[2,3,4-*gh*]perimidine (18aa).[6b] Yellowish orange crystals, mp 207–209 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.70 (1H, d, J = 9.0 Hz, H-3), 7.91 (1H, d, J = 8.7 Hz, H-9), 8.45 (1H, d, J = 8.7 Hz, H-8), 8.46 (1H, s, H-2), 8.51 (1H, d, J = 9.0 Hz, H-4), 9.48 (1H, s, H-6), 13.2 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 111.9, 112.9, 116.3, 120.1, 120.4, 120.6, 124.9, 131.1, 136.4, 147.8, 154.9, 163.0.

2-Methyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18ab).[6b] Yellowish orange crystals, mp 237–238 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.93 (3H, s, Me), 7.65 (1H, d, J = 9.0 Hz, H-3), 7.82 (1H, d, J = 8.7 Hz, H-9), 8.42 (1H, d, J = 8.7 Hz, H-8), 8.46 (1H, s, H-2), 8.50 (1H, d, J = 9.0 Hz, H-4), 13.1 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 26.9, 111.9, 112.9, 116.3, 119.9, 120.5, 120.6, 124.7, 130.8, 136.3, 147.8, 154.9, 163.0.

2-Phenyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18ac).[6b] Yellowish orange crystals, mp 201–203 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.57–7.63 (m, 3H, Ph (H-3,4,5)), 7.78 (d, J = 8.4 Hz, 1H, H-3), 7.96 (d, J = 8.5 Hz, 1H, H-9), 8.39 (s, 1H, H-2), 8.43 (d, J = 8.5 Hz, 1H, H-8), 8.51 (d, J = 8.4 Hz, 1H, H-4), 8.73 (d, J = 7.3 Hz, 2H, Ph (H-2,6)), 13.1 (br. s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 112.51, 112.88, 117.14, 120.51, 120.55, 120.72, 124.83, 128.08 (2C), 128.20 (2C), 129.32, 130.86, 136.28, 140.12, 147.93, 155.14, 160.14.

7-Methyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18ba).[6b] Yellowish orange crystals, mp 259–260 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.98 (3H, s, Me), 7.58 (1H, d, J = 9.0 Hz, H-3), 7.78 (1H, d, J = 8.7 Hz, H-9), 8.31 (1H, d, J = 8.7 Hz, H-8), 8.47 (1H, d, J = 9.0 Hz, H-4), 9.36 (1H, s, H-6), 13.1 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 12.5, 112.0, 112.9, 116.3, 120.1, 120.5, 120.5, 124.7, 130.8, 136.2, 147.8, 155.0, 163.0.

2,7-Dimethyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18bb).[6b] Yellowish orange crystals, mp 271–272 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.86 (3H, s, 7-Me), 2.92 (3H, s, 2-Me), 7.46 (1H, d, J = 9.0 Hz, H-3), 7.64 (1H, d, J = 8.7 Hz, H-9), 8.22 (1H, d, J = 8.7 Hz, H-8), 8.38 (1H, d, J = 9.0 Hz, H-4), 13.1 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 12.4, 27.0, 112.0, 112.8, 116.2, 120.0, 120.4, 120.5, 124.6, 130.7, 136.1, 147.7, 154.9, 162.9.

7-Methyl-2-phenyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18bc).[6b] Yellowish orange crystals, mp 245–246 °C (toluene/petroleum ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.93 (s, 3H, Me), 7.48–7.58 (3H, m, Ph (H-3,4,5)), 7.62 (1H, d, J = 9.0 Hz, H-3), 7.82 (1H, d, J = 8.7 Hz, H-9), 8.29 (1H, d, J = 8.7 Hz, H-8), 8.43 (1H, d, J = 9.0 Hz, H-4), 8.71 (2H, d, J = 8.4 Hz, Ph (H-2,6)), 13.1 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 12.4, 112.7, 112.9, 117.1, 120.5, 120.6, 120.7, 124.9, 128.1 (2C), 128.2 (2C), 129.4, 130.9, 136.2, 140.1, 147.9, 155.1, 159.6.

