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NHC as the Guiding Factor in a Copper-Catalyzed Intramolecular C Arylation of Pyrrolylimidazolium Salts: Synthesis of Luminescent Heterotetracyclic Frameworks

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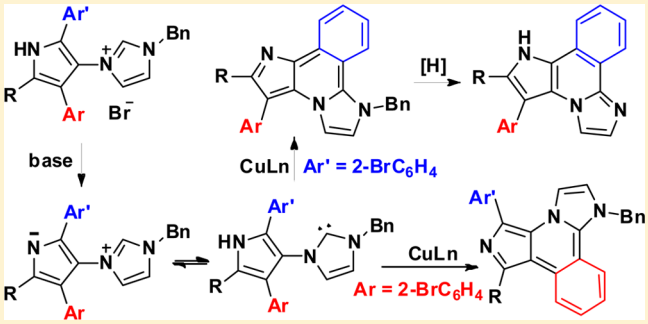
Supporting Information

ABSTRACT: 3-(2/4-(2-Bromophenyl)-1*H*-pyrrol-3-yl)-1*H*-imidazol-3-ium bromides undergo a copper-catalyzed intramolecular direct C arylation under mild conditions to give new heterocyclic frameworks. The cyclizations involve the formation of betaines (imidazoliumylpyrrolides) under basic conditions and the tautomerizaton of the betaines to the corresponding NHCs, which are the reactive species responsible for the selectivity of the arylation via the formation of NHC-Cu complexes. The primary salt arylation products were dehydrohalogenated to obtain the first representatives of 7*H*-imidazo[2,1-*a*]pyrrolo[3,2-*c*]isoquinoline and 1*H*-imidazo-[2,1-*a*]pyrrolo[3,4-*c*]isoquinoline heterocyclic skeletons, which were further transformed into thermodynamically more stable 1*H*- and 6*H*-tautomers, respectively, by removing of the benzyl-PG. The new heterotetracyclic systems are fluorescent in solutions with high quantum yields.



INTRODUCTION

Direct heterocyclic C−H arylation has recently received significant attention as a powerful method for the construction of C−C bonds.[1] One of the main problems in this area is the selectivity of the arylation, which is most often solved by means of directing groups.[1] Direct C−H arylation is commonly achieved by the use of palladium-, rhodium-, or ruthenium-based catalysts. However, from the economical point of view, it is more attractive to use cheap and easily available copper compounds instead of expensive noble metal derivatives. Despite this, not so many examples of copper-catalyzed direct arylations are known to date.[2] Daugulis showed that the key point for successful copper-catalyzed direct arylation of arenes is the acidity of the sp^2 C−H bond.[3] The reaction involves the deprotonation of the arene by an alkali metal base followed by the alkali metal to Cu transmetalation and coupling with arylhalides. The relative acidity of different C−H bonds in the heterocycle is the guiding factor in determining the regioselectivity of the arylation.[3] This approach was successfully applied for arylation of imidazoles[3] though Pd/Cu-mediated reactions were also often used for the functionalization of imidazoles and benzimidazoles to obtain 2-aryl derivatives.[4] It is noteworthy that the mentioned transformations occur at high temperatures, especially when the Cu-mediator is used as a sole metal component (up to 160 °C).[4f] Last year Williams et al. reported the synthesis of 2-arylbenzimidazolium derivatives via the arylation of CuI(NHC)Br complexes (NHC = 1,3-dibenzyl-, 1,3-diphenyl-, or 1,3-bis(2,4,6-trimethyl)phenyl-1,3-dihydrobenzimidazol-2-ylidene) with iodobenzene.[5]

Recently we developed an approach to pyrrolylimidazolium salts of type A,[6] based on the general strategy for the synthesis of 3-heterylpyrroles.[7] These salts react with bases under mild conditions to form betaines **B**, which are in tautomeric equilibrium with the corresponding NHCs **C** (Scheme 1). The presence of the carbene form was proved by the reaction with sulfur forming the corresponding imidazolethiones under very mild conditions.[6b] We hypothesized that NHCs **C** with *ortho*-halogenated Ar or Ar′ substituent, which could be generated under the basic conditions of the copper-catalyzed arylation from the corresponding salts **A**, could undergo selective cyclization through the intermediate formation of the corresponding NHC-Cu complexes. This would provide an easy access to unknown heterocyclic frameworks **D** and **E**.

RESULTS AND DISCUSSION

Two types of imidazolium salts **3a−c** and **3d−f**, differing from each other by the position of the 2-bromophenyl substituent were prepared (Scheme 2).[6] To protect the imidazole nitrogen, we chose the benzyl group, taking into account that it can be easily removed when necessary.

The obtained salts were introduced into intramolecular direct arylation (Scheme 3). To start with, we tried the reaction conditions similar to those used for the intermolecular copper-catalyzed direct C arylation of the caffeine imidazole ring.[8] The cyclization of **3a−c** was performed in DMF with 20 mol % of

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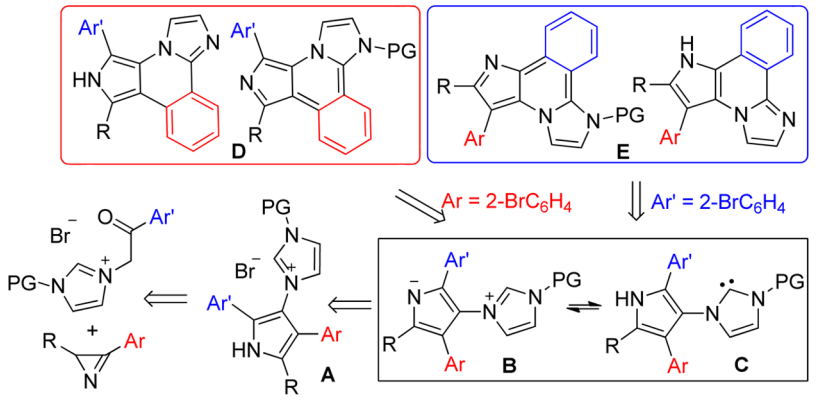
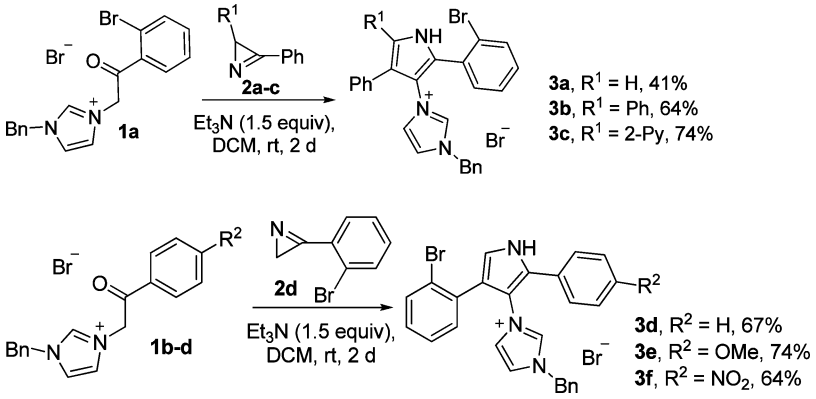
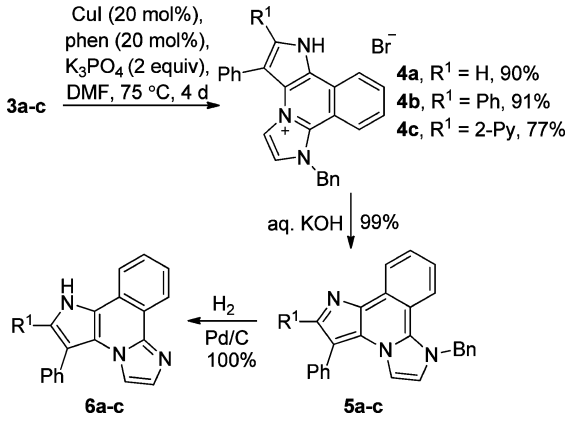
Scheme 1. Retrosynthetic Scheme for the Preparation of Heterocyclic Frameworks D and E



Scheme 2. Synthesis of Pyrrolylimidazolium Salts 3



Scheme 3. Synthesis of Compounds 4a–c, 5a–c, and 6a–c

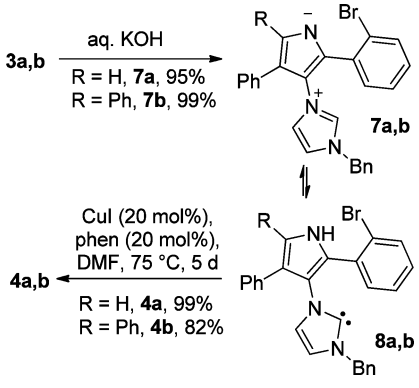


CuI, 20 mol % of phenantroline as a supporting ligand, and 2 equiv of K_3PO_4 as a base. Heating at 75 °C was enough for the arylation to occur. Notably, to the best of our knowledge, this is the only example when the copper-catalyzed direct arylation of heterocycles proceeds at such a low temperature. Usually heating to at least 120 °C, and more often to 140–160 °C, is required.[2−4,8] 7-Benzyl-3-phenyl-1,7-dihydroimidazo[2,1-*a*]-pyrrolo[3,2-*c*]isoquinolin-4-ium bromides **4a–c** were obtained in good yields. They were quantitatively converted into 7-benzyl-3-phenyl-7*H*-imidazo[2,1-*a*]pyrrolo[3,2-*c*]isoquinolines **5a–c** by the reaction with KOH. All new compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy and mass-spectrometry. The structure of **5b** was additionally confirmed by XRD analysis (see Supporting Information). Removal of the benzyl group in **5a–c** leads to formation of compounds **6a–c** which, unlike compounds **5a–c**, may exist in two tautomeric forms (vide infra).

