Synthesis of a Naphtho-pyrido-Annulated Iodonium Salt and Pd-Catalyzed Transformation to 7*H*-Naphtho[1,8-*bc*][1,5]naphthyridine

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Dedicated to Heinz Kolshorn on the occasion of his 70th birthday

Abstract: Nitropyridylnaphthalene is the central intermediate for the synthesis of naphthonaphthyridine and benzo-δ-carboline. Whereas the Cadogan reaction gives the carboline, transformation of the nitro group to iodo followed by oxidation and cyclization results in an iodonium salt. A twofold Pd-catalyzed amination leads to the naphthyridine.

Key words: amination, fused-ring systems, heterocycles, iodine, palladium, catalysis

Carbazole and carbolines are important as scaffolds for a large number of biologically active alkaloids and synthetic derivatives.[1] Several methods for the synthesis of these units are known. The Graebe–Ullmann, the Borsche synthesis, and the Cadogan cyclization are probably the most prominent routes.[2] Nevertheless, all routes have limitations and the need for specific substitution patterns prompted us to search for new routes to these tricyclic systems. In addition to the successful approaches via [2+2+2] cycloaddition,[3] cyclizations of nitrobiaryls and of indoloaminonitriles,[4] we have started to apply hypervalent iodolium salts as intermediates.[5] Diaryliodonium salts are known to be efficient arylating agents for a variety of nucleophiles such as arenes, alkynes, or carbonyl compounds.[6] The copper- and palladium-catalyzed arylation of phenols or anilines using diaryliodonium salts [7] transfers one aryl ring to the heteroatom of the substrate, which results in the formation of iodoarenes as byproducts. The latter are typical substrates in palladium-catalyzed N-arylations, this methodology has been extensively developed by Buchwald and Hartwig.[8]

Recently, we have applied the Cadogan reaction[9] to the synthesis of indolocarbazoles and related extended π-systems.[10] The palladium-catalyzed cross-coupling reaction between boronic acids and *o*-nitrohaloarenes allows a fast access to the required starting materials for the reductive cyclization. Furthermore, these *o*-nitrobiaryls[11] also appeared to be valuable starting materials for the iodolium route, our lately developed new route for the synthesis of (aza)carbazoles.[6i,12] This approach requires the transformation of the *o*-nitrobiaryls to *o*-iodobiaryls. Oxidation of the iodoarenes leads to the iodoso compounds and an intramolecular attack of the protonated iodoso group on the *ortho* position of the remote aryl moiety results in the formation of the bisannulated iodolium salts. In the presence of a Pd/phosphine catalytic system, these salts are able to arylate primary amines. An initial ring opening to a 2-amino-2′-iodobiaryl is followed by intramolecular ring closure delivering the anticipated carbazole or carboline framework. Therefore, *o*-nitrobiaryls are the central intermediates for the iodolium and the Cadogan route to (aza)carbazoles. Furthermore, both methodologies have in common the construction of the pyrrole core. Nevertheless these are complimentary methods. In the Cadogan reaction, the pyrrole is formed in a reductive cyclization with trivalent phosphorus reagents, whereas the first key step of the iodolium route is an oxidative cyclization of an *o*-iodobiaryl to give a hypervalent iodolium salt. Secondly, the twofold palladium-catalyzed amination of the iodolium salts leads to (aza)carbazoles substituted on the pyrrole nitrogen whereas only unsubstituted derivatives are obtained by the classical routes. With almost perfect selectivity, pyrroles are formed in the Cadogan reaction.[9] Most known cyclic iodonium salts are also five-membered rings,[12] only a limited number of larger cyclic iodonium salts have been reported.[13] Whereas the iodolium salts are suitable substrates for twofold arylation, no reports of analogous conversions of six-membered iodonium salts appeared in the literature. Herein, we describe the preferential formation of a six-membered iodonium salt and the first successful transformation of the latter to a pyridine ring, resulting in N-substituted 7*H*-naphtho[1,8-*bc*][1,5]naphthyridine, a hitherto unknown tetracyclic base.

