First Synthesis of Benzopyridoiodolium Salts and Twofold Buchwald–Hartwig Amination for the Total Synthesis of Quindoline

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Dedicated to Prof. Pierre Dixneuf on the occasion of his retirement

Abstract: The first synthesis of cyclic benzopyridoiodolium salts is described. These hypervalent iodine intermediates are used in an efficient strategy for the construction of the δ-carboline core. This novel approach involves a twofold palladium-catalyzed Buchwald–Hartwig reaction between these unprecedented reagents and a primary amine. Our methodology successfully provides the expected N-substituted δ-carboline core and is efficiently applied in the total synthesis of quindoline.

Key words: alkaloids, amination, heterocycles, iodine, total synthesis

Pyrido[x,y-*b*]indoles, better known under the common name carbolines, are divided into four different classes according to the position of the nitrogen atom in the pyridine ring. Whereas a large group of alkaloids is based on the β-carboline core,[1,2] δ-carbolines belong to a much less represented group of pyridoindoles, in nature as well as in synthetic chemistry.

A small number of δ-carbolines have been isolated from natural sources, they are all benzo-fused and also known as quindolines[3] **1**–**5** (Figure 1). All these indolo[3,2-*b*]quinolines were extracted from *Cryptolepis Sanguinolenta* and *Justica betonica*, two indigenous plants from west Africa and India. Extracts of these plants are used in the dyeing of leather and textiles, as well as in traditional medicine in West and Central Africa, including the treatment of malaria, and infections of the respiratory and urinary tracts.[3,4]

Recently, we reported that β- and γ-carbolines can be efficiently synthesized via rhodium- or ruthenium-catalyzed [2+2+2] cycloadditions of nitriles to alkynyl-ynamides.[5] However, this synthetic strategy does not allow the synthesis of the isomeric α- and δ-carbolines.

Only a few synthetic strategies for the construction of the δ-carboline core are described the literature. One of the first applied synthetic routes is based on the Graebe–Ullmann reaction.[6] Similarly to the synthesis of carbazoles, 1-pyridin-3-yl-1*H*-1,2,3-benzotriazoles are used as intermediates to obtain δ-carboline derivatives. Other strategies are based on the combination of two palladium-catalyzed reactions: an amination reaction of halogenobenzenes with β-aminopyridines followed by ring closure.[7–10]

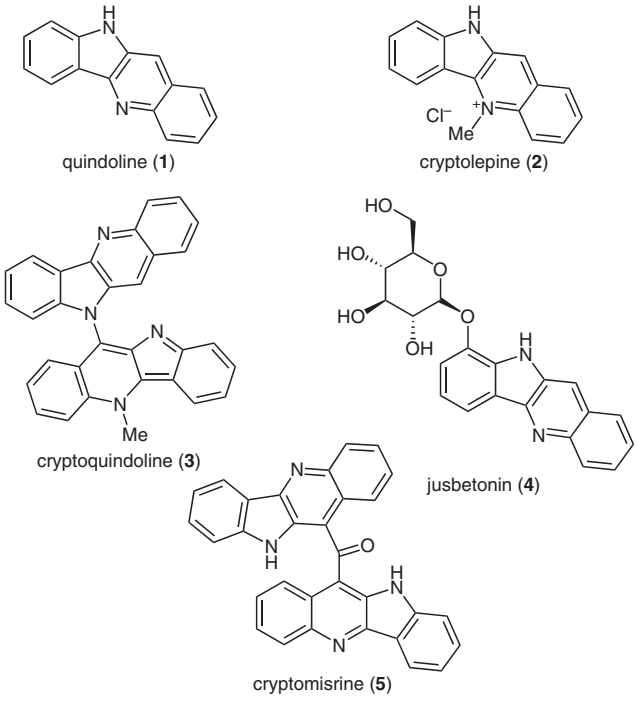

Figure 1 δ-Carbolines isolated from natural sources

Herein we report the synthesis of a new class of iodolium heterocycles and their application in a novel strategy to construct the δ-carboline core.

As part of our interest in carbazoles and related heterocycles,[1,11] we applied Olofsson and Merritt's synthesis of diaryliodonium triflates[12] to the preparation of dibenzoiodolium salts.[13] The oxidation of an *o*-iodobiphenyl with *m*-chloroperoxybenzoic acid to an iodoso derivative followed by protonation with triflic acid results in remote functionalization of the *o*′-position, giving the desired dibenzoiodolium salt with non-nucleophilic triflate as an anion. N-Substituted carbazoles are obtained in twofold palladium-catalyzed aminations with primary amines.[13]

Applying this methodology to 3-iodo-2-phenylpyridine (**9**), we were able to obtain benzopyridoiodolium triflate **10**. To the best of our knowledge, these are the first examples of aza-analogous benzoiodolium salts. The second key step, consists of two successive palladium-catalyzed

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Buchwald–Hartwig reactions of the aforementioned hypervalent iodine compound with a primary amine leading to the desired N-substituted pyrido[3,2-*b*]indole core.

