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ORIGINAL PAPER

Synthesis of imidazo[4,5-*a*]acridones and imidazo[4,5-*a*]acridines as potential antibacterial agents

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Abstract New imidazo[4,5-*a*]acridone derivatives were synthesized from the rearrangement of 3*H*-imidazo [4′,5′:3,4]benzo[*c*]isoxazoles. New imidazo[4,5-*a*]acridines were obtained from the reaction of imidazo[4,5-*a*]acridones in boiling $POCl_3$. All of these compounds exhibited antimicrobial activities comparable to streptomycin as reference drug.

Keywords Imidazo[4, 5-*a*]acridone · Imidazo[4, 5-*a*]acridine · Antibacterial agents · Tanasescu reaction

Introduction

Acridine derivatives, such as acridones, pyridoacridines, and imidazoacridines, are one the oldest classes of bioactive compounds that are widely used as antibacterial [1, 2], antiviral [3, 4], antiprion [5], and antimalarial [6–10] agents. Some work in these areas continues, but recent research has focused mainly on their utility as anticancer [11, 12] and antitumor [13, 14] drugs. This is because of the ability of the acridine and acridone chromophore to intercalate within the double-stranded DNA structure and inhibit topoisomerase enzymes. Also acridines with a suitable functionalization can be used as a fluorophore for fluorescence lifetime studies [15] and fluorescent sensors for anions [16].

There are several methods for the synthesis of these useful compounds, including the Bernthsen reaction [17] as the oldest method for the synthesis of acridines. Other reactions by Ullmann [18], Meyer [19], Koller [20], and several new methods [21–26] have also been cited in the literature. In 1937, Tanasescu and Suciu [27] described a synthetic approach to acridones through rearrangement of benzo[*c*]isoxazoles (anthranil) in the presence of concentrated sulfuric acid containing nitrous acid as catalyst. A literature survey disclosed that 3*H*-imidazo[4′,5′:3,4] benzo[*c*]isoxazoles have not been converted to imidazo[4,5-*a*]acridones by the Tanasescu reaction yet. Owing to our growing interest in the synthesis of bioactive heterocycles [28–33] and evaluation of their biological activities, we became interested in examining the transformation of 3*H*-imidazo[4′,5′:3,4]benzo[*c*]isoxazoles **3a–f** to their new imidazo[4,5-*a*]acridones **4a–f** by this method.

Results and discussion

Chemistry

The new key compounds **3a–f** were obtained via the nucleophilic substitution of hydrogen of *N*-alkyl-5-nitrobenzimidazoles **1a–c** with arylacetonitriles **2a**, **b** in basic MeOH solution [34, 35] (Scheme 1).

Compounds **3a–f** underwent rearrangement in high yields to their corresponding imidazo[4,5-*a*]acridones **4a–f** in concentrated sulfuric acid containing nitrous acid at room temperature (Scheme 2).

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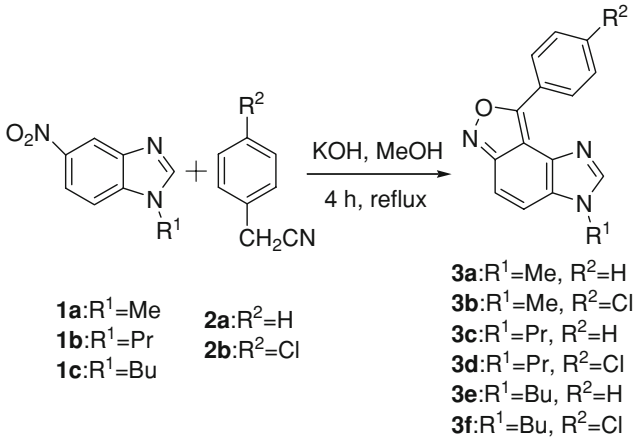
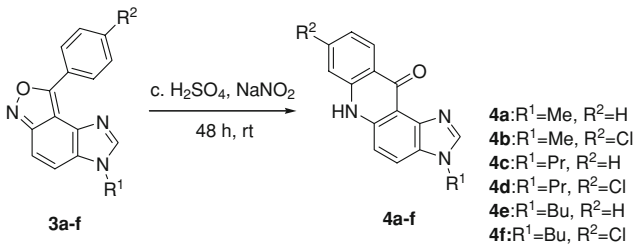