To obtain evidence to show that cyclization proceeds through the intermediate formation of betaines **7**, which are in tautomeric equilibrium with the corresponding NHCs **8**, betaines **7a,b** were prepared in high yields from the salts **3a,b** and subjected to Cu-catalyzed cyclization (Scheme 4).

The cyclization of compounds **7a,b** easily proceeds under the reaction conditions used for the cyclization of salts **3a,b**, but without any base, to give products **4a,b** in high yields. It means that NHCs **8a,b** are the most probable intermediates which

Scheme 4. Cyclization of Betaines 7a,b under Base-Free Conditions



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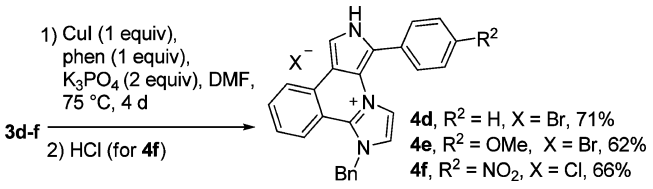
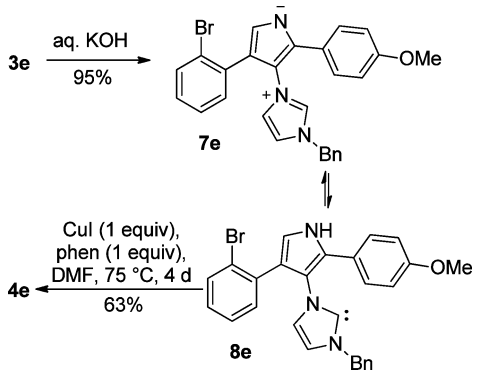
form complexes with copper undergoing further transformation.

The cyclization of salts **3d–f** requires the use of an equimolar quantity of CuI, since using subequimolar quantities of CuI led to substantial tarring of the reaction mixture (Scheme 5).

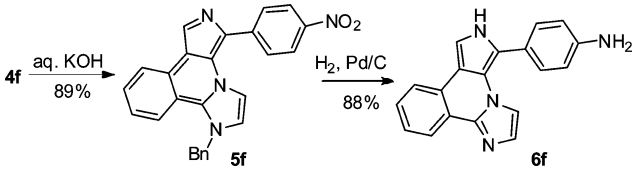
Scheme 5. Cyclization of Salts 3d–f



Scheme 6. Synthesis and Cyclization of Betaine 7e under Base-Free Conditions



Scheme 7. Synthesis of Compounds 5f and 6f



We also tested for this type of salts the base-free protocol for the cyclization of the corresponding betaines. Thus, salt **3e** was transformed into betaine **7e**, which was then cyclized into **4e** in 63% yield (Scheme 6).

Surprisingly, unlike salts **4a–c**, 1-benzyl-5-phenyl-1,6-dihydroimidazo[2,1-*a*]pyrrolo[3,4-*c*]isoquinolin-4-ium bromide **4d** and its MeO-analogue **4e** could not be cleanly dehydrobrominated or debenzylated. In both cases, a complex mixture of products was formed. On the contrary, nitro-substituted isoquinolinium chloride **4f** gave the products of dehydrochlorination **5f** and debenzylation **6f** in 89% and 88% yields, respectively (Scheme 7). The nitro-group in **4f** was reduced to the amino group under the debenzylation conditions.

The following mechanism of the formation of compounds **4** can be proposed (Scheme 8). Pyrrolylimidazolium salts **3** lose HBr under basic conditions (K_3PO_4) and afford betaines **7** which are in tautomeric equilibrium with carbenes **8**. The latter form complexes **9** with Cu(I),[5,9] the intramolecular coupling of which leads to cyclization products **4**.

Compounds **6a–c,f** prepared by reductive debenzylation of **5a–c,f** are new heterocyclic systems (imidazo[2,1-*a*]pyrrolo-[3,2-*c*]isoquinoline, imidazo[2,1-*a*]pyrrolo[3,4-*c*]isoquinoline) that, by contrast to starting compounds **5**, can exist in several tautomeric forms. According to DFT calculations at the B3LYP/6-31G+(d,p) level with the PCM model for DMSO at 298 K, the tautomer with a 1*H*-pyrrol moiety (1*H*-**6a–c**, 6*H*-**6f**) is much more stable than the others (Table 1). The existence of compound **5a–c** in fixed 7*H*-form and compound **6a–c** in the thermodynamically most stable tautomeric 1*H*-form can lead to a substantial difference in their photophysical properties (vide infra).

The novel fused heterocyclic systems (**4**) prepared by intramolecular arylation from pyrrolylimidazoles **3** as well as their dehydrohalogenated (**5**) and debenzylated (**6**) derivatives are luminescent in solutions. The photophysical data for selected compounds are listed in Table 2, and selected examples of the absorption and emission spectra are shown in Figures 1 and 2 (for the excitation spectra see Supporting Information, Tables S1–S7). The quantum yields measured for imidazopyrroloisoquinolines are up to 51% (Table 2).

As shown above, the benzyl group fixes the dehydrohalogenation products of the primary cyclization products **5a–c** in the form of the unstable tautomer, and the removal of this group by hydrogenolysis leads to the more stable tautomer of the heterocycles **6a–c**. This significantly affects the absorption and emission spectra. The largest hypsochromic shift of the long-wave absorption band in going from compounds **5**, having the less thermodynamically stable 7*H*-tautomeric form, fixed by the benzyl group, to compounds **6**, which are 1*H*-tautomers, is observed for diphenyl-substituted derivatives (**5b** (7*H*) → **6b** (1*H*), −45 nm, Table 2, entries 3 and 6). The largest emission shift (**5b** (7*H*) → **6b** (1*H*), −55 nm, Table 2, entries 3 and 6) is also observed for these compounds.

In conclusion, the first copper-catalyzed intramolecular direct C arylation of imidazoles under the betaine (imidazoliumylpyrrolide) − imidazole-NHC tautomeric control was implemented for 2- and 4-(2-bromophenyl)pyrrol-3-yl-substituted imidazolium bromides **3**. The developed cyclizations provide a concise, atom-economical route to novel highly fluorescent heteropolycyclic systems **4–6**. The reactions involve the formation of betaines **7** (imidazoliumylpyrrolides) from bromides **3** under mild basic conditions and at a relatively low temperature. Betaines **7** are in tautomeric equilibrium with

Scheme 8. Proposed Mechanism of Transformations of Salts 3 under the Cyclization Conditions

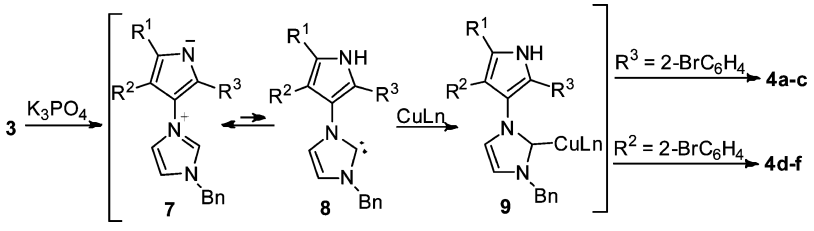


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Table 1. Calculated Relative Gibbs Free Energies for Tautomers of 6a–c,f (DFT B3LYP/6- 31G+(d,p), PCM model for DMSO at 298 K)

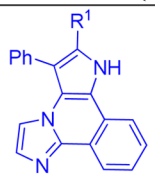
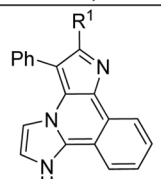
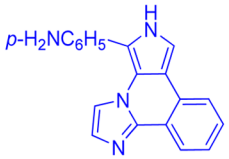
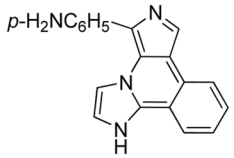
compound	tautomer (ΔG, kcal mol^{-1})	
6a-c	 **1*H*-6a-c** (0)	 **7*H*-6a-c** R^1 = H (13.1), R^1 = Ph (12.3), R^1 = 2-Py (15.1)
6f	 **6*H*-6f** (0)	 **1*H*-6f** (15.5)