The formation of the *o*-iodobiaryl unit was performed by the Suzuki reaction of 2-chloro-3-nitropyridine (**1**) and naphthalen-1-ylboronic acid (**2**) to give nitropyridylnaphthalene **3** in excellent yield (Scheme 1). Catalytic reduction of the nitro group to **4** followed by diazotization and in situ Sandmeyer reaction yields **5** (49%). Among a variety of mixtures of peroxo compounds and strong acids with non-nucleophilic anions, the combination of 3-chloroperoxybenzoic acid and triflic acid appeared to be the best reagent for the remote functionalization.[5] Triflic acid protects the pyridine nitrogen from oxidation and efficiently protonates the iodoso group, thus initiating the intramolecular electrophilic substitution on the naphthalene unit. An 8:1 mixture of two hypervalent iodonium salts **6a**/**6b** was formed that could not be separated by crystallization. In the ^{1}H NMR spectrum, the major compound

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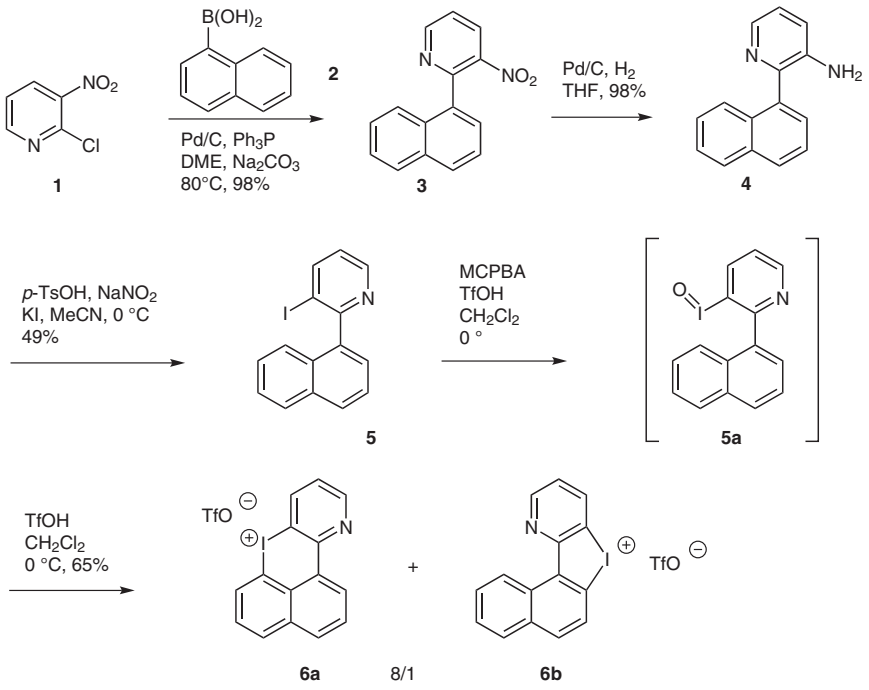
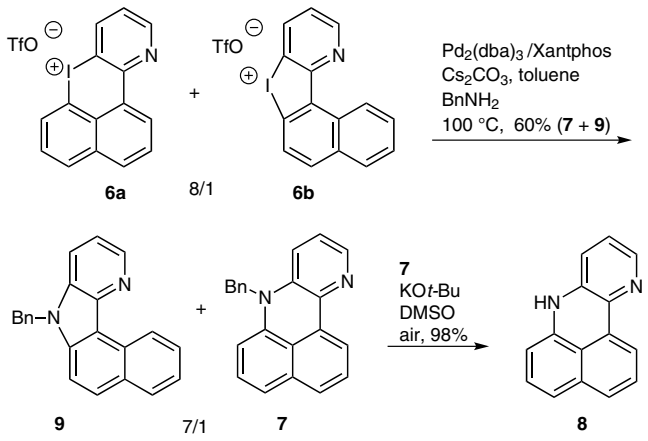


