Palladium-Catalyzed Synthesis of Quino[2,3-*a*]carbazoles and Indolo[2,3-*a*]carbazoles via Intramolecular *ortho*-Arylation

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Abstract: An efficient palladium-catalyzed synthesis of quino[2,3-*a*]carbazoles and indolo[2,3-*a*]carbazoles from indole-3-acetonitrile via Knoevenagel condensation followed by intramolecular *ortho*-arylation has been demonstrated.

Key words: heterocycles, condensation, palladium, arylation

Heteroannulated carbazoles play an essential role in various areas of synthetic and medicinal chemistry that have been comprehensively reviewed;[1] they are versatile compounds due to their biological and pharmacological relevance. As a result, the preparation of heteroannulated carbazoles has received much attention and substantial efforts have been made by several research groups in the area of carbazole chemistry, especially Knölker[1a–d] who extensively reviewed carbazole alkaloids.

Quinocarbazoles have received considerable attention in terms of their biological activity, such as potent antitumor, antibacterial, anti-inflammatory, and antihistamine properties.[2] Hence, several synthetic methodologies have been reported for the preparation of quinocarbazole derivatives.[3] In 2012 a new alkaloid dibromoquinocarbazole derivative (Figure 1) with a indolo[3,2-*k*]phenanthridine skeleton was isolated from the marine sponge *Penares* sp.[3f] Indolocarbazole is a significant heterocyclic template broadly found in many natural products, and many of these compounds have a wide range of medicinal applications.[4] In view of their importance, several research groups have reported the isolation and synthesis of indolocarbazole alkaloids and their derivatives.[5]

For the past decade, transition-metal-catalyzed *ortho*-arylation reactions have had a major impact on the synthesis cyclic compounds, and this is now a well-known method.[6] Recently, much effort has gone into the development of palladium-catalyzed *ortho*-arylation reaction, which is a dominant method in organic synthesis for construction of carbon–carbon and carbon–heteroatom bonds. Herein, we wish to report a palladium-catalyzed *ortho*-arylation reaction for the synthesis of heteroannulated carbazoles from indole-3-acetonitrile. Various chloroquinoline- and chloroindolecarbaldehydes were converted into the corresponding quino- and indolocarbazoles in the presence of palladium(II) acetate in good yields.

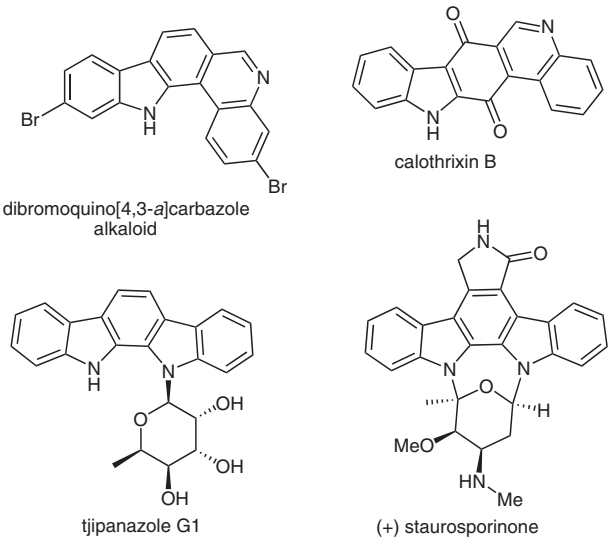

Figure 1 Quino- and indolocarbazole alkaloids

At the outset of our investigation, we chose **1a** and **2a** as model substrate for the intramolecular *ortho*-arylation reaction. The first objective was to prepare the required 1-methyl-1*H*-indole-3-acetonitrile (**1a**) and 2-chloroquinoline-3-carbaldehyde (**2a**); they were prepared by previously reported procedures.[7,8] The original impetus for this research came from an earlier observation that quinocarbazole **3a** could be obtained in 26% yield when **1a** reacted with **2a** in *N*,*N*-dimethylacetamide (DMA) at 130 °C in the presence of 10 mol% of palladium(II) acetate (Table 1, entry 1). To achieve suitable conditions for the synthesis of **3a**, we tested the reaction under various conditions by changing catalysts, bases, solvents, ligands and the results are shown in Table 1. The palladium catalyst (10 mol%) is active in several solvents including *N*,*N*-dimethylacetamide (25%, entry 2), *N*,*N*-dimethylformamide (72%, entry 15), and *N*-methylpyrrolidin-2-one (20%, entry 18) but less active or inactive in toluene, dimethyl sulfoxide, and dioxane (entry 3). When the reaction was carried out at lower temperatures, such as room temperature or 70 °C, the reaction did not occur. When palladium(II) acetate was used without a ligand, only a moderate yield of the anticipated product **3a** was observed (entries 12 and 17). The efficiency of this catalyst was superior to the other palladium catalysts such as palladium(II) chloride, dichlorobis(triphenylphosphine)palladium(II), and palladium(II) trifluoroacetate, which requires at least 20 mol% catalyst and longer reaction times to obtain the