Table 2. Photophysical Characteristics of Selected Imidazopyrroloisoquinolines 5a–c and Their Derivatives 4f and 6a–c in Methanol Solutions at Room Temperature

entry	compd	absorbance, λ_{max} (nm) (ε, $10^{-3}\cdot M^{-1}\cdot cm^{-1}$)	emission, λ_{max} (nm)	excitation, λ_{max} (nm)	QY (%)
1	**4f**	261(49); 307(18); 443(14.5)	467	258, 389	45
2	**5a**	266(60); 358(7)	437	267, 362	37
3	**5b**	268(50); 322(20); 375(16.5)	445	271, 324, 377	51
4	**5c**	268(43); 333(21); 368(21); 380(21)	431	269, 332, 367, 381	37
5	**6a**	268(67); 298(18); 309(15); 331(4); 346(4)	377	270, 298, 309, 331, 346	45
6	**6b**	236(21); 273(37); 331(25)	390	274, 331	50
7	**6c**	243(35); 269(52); 345(47); 363(47)	391	271, 344, 361	0.5

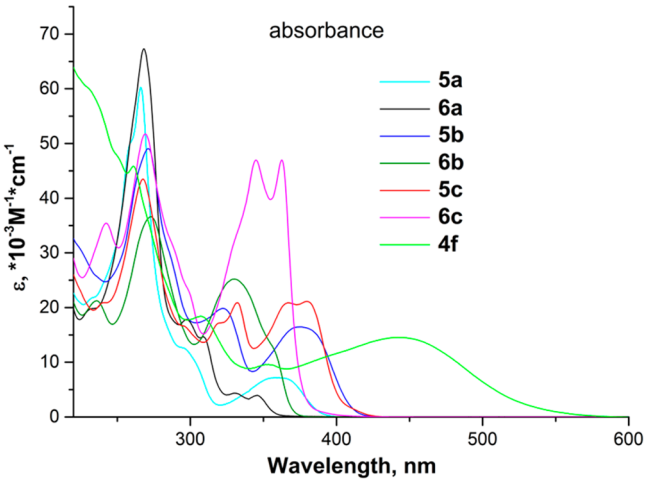


Figure 1. Absorption spectra of selected imidazopyrroloisoquinolines **5a–c** and their derivatives **4f** and **6a–c** in methanol solutions at room temperature.

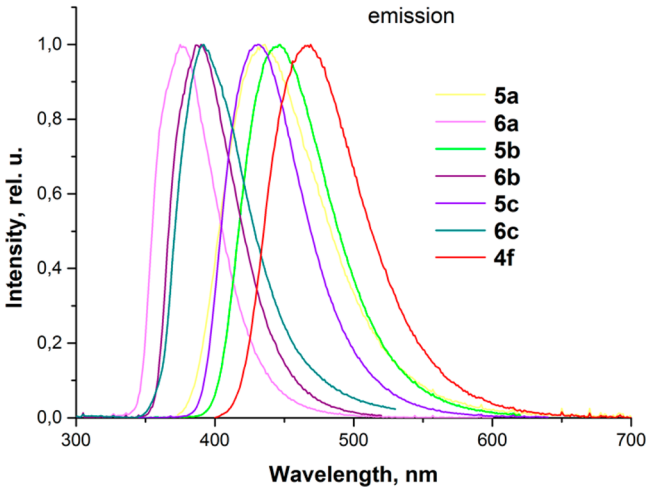


Figure 2. Emission spectra of selected imidazopyrroloisoquinolines **5a–c** and their derivatives **4f** and **6a–c** in methanol solutions at room temperature.

the corresponding imidazole-NHCs **8**, which are responsible for the selectivity of the arylation due to the intermediate formation of NHC-Cu complexes **9**. The primary products of the arylation of pyrrolylimidazoles **3**, 7-benzyl-1,7-dihydroimidazo[2,1-*a*]pyrrolo[3,2-*c*]isoquinolin-4-ium, and 1-benzyl-1,6-dihydroimidazo[2,1-*a*]pyrrolo[3,4-*c*]isoquinolin-4-ium bromides (**4**) can be easily dehydrohalogenated to obtain derivatives of 7-benzyl-7*H*-imidazo[2,1-*a*]pyrrolo[3,2-*c*]-isoquinoline and 1-benzyl-1*H*-imidazo[2,1-*a*]pyrrolo[3,4-*c*]-isoquinoline (**5**). The debenzylation of these compounds leads to their 1*H*- and 6*H*-tautomers, respectively (**6**). The most thermodynamically stable tautomer for all the debenzylated derivatives **6a–c,f** is the tautomer containing a 1*H*-pyrrol fragment.

EXPERIMENTAL SECTION

General Information and Methods. Melting points were determined on a capillary melting point apparatus. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were determined in $CDCl_3$, DMSO-d_6, and MeOH-d_4. Chemical shifts (δ) are reported in parts

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per million downfield from tetramethylsilane (TMS δ = 0.00). ^{1}H NMR spectra were calibrated according to the residual peak of $CDCl_3$ (7.26 ppm), DMSO-d_6 (2.50 ppm), or MeOH-d_4 (3.31 ppm). For all new compounds, ^{13}C {^{1}H} and ^{13}C DEPT135 spectra were recorded and calibrated according to the peak of $CDCl_3$ (77.00 ppm) or DMSO-d_6 (39.51 ppm) and MeOH-d_4 (49.00 ppm). Mass spectra were recorded on an HRMS-ESI-QTOF instument, electrospray ionization, positive mode. Single-crystal X-ray diffraction experiment was performed on a diffractometer at 100 K using monochromated Cu Kα radiation. Thin-layer chromatography (TLC) was conducted on aluminum sheets with 0.2 mm silica gel with a fluorescent indicator. Salts **1b**–**d** were obtained according to literature procedures.[6a]

*1-Benzyl-3-(2-(2-bromophenyl)-2-oxoethyl)-1H-imidazol-3-ium bromide (**1a**).* A solution of 2-bromo-1-(2-bromophenyl)ethan-1-one (1.51 g, 5.43 mmol) and 1-benzyl-1*H*-imidazole (857 mg, 5.43 mmol) in acetone (50 mL) was refluxed for 12 h. Then acetone was evaporated, and the residue was washed with diethyl ether three times (decantation) and dried in vacuum. Product **1a** (2.20 g, 94%) was obtained as colorless, very hydroscopic solid, mp 50–51 °C. ^{1}H NMR ($CDCl_3$): δ 5.46 (s, 2H), 6.28 (s, 2H), 7.19 (t, J = 1.8 Hz, 1H), 7.37–7.45 (m, 6H), 7.46–7.50 (m, 2H), 7.65 (dd, J = 8.0, 0.9 Hz, 1H), 8.09 (dd, J = 7.7, 1.6 Hz, 1H), 10.57 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0 (CH_2), 56.9 (CH_2), 119.3 (C), 122.3 (CH), 124.2 (CH), 128.0 (CH), 128.3 (CH), 128.8 (CH), 129.0 (CH), 130.5 (CH), 134.0 (CH), 134.5 (CH), 134.8 (C), 135.3 (C), 137.4 (CH), 193.0 (C). HRMS (ESI) m/z: 355.0441 calcd for $C_{18}H_{16}BrN_2O^+$ [M − Br]$^+$, found 355.0445.

General Procedure (A) for the Synthesis of 1-Benzyl-3-(2-(2-bromophenyl)-4-phenyl-1*H*-pyrrol-3-yl)-1*H*-imidazol-3-ium Bromides 3a–c and 1-Benzyl-3-(4-(2-bromophenyl)-2-phenyl-1*H*-pyrrol-3-yl)-1*H*-imidazol-3-ium Bromides 3d–f. To a stirred suspension of 1-benzyl-3-(2-(2-bromophenyl)-2-oxoethyl)-1*H*-imidazol-3-ium bromide **1a** or 1-benzyl-3-(2-oxo-2-phenylethyl)-1*H*-imidazol-3-ium bromides (3 mmol) **1b**–**d** and 2*H*-azirines **2** (4.5 mmol, 1.5 equiv) in dichloromethane (DCM) (10 mL), triethylamine (454 mg, 4.5 mmol, 1.5 equiv) was added dropwise, and then the reaction mixture was stirred at rt for 2 days. After the reaction was completed, the precipitate was filtered off, washed with DCM (3 × 3 mL), and dried to obtain an analytically pure product **3**.