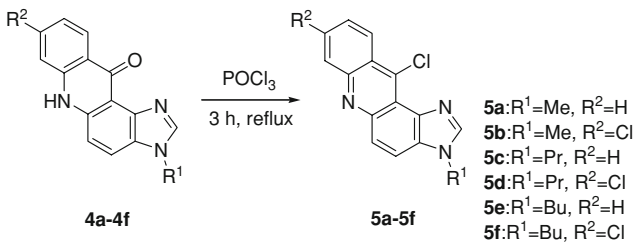
Scheme 1



Scheme 2

The latter compounds decomposed above 300 °C, and they were very insoluble in organic solvents except DMF and DMSO. The structural assignments of compounds **4a–f** were based on the analytical and spectral data. For example, in the ^{1}H NMR spectrum of **4a**, the signal at 11.79 ppm is attributed to one exchangeable proton (NH group). Moreover, the FT-IR spectrum of **4a** in KBr showed two absorption bands at 3,420 and 1,660 cm^{-1} assignable to NH and C=O groups. All this evidence plus microanalytical data strongly support the cyclic structure of **4a**.

Treatment of imidazo[4,5-*a*]acridones **4a–f** in boiling $POCl_3$ gave imidazo[4,5-*a*]acridines **5a–f** in excellent yields (Scheme 3).



Scheme 3

Biological activities

The synthesized compounds **4a–f** and **5a–f** were screened for antibacterial activity against *Escherichia coli HB101* (*BA-7601C*), *Staphylococcus aureus* (*PTCC-1074*), *Pseudomonas aeruginosa* (*PTCC 1431*), *and Bacillus subtilis* (*PTCC 1365*) by filter paper disk diffusion method [36, 37]. Mueller-Hinton agar media were sterilized (15 min at 121 °C) and poured into the plates to a uniform depth of 5 mm and allowed to solidify. The microbial suspension (15×10^8 CFU mL^{-1}) (0.5 McFarland Nephelometery Standards) was streaked over the surface of media using a sterile cotton swab (15 min at 180 °C) to ensure confluent growth of the organisms. The bacteria were grown on agar media (pH = 7.4 ± 0.2 at 25 °C). The disks used were Whatman no. 1 filter papers (6.25 mm in diameter). Stock solutions of compounds **4a–f** and **5a–f** with dimethylsulfoxide (DMSO) were prepared and diluted with ethanol 96% (50–250 μg cm^{-3}). The prepared discs were impregnated with these prepared solutions of compounds **4a–f** and **5a–f** and then placed on the previously inoculated agar surface. The plates were inverted and incubated for 24 h at 37 °C. The negative control of inhibition zones of growth for ethanol and DMSO were studied. All the experiments were conducted three times. Antimicrobial activity was indicated by the assessment of clear inhibition zones around the spot, and the disk diameters were compared with streptomycin (10 μg cm^{-3}) as standard drug. Solvent effects and growth controls were kept, and the zones of inhibition in millimeter were studied as a criterion for its antimicrobial activity. The results of these evaluations are given in Table 1.

As can be concluded from the data in Table 1, imidazo[4,5-*a*]acridines **5a–f** have shown the higher sensitivity against *Escherichia coli HB101* (*BA-7601C*), *Staphylococcus aureus* (*PTCC-1074*), *Pseudomonas aeruginosa* (*PTCC 1431*), and *Bacillus subtilis* (*PTCC 1365*) than imidazo[4,5-*a*]acridones **4a–f**. Compounds **5b**, **d**, and **f** have shown the highest sensitivity against *Escherichia coli HB101* (*BA-7601C*), *Staphylococcus aureus* (*PTCC-1074*), *Pseudomonas aeruginosa* (*PTCC 1431*), and *Bacillus subtilis* (*PTCC 1365*). All the other compounds were found to exhibit moderate activities against the mentioned organisms. These results clearly demonstrate that halogen substituted imidazo[4,5-*a*]acridines exhibited better activity than other substituted imidazo[4,5-*a*]acridones and imidazo[4,5-*a*]acridines.