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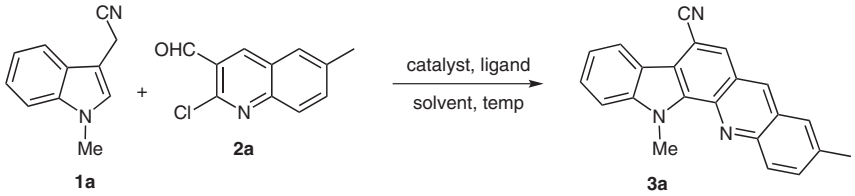
product (entries 9, 7 and 18, respectively). We have also examined other metal catalysts such as ruthenium(III) chloride and chlorotris(triphenylphosphine)rhodium (entries 10 and 11), but neither gave the desired product. Interestingly, the reaction proceeded reasonably even with a lower concentration of the catalyst, such as 5 mol% of palladium(II) acetate, to give **3a** in 48% yield, although a longer reaction time was necessary for the conversion (entry 14).

No reaction occurred in the absence of a palladium catalyst; 30 mol% of triphenylphosphine ligand is sufficient for the reaction, but in its absence or in presence of other ligands, the product was obtained in low yields or did not form (entries 4, 5, and 16). Differences among the bases were observed, potassium acetate and cesium carbonate (entries 1 and 5) gave **3a** in moderate yields, whereas sodium acetate did not give the desired product (entry 4). Further, we found that Lewis acids were unsuccessful in promoting the reaction. After examining various reaction conditions, we were pleased to find that the reaction proceeded smoothly and provided the quinocarbazole **3a** in 72% yield at 120 °C in the presence of 10 mol% of palladium(II) acetate with 30 mol% of triphenylphosphine and 2.5 equiv of potassium carbonate.

With the optimized conditions in hand, various substrates were examined to explore the scope of the reaction (Scheme 1). We proceeded with the preparation of different starting materials **1a**–**e** and **2a**–**c** and reacted them in

Table 1 Optimization Conditions for the Synthesis of the Quinocarbazole **3a**[a]



Entry	Catalyst	Ligand	Base	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	$Pd(OAc)_2$	Ph_3P	KOAc	DMA	130	24	26
2	$Pd(OAc)_2$	Ph_3P	K_2CO_3	DMA	130	20	25
3	$Pd(OAc)_2$	Ph_3P	K_2CO_3	solvent[c]	130	36	–[d]
4	$Pd(OAc)_2$	*i*-Pr_2NH	NaOAc	DMA	120	24	–[d]
5	$Pd(OAc)_2$	Cy_3P	Cs_2CO_3	DMF	140	24	31
6	$Pd(PPh_3)_4$	Ph_3P	K_2CO_3	DMF	120	12	26
7	$PdCl_2(PPh_3)_2$	Ph_3P	K_2CO_3	DMF	120	36	16
8	$Pd(OAc)_2$	Cy_3P	NaOAc	DMF	130	36	–[d]
9	$PdCl_2$	Ph_3P	K_2CO_3	DMF	120	24	15
10	$RuCl_3$	Ph_3P	K_2CO_3	DMF	120	36	–[d]
11	$RhCl(PPh_3)_3$	Ph_3P	K_2CO_3	DMF	120	36	–[d]
12	$Pd(OAc)_2$	–	Cs_2CO_3	DMF	120	18	51
13	–	Ph_3P	K_2CO_3	DMF	130	24	–[d]
14[e]	$Pd(OAc)_2$	Ph_3P	K_2CO_3	DMF	120	24	48
15	$Pd(OAc)_2$	Ph_3P	K_2CO_3	DMF	120	18	72
16	$Pd(OAc)_2$	dppe	K_2CO_3	DMF	130	18	37
17[f]	$Pd(OAc)_2$	–	KOAc	DMF	140	12	32
18	$Pd(OCOCF_3)_2$	Ph_3P	K_2CO_3	NMP	120	24	20

[a] Unless otherwise mentioned, all the reactions were conducted in a Schlenk tube using 1-methyl-1*H*-indole-3-acetonitrile (**1a**, 1.0 equiv), 2-chloro-6-methylquinoline-3-carbaldehyde (**2a**, 1.0 equiv), base (2.5 equiv), catalyst (10 mol%), ligand (30 mol%), solvent (3 mL).
[b] Isolated yields.
[c] Toluene, DMSO, or dioxane.
[d] No result.
[e] 5 mol% of catalyst was used.
[f] 15 mol% of catalyst used.