*1-Benzyl-3-(2-(2-bromophenyl)-4-phenyl-1H-pyrrol-3-yl)-1H-imidazol-3-ium Bromide (**3a**).* Compound **3a** (196 mg, 41%) was obtained from **1a** (1.00 g, 2.3 mmol), 3-phenyl-2*H*-azirine **2a** (403 mg, 3.4 mmol, 1.5 equiv), and triethylamine (347 mg, 3.4 mmol, 1.5 equiv) according to the general procedure A with one exception. In this case the additional amount of **3a** was isolated by evaporation the filtrate and chromatography of the rest on silica gel (DCM/MeOH from 50:1 to 1:1). Colorless solid, mp 250–252 °C. ^{1}H NMR (DMSO-d_6): δ 5.42 (s, 2H), 7.09–7.19 (m, 4H), 7.22–7.32 (m, 3H), 7.35–7.47 (m, 6H), 7.47–7.52 (m, 1H), 7.70 (dd, J = 7.8 Hz, J = 1.2 Hz, 1H), 7.73 (t, J = 1.8 Hz, 1H), 7.90 (t, J = 1.7 Hz, 1H), 9.53 (s, 1H), 12.14 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0 (CH_2), 114.5 (C), 116.9 (CH), 119.4 (C), 123.2 (CH), 123.6 (C), 125.7 (CH), 126.4 (CH), 126.7 (CH), 127.3 (C), 127.5 (CH), 127.9 (CH), 128.6 (CH), 128.9 (CH), 128.94 (CH), 130.2 (C), 131.1 (CH), 132.1 (C), 132.9 (CH), 132.9 (CH), 134.9 (C), 138.0 (CH). HRMS (ESI) m/z: 456.0893 calcd for $C_{26}H_{21}BrN_3^+$ [M − Br]$^+$, found 456.0907.

*1-Benzyl-3-(2-(2-bromophenyl)-4,5-diphenyl-1H-pyrrol-3-yl)-1H-imidazol-3-ium Bromide (**3b**).* Compound **3b** (539 mg, 64%) was obtained from bromide **1a** (600 mg, 1.4 mmol), 2,3-diphenyl-2*H*-azirine **2b** (400 mg, 2.1 mmol, 1.5 equiv), and triethylamine (209 mg, 2.1 mmol, 1.5 equiv) according to the general procedure A. Colorless solid, mp 282–283 °C. ^{1}H NMR (DMSO-d_6): δ 5.37 (s, 2H), 7.03 (dd, J = 6.4 Hz, J = 2.8 Hz, 2H), 7.15 (dd, J = 7.6 Hz, J = 1.7 Hz, 1H), 7.24–7.44 (m, 13H), 7.46–7.51 (m, 1H), 7.61 (dd, J = 7.6 Hz, J = 1.6 Hz, 1H), 7.67 (t, J = 1.7 Hz, 1H), 7.74 (dd, J = 8.0 Hz, J = 1.1 Hz, 1H), 7.79 (s, 1H), 9.47 (s, 1H), 12.32 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 51.8 (CH_2), 117.1 (C), 117.7 (C), 122.8 (CH), 123.6 (C), 125.7 (CH), 126.5 (C), 127.2 (CH), 127.3 (CH), 127.33 (CH), 127.4 (CH), 127.8 (CH), 128.2 (C), 128.5 (CH), 128.5 (CH), 128.8 (CH), 128.9 (CH), 129.7 (CH), 129.9 (C), 131.1 (CH), 131.8 (C), 132.9 (CH), 133.1 (CH), 134.8 (C), 138.0 (CH). HRMS (ESI) m/z: 532.1206 calcd for $C_{32}H_{25}BrN_3^+$ [M − Br]$^+$, found 532.1204.

*1-Benzyl-3-(2-(2-bromophenyl)-4-phenyl-5-(pyridin-2-yl)-1H-pyrrol-3-yl)-1H-imidazol-3-ium Bromide (**3c**).* Compound **3c** (628 mg, 74%) was obtained from bromide **1a** (600 mg, 1.4 mmol), 2-(3-phenyl-2*H*-azirin-2-yl)pyridine **3c** (402 mg, 2.1 mmol, 1.5 equiv), and triethylamine (209 mg, 2.1 mmol, 1.5 equiv) according to the general procedure A with one exception. In this case the reaction mixture was evaporated to dryness, and the product was isolated by column chromatography on silica gel (DCM/MeOH from 50:1 to 1:1). Colorless solid, mp 149–150 °C. ^{1}H NMR (DMSO-d_6): δ 5.38 (s, 2H), 7.01 (dd, J = 6.3 Hz, J = 2.7 Hz, 2H), 7.07 (d, J = 8.1 Hz, 1H), 7.24 (dd, J = 7.0 Hz, J = 5.1 Hz, 1H), 7.27–7.43 (m, 9H), 7.44–7.51 (m, 1H), 7.57–7.67 (m, 3H), 7.70 (d, J = 7.4 Hz, 1H), 7.78 (s, 1H), 8.60 (d, J = 4.4 Hz, 1H), 9.50 (s, 1H), 12.58 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 51.8 (CH_2), 117.5 (C), 119.6 (C), 120.4 (CH), 122.0 (CH), 122.7 (CH), 123.6 (C), 125.7 (CH), 127.2 (C), 127.3 (CH), 127.6 (C), 127.64 (CH), 127.9 (CH), 128.5 (CH), 128.86 (CH), 128.9 (CH), 129.8 (C), 129.9 (CH), 131.1 (CH), 131.6 (C), 132.6 (CH), 133.2 (CH), 134.7 (C), 136.6 (CH), 138.0 (CH), 149.4 (CH). HRMS (ESI) m/z: 533.1179 calcd for $C_{31}H_{24}BrN_4^+$ [M − Br]$^+$, found 533.1164.

*1-Benzyl-3-(4-(2-bromophenyl)-2-phenyl-1H-pyrrol-3-yl)-1H-imidazol-3-ium Bromide (**3d**).* Compound **3d** (400 mg, 67%) was obtained from 1-benzyl-3-(2-oxo-2-phenylethyl)-1*H*-imidazol-3-ium bromide **1b** (400 mg, 1.12 mmol), 3-(2-bromophenyl)-2*H*-azirine **2d** (285 mg, 1.46 mmol, 1.3 equiv), and triethylamine (170 mg, 1.68 mmol, 1.5 equiv) according to the general procedure A. Colorless solid, mp 233–235 °C. ^{1}H NMR (DMSO-d_6): δ 5.42 (s, 2H), 7.09–7.17 (m, 2H), 7.22–7.31 (m, 4H), 7.32–7.43 (m, 8H), 7.63 (d, J = 7.7 Hz, 1H), 7.74 (t, J = 1.7 Hz, 1H), 7.88–7.93 (m, 1H), 9.50–9.54 (m, 1H), 12.25 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0 (CH_2), 114.5 (C), 116.9 (CH), 119.4 (C), 123.2 (CH), 123.6 (C), 125.7 (CH), 126.4 (CH), 126.7 (CH), 127.3 (C), 127.5 (CH), 127.9 (CH), 128.6 (CH), 128.9 (CH), 128.94 (CH), 130.2 (C), 131.1 (CH), 132.1 (C), 132.9 (CH), 132.9 (CH), 134.9 (C), 138.0 (CH). HRMS (ESI) m/z: 456.0893 calcd for $C_{26}H_{21}BrN_3^+$ [M − Br]$^+$, found 456.0907.

*1-Benzyl-3-(4-(2-bromophenyl)-2-(4-methoxyphenyl)-1H-pyrrol-3-yl)-1H-imidazol-3-ium Bromide (**3e**).* Compound **3e** (496 mg, 74%) was obtained from 1-benzyl-3-(2-(4-methoxyphenyl)-2-oxoethyl)-1*H*-imidazol-3-ium bromide **1c** (457 mg, 1.18 mmol), 3-(2-bromophenyl)-2*H*-azirine **2d** (300 mg, 1.53 mmol, 1.3 equiv), and triethylamine (178 mg, 1.76 mmol, 1.5 equiv) according to the general procedure A. Colorless solid, mp 234–235 °C. ^{1}H NMR (DMSO-d_6): δ 3.78 (s, 3H), 5.42 (s, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.11–7.21 (m, 5H), 7.24–7.30 (m, 1H), 7.30–7.35 (m, 2H), 7.35–7.42 (m, 3H), 7.63 (d, J = 7.7 Hz, 1H), 7.71 (t, J = 1.7 Hz, 1H), 7.90 (t, J = 1.6 Hz, 1H), 9.49 (s, 1H), 12.11 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0 (CH_2), 55.21 (CH_3), 113.6 (C), 114.5 (CH), 117.7 (CH), 119.9 (C), 121.5 (C), 123.1 (CH), 123.7 (C), 125.6 (CH), 126.7 (C), 127.4 (CH), 127.6 (CH), 127.7 (CH), 128.6 (CH), 128.9 (CH), 129.5 (CH), 132.4 (CH), 132.6 (CH), 132.8 (C), 134.9 (C), 158.9 (C). HRMS (ESI) m/z: 486.1000 calcd for $C_{27}H_{23}BrN_3O^+$ [M − Br]$^+$, found 486.1017.