Experimental

Melting points were recorded on an Electrothermal type 9100 melting point apparatus. The IR spectra were

Table 1 Antibacterial data of **4a–f** and **5a–f**

Compound	*Escherichia coli HB101 (BA-7601C)*	*Pseudomonas aeruginosa (PTCC-1431)*	*Staphylococcus aureus (PTCC 1074)*	*Bacillus sabtilis (PTCC 1365)*
4a	12 (+)	13 (+)	12 (+)	12 (+)
4b	14 (+)	14 (+)	13 (+)	14 (+)
4c	12 (+)	12.5 (+)	12 (+)	12 (+)
4d	12 (+)	12.5 (+)	12 (+)	13 (+)
4e	12 (+)	12 (+)	12 (+)	13 (+)
4f	13 (+)	14 (+)	13 (+)	14 (+)
5a	13 (+)	13.5 (+)	13 (+)	13 (+)
5b	15 (++)	15 (++)	15 (+)	14 (+)
5c	14 (+)	15 (++)	14 (+)	14 (+)
5d	16 (++)	17 (++)	16 (++)	16 (++)
5e	14 (+)	15 (++)	14 (+)	14 (+)
5f	17 (++)	17 (++)	16 (++)	17 (++)
Streptomycin (standard)	17	10	15	10

Zones of inhibition in millimeters

(++) Highly sensitive = inhibition zone 15

(+) Moderately sensitive = inhibition zone 12–14

obtained on a 4300 Shimadzu spectrometer, and only noteworthy absorptions are listed. The ^{13}C NMR (125 MHz) spectra were recorded on a Bruker Avance DRX-500 spectrometer. The ^{1}H NMR (100 MHz) spectra were recorded on a Bruker AC 100 spectrometer. Chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hz. The mass spectra were scanned on a Varian Mat CH-7 at 70 eV. Elemental analysis was performed on a Thermo Finnigan Flash EA microanalyzer, and results agreed favorably with calculated values. Compounds **1a–c** [38] were obtained according to published methods. Other reagents were commercially available.

*General procedure for the synthesis of **3a–f** from **1a–c***

Compounds **1a–c** (10 mmol) and **2a**, **b** (12 mmol) were added with stirring to a solution of 20 g KOH (357 mmol) in 80 cm^3 methanol. The mixture was refluxed with stirring for 4 h and then poured into water. The precipitate was collected by filtration, washed with water, and air-dried to give **3a–f**.

3-Methyl-8-phenyl-3H-imidazo[4′,5′:3,4]benzo[c]isoxazole (**3a**, $C_{15}H_{11}N_3O$)

Compound **3a** was obtained as pale yellow crystals (methanol), yield 81%, m.p.: 266–268 °C; ^{1}H NMR (100 MHz, $CDCl_3$): $\delta = 3.43$ (s, 3H), 7.41 (d, $J = 8.0$ Hz, 1H), 7.55–7.81 (m, 7H) ppm; MS (70 eV): $m/z = 249$ (M+).

8-(4-Chlorophenyl)-3-methyl-3H-imidazo[4′,5′:3,4]benzo[c]isoxazole (**3b**, $C_{15}H_{10}ClN_3O$)

Compound **3b** was obtained as pale yellow crystals (methanol), yield 86%, m.p.: 292–294 °C; ^{1}H NMR (100 MHz, $CDCl_3$): $\delta = 3.92$ (s, 3H), 7.42 (d, $J = 9.5$ Hz, 1H), 7.58 (d, $J = 9.5$ Hz, 1H), 7.67 (d, $J = 8.8$ Hz, 2H), 7.89 (s, 1H), 8.87 (d, $J = 8.8$ Hz, 2H) ppm; MS (70 eV): $m/z = 285$ (M + 2).