Scheme 1 Synthesis of naphtho-pyrido-iodonium salt **6a**

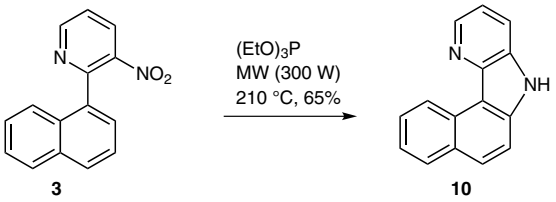
6a showed three AMX spin systems, giving evidence for a cyclization from the iodine into the β-position of the naphthalene core. According to extensive NMR investigations, **6a** contains a six-membered cyclic iodonium ring with a *peri*-annulated naphthalene system. This is probably the first example of the preferential formation of a six-membered ring iodonium salt if both five- and six-membered rings were possible. The second compound is probably the isomeric five-membered-ring iodonium salt **6b**.

Using the successful protocol for the transformation of annulated iodolium salts to pyrroles[12] we succeeded in the twofold Buchwald–Hartwig arylation of benzylamine with **6a** to give compound **7** in 53% yield accompanied by the formation of small amounts of benzo-δ-carboline **9** (Scheme 2). According to all spectroscopic data including HMBC and HSQC experiments, the new base **7** is composed of four six-membered rings. The unsubstituted 7*H*-naphtho[1,8-*bc*][1,5]naphthyridine (**8**) was obtained in nearly quantitative yield via base-induced debenzylation of **8**.



Scheme 2 Palladium-catalyzed arylamination of iodonium salts **6a**,**b** to give naphtho-naphthyridine **7** and benzo-δ-carboline **9**

In an additional experiment, we could prove that the *peri*-functionalization in the formation of **6a** is a unique feature of the iodolium salt route. Microwave-assisted Cadogan reaction of nitro-biaryl **3** results in the exclusive formation of benzocarboline **10** (Scheme 3).



Scheme 3 Synthesis of benzo-δ-carboline **10**

The absorption and emission spectra of the isomeric heterocycles **8** and **10** are significantly different (see the Supporting Information).

The UV-vis absorption spectrum of **8** in cyclohexane is highly structured, three main absorption bands (λ_{max} = 206, 259, 331 nm) appear in the UV and a broad one in the visible spectrum (λ_{max} = 423 nm). The vibrational fine structure is blurred in more polar solvents and a weak positive solvatochromism has to be noted. In cyclohexane, **8** fluoresces intensively with λ^{F}_{max} = 459 nm (2nd max: λ^{F} = 488 nm). According to the rigid molecular structure, the Stokes shift is very small (386 cm^{-1}). Increasing solvent polarity shifts the emission maximum to

λ^F_{max} = 487 nm in dichloromethane and to λ^F_{max} = 512 nm in ethanol. Upon addition of trifluoroacetic acid to solutions of **8** in dichloromethane, a protonated species is formed in 10^{-4} M trifluoroacetic acid, protonation is complete in 10^{-3} M trifluoroacetic acid and protonated **8** absorbs with λ_{max} = 525 nm. This red shift corresponds to a pronounced electronic donor-acceptor structure, resulting from protonation of the lateral pyridine. AM1-INDO/S calculations substantiate this interpretation. Nevertheless, though protonation of **8** in its ground state shifts the electronic transition to lower energies, protonation of its excited state results in quenching of the blue emission (λ^F_{max} = 487 nm) and a new, violet emission (λ^F_{max} = 414 nm in 10^{-2} M TFA) appears. This intense fluorescence is quenched in the presence of high concentrations of trifluoroacetic acid.

The isomeric carboline **10** absorbs only in the UV: λ_{max} = 250 nm, and a band at lower energies with two intense maxima: λ = 319, 333 nm. The light emitted by this species in cyclohexane has a λ^F_{max} = 394 nm, a negative solvatochromism of the emission shifts the maximum to 381 nm in ethanol. An addition of trifluoroacetic acid (10^{-4} M) to the solution of **10** in dichloromethane causes a small shift of the absorption maximum to λ_{max} = 350 nm with a shoulder centered at λ = 390 nm. Higher concentrations of trifluoroacetic acid have only a weak effect on the absorption. Quenching of the fluorescence starts at 10^{-5} M trifluoroacetic acid, only a very weak emission with λ^F_{max} = 452 nm remains in solutions with higher concentrations of trifluoroacetic acid.