To prove the suitability of this approach, a model reaction was investigated for the synthesis of the unsubstituted pyrido[3,2-*b*]indole **12** (Scheme 1). The same synthetic strategy was then successfully applied to the total synthesis of quindoline (**1**, Scheme 2).

3-Iodo-2-phenylpyridine (**9**) was obtained in three steps from commercially available 2-chloro-3-nitropyridine (**6**). A Suzuki cross-coupling reaction with phenylboronic acid led to 3-nitro-2-phenylpyridine (**7**).[14] The nitro group was reduced catalytically (Pd/C, H_2) and the amine **8** converted into the iodo compound **9** in a Sandmeyer reaction. The yields in this sequence were 95, 92, and 33%, respectively. Olofsson and Merritt's one-pot synthesis of diaryliodonium salts requires a molar excess of *m*-chloroperoxybenzoic acid. These conditions are also required for the synthesis of iodolium salts.[13] Though a competing oxidation of the pyridine to its *N*-oxide[15] and therefore reduced yields in the formation of the desired pyrido-annulated iodolium salt **10** were expected, the reaction worked remarkably well. Probably due to the protonation of the pyridine in the presence of three equivalents of triflic acid, oxidation occurred solely on the iodine and the benzopyridoiodolium salt **10** could be isolated in 95% yield.

All spectroscopic data are in agreement with the proposed structure and this was undoubtedly confirmed by an X-ray analysis. Suitable single crystals were obtained by recrystallization from formic acid–diethyl ether (Figure 2).

The crystal consists of parallel stacks of iodolium cations closely associated with the triflic anion, the distances between the iodine and an oxygen of the closest triflate is about 2.79 Å. Packing is controlled by π-stacking with distances of pyridine and benzene rings of about 3.63 Å. In these stacks, the tricyclic cations are arranged with an

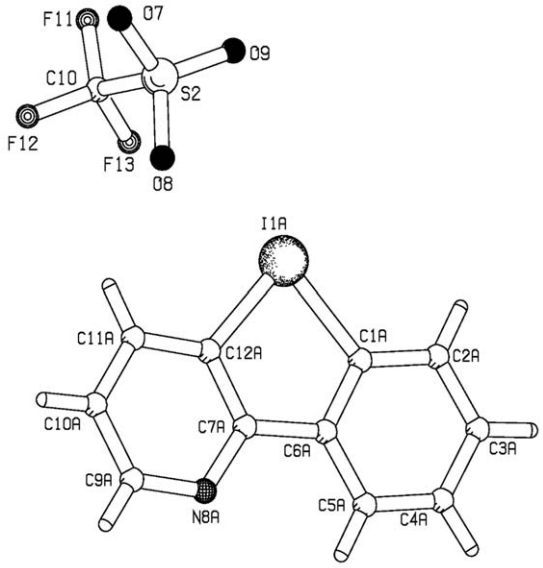
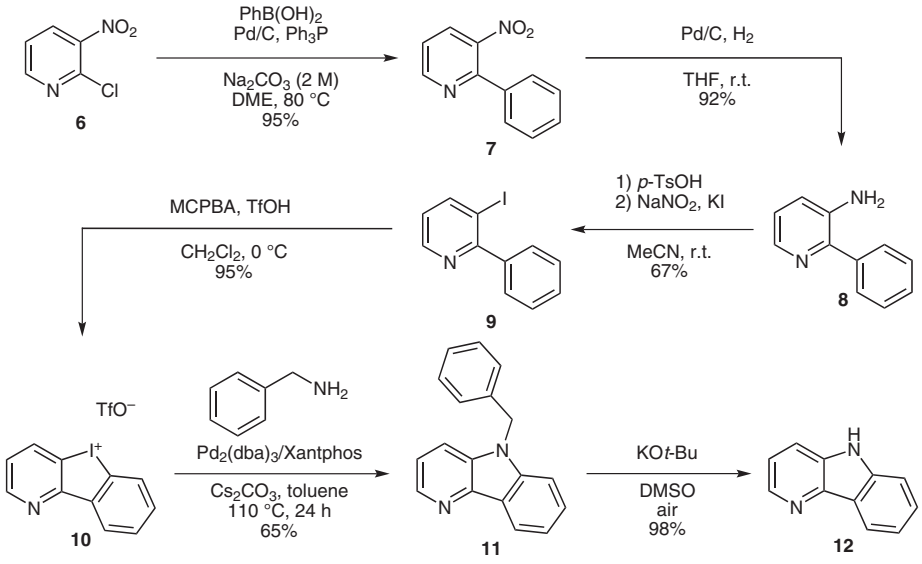