8-Phenyl-3-propyl-3H-imidazo[4′,5′:3,4]benzo[c]isoxazole (**3c**, $C_{17}H_{15}N_3O$)

Compound **3c** was obtained as pale yellow crystals (ethanol), yield 73%, m.p.: 119–122 °C; ^{1}H NMR (100 MHz, $CDCl_3$): $\delta = 0.99$ (t, $J = 7.0$ Hz, 3H), 1.77–2.12 (m, 2H), 4.21 (t, $J = 7.0$ Hz, 2H), 7.47–7.69 (m, 6H), 7.89 (s, 1H), 8.89 (d, $J = 8.0$ Hz, 1H) ppm; MS (70 eV): $m/z = 277$ (M+).

8-(4-Chlorophenyl)-3-propyl-3H-imidazo[4′,5′:3,4]benzo[c]isoxazole (**3d**, $C_{17}H_{14}ClN_3O$)

Compound **3d** was obtained as pale yellow crystals (ethanol), yield 67%, m.p.: 158–160 °C; ^{1}H NMR (100 MHz, $CDCl_3$): $\delta = 1.05$ (t, $J = 7.3$ Hz, 3H), 1.85–2.21 (m, 2H), 4.18 (t, $J = 7.3$ Hz, 2H), 7.40 (d, $J = 9.5$ Hz, 1H), 7.56 (d, $J = 9.5$ Hz, 1H), 7.62 (d, $J = 8.6$ Hz, 2H), 7.86 (s, 1H), 8.89 (d, $J = 8.6$ Hz, 2H) ppm; MS (70 eV): $m/z = 313$ (M + 2).

3-Butyl-8-phenyl-3H-imidazo[4′,5′:3,4]benzo[c]isoxazole (**3e**, $C_{18}H_{17}N_3O$)

Compound **3e** was obtained as pale yellow crystals (ethanol), yield 82%, m.p.: 110–112 °C; ^{1}H NMR

(100 MHz, $CDCl_3$): $\delta = 0.97$ (t, $J = 7.0$ Hz, 3H), 1.21–1.56 (m, 2H), 1.81–2.09 (m, 2H), 4.23 (t, $J = 7.0$ Hz, 2H), 7.47–7.69 (m, 6H), 7.88 (s, 1H), 8.89 (d, $J = 8.0$ Hz, 1H) ppm; MS (70 eV): $m/z = 291$(M+).

3-Butyl-8-(4-chlorophenyl)-3H-imidazo[4′,5′:3,4]benzo[c]isoxazole (**3f**, $C_{18}H_{16}ClN_3O$)
Compound **3f** was obtained as pale yellow crystals (ethanol), yield 83%, m.p.: 157–159 °C; ^{1}H NMR (100 MHz, $CDCl_3$): $\delta = 0.98$ (t, $J = 7.0$ Hz, 3H), 1.23–1.58 (m, 2H), 1.82–2.10 (m, 2H), 4.24 (t, $J = 7.0$ Hz, 2H), 7.41 (d, $J = 9.5$ Hz, 1H), 7.56(d, $J = 9.5$ Hz, 1H), 7.61 (d, $J = 8.6$ Hz, 2H), 7.90 (s, 1H), 8.87 (d, $J = 8.6$ Hz, 2H) ppm; MS (70 eV): $m/z = 327$ (M + 2).

*General procedure for the synthesis of **4a–f** from **3a–f***

Sodium nitrite (5 g, 150 mmol) was added with stirring over half an hour period to a solution of **3a–f** (7 mmol) in 100 cm^3 concentrated sulfuric acid maintained at −10 °C. After the addition was completed, the mixture was allowed to warm to room temperature and to stand at room temperature for 17 h. After pouring this mixture into 500 cm^3 crushed ice and water, the solid that precipitated was removed by filtration, was washed with water, and dried to give **4a–f**.

3-Methyl-6,11-dihydro-3H-imidazo[4,5-a]acridin-11-one (**4a**, $C_{15}H_{11}N_3O$)
Compound **4a** was obtained as yellow crystals (EtOH + CH_3CN), yield 90%, m.p.: >300 °C (decomp); ^{1}H NMR (100 MHz, DMSO-d_6): $\delta = 3.92$ (s, 3H), 7.41 (d, $J = 8.9$ Hz, 1H), 7.45–7.85 (m, 5H), 8.33 (s, 1H), 11.79 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 175.1$, 141.6, 140.3, 140.6, 129.1, 127.7, 126.7, 122.4, 120.0, 119.3, 117.9, 117.5, 117.0, 107.7, 33.3 ppm; IR (KBr): $\bar{\nu} = 3{,}420$ (NH), 1,660 (C=O) cm^{-1}; MS (70 eV): $m/z = 249$ (M+).