*1-Benzyl-3-(4-(2-bromophenyl)-2-(4-nitrophenyl)-1H-pyrrol-3-yl)-1H-imidazol-3-ium Bromide (**3f**).* Compound **3f** (435 mg, 64%) was obtained from 1-benzyl-3-(2-(4-nitrophenyl)-2-oxoethyl)-1*H*-imidazol-3-ium bromide **1d** (474 mg, 1.18 mmol), 3-(2-bromophenyl)-2*H*-azirine **2d** (300 mg, 1.53 mmol, 1.3 equiv), and triethylamine (178 mg, 1.76 mmol, 1.5 equiv) according to the general procedure A. Pale yellow solid, mp 289–292 °C. ^{1}H NMR (DMSO-d_6): δ 5.43 (s, 2H), 7.11–7.19 (m, 2H), 7.26–7.41 (m, 6H), 7.42 (s, 1H), 7.47 (d, J = 8.9 Hz, 2H), 7.64 (d, J = 7.8 Hz, 1H), 7.78 (t, J = 1.7 Hz, 1H), 7.96 (t, J = 1.6 Hz, 1H), 8.21 (d, J = 8.9 Hz, 2H), 9.52 (s, 1H), 12.66 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.1 (CH_2), 116.4 (C), 120.6 (CH), 121.2 (C), 123.6 (CH), 123.7 (C), 124.2 (C), 124.3 (CH), 125.3 (CH), 126.6 (CH), 127.6 (CH), 127.8 (CH), 128.6 (CH), 128.9 (CH), 129.9 (CH), 132.2 (C), 132.4 (CH), 132.7 (CH), 134.8 (C), 135.4 (C), 138.1 (CH), 146.0 (C). HRMS (ESI) m/z: 499.0764 calcd for $C_{26}H_{20}BrN_4O_2^+$ [M − Br]$^+$, found 499.0774.

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General Procedure (B) for Cyclization of 1-Benzyl-3-(2-(2-bromophenyl)-4-phenyl-1*H*-pyrrol-3-yl)-1*H*-imidazol-3-ium Bromides 3a−c and 1-Benzyl-3-(4-(2-bromophenyl)-2-phenyl-1*H*-pyrrol-3-yl)-1*H*-imidazol-3-ium Bromides 3d−f. Salt **3** (0.476 mmol), 1,10-phenanthroline (in the case of salts **3a−c**, 17 mg, 0.0935 mmol, 0.2 equiv; in the case of salts **3d−f**, 85 mg, 0.468 mmol, 1 equiv), K_3PO_4 (198 mg, 0.934 mmol, 2 equiv), and 15 mL of DMF were placed in a flask with screw-cap. Argon was bubbled through this suspension, and CuI (in the case of salts **3a−c** 18 mg, 0.0935 mmol, 0.2 equiv; in the case of salts **3d−f** 90 mg, 0.468 mmol, 1 equiv) was added. Argon was bubbled through reaction mixture again, and the flask was tightly screwed. Reaction mixture was vigorously stirred for 4 days at 75 °C (the temperature of oil bath). Then DMF was evaporated under reduced pressure. The solid residue was dissolved in 20 mL of DCM and washed with 5% aq solution of HCl (20 mL) and brine (20 mL). Then DCM solution was dried under Na_2SO_4, filtered, and evaporated to dryness. The product **4** was isolated by column chromatography on silica gel (DCM/MeOH from 20:1 to 10:1).

General Procedure (C) for the Preparation of Compounds 4a,b,e under Baseless Condition. Betaine **7** (0.476 mmol), 1,10-phenanthroline (in the case of betaines **7a,b** 17 mg, 0.0935 mmol, 0.2 equiv; in the case of the betaine **7e** 85 mg, 0.468 mmol, 1 equiv), and 15 mL of DMF were placed in a flask with a screw-cap. Argon was bubbled through this suspension, and CuI (in the case of betaines **7a,b** 18 mg, 0.0935 mmol, 0.2 equiv; in the case of the betaine **7e** 90 mg, 0.468 mmol, 1 equiv) was added. Argon was bubbled through reaction mixture again, and the flask was tightly screwed. Reaction mixture was vigorously stirred for 4 days at 75 °C (the temperature of oil bath). Then DMF was evaporated under reduced pressure. The solid residue was dissolved in 20 mL of DCM and washed with 5% aq solution of HCl (20 mL) and brine (20 mL). Then DCM solution was dried under Na_2SO_4, filtered, and evaporated to dryness. The product **4** was isolated by column chromatography on silica gel (DCM/MeOH from 20:1 to 10:1).

*7-Benzyl-3-phenyl-1,7-dihydroimidazo[2,1-a]pyrrolo[3,2-c]-isoquinolin-4-ium Bromide (**4a**).* Compound **4a** (190 mg, 90%) was obtained from bromide **3a** (250 mg, 0.467 mmol), CuI (18 mg, 0.0935 mmol, 0.2 equiv), 1,10-phenanthroline (17 mg, 0.0935 mmol, 0.2 equiv), and K_3PO_4 (198 mg, 0.934 mmol, 2 equiv) according to the general procedure B. Colorless solid, mp 213−215 °C. ^{1}H NMR (DMSO-d_6): δ 6.24 (s, 2H), 7.27 (d, J = 7.0 Hz, 2H), 7.30−7.42 (m, 3H), 7.50−7.56 (m, 1H), 7.57−7.69 (m, 5H), 7.80 (s, 1H), 7.92 (d, J = 2.2 Hz, 1H), 7.93−8.00 (m, 1H), 8.27 (d, J = 2.2 Hz, 1H), 8.43 (d, J = 8.5 Hz, 1H), 8.57 (d, J = 8.1 Hz, 1H), 13.16 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.9 (CH_2), 113.1 (C), 113.4 (CH), 113.7 (C), 117.6 (C), 121.0 (CH), 124.4 (C), 124.9 (CH), 126.2 (CH), 126.4 (CH), 126.8 (CH), 127.8 (CH), 128.1 (CH), 128.9 (CH), 129.0 (CH), 129.9 (CH), 131.7 (CH), 132.1 (C), 134.3 (C), 134.4 (C). HRMS (ESI) m/z: 374.1652 calcd for $C_{26}H_{20}N_3^+$ [M − Br]$^+$, found 374.1662.

Bromide (**4a**) was also obtained from 3-(1-benzyl-1*H*-imidazol-3-ium-3-yl)-2-(2-bromophenyl)-4-phenylpyrrol-1-ide **7a** (20 mg, 0.044 mmol), CuI (2 mg, 0.009 mmol, 0.2 equiv), and 1,10-phenanthroline (2 mg, 0.009 mmol, 0.2 equiv) according to the general procedure C, yield 16 mg, 99%.

*7-Benzyl-2,3-diphenyl-1,7-dihydroimidazo[2,1-a]pyrrolo[3,2-c]-isoquinolin-4-ium Bromide (**4b**).* Compound **4b** (236 mg, 91%) was obtained from bromide **3b** (300 mg, 0.491 mmol), CuI (19 mg, 0.0982 mmol, 0.2 equiv), 1,10-phenanthroline (18 mg, 0.0982 mmol, 0.2 equiv), and K_3PO_4 (208 mg, 0.982 mmol, 2 equiv) according to the general procedure B. Colorless solid, mp 235−237 °C. ^{1}H NMR (DMSO-d_6): δ 6.23 (s, 2H), 7.25 (d, J = 7.0 Hz, 2H), 7.30−7.44 (m, 7H), 7.46−7.50 (m, 2H), 7.53−7.66 (m, 6H), 7.9−8.01 (m, 1H), 8.21 (d, J = 2.2 Hz, 1H), 8.44 (d, J = 8.5 Hz, 1H), 8.80 (d, J = 8.0 Hz, 1H), 13.09 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.4 (CH_2), 110.7 (C), 112.6 (CH), 113.2 (C), 119.6 (C), 120.4 (C), 122.0 (CH), 124.2 (C), 125.0 (CH), 126.3 (CH), 126.5 (CH), 127.0 (CH), 128.1 (CH), 128.2 (CH), 128.24 (CH), 128.5 (CH), 128.7 (CH), 129.0 (CH), 129.3 (CH), 130.6 (C), 131.4 (CH), 131.7 (CH), 132.0 (C), 134.4 (C), 134.5 (C), 134.7 (C). HRMS (ESI) m/z: 450.1965 calcd for $C_{32}H_{24}N_3^+$ [M − Br]$^+$, found 450.1958.