2-(4-Chlorophenyl)-7-methyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18bd). Yellowish orange crystals, mp 243–245 °C (toluene); R_f 0.73 (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.97 (3H, s, Me), 7.51 (1H, d, J = 8.6 Hz, Ar (H-3,5)), 7.76 (1H, d, J = 9.2 Hz, H-3), 7.95 (1H, d, J = 8.8 Hz, H-9), 8.14 (1H, d, J = 8.8 Hz, H-4), 8.27 (1H, d, J = 9.2 Hz, H-8), 8.68 (2H, d, J = 8.6 Hz, Ar (H-2,6)), 9.59 (1H, br. s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.8, 113.5, 113.8, 119.2, 119.8, 121.5, 123.1, 125.2, 128.8 (2C), 130.7, 130.2 (2C), 133.9, 135.8, 139.2, 148.9, 156.4, 160.8; FT-IR (NaCl, cm^{-1}): 33 907 (NH), 2991, 1621, 1552, 1491, 1360, 1275, 1181, 1080, 840, 800; HRMS (TOF-ES): calcd for $C_{19}H_{13}ClN_3$ (M + H) 318.0793, found 318.0788 (1.6 ppm).

7-Phenyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18ca).[6b] Yellowish orange crystals, mp 263–265 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.54 (3H, m, Ph (H-3,4,5)), 7.66 (1H, d, J = 9.0 Hz, H-3), 7.79 (1H, d, J = 8.7 Hz, H-9), 8.18 (2H, d, J = 7.7 Hz, Ph (H-2,6)), 8.33 (1H, d, J = 8.7 Hz, H-8), 8.69 (1H, d, J = 9.0 Hz, H-4), 9.33 (1H, s, H-6), 13.3 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 112.0, 112.2, 117.9, 120.9, 121.2, 122.3, 126.2, 127.2 (2C), 128.5, 129.3 (2C), 129.4, 131.0, 132.2, 148.4, 154.6, 163.5.

7-Benzyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18da). Yellowish orange crystals, mp 251–252 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.72 (2H, s, CH_2), 7.24 (1H, t, J = 7.4 Hz, Ph (H-4)), 7.34 (2H, dd, J = 7.8, 7.4 Hz, Ph (H-3,5)), 7.42 (2H, d, J = 7.8 Hz, Ph (H-2,6)), 7.58 (1H, d, J = 9.1 Hz, H-3), 7.81 (1H, d, J = 8.8 Hz, H-9), 8.32 (1H, d, J = 9.1 Hz, H-8), 8.35 (1H, d, J = 8.8 Hz, H-4), 9.39 (1H, s, H-6), 13.35 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.4, 113.0, 114.2, 117.7, 120.4, 121.2, 125.2, 126.6, 126.8 (2C), 128.5, 129.7, 129.8, 131.2 (2C), 130.9, 139.0, 147.7, 155.0; FT-IR (NaCl, cm^{-1}): 3407 (NH), 3214, 3028, 2814, 1618, 1494, 1373; HRMS (TOF-ES): calcd for $C_{19}H_{14}N_3$ (M + H), 284.1182, found 284.1180 (0.9 ppm).

7-Benzyl-2-methyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18db). Yellowish orange crystals, mp 223–225 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.86 (3H, s, Me), 4.68 (2H, s, CH_2), 7.23 (1H, t, J = 7.3 Hz, Ph (H-4)), 7.33 (2H, dd, J = 7.7, 7.3 Hz, Ph (H-3,5)), 7.43 (2H, d, J = 7.7 Hz, Ph (H-2,6)), 7.48 (1H, d, J = 9.1 Hz, H-3), 7.69 (1H, d, J = 8.8 Hz, H-9), 8.24 (1H, d, J = 9.1 Hz, H-8), 8.27 (1H, d, J = 8.8 Hz, H-4), 13.12 (1H, br. s, NH); ^{13}C NMR (100

MHz, DMSO-d_6): δ 27.1, 33.2, 112.1, 112.6, 117.0, 120.5, 120.7, 120.8, 124.9, 126.6, 127.5, 128.2, 128.7 (2C), 128.9 (2C), 130.9, 138.9, 155.0, 163.2; FT-IR (NaCl, cm^{-1}): 3387 (NH), 3069, 2793, 2345, 1501, 1367; HRMS (TOF-ES): calcd for $C_{20}H_{16}N_3$ (M + H) 298.1339, found 298.1343 (1.3 ppm).