Figure 2 X-ray crystal structure of benzo[4,5]pyrido[3,2-*b*]iodol-5-ium trifluoromethanesulfonate (**10**)

alternating orientation of the iodonium side. Furthermore, the pyridine/benzene orientation is disordered. The C–I bonds in the iodolium ring are 2.103 and 2.096 Å, and the C–I–C bond angle is 81.94°. A dibenzoiodolium salt shows C–I bond lengths of 2.136 and 2.113 Å, but with 89.1° the C–I–C angle is nearly identical.[16] With 1.360 and 1.356 Å, the C–N bonds in the pyridine ring adopt typical values found in δ-carbolines.[17]

Taking into account that diaryliodonium salts are good arylating agents and that a broad range of palladium-catalyzed arylation reactions on primary and secondary amines have been reported,[18,19] we considered this new hypervalent iodine compound as an intermediate for a novel direct route to δ-carbolines. Different catalytic systems were investigated and the combination of the complex $Pd(dba)_2$/Xantphos with cesium carbonate as a base



Scheme 1 Synthesis of 5*H*-pyrido[3,2-*b*]indole (**12**)

afforded the best results. In the presence of 4 mol% of the catalyst, the subsequent twofold palladium-catalyzed amination proceeds efficiently and the expected *N*-benzylpyrido[3,2-*b*]indole **11** could be isolated in 65% yield as colorless crystals.[17] Deprotection with potassium *tert*-butoxide in dimethyl sulfoxide proceeds quantitatively to afford the desired 5*H*-pyrido[3,2-*b*]indole (**12**).

The various interesting biological activities of cryptolepines and their derivatives have resulted in the establishment of several related synthetic pathways. The first total synthesis of quindoline (**1**) was published before its isolation from natural sources.[20] Quindoline (**1**) has been prepared via different approaches. Key steps were either the condensation of diacetylindoxyl and isatinic acid, N-arylation of 3-aminoquinoline followed by oxidative cyclization with palladium(II) acetate,[21] intramolecular nucleophilic cyclization of a 2-acyl-1-(phenylsulfonyl)indole, or Suzuki reaction of pivaloylaminophenylboronic acid with substituted quinolines. More recently, Rocca and Quéguiner[22] reported the first halogen-dance reaction for the synthesis of 3-fluoro-2-iodoquinoline and applied this in a new convergent synthesis of quindoline (**1**).

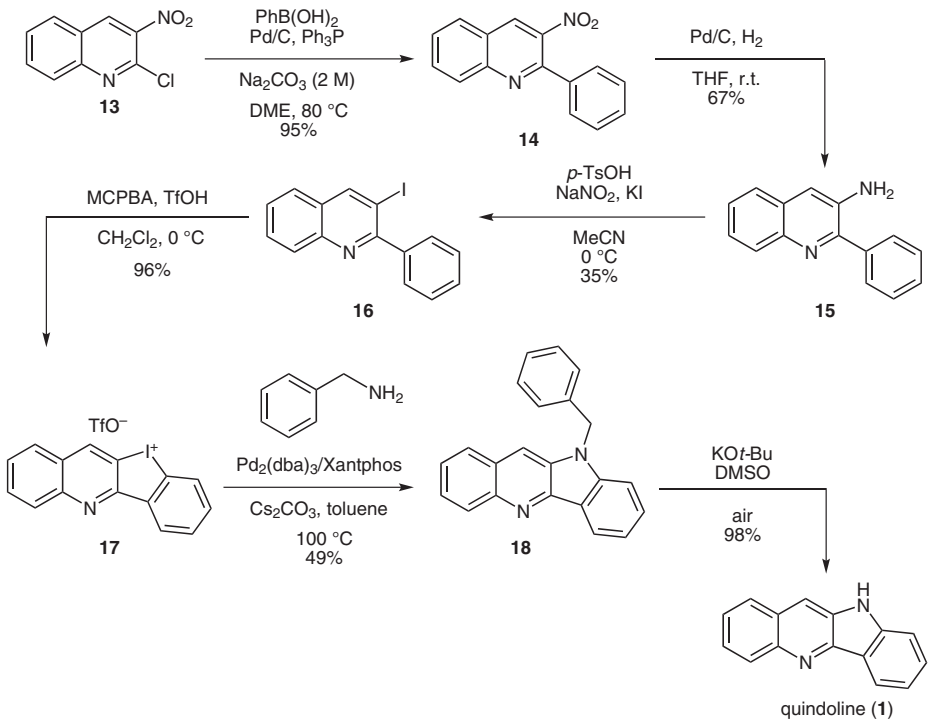
Our approach for the synthesis of quindoline (**1**) is based on the iodolium salt methodology leading to δ-carboline **12**. 2-Chloro-3-nitroquinoline (**13**) was prepared from quinoline in three steps.[23] This intermediate was subjected to the same chemical transformation sequence as for the previously described 2-chloro-3-nitropyridine (**6**). Suzuki coupling with phenylboronic acid led almost quantitatively to the desired 3-nitro-2-phenylquinoline (**14**).[14]

