One-Pot Synthesis of Imidazopyridine Derivatives

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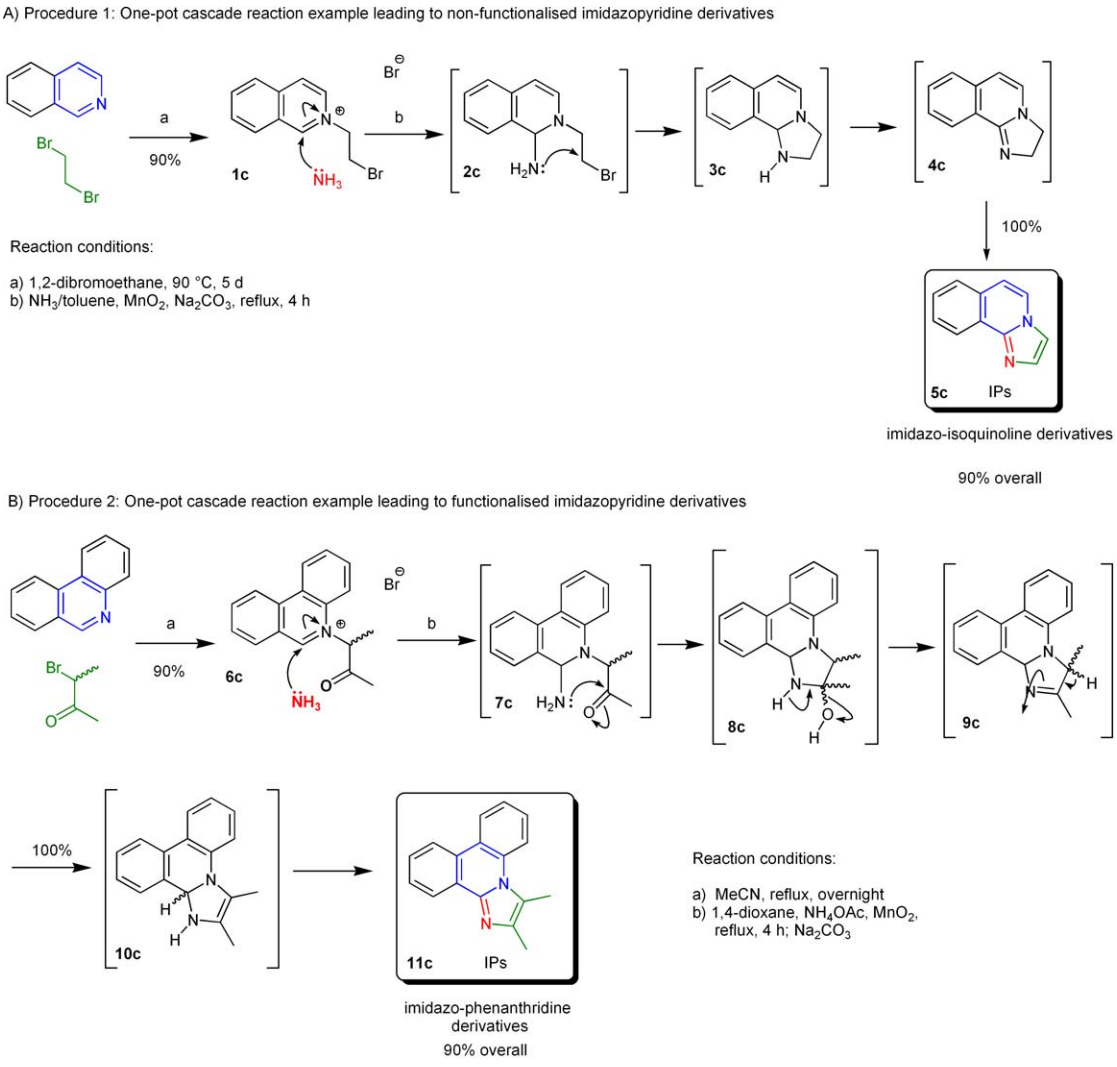
Abstract: Two highly efficient and general one-pot annulation reactions are described for the synthesis of imidazopyridine derivatives (IPs). The two procedures are complementary to each other: Whereas the first one allows the production of simpler IPs, the second leads to IPs with functionalized imidazole moiety. Both methodologies consist of an activation step, which raises the electrophilicity of the N-heterocyclic starting material (i.e., quaternarization of the N-heterocycle), followed by a cascade reaction involving nucleophilic addition, substitution, rearrangement, and oxidation steps. These methodologies can be used in the synthesis of a library of drug-like molecules.

Key words: annulation reaction, one-pot reaction, cascade reaction, N-heterocycles, imidazole derivatives



Scheme 1 The 'one-pot' reaction methodologies leading to nonfunctionalized (Procedure 1) and functionalized (Procedure 2) imidazopyridine derivatives (IPs)

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Introduction

Heterocycles are present as fundamental components in the skeleton of more than half of the biologically active compounds produced by nature.[1] As a consequence, the ongoing interest for developing new versatile and efficient syntheses of heterocycles has always been a thread in the synthetic community. Recently, however, it has become not only a question of what can be synthesized, but how the synthesis can be achieved in the most atom efficient manner. Critical objectives in modern organic chemistry are the improvement of efficiency, avoidance of toxic reagents, reduction of waste, and the responsible treatment of resources.[2,3] Multi-step one-pot reactions, also called cascade reactions, address many of these objectives. As they do not require workup and isolation of intermediates, cascade reactions are indeed cleaner, quicker as well as more efficient than traditional 'step by step methodologies'.[4,5] Therefore, the concept of increasing the molecular complexity while decreasing the number of synthetic steps is becoming more and more attractive.