7-Benzyl-2-phenyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18dc). Yellowish orange crystals, mp 195–197 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.72 (2H, s, CH_2), 7.25 (1H, t, J = 7.4 Hz, Ph (H-4)), 7.34 (2H, dd, J = 7.7, 7.4 Hz, Ph (H-3,5)), 7.45 (2H, d, J = 7.7 Hz, Ph (H-2,6)), 7.49–7.57 (m, 3H, Ph (H-3,4,5)), 7.65 (1H, d, J = 9.1 Hz, H-3), 7.87 (1H, d, J = 8.8 Hz, H-9), 8.33 (1H, d, J = 9.1 Hz, H-8), 8.35 (1H, d, J = 8.8 Hz, H-4), 8.69 (2H, dd, J = 8.5, 1.6 Hz, Ph (H-2,6)), 13.31 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.4, 113.0, 118.1, 120.8, 121.4, 121.6, 125.4, 126.9, 128.3 (2C), 128.6 (2C), 128.9 (2C), 129.1 (2C), 129.8, 130.9, 131.4, 138.9, 139.0, 140.2, 148.3, 155.3, 160.0; FT-IR (NaCl, cm^{-1}): 3373 (NH), 2924, 2842, 2366, 1745, 1625, 1535, 1497, 1367, 1342, 1274; HRMS (TOF-ES): calcd for $C_{25}H_{18}N_3$ (M + H) 360.1495, found 360.1501 (1.6 ppm).

7-Pentyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18ea). Yellowish orange crystals, mp 156–158 °C (toluene–petroleum ether); R_f 0.62 (EtOAc/EtOH 3 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.87 (3H, t, J = 7.0 Hz, Me), 1.36 (4H, m, CH_2CH_2), 1.93 (2H, m, CH_2), 3.36 (2H + H_2O, m, CH_2 + H_2O), 7.60 (1H, d, J = 9.1 Hz, H-3), 7.80 (1H, d, J = 8.7 Hz, H-9), 8.35 (1H, d, J = 8.7 Hz, H-4), 8.52 (1H, d, J = 9.1 Hz, H-8), 9.38 (1H, s, H-6), 13.24 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.8, 20.7, 21.8, 29.4, 31.0, 111.7, 114.1, 117.0, 120.2, 120.5, 120.7, 124.8, 131.1, 140.7, 147.4, 154.6, 154.8; FT-IR (NaCl, cm^{-1}): 3507 (NH), 2958, 2438, 1631, 1572, 1490, 1255, 1190, 1082; HRMS (TOF-ES): calcd for $C_{17}H_{18}N_3$ (M + H) 264.1495, found 264.1493 (0.8 ppm).

2-(4-Chlorophenyl)-7-pentyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18ed). Yellowish orange crystals, mp 211–213 °C (toluene/petroleum ether); R_f 0.74 (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (3H, t, J = 7.1 Hz, Me), 1.35–1.47 (4H, m, CH_2CH_2), 1.93–2.00 (2H, m, CH_2), 3.30 (2H, J = 7.7 Hz, CH_2), 7.51 (1H, d, J = 8.6 Hz, Ar (H-3,5)), 7.78 (1H, d, J = 9.2 Hz, H-3), 7.97 (1H, d, J = 8.8 Hz, H-9), 8.16 (1H, d, J = 8.8 Hz, H-4), 8.30 (1H, d, J = 9.2 Hz, H-8), 8.69 (2H, d, J = 8.6 Hz, Ar (H-2,6)), 9.71 (1H, br. s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 22.4, 28.0, 29.8, 31.6, 113.3, 113.5, 119.0, 119.7, 121.4, 122.8, 124.9, 128.6 (2C), 130.1 (2C), 130.3, 135.7, 139.0, 139.1, 148.6, 156.1, 160.6; FT-IR (NaCl, cm^{-1}): 33 907 (NH), 2991, 1621, 1552, 1491, 1360, 1275, 1181, 1080, 840, 800; HRMS (TOF-ES): calcd for $C_{23}H_{21}ClN_3$ (M + H) 374.1419, found 374.1423 (1.1 ppm).

7-(3-Chlorophenyl)-2-methyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18fb). Yellowish orange crystals, mp 283–284 °C (toluene); R_f 0.44 (EtOAc/EtOH 3 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.00 (3H, s, Me), 7.37 (1H, d, J = 7.9 Hz, Ar (H-4)), 7.45 (1H, dd, J = 7.9, J = 7.7 Hz, Ar (H-5)), 7.68 (1H, d, J = 9.2 Hz, H-3), 7.75 (1H, d, J = 8.8 Hz, H-9), 7.82 (1H, d, J = 7.7 Hz, Ar (H-6)), 7.92 (1H, s, Ar (H-2)), 8.00 (1H, d, J = 8.8 Hz, H-4), 8.40 (1H, d, J = 9.2 Hz, H-8), 9.51 (1H, br. s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.8, 111.4, 112.1, 117.9, 119.8, 122.0, 124.3, 125.3, 126.1, 127.7, 129.8, 130.0, 132.4, 133.6, 134.5, 134.8, 147.0, 153.6, 162.6; FT-IR (NaCl, cm^{-1}): 3317 (NH), 2985, 2825, 2240, 1641, 1554, 1490, 1383, 1273, 1181, 840, 800; HRMS (TOF-ES): calcd for $C_{19}H_{13}ClN_3$ (M + H) 318.0793, found 318.0787 (1.9 ppm).