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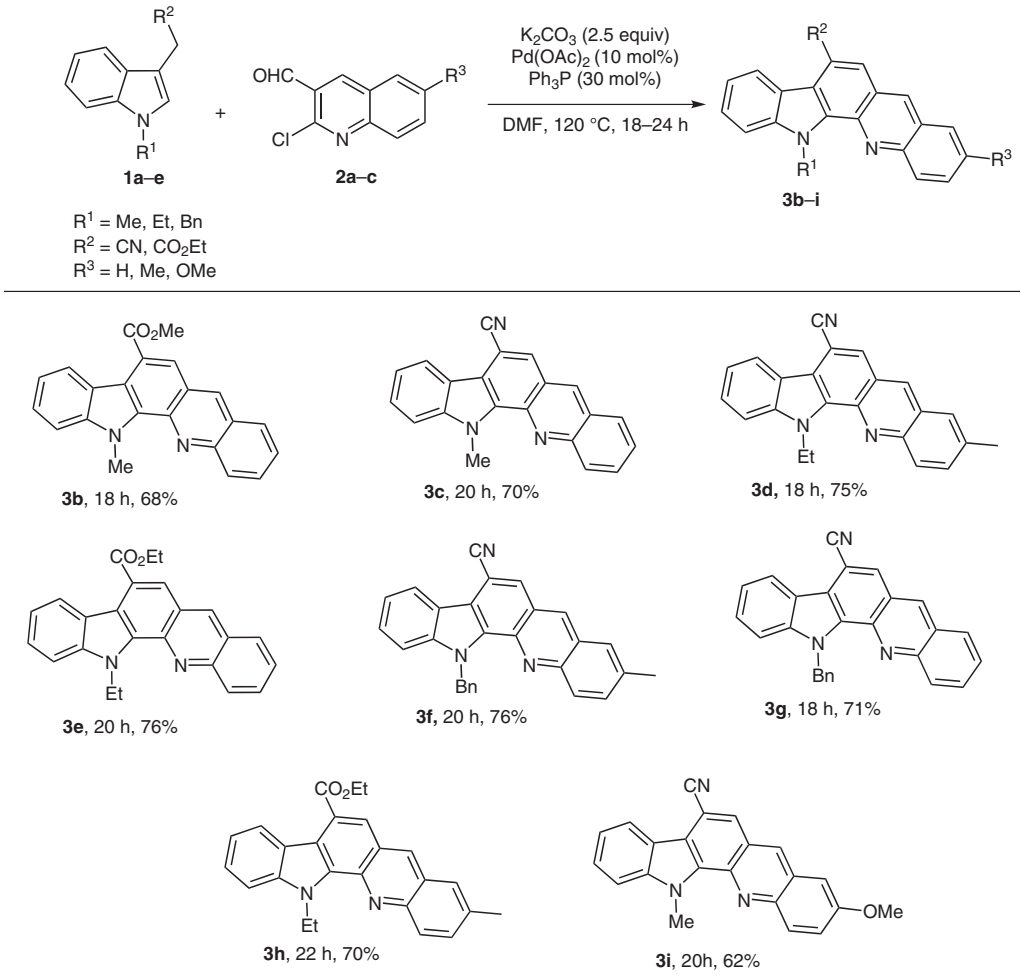

Scheme 1 Synthesis of quino[2,3-*a*]carbazole derivatives; all reactions were conducted in a Schlenk tube using **1a**–**e** (1.0 equiv), 2-chloroquinoline-3-carbaldehyde **2a**–**c** (1.0 equiv), $Pd(OAc)_2$ (10 mol%), Ph_3P (30 mol%), K_2CO_3 (2.5 equiv), DMF (3 mL) at 120 °C. Yields are isolated yields.

the presence of palladium(II) acetate and triphenylphosphine, potassium carbonate in *N*,*N*-dimethylformamide to afford quino[2,3-*a*]carbazoles **3b**–**i** in 62–76% yields. The observed result clearly demonstrates that this method is useful for synthesis of **3b**–**i** under the optimized reaction conditions. Though this reaction worked well with electron-donating substituents like Me and OMe on the 2-chloroquinoline-3-carbaldehyde moiety, when electron-withdrawing substituents, such as Cl, Br, or CO_2Me, were present, the reaction gave an inseparable mixture of the corresponding products in low yields. Next, using an indole-3-acetonitrile with the indole nitrogen free or protected with Boc did not give the desire products. Further, we extended this *ortho*-arylation strategy to 2-chloro-1-ethyl-1*H*-indole-3-carbaldehyde (**2d**) with a view to synthesizing indolo[2,3-*a*]carbazole frameworks **3j**,**k** (Scheme 2). Thus, we obtained the substituted indolo[2,3-*a*]carbazoles **3j**,**k** in good yields from 2-chloroindole-3-carbaldehyde **2d** under the optimized reaction conditions.

On the basis of the previous reports[9] a plausible mechanistic scenario for the formation of the product via Knoevenagel condensation followed by intramolecular *ortho*-arylation is described in Scheme 3. Base-induced Knoevenagel condensation reaction between **1** and **2** gives an intermediate **4**. Thus, the oxidative addition of the C–Cl bond to the Pd(0) species provides an intermediate (aryl)Pd complex **5**. Then, intramolecular *ortho*-arylation to the adjacent aryl C–H bond gives the seven-membered palladacycle intermediate **6**, followed by reductive elimination, thus yielding the desired product **3** and regenerating the Pd(0) catalyst.