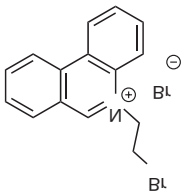
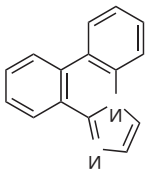
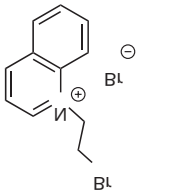
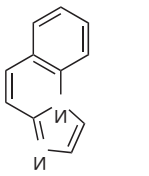
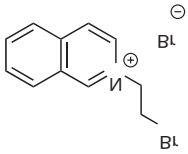
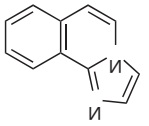
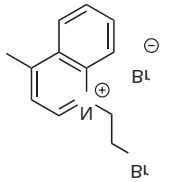
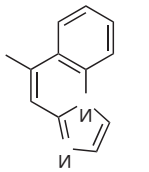
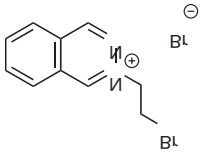
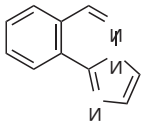
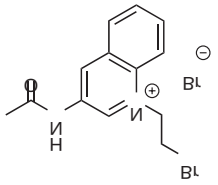
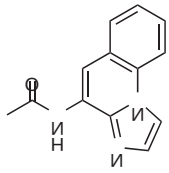
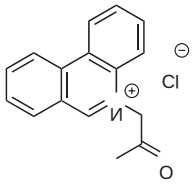
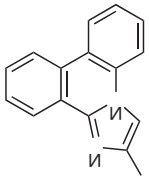
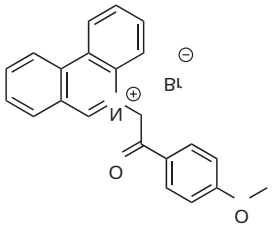
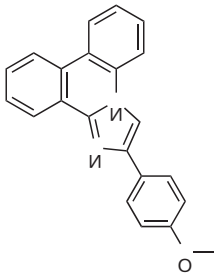
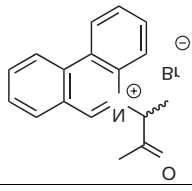
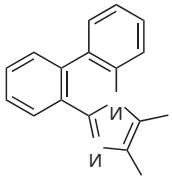
Recently, we have exploited the reactivity of two dielectrophiles, 2-bromoethylphenanthridinium and 2-acetylphenanthridinium derivatives, in two annulation reactions, producing a number of imidazo-based heterocyclic frameworks.[6,7] Also, it was discovered that some of the resulting heterocycles had interesting photochromic properties.[7]