X-ray analysis of 7-benzylnaphthonaphthyridine **7** gave final proof of the molecular structure (Figure 1). The monoclinic crystals are formed from centrosymmetric pairs of **7**, connected via π-stacking with a distance of 3.491(1) Å between the centroids of the central pyridine ring of one molecule and the lateral pyridine ring of the other. With an angle of 80.1(1)°, the plane of the benzyl ring is close to orthogonal to the plane of the completely flat naphthonaphthyridine. The C–N8 bond lengths of 1.330 Å and 1.340 Å in the lateral ring correspond to a normal pyridine system whereas the C–N1 bond lengths in the central ring are significantly longer (1.391, 1.397 Å). Similarly, the bond C7A–C7B (1.465 Å), connecting the pyridine and naphthalene units, is much longer than all other bonds in the tetracyclic framework.

The Cadogan reaction of *o*-nitrobiaryl units with trivalent phosphorus reagents belongs to the most important synthetic routes to carbazoles and has recently also been applied to the synthesis of carboline derivatives.[14] This reductive cyclization is characterized by the exclusive formation of pyrrole rings,[9] probably via electrocyclization of an intermediary 1-azapentadiene anion. In our approach, the functionalization of the remote aromatic ring is performed via an electrophilic attack of the protonated *o′*-iodoso group. The regioselectivity is controlled by the charge density in the sterically accessible positions. AM1-calculations predict a charge density on the *peri*-position of the naphthalene system in **5b** (iodoso) about 33% higher than in the β-position. With a successive protonation of pyridine and iodoso group, the relative charge density *peri*/β increases to 180:1, therefore directing the electrophilic attack into the *peri*-position. Under the conditions of a Buchwald–Hartwig arylation, iodonium salt **6a** reacts with benzylamine. In the first step, ring opening to an iodo-amino derivative occurs and the pyridine ring is closed in an intramolecular palladium-catalyzed arylation to yield 53% of **7**. Up to now, the iodolium and the Cadogan route have been regarded as alternative methods for the cyclization of nitrobiaryls to (aza)carbazoles. In the special case of a possible *peri*-functionalization,[15] the iodolium route allows access to six-membered cyclic iodonium salts. Furthermore, we could show that these are suitable substrates for the palladium-catalyzed formation of pyridine rings, opening a new route to annulated naphthyridines.[16] For comparison purposes, we subjected **3** to the conditions of the Cadogan reaction.[10] The yield of the anticipated benzocarboline **10** was 65%, spectroscopy did not give any evidence for the formation of the isomeric compound **8**.

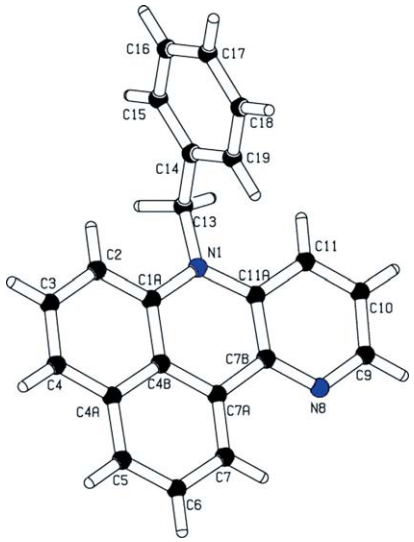


Figure 1 Molecular structure of benzyl-naphthonaphthyridine **7**

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. ^{1}H and ^{13}C NMR spectra: Bruker AC 300 (300 MHz), Bruker AV 400 (400 MHz), and Bruker ARX 400 (400 MHz); $CDCl_3$ or DMSO-d_6. The H and C signals were assigned on the basis of DEPT, COSY 45, HMQC, and HMBC experiments; atom numbering for **6**–**10** is shown in Figure 2. Melting points: Büchi HWS SG 200. IR spectra: Jasco 4100 FT-IR (ATR). FD-MS spectra: Mat 95 (Finnigan); HRMS (ESI): Q-TOF-ULTIMA 3 with Lock Spray device (Waters-Micromass), NaICsI as reference. UV-vis spectra: Perkin-Elmer Lambda 16. Fluorescence spectra: Perkin-Elmer LS 50B. Elemental analyses: Vario EL. Semiempirical calculations of structures and charge densities were performed on the AM1 level using the MOPAC package. Column chromatography on silica gel; PE = petroleum ether.