7-Benzyl-2,3-diphenyl-1,7-dihydroimidazo[2,1-*a*]pyrrolo[3,2-*c*]-isoquinolin-4-ium bromide (**4b**) was also obtained from 3-(1-benzyl-1*H*-imidazol-3-ium-3-yl)-2-(2-bromophenyl)-4,5-diphenyl-3*H*-pyrrol-3-ide **7b** (100 mg, 0.189 mmol), CuI (197 mg, 0.0377 mmol, 0.2 equiv), and 1,10-phenanthroline (7 mg, 0.0377 mmol, 0.2 equiv) according to the general procedure C, yield 82 mg, 82%.

*7-Benzyl-3-phenyl-2-(pyridin-2-yl)-1,7-dihydroimidazo[2,1-a]-pyrrolo[3,2-c]isoquinolin-4-ium Bromide (**4c**).* Compound **4c** (201 mg, 77%) was obtained from bromide **3c** (300 mg, 0.491 mmol), CuI (19 mg, 0.0982 mmol, 0.2 equiv), 1,10-phenanthroline (18 mg, 0.0982 mmol, 0.2 equiv), and K_3PO_4 (208 mg, 0.982 mmol, 2 equiv) according to the general procedure B. Yellowish solid, mp 240−242 °C. ^{1}H NMR (DMSO-d_6): δ 6.21 (s, 2H), 7.02 (d, J = 8.1 Hz, 1H), 7.22−7.29 (m, 3H), 7.30−7.41 (m, 4H), 7.60−7.72 (m, 7H), 7.93−7.99 (m, 1H), 8.19 (d, J = 2.1 Hz, 1H), 8.43 (d, J = 8.5 Hz, 1H), 8.75 (d, J = 4.3 Hz, 1H), 9.10 (d, J = 8.2 Hz, 1H), 13.44 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.5 (CH_2), 112.0 (C), 112.6 (CH), 113.8 (C), 129.7 (C), 120.9 (C), 121.4 (CH), 122.5 (CH), 122.9 (CH), 124.2 (C), 124.9 (CH), 126.3 (CH), 126.9 (CH), 127.0 (CH), 128.1 (CH), 129.0 (CH), 129.2 (CH), 129.7 (CH), 131.1 (CH), 131.8 (CH), 131.9 (C), 133.1 (C), 134.3 (C), 134.7 (C), 136.8 (CH), 148.9 (C), 149.6 (CH). HRMS (ESI) m/z: 451.1917 calcd for $C_{31}H_{23}N_4^+$ [M − Br]$^+$, found 451.1922.

*1-Benzyl-5-phenyl-1,6-dihydroimidazo[2,1-a]pyrrolo[3,4-c]-isoquinolin-4-ium Bromide (**4d**).* Compound **4d** (30 mg, 71%) was obtained from bromide **3d** (50 mg, 0.0935 mmol), CuI (18 mg, 0.0935 mmol, 1 equiv), 1,10-phenanthroline (17 mg, 0.0935 mmol, 1 equiv), and K_3PO_4 (40 mg, 0.187 mmol, 2 equiv) according to the general procedure B. Yellow solid, mp 150−152 °C. ^{1}H NMR (DMSO-d_6): δ 6.16 (s, 2H), 7.24−7.43 (m, 5H), 7.45−7.52 (m, 1H), 7.56−7.61 (m, 1H), 7.62−7.68 (m, 2H), 7.69−7.75 (m, 2H), 7.79−7.85 (m, 1H), 7.89 (d, J = 2.1 Hz, 1H), 8.14 (d, J = 2.1 Hz, 1H), 8.20−8.26 (m, 2H), 8.43 (d, J = 8.1 Hz, 1H), 12.8 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.5 (CH_2), 112.2 (C), 112.9 (CH), 114.2 (C), 114.3 (CH), 114.5 (C), 118.5 (C), 123.5 (CH), 125.2 (CH),126.3 (CH), 126.32 (CH), 126.6 (CH), 128.2 (CH), 128.9 (CH), 129.1 (CH), 129.2 (CH), 129.8 (CH), 129.9 (C), 130.0 (C), 132.1 (CH), 134.3 (C), 136.2 (C). HRMS (ESI) m/z: 374.1652 calcd for $C_{26}H_{20}N_3^+$ [M − Br]$^+$, found 374.1665.

*1-Benzyl-5-(4-methoxyphenyl)-1,6-dihydroimidazo[2,1-a]-pyrrolo[3,4-c]isoquinolin-4-ium Bromide (**4e**).* Compound **4e** (64 mg, 62%) was obtained from bromide **3e** (122 mg, 0.215 mmol), CuI (41 mg, 0.215 mmol, 1 equiv), 1,10-phenanthroline (39 mg, 0.215 mmol, 1 equiv), and K_3PO_4 (91 mg, 0.43 mmol, 2 equiv) according to the general procedure B. Colorless solid, mp 231−232 °C ^{1}H NMR (DMSO-d_6): δ 3.88 (s, 3H), 6.15 (s, 2H), 7.18−7.23 (m, 2H), 7.26−7.30 (m, 2H), 7.31−7.37 (m, 1H), 7.37−7.43 (m, 2H), 7.45−7.50 (m, 1H), 7.61−7.66 (m, 2H), 7.77−7.83 (m, 1H), 7.86 (d, J = 2.1 Hz, 1H), 8.13−8.18 (m, 2H), 8.23 (d, J = 8.4 Hz, 1H), 8.41 (d, J = 7.3 Hz, 1H), 12.75 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.5 (CH_2), 55.4 (CH_3), 112.0 (C), 112.3 (CH), 114.2 (C), 114.21 (C), 114.25 (CH), 114.61 (CH), 118.4 (C), 122.1 (C), 123.5 (CH), 125.2 (CH), 126.2 (CH), 126.6 (CH), 128.1 (CH), 129.1 (CH), 130.0 (C), 131.3 (CH), 132.1 (CH), 134.4 (C), 136.0 (C), 159.7 (C). HRMS (ESI) m/z: 404.1757 calcd for $C_{27}H_{22}N_3O^+$ [M − Br]$^+$, found 404.1776. Anal. Calcd for $C_{27}H_{22}BrN_3O$: C, 66.95; H, 4.58; N, 8.67. Found: C, 67.34; H, 4.55 N, 8.62.

1-Benzyl-5-(4-methoxyphenyl)-1,6-dihydroimidazo[2,1-*a*]pyrrolo-[3,4-*c*]isoquinolin-4-ium bromide (**4e**) was also obtained from 3-(1-benzyl-1*H*-imidazol-3-ium-3-yl)-4-(2-bromophenyl)-2-(4-methoxyphenyl)pyrrol-1-ide **7e** (80 mg, 0.165 mmol), CuI (31 mg, 0.165 mmol, 1 equiv), and 1,10-phenanthroline (30 mg, 0.165 mmol, 1 equiv) according to the general procedure C, yield 46 mg, 63%.

*1-Benzyl-5-(4-nitrophenyl)-1,6-dihydroimidazo[2,1-a]pyrrolo[3,4-c]isoquinolin-4-ium Chloride (**4f**).* Compound **4f** (65 mg, 66%) was obtained from bromide **3f** (122 mg, 0.215 mmol), CuI (41 mg, 0.215 mmol, 1 equiv), 1,10-phenanthroline (39 mg, 0.215 mmol, 1 equiv), and K_3PO_4 (91 mg, 0.43 mmol, 2 equiv) according to the general procedure B with one exception. The dark red solid, obtained after evaporation of DMF, which seemed to be a copper polymer insoluble

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in organic solvents and water, was washed with water and DCM. Then it was suspended in aq 5% HCl, and soon it turned into yellow solid. The solid was filtered off and dried, and compound **4f** was isolated by column chromatography on silica gel (DCM/MeOH from 20:1 to 10:1). Yellow solid, mp 233−234 °C. ^{1}H NMR (DMSO-d_6): δ 6.18 (s, 2H), 7.27−7.44 (m, 5H), 7.48−7.55 (m, 1H), 7.81−7.87 (m, 1H), 8.01 (d, J = 8.8 Hz, 2H), 8.07 (d, J = 2.2 Hz, 1H), 8.22−8.27 (m, 2H), 8.38 (s, 1H), 8.44−8.50 (m. 3H), 13.29 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.5 (CH), 113.0 (C), 114.3 (C), 115.0 (CH), 115.2 (CH), 114.8 (C), 116.5 (C), 123.6 (CH), 124.3 (CH), 125.2 (CH), 126.2 (CH), 126.6 (CH), 128.2 (CH), 129.1 (CH), 129.6 (C), 130.4 (CH), 132.2 (CH), 134.3 (C), 136.5 (C), 136.6 (C), 146.9 (C). HRMS (ESI) m/z: 419.1503 calcd for $C_{26}H_{19}N_4O_2^+$ [M − Cl]$^+$, found 419.1525. Anal. calcd for $C_{26}H_{19}ClN_4O_4 \cdot 0.2CH_2Cl_2$: C, 66.69; H, 4.14; N, 11.87. Found: C, 66.35; H, 4.31; N, 12.05.