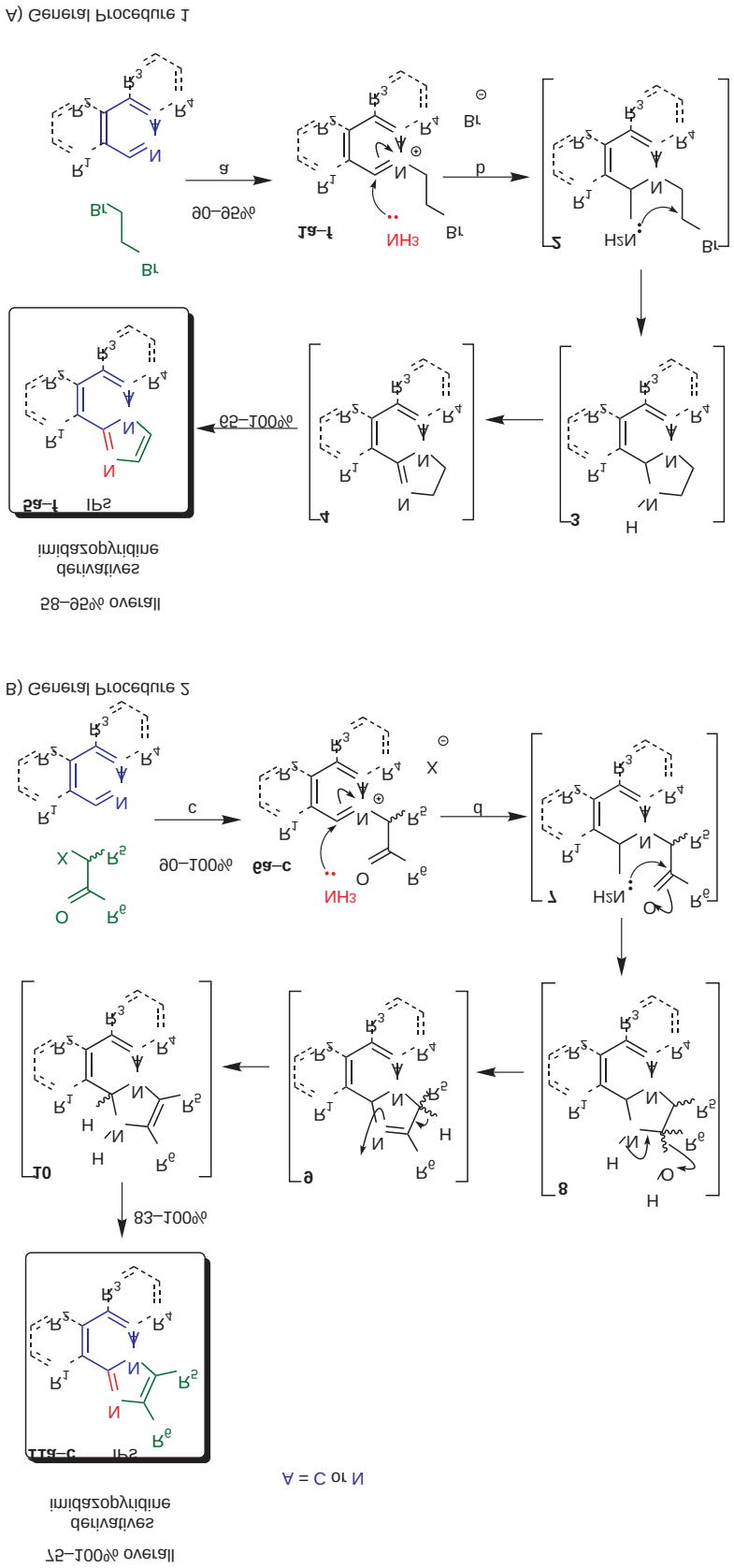
The dielectrophilic starting materials **1** and **6** (Scheme 1 and Scheme 2, A and B) are easily prepared by reacting the corresponding N-heterocycles with an excess of 1,2-dibromoethane or 2-bromoacetyl derivatives respectively (see experimental). Various spectroscopic evidences were gathered to allow us to propose the following reaction mechanism for the two annulation reactions.[6–9]

The synthesis of IP derivatives **5a**–**f** (Procedure 1, Scheme 2A) is initiated in an NH_3/toluene biphasic system via a nucleophilic addition of ammonia onto the iminium moiety of the dielectrophile starting material **1a**–**f**. The resulting secondary amine **2** undergoes a five-membered ring cyclization to give the imidazolidine intermediate **3**, which shifts to the toluene phase to undergo two successive oxidation steps leading to **4** and IPs **5a**–**f**.[6,7]

The synthesis of substituted IP derivatives **11a**–**c** (Procedure 2, Scheme 2B) is achieved by nucleophilic addition of ammonium acetate onto the iminium moiety of the dielectrophile starting materials **6a**–**c**. The resulting secondary amine **7** undertakes a five-membered-ring cyclization to form the imine **9** that rearranges to the stabilized enamine **10** under the slightly acidic reaction conditions. The resulting dihydroimidazole moiety of **10** is subsequently oxidized by MnO_2 in the reaction medium leading to the substituted IPs **11a**–**c**. In both procedures, the final products IPs **5a**–**f** and **11a**–**c** are recovered in a pure form, after removing the inorganic residue of the reactions by filtration (Table 1).

Table 1 Examples of IP Molecules Obtained Using Procedures 1 and 2

Starting material	Product	Yield (%)
1a 	**5a** 	quant.
1b 	**5b** 	65
1c 	**5c** 	quant.
1d 	**5d** 	quant.
1e 	**5e** 	92
1f 	**5f** 	98
6a 	**11a** 	85
6b 	**11b** 	88
6c 	**11c** 	quant.

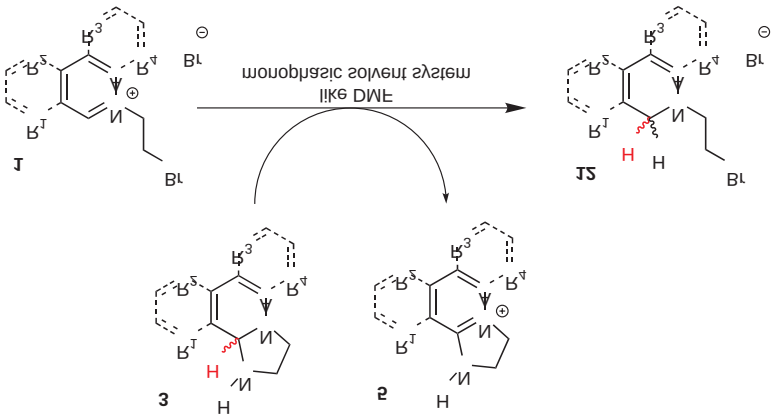


Scheme 2 General scheme for Procedures 1 and 2. *Reagents and conditions*: a) 1,2-dibromoethane, 90 °C, 5 d; b) NH_3/toluene, MnO_2, Na_2CO_3, 4 h, reflux; c) MeCN, reflux, overnight; d) 1,4-dioxane, NH_4OAc, MnO_2, reflux, 4 h; Na_2CO_3.