Further, we studied the mechanistic pathway of the reaction, where we isolated the intermediate to verify whether the first step was formation of the Knoevenagel condensation intermediate or not. We isolated the intermediate in 74% yield, with some starting material remaining, by treating 2-chloroquinoline-3-carbaldehyde (**2a**) and **1a** in the presence of potassium carbonate in dry *N*,*N*-dimethylformamide at 120 °C after six hours (Scheme 4). Next, we treated the intermediate with palladium(II) acetate (10 mol%), triphenylphosphine (30 mol%), and potassium carbonate (2.5 equiv) in dry *N*,*N*-dimethylformamide at 120 °C for 20 hours, but the reaction did not go to completion and we obtained **3a** in only 52% yield.

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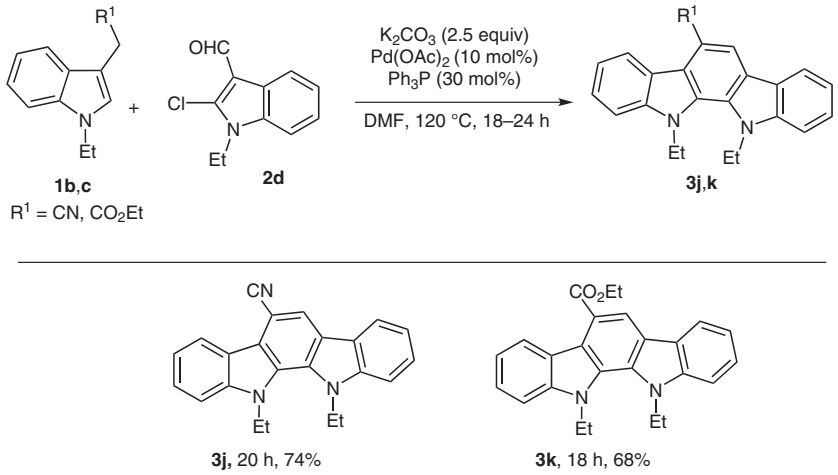
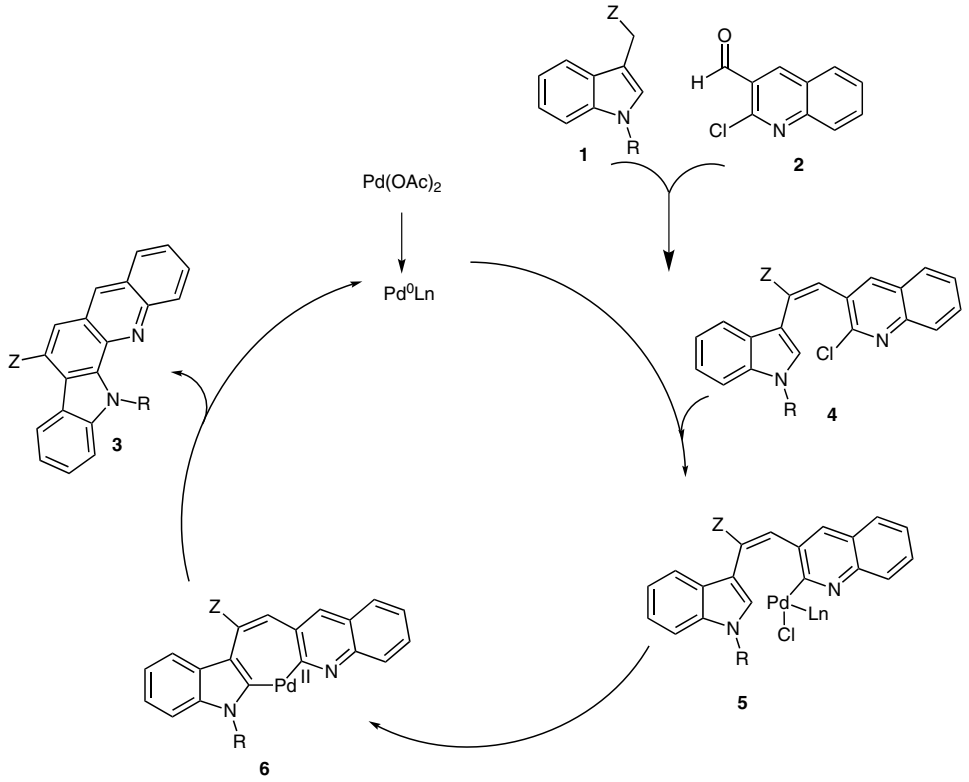
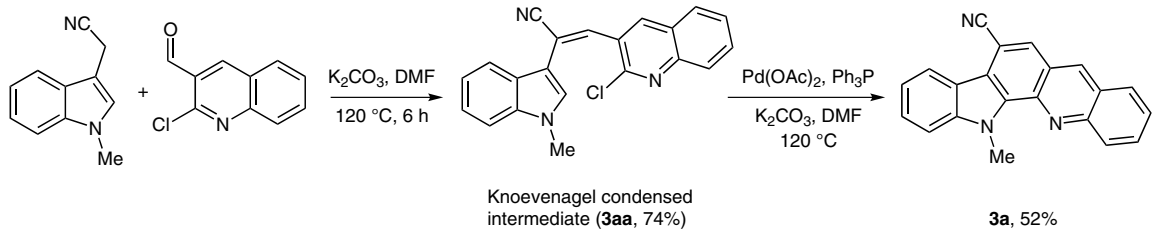