The Michael addition of *o*-aminobenzaldehyde to β-nitrostyrene followed by condensation in the presence of DABCO was explored as an alternative route to this compound.[24] This procedure requires only three steps, nevertheless, the overall yield was considerably lower and the reaction was not reproducible on a large scale.

Reduction of the nitro group in **14** with palladium on activated carbon under a hydrogen atmosphere occurred rapidly at room temperature to give **15** (67% yield), and diazotation/Sandmeyer reaction led[25] to the iodoquinoline **16** in 35% yield. Oxidation with 3-chloroperoxybenzoic acid in the presence of three equivalents of triflic acid selectively gave the benzoquinoloiodolium triflate **17** in excellent yield (96%) in less than an hour. For further transformations, the highly hygroscopic salt had to be carefully protected from light and moisture.

As well as for the benzopyridoiodolium salt **10**, there are no other reports of similar iodolium salts containing a quinoline moiety. The palladium-catalyzed double amination reaction was performed under the previously optimized conditions namely $Pd_2(dba)_3$/Xantphos with cesium carbonate and the expected *N*-benzylquindoline **18** was obtained in a moderate yield of 49%. Finally, deprotection with potassium *tert*-butoxide in dimethyl sulfoxide in the presence of air[26] afforded pure quindoline (**1**) in quantitative yield as a pale-yellow solid.

To summarize, we have succeeded in the first synthesis of benzopyridoiodolium salt **10** and its complete structural characterization. The twofold palladium-catalyzed amination on this salt opens a new access to δ-carbolines. The utility of this procedure has been demonstrated by the total synthesis of quindoline (**1**) via a benzoquinolinoiodolium salt **17**.



Scheme 2 Total synthesis of quindoline (**1**)

All reactions were carried out under dry argon or N_2 unless otherwise indicated. Commercially available reagents were used without further purification unless otherwise indicated; solvents and gases were dried by standard procedures. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated; PE = petroleum ether. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC 300 (300 MHz), Bruker AV 400 (400 MHz), and Bruker ARX 400 (400 MHz) spectrometers in $CDCl_3$ or DMSO-d_6. Melting points were determined by using a Büchi HWS SG 200 instrument. IR spectra were obtained with a Jasco 4100 FTIR (ATR). FD-MS spectra were obtained with a Mat 95 (Finnigan) spectrometer. HRMS-ESI spectra were obtained with a Q-TOF-ULTIMA 3 with Lock Spray device (Waters-Micromass). Elemental analyses were carried out by using a Vario EL analyzer.

2-Phenylpyridin-3-amine (8)

3-Nitro-2-phenylpyridine (**7**, 540 mg, 2.70 mmol) and Pd/C 10% (144 mg, 0.13 mmol) were added to freshly distilled THF (40 mL) in a dry sealed tube fitted with a H_2 balloon. The mixture was stirred for 16 h at r.t. After filtration through Celite, the solvent was removed under reduced pressure and the crude mixture was purified by chromatography (silica gel, PE–EtOAc, 4:1) to afford pure **8**; yield: 422 mg (2.48 mmol, 92%); mp 63 °C.

IR (neat, ATR): 3325, 1617, 1577, 1494, 1448, 1436, 1307, 1290, 1134, 1063, 1017, 919, 847, 808, 792, 743, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (dd, *J* = 4.0, 2.0 Hz, 1 H), 7.67 (m, 2 H), 7.48 (m, 2 H), 7.39 (m, 1 H), 7.05 (m, 2 H), 3.85 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0, 140.0, 139.9, 138.6, 128.8, 128.4, 128.2, 123.0, 122.6.