8-Chloro-3-methyl-6,11-dihydro-3H-imidazo[4,5-a]acridin-11-one (**4b**, $C_{15}H_{10}ClN_3O$)
Compound **4b** was obtained as yellow crystals (EtOH + CH_3CN), yield 85%, m.p.: >300 °C (decomp); ^{1}H NMR (100 MHz, DMSO-d_6): $\delta = 4.04$ (s, 3H), 7.32 (dd, $J = 9.5$ Hz, $J = 2.1$ Hz, 1H), 7.78 (d, $J = 9.4$ Hz, 1H), 7.85 (d, $J = 9.4$ Hz, 1H), 8.12 (d, $J = 2.1$ Hz, 1H), 8.25 (d, $J = 9.5$ Hz, 1H) 8.45 (s, 1H), 11.83 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 175.1$, 141.9, 141.4, 140.6, 138.2, 127.0, 126.4, 122.2, 119.9, 119.2, 117.9, 117.3, 117.0, 107.4, 33.4 ppm; IR (KBr): $\bar{\nu} = 3{,}415$ (NH), 1,660 (C=O) cm^{-1}; MS (70 eV): $m/z = 285$ (M + 2).

3-Propyl-6,11-dihydro-3H-imidazo[4,5-a]acridin-11-one (**4c**, $C_{17}H_{15}N_3O$)
Compound **4c** was obtained as yellow crystals (EtOH + CH_3CN), yield 80%, m.p.: >300 °C (decomp); ^{1}H NMR (100 MHz, DMSO-d_6): $\delta = 0.79$ (t, $J = 7.0$ Hz, 3H), 1.71–2.06 (m, 2H), 4.26 (t, $J = 7.0$ Hz, 2H), 7.15–8.15 (m, 6H), 8.30 (s, 1H), 11.86 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 175.0$, 140.2, 139.4, 138.5, 129.3, 127.1, 126.1, 122.1, 119.5, 118.8, 117.2, 117.0, 116.6, 106.9, 52.5, 21.6, 10.0 ppm; IR (KBr): $\bar{\nu} = 3{,}415$ (NH), 1,660 (C=O) cm^{-1}; MS (70 eV): $m/z = 277$ (M+).

8-Chloro-3-propyl-6,11-dihydro-3H-imidazo[4,5-a]acridin-11-one (**4d**, $C_{17}H_{14}ClN_3O$)
Compound **4d** was obtained as yellow crystals (EtOH + CH_3CN), yield 73%, m.p.: >300 °C (decomp); ^{1}H NMR (100 MHz, DMSO-d_6): $\delta = 0.83$ (t, $J = 7.1$ Hz, 3H), 1.69–1.95 (m, 2H), 4.29 (t, $J = 7.1$ Hz, 2H), 7.25 (dd, $J = 9.5$ Hz, $J = 2.1$ Hz, 1H), 7.68 (d, $J = 9.4$ Hz, 1H), 7.75 (d, $J = 9.4$ Hz, 1H), 8.17 (d, $J = 2.1$ Hz, 1H), 8.25 (d, $J = 9.5$ Hz, 1H), 8.35 (s, 1H), 11.80 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 175.1$, 140.2, 140.0, 139.56, 137.4, 128.4, 126.1, 121.9, 119.1, 119., 117.7, 117.1, 115.2, 106.7, 52.8, 21.6, 10.1 ppm; IR (KBr): $\bar{\nu} = 3{,}415$ (NH), 1,660 (C=O) cm^{-1}; MS (70 eV): $m/z = 313$ (M + 2).