2-(Naphthalen-1-yl)-3-nitropyridine (3)
A mixture of **1** (200 mg, 1.26 mmol), **2** (270 mg, 1.58 mmol), Ph_3P (34 mg, 0.13 mmol), DME (5 mL), 2 M aq Na_2CO_3 (2.5 mL), and 10% Pd/C (60 mg, 0.06 mmol) was stirred for 16 h at 80 °C, followed by filtration through Celite and washing the filter cake with EtOAc (4 × 7 mL). The combined filtrates were washed with 10% NaOH and brine, dried ($MgSO_4$), and concentrated, and the residue was purified by chromatography (PE–EtOAc, 5:1) to give **3** (312 mg, 98%) as a yellow oil. Previously reported analytical data[14] for **3** are incorrect.

IR (neat, ATR): 1590, 1560, 1524, 1392, 1348, 1232, 1082, 862, 803, 777, 726, 661 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.98 (dd, *J* = 4.7, 1.6 Hz, 1 H, 6-CH), 8.37 (dd, *J* = 8.2, 1.4 Hz, 1 H), 7.95 (m, 2 H), 7.45–7.60 (m, 6 H).

^{13}C NMR (75 MHz, CDC l_3): δ = 153.4 (s), 152.6 (d), 147.2 (s), 134.4 (s), 133.6 (s), 132.3 (d), 130.9 (s), 129.7 (d), 128.6 (d), 126.9 (d), 126.4 (d), 126.2 (d), 125.2 (d), 124.2 (d), 123.0 (d).

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

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}N_2O_2$: 251.0821; found: 251.0825.

2-(Naphthalen-1-yl)pyridin-3-amine (4)
To **3** (15.00 g, 59.94 mmol) in anhyd THF (100 mL) was added 10% Pd/C (3.20 g), and the mixture was stirred for 16 h under a H_2 atmosphere. The mixture was filtered through celite and the residue washed with EtOAc. The combined organic layers were washed with 10% Na_2CO_3 (15 mL), brine (2 × 20 mL), and dried ($MgSO_4$) and the solvent was removed. The residue purified by chromatography (PE–EtOAc, 3:2) to yield **4** (12.95 g, 98%) as a colorless oil.

IR (neat, ATR): 3473, 1611, 1577, 1449, 1309, 1250, 1136, 1017, 971, 906, 799, 778, 764, 727 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 4.6 Hz, *J*′ = 0.7 Hz, 1 H), 7.91 (m, 2 H), 7.56 (m, 3 H), 7.49 (t, *J* = 7.2 Hz, 1 H), 7.42 (t, *J* = 7.2 Hz, 1 H), 7.15 (dd, *J* = 8.1 Hz, *J*′ = 4.6 Hz, 1 H), 7.07 (dd, *J* = 4.6, 0.8 Hz, 1 H), 3.56 (br, 2 H).

^{13}C NMR (75 MHz, CDC l_3): δ = 144.4 (s), 140.9 (s), 139.5 (d), 135.5 (s), 133.9 (s), 131.0 (s), 128.8 (d), 128.3 (d), 127.1 (d), 126.4 (d), 126.0 (d), 125.7 (d), 125.3 (d), 123.3 (d), 122.1 (d).

MS (FD): *m*/*z* (%) = 220.1 (100) $[C_{15}H_{12}N_2]^+$.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}N_2$: 221.1079; found: 221.1089.

3-Iodo-2-(naphthalen-1-yl)pyridine (5)
To a solution of *p*-TsOH (13.0 g, 68.10 mmol) in MeCN (100 mL) was added **4** (5.00 g, 22.70 mmol). At 10–15 °C, a solution of $NaNO_2$ (3.13 g) and KI (9.40 g) in H_2O was added gradually to the suspension and stirring was continued for 1 h; the solution was allowed to come to 20 °C. H_2O (150 mL) was added and $NaHCO_3$ until pH 9, $Na_2S_2O_3$ was added to reduce iodine. The mixture was extracted with Et_2O (3 × 30 mL), washed with brine, dried ($MgSO_4$), and concentrated. Purification by chromatography (PE–EtOAc, 6:1) afforded pure **5** (3.77 g, 49%) as a pale yellow solid; mp 108–109 °C.