Scheme 2 Synthesis of indolo[2,3-*a*]carbazole derivatives; all reactions were conducted in a Schlenk tube using **1b**,**c** (1.0 equiv), 2-chloro-1-ethyl-1*H*-indole-3-carbaldehyde (**2d**, 1.0 equiv), $Pd(OAc)_2$ (10 mol%), Ph_3P (30 mol%), K_2CO_3 (2.5 equiv), DMF (3 mL) at 120 °C. Yields are isolated yields.



Scheme 3 Plausible mechanism



Scheme 4 Mechanistic proof

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In summary, we have developed a novel palladium(II) acetate catalyzed intramolecular *ortho*-arylation reaction of indole-3-acetonitrile with 2-chloroquinoline-3-carbaldehyde, which afforded quino[2,3-*a*]carbazole derivatives in good yields. This methodology also extended to the synthesis of indolo[2,3-*a*]carbazoles in good yields, starting from 2-chloroindole-3-carbaldehyde.

All ^{1}H and ^{13}C NMR spectra were recorded on a AV-400 spectrometer operating at 400 and 100 MHz respectively relative to TMS (δ = 0.00) or $CDCl_3$ (δ_C = 77.0).Chemical shifts of common trace ^{1}H NMR impurities ($CDCl_3$): δ = 1.56 (H_2O); 1.26, 2.05, 4.12 (EtOAc); 5.30 (CH_2Cl_2); 7.26 ppm ($CDCl_3$). IR spectra were recorded on FT/IR-5300 spectrophotometer. Mass spectra were recorded on either using EI technique or LCMS-2010A mass spectrometer. Elemental analyses (C, H, and N) were recorded on EA 1112 analyzer in the School of Chemistry, University of Hyderabad. Routine monitoring of the reactions was performed by TLC silica gel plates 60 F254 were used. Compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with I_2. Column chromatography was carried out employing silica gel 100 mesh. Commercially available reagents and solvents were used without further purification and were purchased. Melting points were measured in open capillary tubes and are uncorrected. LCMS system, whereas MS (EI) were recorded with a Jeol JMS600H mass spectrometer. HRMS (ESI) were recorded using a Bruker Maxis mass spectrometer.

9,13-Dimethyl-13*H*-indolo[3,2-*c*]acridine-5-carbonitrile (3a); Typical Procedure

1-Methyl-1*H*-indole-3-acetonitrile (**1a**, 1.0 equiv), 2-chloro-6-methylquinoline-3-carbaldehyde (**2a**, 1.0 equiv), K_2CO_3 (2.5 equiv), $Pd(OAc)_2$ (10 mol%), and Ph_3P (30 mol%) were transferred to an oven-dried 25-mL Schlenk tube. The tube was evacuated and refilled with N_2 (3 ×). After addition of DMF (3 mL) under a positive pressure of N_2 via syringe, the Schlenk tube was placed in a 120 °C oil bath and stirred for 18 h. Upon completion of the reaction (TLC monitoring), the mixture was poured into H_2O (25 mL) and the contents were extracted with EtOAc (2 × 20 mL). Then the combined organic extracts were dried (anhyd Na_2SO_4) and concentrated under reduced pressure to obtain crude **3a**. The crude product was purified by column chromatography (silica gel, hexanes–EtOAc, 95:5) to afford **3a** as a yellow-colored solid; yield: 0.030 g (72%); mp 68 °C; R_f = 0.36 (hexanes–EtOAc, 7:3).

IR (KBr): 3408, 2912, 1701, 1587, 1477, 1338, 1331, 1252, 1180, 1087, 1020, 992, 781 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, *J* = 8.0 Hz, 1 H), 8.56 (s, 1 H), 8.09 (d, *J* = 8.8 Hz, 1 H), 7.90 (s, 1 H), 7.66 (s, 1 H), 7.63–7.61 (m, 1 H), 7.59–7.57 (m, 2 H), 7.42–7.38 (m, 1 H), 4.78 (s, 3 H), 2.58 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.0, 140.6, 140.4, 136.2, 135.7, 133.8, 133.5, 129.0, 127.1, 126.3, 125.8, 125.6, 124.6, 121.1, 120.7, 120.5, 118.8, 116.0, 109.7, 104.0, 33.3, 21.8.

HRMS: *m*/*z* [M + H] calcd for $C_{22}H_{16}N_3$: 322.1345; found: 322.1345.

Methyl 13-Methyl-13*H*-indolo[3,2-*c*]acridine-5-carboxylate (3b)

Yellow-colored solid; yield: 0.029 g (68%); mp 78 °C; R_f = 0.56 (hexanes–EtOAc, 7:3).