3-Butyl-6,11-dihydro-3H-imidazo[4,5-a]acridin-11-one (**4e**, $C_{18}H_{17}N_3O$)
Compound **4e** was obtained as yellow crystals (EtOH + CH_3CN), yield 87%, m.p.: >300 °C (decomp); ^{1}H NMR (100 MHz, DMSO-d_6): $\delta = 0.87$ (t, $J = 7.0$ Hz, 3H), 1.16–1.51 (m, 2H), 1.75–2.03 (m, 2H), 4.30 (t, $J = 7.0$ Hz, 2H), 7.10–8.10 (m, 6H), 8.31 (s, 1H), 11.81 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 175.1$, 140.3, 138.9, 138.0, 129.3, 127.2, 126.2, 122.1, 119.5, 118.9, 117.3, 117.0, 116.6, 107.0, 49.7, 30.8, 20.4, 11.1 ppm; IR (KBr): $\bar{\nu} = 3{,}415$ (NH), 1,660 (C=O) cm^{-1}; MS (70 eV): $m/z = 291$(M+).

3-Butyl-8-chloro-6,11-dihydro-3H-imidazo[4,5-a]acridin-11-one (**4f**, $C_{18}H_{16}ClN_3O$)
Compound **4f** was obtained as yellow crystals (EtOH + CH_3CN), yield 80%, m.p.: >300 °C (decomp); ^{1}H NMR (100 MHz, DMSO-d_6): $\delta = 0.86$ (t, $J = 6.5$ Hz, 3H), 1.13–1.48 (m, 2H), 1.73–2.01 (m, 2H), 4.33 (t, $J = 6.5$ Hz, 2H), 7.21(dd, $J = 9.5$ Hz, $J = 2.1$ Hz, 1H), 7.58 (d, $J = 9.4$ Hz, 1H), 7.65 (d, $J = 9.4$ Hz, 1H), 8.15 (d, $J = 2.1$ Hz, 1H), 8.25 (d, $J = 9.5$ Hz, 1H) 8.30 (s, 1H), 11.91 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 175.1$, 140.3, 139.7, 139.1, 137.4, 128.4, 126.2, 121.9, 119.2, 119.0, 117.7, 117.2, 115.2, 107.4, 49.9, 30.7, 20.4,

11.1 ppm; IR (KBr): $\bar{\nu}$ = 3,415 (NH), 1,660 (C=O) cm^{-1}; MS (70 eV): *m*/*z* = 327 (M + 2).

General procedure for the synthesis of ***5a–f*** *from* ***4a–f***

A mixture of **4a–f** (4 mmol) and 6 cm^3 $POCl_3$ was refluxed with stirring for 3 h. After cooling to rt, the reaction mixture was poured onto crushed ice and neutralized with ammonia solution. The product was extracted with 2 × 50 cm^3 EtOAc. The extract was dried and evaporated to give **5a–f**.

3-Methyl-3H-imidazo[4,5-a]acridine (**5a**, $C_{15}H_{10}ClN_3$)
Compound **5a** was obtained as yellow crystals (CH_3CN), yield 75%, m.p.: 240–241 °C; ^{1}H NMR (100 MHz, $CDCl_3$): δ = 4.02 (s, 3H), 7.61 (d, *J* = 8.9 Hz, 1H), 7.65–8.05 (m, 5H), 8.65 (dd, *J* = 9.0 Hz, *J* = 2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9, 156.7, 150.3, 142.6, 134.6, 131.6, 131.3, 130.7, 127.4, 125.8, 122.0, 119.0, 111.7, 110.6, 33.2 ppm; MS (70 eV): *m*/*z* = 267 (M+).

8-Chloro-3-methyl-3H-imidazo[4,5-a]acridine
(**5b**, $C_{15}H_9Cl_2N_3$)
Compound **5b** was obtained as yellow crystals (CH_3CN), yield 80%, m.p.: 282–284 °C; ^{1}H NMR (100 MHz, $CDCl_3$): δ = 4.05 (s, 3H), 7.62 (dd, *J* = 9.5 Hz, *J* = 2.1 Hz, 1H), 7.85 (d, *J* = 9.4 Hz, 1H), 8.03 (d, *J* = 9.4 Hz, 1H), 8.13 (s, 1H), 8.30 (d, *J* = 2.1 Hz, 1H), 8.62 (d, *J* = 9.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9, 157.0, 150.3, 142.6, 139.7, 134.6, 131.8, 130.9, 127.9, 125.9, 121.7, 119.1, 111.6, 110.9, 33.3 ppm; MS (70 eV): *m*/*z* = 304 (M + 2).