MS (FD): *m*/*z* (%) = 170.3 (100) $[C_{11}H_{10}N_2]^+$.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{11}N_2$: 171.0917; found: 171.0920.

3-Iodo-2-phenylpyridine (9)

To a solution of *p*-TsOH (3.42 g, 18.00 mmol) in MeCN (25 mL) was added **8** (1.02 g, 6.00 mmol). The resulting suspension was cooled to 10–15 °C and a solution of $NaNO_2$ (830 mg, 12.00 mmol) and KI (2.50 g, 15.00 mmol) in H_2O (10 mL) was added gradually. The mixture was stirred for 10 min, then allowed to come up to 20 °C and stirred for 1 h. H_2O was added, $NaHCO_3$ was added until the mixture was pH 9, and then $Na_2S_2O_3$ was added until complete reduction of the iodine. The crude mixture was extracted with Et_2O (3 × 60 mL), washed with brine, dried ($MgSO_4$), and filtered. The solvent was removed under reduced pressure and the crude mixture was purified by chromatography (silica gel, PE–EtOAc, 6:1) afforded pure **9** as a yellow solid; yield: 560 mg (2.01 mmol, 33%); mp 98 °C.

IR (neat, ATR): 1610, 1561, 1515, 1418, 1293, 1244, 1037, 1019, 1004, 834, 808, 767, 731 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (dd, *J* = 4.7, 1.5 Hz, 1 H), 8.26 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.59 (m, 2 H), 7.44 (m, 3 H), 6.99 (dd, *J* = 8.0, 4.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1, 159.9, 148.6, 147.7, 134.4, 130.7, 122.8, 113.3, 94.2.

MS (FD): *m*/*z* (%) = 281.0 (100) $[C_{11}H_8IN]^+$.

Benzo[4,5]pyrido[3,2-*b*]iodol-5-ium Trifluoromethanesulfonate (10)

In a dry sealed tube under argon atmosphere, **9** (1.00 g, 3.55 mmol) was dissolved in anhyd CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and MCPBA (1.23 g, 7.11 mmol) was added. The mixture was stirred at 0 °C for 10 min and TfOH (950 μL, 10.67 mmol) was slowly added. After 30 min stirring at 0 °C, the solvent was evaporated under reduced pressure and anhyd Et_2O (20 mL) was added to the pale-yellow residue. After a few min, the white solid was filtered off and washed several times with cold Et_2O to afford the pure **10** as a white solid; yield: 1.51 g (3.52 mmol, 95%); decomposes at 295 °C.

IR (neat, ATR): 3099, 1620, 1433, 1298, 1260, 1232, 1206, 1165, 1079, 1014, 995, 811, 786, 728, 667 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6) : δ = 8.99 (dd, *J* = 4.6, 1.2 Hz, 1 H), 8.57 (dd, *J* = 8.3, 1.2 Hz, 1 H), 8.44 (dd, *J* = 7.6, 1.6 Hz, 1 H), 8.27 (d, *J* = 8.0 Hz, 1 H), 7.82–7.91 (m, 2 H), 7.75 (dd, *J* = 8.3, 4.5 Hz, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.5, 151.4, 139.3, 139.2, 133.0, 130.8, 130.2, 128.3, 125.9, 121.7, 119.5.

MS (FD): *m*/*z* (%) = 280.1 (100), 281.1 (17) $[C_{11}H_7IN^+]$.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{11}H_7IN$: 279.9623; found: 279.9634.

5-Benzyl-5*H*-pyrido[3,2-*b*]indole (11)

Iodol-5-ium triflate **10** (400 mg, 0.93 mmol), $Pd_2(dba)_3$ (34 mg, 0.04 mmol), Xantphos (64 mg, 0.11 mmol), and Cs_2CO_3 (850 mg, 2.61 mmol) were suspended in freshly distilled toluene (5 mL) in a sealed tube. The mixture was stirred for 5 min at r.t. and freshly distilled $BnNH_2$ (122 μL, 1.12 mmol) was added. After stirring for 16 h at 100 °C, the mixture was filtered through Celite, the solvent was evaporated under reduced pressure, and the crude product was purified by chromatography (silica gel, PE–EtOAc, 4:1) to afford pure **11** as a white crystalline solid; yield: 156 mg (0.60 mmol, 65%); mp 142 °C.