IR (KBr): 3477, 2959, 2928, 2851, 1727, 1635, 1587, 1477, 1450, 1228, 1180, 1151, 1087, 1008, 915 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (s, 1 H), 8.69 (d, *J* = 8.2 Hz, 1 H), 8.31 (d, *J* = 8.6 Hz, 1 H), 8.28 (s, 1 H), 8.04 (d, *J* = 8.4 Hz, 1 H), 7.84 (t, *J* = 7.6 Hz, 1 H), 7.66–7.64 (m, 1 H), 7.58 (q, *J* = 7 Hz, 2 H), 7.37 (t, *J* = 8.0 Hz, 1 H), 4.94 (s, 3 H), 4.15 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 148.0, 142.1, 141.0, 137.1, 134.3, 130.3, 129.6, 128.2, 125.7, 125.5, 125.3, 124.7, 124.0, 123.8, 121.7, 120.1, 116.6, 109.5, 52.4, 33.6.

HRMS: *m*/*z* [M + H] calcd for $C_{22}H_{17}N_2O_2$: 341.1291; found: 341.1293.

13-Methyl-13*H*-indolo[3,2-*c*]acridine-5-carbonitrile (3c)

Orange-colored solid; yield: 0.029 g (70%); mp 240 °C; R_f = 0.62 (hexanes–EtOAc, 7:3).

IR (KBr): 3398, 2928, 2818, 1707, 1450, 1375, 1331, 1128, 1111, 1047, 1020, 889, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.84 (s, 1 H), 8.71 (d, *J* = 8.0 Hz, 1 H), 8.31 (d, *J* = 8.4 Hz, 1 H), 8.09 (s, 1 H), 8.05 (d, *J* = 8.4 Hz, 1 H), 7.88 (t, *J* = 8.0 Hz, 1 H), 7.68–7.60 (m, 2 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 4.90 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6, 140.7, 136.5, 130.4, 128.7, 127.7, 126.7, 125.6, 125.3, 125.0, 124.5, 123.8, 121.2, 120.1, 119.4, 118.4, 117.9, 116.1, 115.4, 109.3, 33.1.

LC-MS (–): *m*/*z* = 306 $(M - H)^-$.

Anal. Calcd for $C_{21}H_{13}N_3$: C, 82.06; H, 4.26; N, 13.67. Found: C, 82.16; H, 4.21; N, 13.58.

13-Ethyl-9-methyl-13*H*-indolo[3,2-*c*]acridine-5-carbonitrile (3d)

Yellow-colored solid; yield: 0.032 g (75%); mp 98 °C; R_f = 0.45 (hexanes–EtOAc, 7:3).

IR (KBr): 3238, 2968, 2918, 2538, 1707, 1450, 1365, 1341, 1258, 1151, 1087, 1020, 989, 785 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (d, *J* = 8.2 Hz, 1 H), 8.77 (s, 1 H), 8.72 (d, *J* = 7.8 Hz, 1 H), 8.20 (d, *J* = 8.6 Hz, 1 H), 8.11 (s, 1 H), 7.81 (s, 1 H), 7.71 (d, *J* = 8.2 Hz, 2 H), 7.55–7.52 (m, 1 H), 4.89 (q, *J* = 7.2 Hz, 2 H), 2.63 (s, 3 H), 1.65 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.0, 136.3, 135.9, 133.8, 129.3, 128.5, 127.2, 127.1, 126.4, 125.97, 125.92, 124.9, 124.3, 122.2, 121.5, 120.8, 120.7, 120.5, 109.7, 108.9, 38.7, 21.8, 14.9.

LC-MS (+): *m*/*z* = 336 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{17}N_3$: C, 82.36; H, 5.11; N, 12.53. Found: C, 82.12; H, 5.16; N, 12.56.

Ethyl 13-Ethyl-13*H*-indolo[3,2-*c*]acridine-5-carboxylate (3e)

Orange-colored solid; yield: 0.033 g (76%); mp 136 °C; R_f = 0.52 (hexanes–EtOAc, 7:3).

IR (KBr): 3412, 3151, 2458, 1717, 1532, 1477, 1370, 1321, 1228, 1140, 1101, 1087, 889, 781, 728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.91 (s, 1 H), 8.70 (d, *J* = 8.0 Hz, 1 H), 8.32–8.30 (m, 2 H), 8.06 (d, *J* = 8.4 Hz, 1 H), 7.86–7.82 (m, 1 H), 7.72–7.70 (m, 1 H), 7.62–7.55 (m, 2 H), 7.36 (t, *J* = 7.2 Hz, 1 H), 5.60 (q, *J* = 7.0 Hz, 2 H), 4.64 (q, *J* = 7.2 Hz, 2 H), 1.66 (t, *J* = 7.0 Hz, 3 H), 1.56 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 148.3, 141.7, 139.9, 139.3, 136.9, 130.2, 129.7, 128.1, 126.1, 125.7, 125.2, 124.8, 124.1, 123.5, 121.9, 120.0, 116.7, 114.0, 109.4, 61.4, 40.8, 15.3, 14.4.