7-(3-Chlorophenyl)-2-phenyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18fc). Yellowish orange crystals, mp 150–152 °C (toluene/petroleum ether); R_f 0.75 (EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.51–7.66 (5H, m, ArH), 7.67 (1H, d, J = 9.2 Hz, H-3), 7.79 (1H, d, J = 8.8 Hz, H-9), 7.92–7.95 (2H, m, ArH), 8.33 (1H, dd, J = 8.8, J = 6.8, Hz, ArH), 8.69–8.73 (3H, m, ArH), 13.62 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 112.8, 113.0, 120.33, 121.1, 121.6, 122.9, 123.7, 126.1, 126.5, 126.7, 128.4 (2C), 128.6 (2C), 129.9, 130.5, 131.5, 133.5, 133.8, 134.4, 140.8, 148.9, 154.6, 160.3; FT-IR (NaCl, cm^{-1}): 3518 (NH), 2380, 1690, 1621, 1554, 1551, 1363, 1270, 800, 700; HRMS (TOF-ES): calcd for $C_{24}H_{15}ClN_3$ (M + H) 380.0949, found 380.0942 (1.8 ppm).

7-(4-Methoxyphenyl)-2-methyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18gb). Yellowish orange crystals, mp 277–279 °C (toluene); R_f 0.32 (EtOAc : EtOH 3 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.89 (3H, s, Me), 3.88 (3H, s, OMe), 7.21 (2H, d, J = 8.6 Hz, Ar (H-3,5)), 7.63 (1H, d, J = 9.2 Hz, H-3), 7.75 (1H, d, J = 8.7 Hz, H-9), 8.14 (2H, d, J = 8.6 Hz, Ar (H-2,6)), 8.30 (1H, d, J = 8.7 Hz, H-4), 8.70 (1H, d, J = 9.2 Hz, H-8), 13.43 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 27.6, 55.9, 111.8, 112.8, 115.6 (2C), 118.4, 121.1, 121.7, 122.5, 124.7, 126.1, 129.2 (2C), 132.0, 136.3, 148.8, 155.2, 160.3, 164.0; FT-IR (NaCl, cm^{-1}): 3097 (NH), 2938, 1611, 1556, 1490, 1373, 1253, 1181, 1022; HRMS (TOF-ES): calcd for $C_{20}H_{16}N_3O$ (M + H) 314.1288, found 314.1285 (1.0 ppm).

7-(4-Chlorophenyl)-2-phenyl-6*H*-pyrrolo[2,3,4-*gh*]perimidine (18hc). Yellowish orange crystals, mp 172–174 °C (toluene/petroleum ether); R_f 0.80 (EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.50–7.60 (3H, m, Ph (H-3,4,5)), 7.72 (2H, d, J = 8.6 Hz, Ar (H-3,5)), 7.87 (1H, d, J = 9.2 Hz, H-3), 8.00 (1H, d, J = 8.8 Hz, H-9), 8.24 (2H, d, J = 8.6 Hz, Ar (H-2,6)), 8.33 (1H, dd, J = 8.8, J = 6.8, Hz, ArH), 8.43 (1H, d, J = 8.8 Hz, H-8), 7.82 (1H, d, J = 9.2 Hz, H-4), 13.71 (1H, br. s, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 112.4, 112.9, 119.9, 121.1, 121.6, 123.4, 126.5, 126.9, 128.2 (2C), 128.5 (2C), 128.9 (2C), 129.6 (2C), 129.8, 130.5, 131.6, 133.4, 139.8, 148.7, 154.6, 160.2; FT-IR (NaCl, cm^{-1}): 3350 (NH), 2995, 2850, 2380, 1570, 1361, 1240, 1150, 800, 700; HRMS (TOF-ES): calcd for $C_{24}H_{15}ClN_3$ (M + H) 380.0949, found 380.0944 (1.3 ppm).

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