IR (neat, ATR): 1621, 1588, 1482, 1451, 1412, 1334, 1318, 1242, 1193, 1115, 1012, 913, 845, 781, 742, 730, 721, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (dd, *J* = 4.7, 1.2 Hz, 1 H), 8.43 (d, *J* = 7.8 Hz, 1 H), 7.64 (dd, *J* = 8.2, 1.2 Hz, 1 H), 7.53 (td, *J* = 8.3, 1.2 Hz, 1 H), 7.42 (d, *J* = 8.2 Hz, 1 H), 7.26–7.34 (m, 5 H), 7.12 (m, 2 H), 5.52 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.9, 141.8, 141.4, 136.5, 134.0, 128.9, 127.9, 127.7, 126.3, 122.2, 120.9, 120.1, 120.0, 115.8, 109.2, 46.5.

MS (FD): *m*/*z* = 258.1 $[C_{18}H_{14}N_2]^+$.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{15}N_2$: 259.1230; found: 259.1230.

5*H*-Pyrido[3,2-*b*]indole (12)

5-Benzyl-5*H*-pyrido[3,2-*b*]indole (**11**, 10 mg, 0.04 mmol) was dissolved in DMSO (1 mL) in a dry sealed tube. While stirring the solution at r.t., KO*t*-Bu (22 mg, 0.19 mmol) was added. The mixture was stirred for 30 min and the reaction was quenched with sat. NH_4Cl solution. The mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The product was purified by chromatography (silica gel, PE–EtOAc, 3:2); yield: 6 mg (0.038 mmol, 98%). The ^{1}H and ^{13}C NMR spectra were in agreement with the literature.[9]

IR (neat, ATR): 3054, 2918, 1627, 1560, 1504, 1458, 1395, 1318, 1220, 1153, 1009, 890, 776, 722 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.44 (s, 1 H), 8.45 (dd, *J* = 4.5, 1.0 Hz, 1 H), 8.18 (d, *J* = 7.8 Hz, 1 H), 7.88 (dd, *J* = 8.2, 1.0 Hz, 1 H), 7.56 (d, *J* = 8.1 Hz, 1 H), 7.50 (t, *J* = 7.5 Hz, 1 H), 7.39 (dd, *J* = 8.2, 4.6 Hz, 1 H), 7.24 (t, *J* = 7.4 Hz, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 141.1 (2 C), 140.5, 132.9, 127.4, 121.5, 120.2, 120.0, 119.3, 117.9, 111.7.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9N_2$: 169.0760; found: 169.0762.

3-Nitro-2-phenylquinoline (14)

To a solution of 2-chloro-3-nitroquinoline (**13**, 200 mg, 0.96 mmol), $PhB(OH)_2$ (140 mg, 1.15 mmol), and Ph_3P (25 mg, 0.10 mmol) in DME (5 mL) were added 2 M Na_2CO_3 solution (2 mL) and Pd/C 10% (45 mg, 0.04 mmol). The mixture was stirred for 16 h at 80 °C, filtered through Celite, and the filter cake was washed with EtOAc (4 × 20 mL). The combined organic layers were washed with H_2O and brine, and dried ($MgSO_4$). After filtration, the solvent was removed under reduced pressure and the residue was purified by chromatography (silica gel, PE–EtOAc, 5:1) to give **14** as a yellow solid; yield: 228 mg (0.91 mmol, 95%); mp 148 °C.

IR (neat, ATR): 1596, 1547, 1524, 1497, 1453, 1328, 1146, 1132, 933, 874, 832, 764, 697 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.70 (s, 1 H,), 8.24 (d, *J* = 8.5 Hz, 1 H), 7.99 (d, *J* = 8.2 Hz, 1 H), 7.91 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1 H), 7.74–7.62 (m, 3 H), 5.53–7.47 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1, 148.4, 137.1, 132.3, 132.7, 129.8, 129.6, 128.8, 128.6, 128.5, 128.1, 125.5.

MS (FD): *m*/*z* = 250.1 $[C_{15}H_{10}N_2O_2]^+$.

Anal. Calcd for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.19. Found: C, 71.92; H, 4.05; N, 11.16.

2-Phenylquinolin-3-amine (15)

Pd/C 10% (430 mg, 0.40 mmol) was added to a solution of 3-nitro-2-phenylquinoline (**14**, 1.00 g, 4.00 mmol) in anhyd THF (40 mL) in a sealed tube. The tube was then connected to a H_2 balloon and the mixture was stirred for 16 h at r.t. After filtration through Celite, the solvent was removed under reduced pressure and the crude solid was purified by chromatography (silica gel, PE–EtOAc, 4:1) to afford pure **15** as a pale-yellow solid; yield: 590 mg (2.68 mmol, 67%); mp 123 °C. The ^1H NMR spectrum was in agreement with the literature.[27]

IR (neat, ATR): 3387, 3052, 1618, 1429, 1352, 1266, 1188, 1009, 881, 846, 762, 740, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 7.7 Hz, 1 H), 7.75 (m, 2 H), 7.63 (m, 1 H), 7.50 (m, 2 H), 7.47 (m, 3 H), 7.41 (s, 1 H), 4.26 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.6, 142.7, 138.3, 138.1, 129.2, 129.0, 128.9, 128.8, 128.6, 126.7, 125.7, 125.3, 116.1.