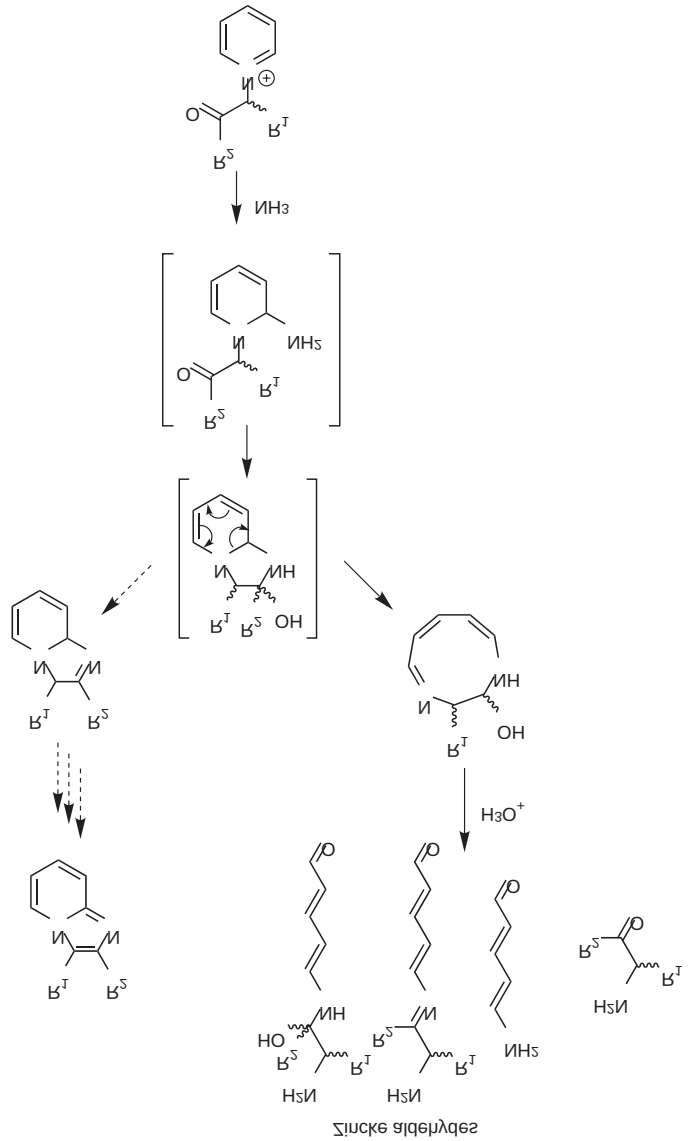
Scope and Limitations

To the best of our knowledge, these procedures have the following limitations:

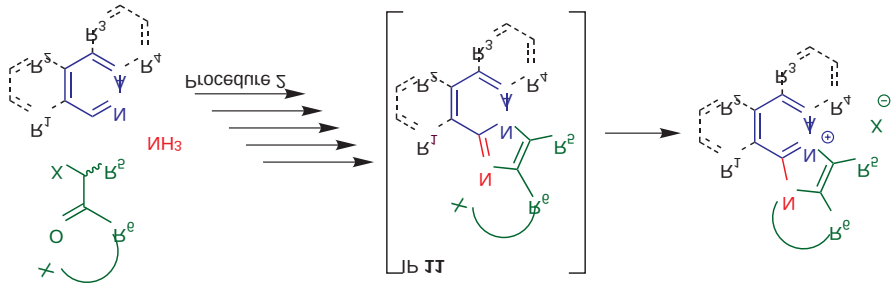
(1) In Procedure 1 (Scheme 2A), the biphasic condition set up between NH_3/toluene is crucial for the reaction to be successful. In these conditions, the ammonia phase partitions the electron-deficient starting material **1** away from the electron-rich intermediates **2** and **3** dissolved in the



Scheme 3 Redox side reaction when the reaction is undertaken in a monophasic system



Scheme 4 Pyridinium starting material cannot be used in the procedures



Scheme 5 Possible extension of the methodology to the annulation of a second cycle

toluene phase, preventing a redox side reaction from occurring (Scheme 3).[8]

(2) In Procedure 2, liquid ammonia could not be used as nucleophile since the carbonyl moiety of **6** enhances the acidity of the adjacent methylene position next to the ammonium moiety and leads, in such basic condition, to an ylide that undertakes cycloaddition side reactions.[10] Instead, ammonium acetate was used as a mild source of ammonia.

(3) The procedures were found to be general for all the N-heterocyclic derivatives tested (quinoline, isoquinoline, phenanthridine, and phthalazine), except for the simpler pyridine. It is believed that in our reaction conditions, the pyridinium salt would undertake a ring-opening side reaction upon addition of ammonia in a similar way to the Zincke reaction[11,12] leading to a mixture of side products (Scheme 4). Therefore, it seems that the N-heterocycle starting materials need at least one flanking aromatic system in order to stabilize at least one of the two double bonds of the N-heterocyclic moiety of intermediates **3** and **8** (Scheme 2).

Finally, further work is ongoing to exploit the nucleophilicity of the imidazole moiety of IP framework **11** (Scheme 5) in a second spontaneous annulation reaction with an electrophilic moiety on R^6.