HRMS: *m*/*z* [M + Na] calcd for $C_{24}H_{20}N_2NaO_2$: 391.1423; found: 391.1423.

13-Benzyl-9-methyl-13*H*-indolo[3,2-*c*]acridine-5-carbonitrile (3f)

Yellow-colored solid; yield: 0.033 g (76%); mp 212 °C; R_f = 0.48 (hexanes–EtOAc, 7:3).

IR (KBr): 3451, 1637, 1262, 1221, 1019, 1008, 920, 889, 781, 729 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (d, *J* = 8.0 Hz, 1 H), 8.60 (s, 1 H), 8.05 (d, *J* = 8.8 Hz, 1 H), 8.00 (s, 1 H), 7.67 (s, 1 H), 7.63–7.61

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(m, 2 H), 7.56–7.52 (m, 1 H), 7.45–7.41 (m, 1 H), 7.29–7.28 (m, 1 H), 7.24–7.16 (m, 4 H), 6.77 (s, 2 H), 2.56 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.2, 140.4, 140.2, 138.7, 136.3, 135.9, 133.9, 133.2, 129.1, 128.5, 127.7, 127.1, 126.9, 126.3, 126.1, 125.8, 124.7, 121.5, 121.1, 120.7, 118.7, 116.5, 110.5, 104.1, 49.2, 21.8.

LC-MS (+): *m*/*z* = 398 $[M + H]^+$.

Anal. Calcd for $C_{28}H_{19}N_3$: C, 84.61; H, 4.82; N, 10.57. Found: C, 84.52; H, 4.76; N, 10.45.

13-Benzyl-13*H*-indolo[3,2-*c*]acridine-5-carbonitrile (3g)
Yellow-colored solid; yield: 0.031 g (71%); mp 180 °C; R_f = 0.52 (hexanes–EtOAc, 7:3).

IR (KBr): 3412, 3001, 2868, 2858, 1707, 1687, 1450, 1365, 1331, 1228, 1180, 1151, 1087, 1020, 889, 721 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (s, 1 H), 8.71 (d, *J* = 8.0 Hz, 1 H), 8.17 (d, *J* = 8.6 Hz, 1 H), 8.05 (s, 1 H), 7.98 (d, *J* = 8.4 Hz, 1 H), 7.83–7.79 (m, 1 H), 7.63–7.61 (m, 1 H), 7.59–7.53 (m, 2 H), 7.45–7.42 (m, 1 H), 7.31–7.29 (m, 2 H), 7.23–7.15 (m, 3 H), 6.77 (s, 2 H).

^{13}C NMR (500 MHz, $CDCl_3$): δ = 148.4, 141.0, 140.4, 138.6, 137.0, 133.1, 131.0, 129.5, 128.55, 128.50, 128.2, 127.7, 127.0, 126.8, 126.3, 125.7, 124.7, 121.5, 121.2, 120.8, 118.6, 116.9, 110.5, 104.5, 49.3.

HRMS: *m*/*z* [M + H] calcd for $C_{27}H_{18}N_3$: 384.1501; found: 384.1500.

Ethyl 13-Ethyl-9-methyl-13*H*-indolo[3,2-*c*]acridine-5-carboxylate (3h)
Yellow-colored solid; yield: 0.029 g (70%); mp 184 °C; R_f = 0.45 (hexanes–EtOAc, 7:3).

IR (KBr): 3352, 3011, 2928, 2818, 1707, 1525, 1477, 1355, 1331, 1228, 1110, 1087, 1020, 880, 781 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 8.70 (d, *J* = 8.0 Hz, 1 H), 8.29 (s, 1 H), 8.22 (d, *J* = 8.8 Hz, 1 H), 7.81 (s, 1 H), 7.69 (t, *J* = 8.2 Hz, 2 H), 7.57–7.54 (m, 1 H), 7.37–7.33 (m, 1 H), 5.60 (q, *J* = 7.2 Hz, 2 H), 4.63 (q, *J* = 7.2 Hz, 2 H), 2.63 (s, 3 H), 1.68–1.64 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 148.1, 144.5, 141.7, 139.1, 138.3, 137.0, 135.2, 133.1, 132.6, 131.1, 127.3, 126.2, 125.4, 124.2, 122.8, 120.2, 118.1, 114.4, 109.4, 59.8, 38.6, 21.3, 14.7, 14.2.

LC-MS (+): *m*/*z* = 383 $[M + H]^+$.

Anal. Calcd for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.32. Found: C, 78.36; H, 5.72; N, 7.23.

9-Methoxy-13-methyl-13*H*-indolo[3,2-c]acridine-5-carbonitrile(3i)
Yellow-colored solid; yield: 0.047 g (62%); mp 184 °C; R_f = 0.6 (hexanes–EtOAc, 7:3).