General Procedure D for the Synthesis of Pyrrol-1-ides 7. A suspension of salt **3** (0.4 mmol) in aq solution of KOH (45 mg, 0.8 mmol, 2 equiv, 5 mL H_2O) was sonicated for 30 min and then vigorously stirred for 12 h. The precipitate was filtered, washed with small amount of water, and thoroughly dried to obtain analytically pure product **7** in almost quantitative yield.

*3-(1-Benzyl-1H-imidazol-3-ium-3-yl)-2-(2-bromophenyl)-4-phenylpyrrol-1-ide (**7a**).* Compound **7a** (37 mg, 95%) was obtained from bromide **3a** (45 mg, 0.0860 mmol) and aq solution of KOH (10 mg, 0.172 mmol, 2 equiv, 5 mL H_2O) according to the general procedure D. Colorless solid, mp 190−192 °C. ^{1}H NMR (DMSO-d_6): δ 5.38 (s, 2H), 6.88−7.01 (m, 4H), 7.03−7.17 (m, 3H), 7.19−7.29 (m, 3H), 7.33−7.46 (m, 6H), 7.75 (s, 1H), 9.14 (s, 1H). NMR (DMSO-d_6): δ 51.6 (CH_2), 112.3 (C), 117.4 (C), 122.1 (CH), 122.4 (C), 123.4 (CH), 124.9 (CH), 125.6 (CH), 126.92 (CH), 126.96 (CH), 127.2 (CH), 127.5 (CH), 128.45 (CH), 128.8 (CH), 132.2 (CH), 132.8 (CH), 133.9 (C), 135.3 (C), 136.5 (C), 136.8 (CH), 138.4 (C). HRMS (ESI) m/z: 454.0913 calcd for $C_{26}H_{21}BrN_3^+$ [M + H]$^+$, found 454.0902.

*3-(1-Benzyl-1H-imidazol-3-ium-3-yl)-2-(2-bromophenyl)-4,5-diphenylpyrrol-1-ide (**7b**).* Compound **7b** (172 mg, 99%) was obtained from bromide **3b** (200 mg, 0.327 mmol) and aq solution of KOH (36 mg, 0.654 mmol, 2 equiv, 10 mL H_2O) according to the general procedure D. Yellow solid, mp 132−135 °C. ^{1}H NMR (DMSO-d_6): δ 5.31 (s, 2H), 6.87−6.94 (m, 1H), 7.02−7.13 (m, 7H), 7.13−7.24 (m, 4H), 7.27−7.33 (m, 1H), 7.34−7.42 (m, 5H), 7.46 (d, J = 7.9 Hz, 1H), 7.55 (dd, J = 7.7, 1.5 Hz, 1H), 7.61 (s, 1H), 8.96 (s, 1H). NMR (DMSO-d_6): δ 51.5 (CH_2), 115. Six (C), 116.8 (C), 121.7 (CH), 122.2 (C), 123.4 (CH), 125.1 (CH), 125.5 (CH), 126.2 (CH), 127.1 (CH), 127.39 (CH), 127.40 (CH), 127.41 (CH), 128.2 (CH), 128.4 (CH), 128.8 (CH), 129.7 (CH), 132.3 (CH), 132.5 (C), 133.1 (CH), 135.2 (C), 136.6 (CH), 136.9 (C), 138.0 (C), 139.4 (C). HRMS (ESI) m/z: 530.1226 calcd for $C_{32}H_{25}BrN_3^+$ [M + H]$^+$, found 530.1205.

*3-(1-Benzyl-1H-imidazol-3-ium-3-yl)-4-(2-bromophenyl)-2-(4-methoxyphenyl)pyrrol-1-ide (**7e**).* Compound **7e** (162 mg, 95%) was obtained from bromide **3e** (200 mg, 0.354 mmol) and aq solution of KOH (40 mg, 0.708 mmol, 2 equiv, 10 mL H_2O) according to the general procedure D. Colorless solid, mp 182−185 °C. ^{1}H NMR (DMSO-d_6): δ 3.70 (s, 3H), 5.40 (s, 2H), 6.70 (d, J = 8.8 Hz, 2H), 6.82 (s, 1H), 6.96−7.09 (m, 4H), 7.12−7.17 (m, 1H), 7.20−7.26 (m, 2H), 7.38−7.43 (m, 3H), 7.49−7.53 (m, 2H), 7.80 (t, J = 1.7 Hz, 1H), 9.25 (s, 1H). NMR (DMSO-d_6): δ 51.7 (CH_2), 54.9 (CH_3), 111.9 (C), 113.6 (CH), 118.2 (C), 122.4 (CH), 123.1 (C), 125.8 (CH), 126.0 (CH), 126.5 (CH), 127.3 (CH), 127.4 (CH), 127.5 (CH), 128.5 (CH), 128.9 (CH), 129.9 (C), 131.1 (CH), 131.9 (C), 132.7 (CH), 135.4 (C), 136.9 (C), 137.4 (CH), 156.3 (C). HRMS (ESI) m/z: 484.1019 calcd for $C_{27}H_{23}BrN_3O^+$ [M + H]$^+$, found 484.1016.

General Procedure E for the Synthesis of Compounds 5. A suspension salt **4** (0.4 mmol) in aq solution of KOH (45 mg, 0.8 mmol, 2 equiv, 5 mL H_2O) was sonicated for 30 min and then vigorously stirred for 12 h. The precipitate was filtered, washed with small amount of water, and thoroughly dried to obtain analytically pure isoquinoline **5** in almost quantitative yields.

*7-Benzyl-3-phenyl-7H-imidazo[2,1-a]pyrrolo[3,2-c]isoquinoline (**5a**).* Compound **5a** (40 mg, 99%) was obtained from bromide **4a** (50 mg, 0.110 mmol) and aq solution of KOH (12 mg, 0.220 mmol, 2 equiv, 5 mL H_2O) according to the general procedure E. Yellow solid, mp 225−228 °C. ^{1}H NMR (DMSO-d_6): δ 6.12 (s, 2H), 7.09−7.15 (m, 1H), 7.17−7.24 (m, 3H), 7.27 (s, 1H), 7.28−7.41 (m, 5H), 7.60−7.65 (m, 1H), 8.03 (d, J = 7.4 Hz, 2H), 8.19 (d, J = 8.5 Hz, 1H), 8.24 (d, J = 1.7 Hz, 1H), 8.55 (d, J = 8.1 Hz, 1H), 8.58 (d, J = 1.8 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 53.0 (CH_2), 89.9 (CH), 110.1 (C), 112.9 (CH), 121.2 (CH), 122.0 (CH), 123.8 (C), 124.0 (CH), 124.7 (CH), 124.9 (CH), 125.9 (CH), 126.1 (CH), 127.9 (CH), 128.2 (CH), 129.1 (CH), 129.6 (CH), 129.9 (C), 130.4 (C), 131.8 (C), 135.4 (C), 139.2 (C), 146.7 (C). HRMS (ESI) m/z: 374.1652 calcd for $C_{26}H_{20}N_3^+$ [M + H]$^+$, found 374.1662.

*7-Benzyl-2,3-diphenyl-7H-imidazo[2,1-a]pyrrolo[3,2-c]-isoquinoline (**5b**).* Compound **5** (100 mg, 99%) was obtained from bromide **4b** (118 mg, 0.222 mmol) and aq solution of KOH (25 mg, 0.444 mmol, 2 equiv, 10 mL H_2O) according to the general procedure E. Yellow-orange solid, mp 269−270 °C. ^{1}H NMR (DMSO-d_6): δ 6.11 (s, 2H), 7.00−7.06 (m, 1H), 7.11−7.26 (m, 5H), 7.27−7.32 (m, 1H), 7.33−7.40 (m, 3H), 7.42−7.54 (m, 5H), 7.56−7.60 (m, 2H), 7.63−7.69 (m, 1H), 8.03 (d, J = 2.2 Hz, 1H), 8.21 (d, J = 8.6 Hz, 1H), 8.61 (d, J = 7.6 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 53.0 (CH_2), 108.4 (C), 110.1 (C), 110.8 (CH), 120.7 (C), 121.3 (CH), 122.3 (CH), 124.0 (CH), 124.7 (CH), 125.7 (CH), 126.1 (CH), 126.7 (CH), 127.1 (CH), 127.5 (CH), 127.9 (CH), 128.7 (CH), 129.0 (CH), 129.3 (C), 129.8 (CH), 130.1 (C), 131.5 (CH), 132.5 (C), 135.3 (C), 137.5 (C), 139.2 (C), 143.9 (C). HRMS (ESI) m/z: 450.1965 calcd for $C_{32}H_{24}N_3^+$ [M + H]$^+$, found 450.1970.