Procedures

All starting materials and solvents were commercially available (reagent grade) and used as supplied, from Aldrich Chemical Co., without further purification. ^{1}H NMR and ^{13}C NMR were recorded using a Bruker DPX 400 spectrometer operating at 400 and 100 MHz, respectively. Chemical shifts (δ) are given in ppm relative to residual solvent peak. Coupling constants (*J*) are given in Hz. IR spectral analyses were performed on a JASCO 410 spectrophotometer, using a KBr disc; peaks are quoted in wave numbers (cm^{-1}). Mass spectra were obtained using a JEOL JMS 700 spectrometer operating in FAB, EI, or CI mode. Microanalyses were performed on a CE-440 elemental analyzer. Melting points were determined on a digital IA9000 series melting point apparatus, using capillary tubes.

2-Bromoethylpyridinium Derivatives 1a–f; General Procedure

The appropriate pyridine derivative (30 mmol) was dissolved in 1,2-dibromoethane (114.2 g, 50 mL, 608 mmol) and stirred at 90 °C for 5 d. Any precipitate formed during the reaction was recovered daily by filtration. After each filtration, the precipitate was rinsed with an additional amount of 1,2-dibromoethane (5 mL) and the mother liquor stirred at 90 °C until the next filtration. The reaction was complete when no more precipitate was formed. The precipitates were combined and washed with acetone (3 × 20 mL) to give, after drying, the corresponding 2-bromoethylpyridinium derivative **1a–f** as a beige powder.

CAUTION! Products **1a–f** were found to be extreme irritants and allergenics. Appropriate safety protection and utmost care are required while preparing and handling these compounds.

2-Bromoethylquinolinium Bromide (1b)

Compound **1b** (9.05 g, 95%) was isolated as a beige powder; mp 289–290 °C (dec.).

IR (KBr): 3437 (s), 3045 (w), 2981 (m), 2947 (m), 1624 (s), 1599 (m), 1585 (m), 1525 (s), 1489 (w), 1450 (m), 1400 (m), 1363 (s), 1242 (s), 1126 (m), 1161 (m), 1144 (m), 1049 (w), 874 (w), 816 (m), 800 (m), 775 cm^{-1} (s).

^{1}H NMR (D_2O, 400 MHz): δ = 9.24 (d, *J* = 8.4 Hz, 1 H), 9.12 (d, *J* = 8.4 Hz, 1 H), 8.87 (d, *J* = 8.4 Hz, 1 H), 8.33 (d, *J* = 8.4 Hz, 1 H), 8.20 (t, *J* = 8.4 Hz, 1 H), 7.98 (m, 2 H), 5.41 (t, *J* = 5.8 Hz, 2 H), 4.05 (t, *J* = 5.8 Hz, 2 H).

^{13}C NMR (D_2O, 100 MHz): δ = 149.80 (C), 149.20 (CH), 138.08 (C), 136.66 (CH), 131.43 (CH), 130.68 (CH), 130.55 (CH), 121.59 (CH), 118.08 (CH), 58.59 (CH_2), 29.28 (CH_2).

MS (FAB): *m/z* (%) = 237 (M – Br, 98), 236 (100), 209.9 (2), 172 (2), 156 (12), 129.1 (6), 107.2 (2), 89.5 (2), 72.7 (1), 59.9 (1).

Anal. Calcd for $C_{11}H_{11}Br_2N$: C, 41.67; H, 3.49; N, 4.42. Found: C, 41.75; H, 3.50; N, 4.51.

Analytical and spectral data for the other pyridinium derivatives are available in the published literature.[7]

Acetylpyridinium Derivatives 6a–c; General Procedure

The appropriate pyridine derivative (30 mmol) was dissolved in MeCN (40 mL) and the 2-halogenoacetyl derivative (33 mmol) was added to the stirred solution. The mixture was refluxed overnight and left to cool down to r.t. before adding Et_2O (20 mL). The resulting precipitate was recovered by filtration, washed with acetone (3 × 20 mL), and dried under vacuum to give the corresponding acetylpyridinium derivative **6a–c** as a beige powder.

CAUTION! Products **6a–c** were found to be extreme irritants and allergenics. Appropriate safety protection and utmost care are required while preparing and handling these compounds.

5-(2-Oxopropyl)phenanthridinium Chloride (6a)

Compound **6a** (7.17 g, 88%) was isolated as a brown powder; mp 139–141 °C (dec.)

IR (KBr): 3465 (s), 3415 (s), 3238 (w), 3066 (m), 3019 (m), 2963 (m), 2672 (w), 1851 (w), 1735 (s), 1625 (s), 1578 (m), 1533 (m), 1447 (s), 1347 (s), 1264 (m), 1170 (s), 1039 cm^{-1} (w).

^{1}H NMR (D_2O, 400 MHz): δ = 9.50 (s, 1 H), 8.50 (d, *J* = 8.0 Hz, 1 H), 8.45 (d, *J* = 8.0 Hz, 1 H), 8.17 (d, *J* = 8.0 Hz, 1 H), 8.03 (t,

J = 8.0 Hz, 1 H), 7.85 (t, *J* = 9.0 Hz, 1 H), 7.80 (d, *J* = 9.0 Hz, 1 H), 7.74 (m, 2 H), 6.05 (s, 2 H), 2.47 (s, 3 H).