3-Propyl-3H-imidazo[4,5-a]acridine (**5c**, $C_{17}H_{14}ClN_3$)
Compound **5c** was obtained as yellow crystals (CH_3CN), yield 79%, m.p.: 185–187 °C; ^{1}H NMR (100 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.2 Hz, 3H), 1.88–2.11 (m, 2H), 4.30 (t, *J* = 7.2 Hz, 2H), 7.68–8.32 (m, 6H), 8.67 (dd, *J* = 9.0 Hz, *J* = 2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.7, 156.6, 148.3, 142.3, 134.6, 131.7, 130.8, 130.3, 127.0, 125.6, 121.5, 118.8, 111.5, 110.5, 52.3, 21.6, 10.1 ppm; MS (70 eV): *m*/*z* = 295 (M+).

8-Chloro-3-propyl-3H-imidazo[4,5-a]acridine
(**5d**, $C_{17}H_{13}Cl_2N_3$)
Compound **5d** was obtained as yellow crystals (CH_3CN), yield 80%, m.p.: 205–207 °C; ^{1}H NMR (100 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.1 Hz, 3H), 1.81–207 (m, 2H), 4.32 (t, *J* = 7.1 Hz, 2H), 7.60 (dd, *J* = 9.5 Hz, *J* = 2.1 Hz, 1H), 7.90 (d, *J* = 9.4 Hz, 1H), 8.10 (d, *J* = 9.4 Hz, 1H), 8.25 (s, 1H), 8.31 (d, *J* = 2.1 Hz, 1H), 8.64 (d, *J* = 9.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.8, 156.9, 148.8, 142.5, 139.7, 134.1, 131.7, 130.9, 128.0, 125.7, 121.5, 119.1, 111.7, 110.8, 52.5, 21.5, 10.2 ppm; MS (70 eV): *m*/*z* = 332 (M + 2).

3-Butyl-3H-imidazo[4,5-a]acridine (**5e**, $C_{18}H_{16}ClN_3$)
Compound **5e** was obtained as yellow crystals (CH_3CN), yield 75%, m.p.: 172–174 °C; ^{1}H NMR (100 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.0 Hz, 3H), 1.26–1.61 (m, 2H), 1.88–2.16 (m, 2H), 4.35 (t, *J* = 7.0 Hz, 2H), 7.69–8.34 (m, 6H), 8.68 (dd, *J* = 9.0 Hz, *J* = 2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.7, 156.5, 147.7, 141.9, 134.5, 131.6, 130.8, 130.3, 126.9, 125.6, 121.4, 118.7, 111.2, 110.1, 49.7, 30.8, 20.4, 11.1 ppm; MS (70 eV): *m*/*z* = 309 (M+).

3-Butyl-8-chloro-3H-imidazo[4,5-a]acridine
(**5f**, $C_{18}H_{15}Cl_2N_3$)
Compound **5f** was obtained as yellow crystals (CH_3CN), yield 82%, m.p.: 183–185 °C; ^{1}H NMR (100 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 6.8 Hz, 3H), 1.25–1.60 (m, 2H), 1.73–2.01 (m, 2H), 4.38 (t, *J* = 6.8 Hz, 2H), 7.62 (dd, *J* = 9.5 Hz, *J* = 2.1 Hz, 1H), 7.91 (d, *J* = 9.4 Hz, 1H), 8.11 (d, *J* = 9.4 Hz, 1H), 8.21 (s, 1H), 8.41 (d, *J* = 2.1 Hz, 1H), 8.62 (d, *J* = 9.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9, 156.7, 148.6, 142.6, 139.4, 133.9, 131.6, 130.9, 127.9, 125.7, 121.3, 119.0, 111.5, 110.2, 49.8, 30.8, 20.4, 11.1 ppm; MS (70 eV): *m*/*z* = 346 (M + 2).

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