IR (KBr): 3117, 2926, 2224, 1687, 1632, 1479, 1221, 909, 739 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 2 H), 8.20 (d, *J* = 9.2 Hz, 1 H), 8.07 (s, 1 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.62 (t, *J* = 8.0 Hz, 1 H), 7.55 (dd, *J* = 9.2, 2.8 Hz 1 H), 7.46–7.43 (m, 1 H), 7.22 (d, *J* = 2.4 Hz, 1 H), 4.90 (s, 3 H), 4.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 145.4, 140.6, 139.7, 134.7, 134.0, 131.1, 126.8, 126.7, 126.0, 125.8, 125.1, 121.3, 120.8, 120.6, 118.9, 115.9, 109.8, 104.4, 103.4, 55.7, 33.4.

HRMS: *m*/*z* [M + H] calcd for $C_{22}H_{16}N_3O$: 338.1293; found: 338.1290.

11,12-Diethyl-11,12-dihydroindolo[2,3-*a*]carbazole-5-carbonitrile (3j)
Orange-colored solid; yield: 0.034 g (74%); mp 204 °C; R_f = 0.36 (hexanes–EtOAc, 7:3).

IR (KBr): 3477, 3051, 2960, 2928, 2868, 1607, 1477, 1450, 1375, 1351, 1228, 1151, 1087, 1008, 920 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 8.0 Hz, 1 H), 8.22 (s, 1 H), 8.19 (d, *J* = 7.6 Hz, 1 H), 7.59–7.54 (m, 2 H), 7.47–7.44 (m, 2 H), 7.34–7.30 (m, 2 H), 4.80 (q, *J* = 7.2 Hz, 2 H), 4.48 (q, *J* = 7.2 Hz, 2 H), 1.58 (t, *J* = 7.2 Hz, 3 H), 1.49 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.5, 141.2, 135.8, 134.2, 127.1, 126.8, 123.6, 123.0, 122.1, 122.0, 121.0, 120.1, 119.5, 119.0, 118.5, 108.9, 108.4, 104.5, 82.8, 38.5, 37.7, 14.8, 13.9.

LC-MS (+): *m*/*z* = 338 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68; N, 12.45. Found: C, 81.76; H, 5.61; N, 12.36.

Ethyl 11,12-Diethyl-11,12-dihydroindolo[2,3-*a*]carbazole-5-carboxylate (3k)
Orange-colored solid; yield: 0.031 g (68%); mp 186 °C; R_f = 0.58 (hexanes–EtOAc, 7:3).

IR (KBr): 3462, 3041, 2963, 2912, 2858, 1587, 1467, 1375, 1311, 1248, 1180, 1151, 1087, 1020, 891 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81–8.79 (m, 2 H), 8.50 (s, 1 H), 8.30–8.28 (m, 2 H), 7.60–7.58 (m, 1 H), 7.53–7.49 (m, 1 H), 7.40–7.33 (m, 2 H), 4.94 (q, *J* = 7.2 Hz, 2 H), 4.61 (q, *J* = 7.2 Hz, 2 H), 4.47 (q, *J* = 7.2 Hz, 2 H), 1.80 (t, *J* = 7.2 Hz, 3 H), 1.58–1.53 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 142.5, 141.1, 140.5, 135.4, 126.5, 125.8, 125.0, 124.6, 124.2, 124.1, 122.6, 121.7, 121.5, 119.6, 117.4, 108.5, 107.7, 98.1, 61.0, 40.8, 37.7, 15.3, 14.5, 13.4.

LC-MS (+): *m*/*z* = 385 $[M + H]^+$.

Anal. Calcd for $C_{25}H_{24}N_2O_2$: C, 78.10; H, 6.29; N, 7.29. Found: C, 78.21; H, 6.21; N, 7.36.

(*E*)-3-(2-Chloroquinolin-3-yl)-2-(1-methyl-1*H*-indol-3-yl)acrylonitrile (3aa)
Yellow-colored solid; yield: 0.065 g (74%); mp 142 °C; R_f = 0.45 (hexanes–EtOAc, 7:3).

IR (KBr): 2953, 2920, 1687, 1627, 1539, 1473, 1320, 1221, 1024, 821, 734 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (s, 1 H), 8.07 (d, *J* = 8.0 Hz, 1 H), 8.04 (d, *J* = 8.4 Hz, 1 H), 7.96 (s, 2 H), 7.78 (t, *J* = 7.2 Hz, 1 H), 7.62 (d, *J* = 7.6 Hz, 1 H), 7.58 (s, 1 H), 7.43–7.34 (m, 3 H), 3.87 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.0, 147.1, 138.1, 136.9, 131.3, 130.1, 128.3, 128.2, 127.6, 127.5, 127.0, 124.5, 123.4, 121.7, 120.0, 117.7, 111.2, 110.4, 110.3, 33.3.

HRMS: *m*/*z* [M + H] calcd for $C_{21}H_{15}Cl^{35}N_3$: 344.0955; found: 344.0954; *m*/*z* [M + H] calcd for $C_{21}H_{15}Cl^{37}N_3$: 346.0925; found: 346.0923.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis. Included are NMR, HRMS, LC-MS and elemental analysis data.

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