^{13}C NMR (D_2O, 100 MHz): δ = 202.36 (C), 155.52 (CH), 138.76 (CH), 135.03 (C), 133.20 (C), 132.68 (CH), 132.15 (CH), 130.39 (CH), 130.33 (CH), 125.56 (C), 124.40 (CH), 123.03 (C), 122.56 (CH), 118.67 (CH), 68.00 (CH_2), 26.99 (CH_3).

MS (CI): *m*/*z* (%) = 236.13 (M – Cl, 20), 180.12 (40), 139.14 (5), 127.15 (10), 113.17 (15), 85.14 (70), 69.08 (100).

Analytical and spectral data for the other acetylpyridinium derivatives are available in the published literature.[7]

Procedure 1: Imidazopyridines 5a–f

Under stirring, liquid ammonia (40 mL) was added to an open round-bottomed flask containing toluene (40 mL). To the resulting cold biphasic solution was added under stirring the corresponding 2-bromoethylpyridinium bromide derivative **1a–f** (4 mmol), followed by addition of MnO_2 (3.5 g, 40 mmol, 10 equiv) and Na_2CO_3 (2.12 g, 20 mmol, 5 equiv). The mixture was left stirring until complete evaporation of the ammonia phase (i.e., 1 to 2 h, until the mixture reached r.t.) and the toluene was maintained at reflux for 4 h. The mixture was then filtered on glass frit (no. 4) and the residue was rinsed extensively with acetone. Finally, the mother liquor was concentrated to dryness to afford analytically pure imidazopyridines **5a–f**, without further purification.

Imidazo[1,2-*f*]phenanthridine (5a)

Yield: 870 mg (quant); yellow powder; mp 77–78 °C; R_f = 0.3 (EtOAc).

IR (KBr): 3432 (s), 1629 (m), 1532 (m), 1495 (w), 1463 (m), 1439 (m), 1316 (m), 1262 (s), 1104 (s), 803 (m), 719 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.79 (m, 1 H), 8.51 (dd, *J* = 8.0, 1.0 Hz, 1 H), 8.42 (m, 1 H), 8.05 (d, *J* = 1.2 Hz, 1 H), 7.93 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.7 (m, 3 H), 7.68 (d, *J* = 1.2 Hz, 1 H), 7.58 (td, *J* = 8.0, 1.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 142.08 (C), 131.49 (C), 130.45 (C), 129.19 (CH), 129.06 (CH), 128.86 (CH), 127.68 (C), 125.53 (CH), 124.59 (CH), 124.29 (CH), 122.42 (CH), 121.91 (C), 115.94 (CH), 112.15 (CH).

MS (FAB): *m*/*z* (%) = 219.4 (M + 1, 100), 178.7 (3), 164.9 (2), 98.8 (5), 71.2 (7), 57.4 (10).

Anal. Calcd for $C_{15}H_{10}N_2$: C, 82.55; H, 4.62; N, 12.84. Found: C, 82.40; H, 4.65; N, 12.90.

Imidazo[1,2-*a*]quinoline (5b)

Yield: 440 mg (65%); brown oil; R_f = 0.2 (EtOAc).

IR (KBr): 3367 (s), 1613 (s), 1557 (s), 1536 (s), 1487 (m), 1446 (s), 1419 (s), 1317 (s), 1279 (m), 1217 (s), 1088 (s), 870 cm^{-1} (m).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (d, *J* = 1.6 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 7.58 (d, *J* = 1.6 Hz, 1 H), 7.57 (t, *J* = 8.0 Hz, 1 H), 7.50 (d, *J* = 9.6 Hz, 1 H), 7.43 (d, *J* = 9.6 Hz, 1 H), 7.39 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.98 (C), 132.73 (C), 132.52 (CH), 129.15 (CH), 128.78 (CH), 126.06 (CH), 124.76 (CH), 123.43 (C), 117.33 (CH), 115.16 (CH), 111.05 (CH).

MS (EI): *m*/*z* (%) = 168.1 (M^+, 100), 140 (12), 128 (28), 114 (20), 84 (11), 63 (8), 51 (5).

HRMS (EI): *m*/*z* calcd for $C_{11}H_8N_2$: 168.0687 (M^+); found: 168.0689.

Imidazo[2,1-*a*]isoquinoline (5c)

Yield: 670 mg (quant); brown powder; mp 69–70 °C; R_f = 0.25 (EtOAc).

IR (KBr): 3444 (s), 3069 (s), 2743 (s), 2451 (w), 1960 (m), 1934 (m), 1725 (m), 1638 (s), 1607 (s), 1518 (s), 1449 (s), 1385 (s), 1317 (s), 1224 (s), 1141 (s), 1095 (s), 953 (s), 910 (s), 882 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.63 (d, *J* = 8.0 Hz, 1 H), 7.86 (d, *J* = 7.2 Hz, 1 H), 7.65 (d, *J* = 8.0 Hz, 1 H), 7.59 (t, *J* = 8.0 Hz, 1 H), 7.55 (d, *J* = 1.2 Hz, 1 H), 7.54 (t, *J* = 8.0 Hz, 1 H), 7.51 (d, *J* = 1.2 Hz, 1 H), 7.02 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.05 (C), 131.22 (CH), 129.46 (C), 128.30 (CH), 128.25 (CH), 126.94 (CH), 123.85 (C), 123.29 (CH), 123.09 (CH), 114.28 (CH), 113.27 (CH).