Anal. Calcd for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.44; H, 5.75; N, 12.87.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{13}N_2$: 221.1073; found: 221.1075.

3-Iodo-2-phenylquinoline (16)

To a solution of *p*-TsOH (1.60 g, 8.40 mmol) in MeCN (15 mL) was added **15** (617 mg, 2.80 mmol). The resulting suspension was cooled to 10–15 °C and a solution of $NaNO_2$ (380 mg, 5.60 mmol) and KI (1.16 g, 7.00 mmol) in H_2O (5 mL) was added gradually. The mixture was stirred for 10 min and then allowed to come up to 20 °C and stirred for 1 h. H_2O was added, $NaHCO_3$ was added until the mixture was pH 9, and then $Na_2S_2O_3$ was added until complete reduction of the iodine. The crude mixture was extracted with Et_2O (3 × 20 mL), washed with brine, dried ($MgSO_4$), and filtered. The solvent was removed under reduced pressure and the crude mixture was purified by chromatography (silica gel, PE–EtOAc, 6:1) to afford pure **15**; yield: 973 mg (2.94 mmol, 96%). The ^1H and ^{13}C NMR spectra were in agreement with the literature.[28]

IR (neat, ATR): 1569, 1482, 1440, 1395, 1131, 1070, 1022, 947, 901, 872, 784, 759, 751, 717, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 8.12 (d, *J* = 8.8 Hz, 1 H), 7.76 (m, 2 H), 7.67 (m, 2 H), 7.57 (m, 1 H), 7.52 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.7, 147.2, 146.7, 142.0, 130.4, 129.4, 129.3, 128.8, 128.5, 128.0, 127.3, 126.3, 91.2.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{11}IN$: 331.9936; found: 331.9926.

Anal. Calcd for $C_{15}H_{10}IN$: C, 54.40; H, 3.04; N, 4.23. Found: C, 54.55; H, 3.04; N, 4.20.

Benzo[4,5]quinolo[3,2-*b*]iodol-10-ium Trifluoromethanesulfonate (17)

3-Iodo-2-phenylquinoline (**16**, 500 mg, 1.51 mmol) was dissolved in anhyd CH_2Cl_2 (5 mL) in a dry sealed tube under argon atmosphere. The mixture was cooled to 0 °C and stirred for 15 min. MCPBA (680 mg, 4.53 mmol) was added and the mixture was stirred for further 10 min at 0 °C. TfOH (402 μL, 4.53 mmol) was slowly added to the white suspension. After 30 min stirring, the solvent was evaporated under reduced pressure and anhyd Et_2O (20 mL) was added to the brown residue. The pale-yellow solid was filtered off, washed with cold Et_2O and dried under high vacuum; yield: 694 mg (1.45 mmol, 96%).

IR (neat, ATR): 1635, 1585, 1381, 1364, 1294, 1279, 1242, 1231, 1215, 1154, 1024, 975, 956, 770 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 9.13 (s, 1 H), 8.61 (dd, *J* = 7.6, 2.0 Hz, 1 H), 8.29 (m, 3 H), 8.05 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1 H), 7.94 (m, 2 H), 7.87 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 156.5, 147.1, 139.6, 138.6, 133.9, 132.5, 131.0, 130.3, 128.8, 128.8, 128.8, 128.4, 128.2, 121.6, 114.8.

MS (FD): *m*/*z* (%) = 330.1 (100), 331.1 (15) $[C_{15}H_9IN^+]$.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{15}H_9IN$: 329.9780; found: 329.9787.