*7-Benzyl-3-phenyl-2-(pyridin-2-yl)-7H-imidazo[2,1-a]pyrrolo[3,2-c]isoquinoline (**5c**).* Compound **5c** (24 mg, 99%) was obtained from bromide **4c** (28 mg, 0.053 mmol) and aq solution of KOH (6 mg, 0.106 mmol, 2 equiv, 5 mL H_2O) according to the general procedure E. Yellow solid, mp 206−209 °C. ^{1}H NMR (DMSO-d_6): δ 6.11 (s, 2H), 6.95−7.00 (m, 1H), 7.17−7.22 (m, 2H), 7.23−7.40 (m, 6H), 7.40−7.47 (m, 4H), 7.59−7.65 (m, 1H), 7.65−7.71 (m, 1H), 7.99−8.05 (m, 2H), 8.18 (d, J = 3.9 Hz, 1H), 8.22 (d, J = 8.6 Hz, 1H), 8.62 (d, J = 7.5 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 53.1 (CH_2), 110.3 (C), 110.7 (C), 111.1 (CH), 119.7 (CH), 120.7 (C), 121.3 (CH), 121.7 (CH), 122.7 (CH), 124.1 (CH), 125.6 (CH), 125.9 (CH), 126.1 (CH), 127.8 (CH), 127.9 (CH), 129.1 (CH), 129.6 (C), 130.0 (CH), 130.4 (C), 131.6 (CH), 132.8 (C), 135.2 (CH), 137.7 (C), 143.5 (C), 148.0 (CH), 157.9 (C). HRMS (ESI) m/z: 451.1917 calcd for $C_{31}H_{23}N_4^+$ [M + H]$^+$, found 451.1927.

*1-Benzyl-5-(4-nitrophenyl)-1H-imidazo[2,1-a]pyrrolo[3,4-c]-isoquinoline (**5f**).* Compound **5f** (16 mg, 89%) was obtained from chloride **4f** (20 mg, 0.044 mmol) and aq solution of KOH (5 mg, 0.088 mmol, 2 equiv, 5 mL H_2O) according to the general procedure E. Red solid, mp 233−234 °C. ^{1}H NMR (DMSO-d_6): 6.13 (s, 2H), 7.11−7.50 (m, 6H), 7.61−7.70 (m, 1H), 7.83−8.02 (m, 3H), 8.10−8.32 (m, 6H). ^{13}C NMR (DMSO-d_6): δ 53.2 (CH_2), 111.3 (C), 114.3 (CH), 115.1 (C), 116.9 (C), 122.4 (CH), 123.1 (CH), 123.8 (CH), 124.2 (C), 124.5 (CH), 125.0 (CH), 125.6 (CH), 126.1 (CH), 127.8 (CH), 128.0 (CH), 129.1 (CH), 131.1 (CH), 131.3 (C), 134.5 (C), 135.0 (C), 143.3 (C), 145.4 (C). HRMS (ESI) m/z: 419.1503 calcd for $C_{26}H_{19}N_4O_2^+$ [M + H]$^+$, found 419.1493.

General Procedure F for the Debenzylation of Compounds 5. Pd/C (10 wt %) was added to a solution of compound **5** (0.1 mmol) in MeOH (5 mL). The resulting suspension was hydrogenated under stirring at rt using a rubber balloon with hydrogen for 12 h. The conversion was monitored by TLC (MeOH/DCM 1:10). After the completion of the reaction the reaction mixture was filtered off and evaporated to dryness to afford analytically pure product.

*3-Phenyl-1H-imidazo[2,1-a]pyrrolo[3,2-c]isoquinoline (**6a**).* Compound **6a** (6 mg, 100%) was obtained from compound **5a** (10 mg, 0.022 mmol) according to the general procedure F. Colorless solid, mp 252−253 °C. ^{1}H NMR (DMSO-d_6): δ 7.39−7.47 (m, 3H), 7.49−7.59 (m, 6H), 7.63−7.70 (m, 1H), 8.26 (d, J = 7.9 Hz, 1H), 8.52 (d, J = 7.5 Hz, 1H), 12.48 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 112.1 (CH), 113.5 (C), 118.8 (C), 118.9 (C), 120.0 (C), 120.1 (CH), 121.0 (CH),

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122.2 (C), 123.7 (CH), 125.4 (CH), 127.1 (CH), 128.1 (CH), 128.6 (CH), 129.7 (CH), 130.0 (CH), 133.7 (C), 141.3 (C). HRMS (ESI) m/z: 284.1182 calcd for $C_{19}H_{14}N_3^+$ $[M + H]^+$, found 284.1184.

*2,3-Diphenyl-1H-imidazo[2,1-a]pyrrolo[3,2-c]isoquinoline (**6b**).* Compound **6b** (31 mg, 100%) was obtained from compound **5b** (39 mg, 0.0867 mmol) according to the general procedure F. Colorless solid, mp 212−214 °C. ^{1}H NMR (DMSO-d_6): δ 6.98 (d, J = 1.2 Hz, 1H), 7.24−7.30 (m, 1H), 7.31−7.37 (m, 3H), 7.42−7.57 (m, 8H), 7.66−7.71 (m, 1H), 8.47−8.54 (m, 2H), 12.38 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 110.7 (C), 111.5 (CH), 118.3 (C), 120.2 (C), 120.7 (CH), 121.1 (C), 121.9 (C), 123.7 (CH), 125.5 (CH), 127.3 (CH), 127.6 (CH), 128.0 (CH), 128.1 (CH), 128.4 (CH), 128.9 (CH), 130.1 (CH), 131.3 (CH), 131.5 (C), 131.7 (C), 133.7 (C), 141.3 (C). HRMS (ESI) m/z: 360.1495 calcd for $C_{25}H_{18}N_3^+$ $[M + H]^+$, found 360.1488.

*3-Phenyl-2-(pyridin-2-yl)-1H-imidazo[2,1-a]pyrrolo[3,2-c]-isoquinoline (**6c**).* Compound **6** (10 mg, 100%) was obtained from compound **5c** (12 mg, 0.0266 mmol) according to the general procedure F. Yellowish solid, mp 213−216 °C. ^{1}H NMR (DMSO-d_6): δ 6.86 (d, J = 0.8 Hz, 1H), 7.1 (br. s, 1H), 7.17−7.23 (m, 1H), 7.30 (s, 1H), 7.48−7.67 (m, 8H), 8.49 (d, J = 8.0 Hz, 1H), 8.63 (br. s, 1H), 8.74 (d, J = 7.6 Hz, 1H), 12.78 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 111.4 (CH), 112.0 (C), 119.5 (C), 120.6 (CH), 120.63 (C), 121.4 (C), 121.6 (CH), 121.68 (CH), 122.3 (C), 123.6 (CH), 125.8 (CH), 128.1 (CH), 128.4 (CH), 129.2 (CH), 130.1 (CH), 130.6 (C), 131.1 (CH), 134.0 (C), 136.4 (CH), 141.2 (C), 149.2 (CH), 150.3 (C). HRMS (ESI) m/z: 361.1448 calcd for $C_{24}H_{17}N_4^+$ $[M + H]^+$, found 361.1461.

*4-(6H-Imidazo[2,1-a]pyrrolo[3,4-c]isoquinolin-5-yl)aniline (**6f**).* Compound **6f** (10 mg, 88%) was obtained from compound **5f** (16 mg, 0.054 mmol) according to the general procedure F. Colorless solid, mp 224−226 °C. ^{1}H NMR (DMSO-d_6): δ 5.37 (s, 2H), 6.73 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 7.27 (s, 1H), 7.37−7.44 (m, 1H), 7.47−7.54 (m, 2H), 7.73 (d, J = 3.0 Hz, 1H), 8.08 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 7.8 Hz, 1H), 11.76 (s, 1H). ^{13}C NMR (MeOH-d_4): δ 111.1 (CH), 113.4 (C), 114.5 (CH), 116.3 (CH), 117.8 (C), 119.3 (C), 122.0 (C), 122.3 (C), 123.5 (CH), 124.9 (CH), 126.6 (CH), 129.2 (C), 129.4 (CH), 129.8 (CH), 131.8 (CH), 144.1 (C), 149.5 (C). HRMS (ESI) m/z: 299.1291 calcd for $C_{19}H_{15}N_4^+$ $[M + H]^+$, found 299.1279.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02627.

NMR spectra for all new compounds and computation details: energies of compounds and their Cartesian coordinates (PDF)

Crystallographic data for **5b** (CIF)

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Notes

The authors declare no competing financial interest.

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