MS (EI): *m*/*z* (%) = 168.1 (M^+, 100), 141 (12), 114 (30), 113 (5), 70.5 (10), 63 (5), 49 (3).

HRMS: *m*/*z* calcd for $C_{11}H_8N_2$: 168.0687 (M^+); found: 168.0689.

5-Methylimidazo[1,2-*a*]quinoline (5d)

Yield: 730 mg (quant); brown oil; R_f = 0.2 (EtOAc).

IR (KBr): 3407 (s), 2912 (w), 1621 (s), 1455 (s), 1420 (s), 1325 (s), 1198 (s), 1148 (m), 865 cm^{-1} (m).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.90 (s, 1 H), 7.83 (d, *J* = 7.8 Hz, 1 H), 7.81 (d, *J* = 7.8 Hz, 1 H), 7.55 (t, *J* = 7.8 Hz, 1 H), 7.50 (d, *J* = 1.2 Hz, 1 H), 7.41 (t, *J* = 7.8 Hz, 1 H), 7.32 (d, *J* = 1.2 Hz, 1 H), 2.53 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 133.04 (C), 128.62 (CH), 128.28 (C), 125.81 (CH), 124.59 (CH), 123.88 (C), 121.87 (CH), 116.51 (CH), 115.36 (CH), 110.58 (CH), 19.29 (CH_3).

MS (EI): *m*/*z* (%) = 182.1 (M^+, 100), 181.1 (98), 154.1 (20), 127 (29), 91 (19), 77 (12), 63 (11), 51 (10).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}N_2$: 182.0844 (M^+); found: 182.0840.

Imidazo[2,1-*a*]phthalazine (5e)

Yield: 620 mg (92%); yellow powder; mp 74–75 °C; R_f = 0.3 (EtOAc).

IR (KBr): 3110 (s), 2382 (m), 1984 (m), 1964 (m), 1855 (m), 1721 (m), 1656 (s), 1557 (s), 1523 (s), 1449 (s), 1337 (s), 1240 (s), 1141 (s), 1068 (s), 904 (s) 862 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.59 (s, 1 H), 8.56 (d, *J* = 8.0 Hz, 1 H), 7.85 (d, *J* = 1.6 Hz, 2 H), 7.83 (m, 2 H), 7.65 (t, *J* = 8.0 Hz, 1 H), 7.58 (d, *J* = 1.6 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 145.78 (CH), 133.31 (CH), 131.88 (C), 129.73 (CH), 129.11 (CH), 127.65 (CH), 125.45 (C), 122.86 (C), 122.49 (CH), 117.54 (CH).

MS (CI+): *m*/*z* (%) = 170.12 (M + H, 100), 169.12 (25), 147.11 (20), 131.12 (12), 115.10 (3).

HRMS (EI): *m*/*z* calcd for $C_{10}H_7N_3$: 169.0640 (M^+); found: 169.0637.

***N*-Imidazo[1,2-*a*]quinolin-4-ylacetamide (5f)**

Yield: 880 mg (98%); pale yellow powder; mp 153–154 °C; R_f = 0.2 (EtOAc).

IR (KBr): 3446 (w), 3147 (m), 2924 (m), 2770 (w), 1681 (s), 1557 (s), 1520 (s), 1458 (m), 1421 (s), 1369 (m), 1331 (s), 1310 (m), 1260 (s), 1142 (m), 1003 (w) 872 (m), 846 cm^{-1} (m).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.2 (s, 1 H), 8.61 (s, 1 H), 8.04 (d, *J* = 1.6 Hz, 1 H), 7.81 (t, *J* = 7.8 Hz, 2 H), 7.58 (d, *J* = 1.6 Hz, 1 H), 7.54 (t, *J* = 7.8 Hz, 1 H), 7.45 (t, *J* = 7.8 Hz, 1 H), 2.31 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 130.13 (CH), 129.79 (CH), 128.42 (CH), 121.50 (CH), 119.56 (CH), 114.68 (CH), 75 (CH_3).

MS (EI): *m*/*z* (%) = 225.1 (M^+, 35), 183.1 (100), 155.1 (20), 128 (5), 101 (5), 82.9 (5), 49 (3).

Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.66. Found: C, 69.12; H, 4.83; N, 18.45.

Procedure 2: Imidazopyridines 11a–c

To a stirred suspension of the appropriate acetylpyridinium derivative **6a–c** (4 mmol) in 1,4-dioxane (40 mL) at r.t. was added NH_4OAc (1.23 g, 16 mmol, 4 equiv), followed by MnO_2 (3.5 g, 40 mmol, 10 equiv). The mixture was refluxed for 4 h before adding Na_2CO_3 (4.24 g, 40 mmol, 10 equiv). The suspension was then cooled down to r.t. and Et_2O (10 mL) was added to precipitate any inorganic side products. The mixture was filtered on glass frit (no. 4) and the residue was rinsed extensively with acetone. Finally, the mother liquor was concentrated to dryness to afford analytically pure IPs **11a–c**, without further purification.