10-Benzyl-10*H*-indolo[3,2-*b*]quinoline (18)

Iodol-10-ium triflate **17** (445 mg, 0.93 mmol), $Pd_2(dba)_3$ (34 mg, 0.04 mmol), Xantphos (64 mg, 0.11 mmol), and Cs_2CO_3 (850 mg, 2.61 mmol) were added to a sealed tube. Freshly distilled toluene was added and the solution was stirred for 5 min at r.t. $BnNH_2$ (122 μL, 1.12 mmol) was added and the mixture was stirred for 16 h at 110 °C. The residue was filtered through Celite and the solvent was evaporated under reduced pressure. The crude mixture was purified by chromatography (silica gel, PE–EtOAc, 4:1) to afford pure **18** as a white crystalline solid; yield: 141 mg, (0.46 mmol, 49%). The ^1H NMR spectrum was in agreement with the literature.[3]

^1H NMR (400 MHz, $CDCl_3$): δ = 8.60 (d, *J* = 7.7 Hz, 1 H), 8.34 (d, *J* = 8.1 Hz, 1 H), 7.90 (d, *J* = 7.0 Hz, 1 H), 7.90 (s, 1 H), 7.66 (ddd, *J* = 8.4, 6.7, 1.4 Hz, 1 H), 7.63 (m, 1 H), 7.55 (m, 1 H), 7.37 (m, 2 H), 7.27 (m, 3 H), 7.19 (m, 2 H), 5.55 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.1, 144.6, 144.2, 136.4, 133.8, 129.9, 129.2, 128.9, 127.7, 127.2, 126.9, 126.4, 126.4, 125.3, 122.2, 121.9, 120.1, 111.3, 108.9, 46.7.

MS (FD): *m*/*z* = 308.1 $[C_{22}H_{16}N_2^+]$.

10*H*-Indolo[3,2-*b*]quinoline (1)

10-Benzyl-10*H*-indolo[3,2-*b*]quinoline (**18**, 40 mg, 0.13 mmol) was dissolved in DMSO (100 μL, 1.3 mmol) and introduced into a dry sealed tube. While stirring the solution at r.t., KO*t*-Bu (102 mg, 0.91 mmol) was added. Air was bubbled into the solution, via a gas dispersion tube for 10 min. The mixture turned rapidly deep violet. The reaction was quenched with sat. NH_4Cl solution and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The product was purified by chromatography (silica gel, PE–EtOAc, 3:2); yield: 28 mg (0.13 mmol, 98%). The ^1H and ^{13}C NMR spectra were in agreement with the literature.[4]

IR (neat, ATR): 3146, 1614, 1490, 1461, 1398, 1337, 1222, 1125, 879, 849, 818, 756, 735, 715, 690 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.42 (s, 1 H), 8.35 (d, J = 7.7 Hz, 1 H), 8.28 (s, 1 H), 8.19 (d, J = 8.5 Hz, 1 H), 8.10 (d, J = 7.5 Hz), 7.55 (m, 2 H), 7.63 (m, 2 H), 7.28 (m, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 145.7, 144.0, 143.4, 132.4, 129.7, 128.7, 127.5, 126.7, 126.0, 124.9, 121.4, 121.0, 119.3, 113.0, 111.5.

MS (FD): m/z = 218.1 [$C_{15}H_{10}N_2^+$].

X-ray Crystal Structure Determination of 10

X-ray crystallographic analysis was performed with an Enraf–Nonius Turbo-Cad 4 instrument equipped with a rotating anode by using a colorless plate (Cu-Kα, graphite monochromator; λ = 1.54180 Å). Crystal data: $C_{12}H_7F_3INO_3S$, M = 429.2 g mol^{-1}, 0.3 × 0.3 × 0.4 mm^3, triclinic, space group: $P\overline{1}$, T = 193 K, unit cell dimensions: a = 10.412(4) Å, b = 12.352(5) Å, c = 13.336(6) Å, α = 62.653(10)°, β = 88.205(1)°, γ = 65.679(10)°, V = 1361.5(2) $Å^3$, z = 4, d_{calc} = 2.094 g cm^{-3}, absorption μ = 2.55 mm^{-1}, the θ range for data collection was 2–28°; index ranges were $-13 \le h \le 13$, $-16 \le k \le 16$, $-17 \le l \le 17$. Number of reflections collected: 49739; independent reflections: 6496 [R_{int} = 0.0202]. The structure was solved by direct methods (program SIR 97, refinement by SHELXL 97).[29] Structure refinement was performed by full-matrix least squares on 405 parameters, weighted refinement: $w = 1/[\sigma^2(F_o^2) + (0.0195\ P)^2 + 0.85\ P]$ with $P = [\max(F_o^2,0) + 2F_o^2]/3$ and hydrogen atoms located from difference Fourier synthesis and refined isotropically assuming a riding motion model, non-hydrogen atoms improved with anisotropic temperature factors. Goodness-of-fit on S = 1.058, maximal range of parameters: 0.001(e.s.d.), final R indices: R_1 = 0.0157, wR_2 = 0.0404, the final difference Fourier map showed minimum and maximum values of 0.64 and –0.53 $eÅ^{-3}$, respectively. CCDC-828718 (**10**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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