2-Methylimidazo[1,2-*f*]phenanthridine (11a)

Yield: 790 mg (85%); brown powder; mp 130–131 °C; R_f = 0.4 (EtOAc).

IR (KBr): 3372 (w), 3146 (m), 3067 (w), 2915 (m), 1607 (m), 1591 (s), 1550 (s), 1591 (s), 1550 (s), 1530 (s), 1460 (s), 1433 (s), 1392 (s), 1349 (m), 1313 (s) 1233 (w), 1109 (m), 1036 cm^{-1} (w).

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.46 (d, *J* = 8.0 Hz, 1 H), 8.14 (d, *J* = 8.0 Hz, 1 H), 8.10 (d, *J* = 8.0 Hz, 1 H), 7.48 (t, *J* = 8.0 Hz, 1 H), 7.44 (m, 3 H), 7.34 (t, *J* = 8.0 Hz, 1 H), 7.22 (t, *J* = 8.0 Hz, 1 H), 2.38 (s, 3 H).

^{13}C NMR $CDCl_3$, 100 MHz): δ = 141.73 (C), 140.86 (C), 131.39 (C), 128.55 (CH), 128.23 (CH), 127.21 (C), 124.51 (CH), 123.89 (CH), 123.86 (CH), 123.22 (C), 122.44 (CH), 122.20 (CH), 121.26 (CH), 115.49 (CH), 108.86 (CH), 14.31 (CH_3).

MS (EI): *m*/*z* (%) = 232.1 (M^+, 100), 204.1 (10), 178.1 (11), 177.1 (10), 116 (15), 82.9 (12), 76 (5), 49 (5).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{12}N_2$: 232.1000 (M^+); found: 232.0998.

2-(4-Methoxyphenyl)imidazo[1,2-*f*]phenanthridine (11b)

Yield: 1.14 g (88%); beige powder; mp 160–161 °C; R_f = 0.7 (EtOAc).

IR (KBr): 3442 (s), 3143 (w), 2939 (w), 2837 (w), 2898 (m), 1561 (m), 1462 (s), 1436 (s), 1399 (m), 1295 (w), 1245 (s), 1033 (s), 943 (w), 828 cm^{-1} (s).

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.69 (d, *J* = 7.2 Hz, 1 H), 8.40 (d, *J* = 8.0 Hz, 1 H), 8.32 (d, *J* = 7.2 Hz, 1 H), 8.09 (s, 1 H), 7.91 (d, *J* = 8.8 Hz, 2 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.57 (m, 3 H), 7.44 (t, *J* = 7.2 Hz, 1 H), 6.94 (d, *J* = 8.8 Hz, 2 H), 3.80 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.35 (C), 144.03 (C), 142.61 (C), 131.70 (C), 128.84 (CH), 128.58 (CH), 128.51 (CH), 127.52 (C), 127.05 (CH), 126.75 (C), 124.94 (CH), 124.45 (CH), 124.21 (C), 123.59 (C), 123.59 (C), 122.35 (CH), 121.76 (C), 115.80 (CH), 114.18 (CH), 106.69 (CH), 55.36 (CH_3).

MS (EI): *m*/*z* = 324.1 (M^+, 100), 309.1 (22), 281.1 (20), 246.1 (25), 245.1 (18), 179.1 (20), 178.1 (15), 162.1 (11), 140.1 (10), 69 (10), 44 (50).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}ON_2$: 324.1263 (M^+); found: 324.1264.

2,3-Dimethylimidazo[1,2-*f*]phenanthridine (11c)

Yield: 985 mg (~100%); beige powder; mp 135–136 °C; R_f = 0.4 (EtOAc).

IR (KBr): 3383 (m), 3054 (m), 2975 (m), 2919 (m), 2858 (m), 1945 (m), 1664 (m), 1595 (s), 1573 (s), 1531 (s), 1542 (s), 1398 (s), 1372 (s), 1040 (m), 945 (m), 817 cm^{-1} (m).

^1H NMR ($CDCl_3$, 400 MHz): δ = 8.61 (d, *J* = 8.0 Hz, 1 H), 8.37 (d, *J* = 8.0 Hz, 1 H), 7.47 (t, *J* = 8.0 Hz,1 H), 7.39 (t, *J* = 8.0 Hz, 1 H), 2.75 (s, 3 H), 2.39 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 140.90 (C), 136.97 (C), 133.80 (C), 128.58 (CH), 128.44 (CH), 128.22 (CH), 127.13 (C), 124.56 (CH), 124.18 (CH), 124.13 (CH), 122.49 (C), 122.05 (C), 120.88 (C), 116.29 (CH), 14.30 (CH_3), 12.92 (CH_3).

MS (EI): *m*/*z* (%) = 246.1 (M^+, 100), 245.1 (50), 231.1 (10), 204.1 (10), 178.1 (10), 177.1 (10), 123.1 (9), 122.1 (3), 84 (4), 82.9 (4), 49 (4).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{14}N_2$: 246.1157 (M^+); found: 246.1158.

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