IR (neat, ATR): 1561, 1432, 1419, 1386, 1118, 1065, 1012, 970, 862, 800, 774, 721 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.72 (dd, *J* = 4.7, 1.6 Hz, 1 H, 6-CH), 8.32 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.93 (m, 2 H), 7.57 (dd, *J* = 8.2, 7.0 Hz, 1 H), 7.37–7.52 (m, 4 H), 7.10 (dd, *J* = 8.0, 4.7 Hz, 1 H, 5-CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (s), 148.6 (d), 146.9 (d), 140.1 (s), 133.6 (s), 130.9 (s), 128.9 (d), 128.3 (d), 126.7 (d), 126.4 (d), 126.0 (d), 125.3 (d), 125.1 (d), 123.6 (d), 97.1 (s).

MS (FD): *m*/*z* (%) = 331.0 (100) $[C_{15}H_{10}IN]^+$.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}IN$: 331.9936; found: 331.9946.

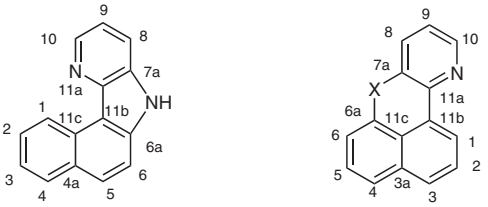


Figure 2 Atom numbering in **6–10**

Naphtho[1,8-*de*]pyrido[3,2-*b*]iodinin-7-ium Trifluoromethanesulfonate (6a) and Naphtho[1,2-*d*]pyrido[3,2-*b*]iodolium Trifluoromethanesulfonate (6b)
Iodo compound **5** (2.00 g, 6.04 mmol) was dissolved in CH_2Cl_2 (20 mL) in a sealed tube under argon. At 0 °C MCPBA (2.07 g, 12.01 mmol) was added, and after stirring for 10 min, TfOH (1.61 mL, 18.12 mmol) was added dropwise. The black solution was stirred for 1 h and evaporated in vacuo. Et_2O was added and the sealed tube cooled to –25 °C. After 30 min the solid was isolated by suction filtration and washed with cold Et_2O to give **6a**/**6b** (ratio 8:1, 1.88 g, 65%) as a yellow solid.

IR (neat, ATR): 1608, 1522, 1279, 1214, 1160, 1022, 820, 791, 755 cm^{-1}.

^1H NMR COSY, HSQC, HMBC (400 MHz, 100.6 MHz, DMSO-d_6): δ (**6a**) = 8.98 (dd, *J* = 7.6, 1.2 Hz, 1 H, 1-CH), 8.79 (dd, *J* = 4.5, 1.4 Hz, 1 H, 10-CH), 8.51 (dd, *J* = 8.2, 1.4 Hz, 1 H, 8-CH), 8.29 (dd, *J* = 7.6, 1.2 Hz, 1 H, 6-CH), 8.19 (m, 2 H, 4-CH, 3-CH), 7.82 (t, *J* = 8.0 Hz, 1 H, 2-CH), 7.68 (t, *J* = 8.0 Hz, 1 H, 5-CH), 7.57 (dd, *J* = 8.2, 4.5 Hz, 1 H, 9-CH).

^1H NMR (400 MHz, 100.6 MHz, DMSO-d_6): δ (**6b**) = 9.18 (d, 1 H), 8.79 (dd, 1 H), 8.53 (d, *J* = 8.2 Hz, 1 H), 8.47 (d, 1 H), 8.22 (1 H, sup.), 8.09 (t, 2 H), 7.93 (d, 1 H), 7.63 (dd, 1 H).

^{13}C NMR HSQC, HMBC (100.6 MHz, 400 MHz, DMSO-d_6): δ (**6a**) = 151.9 (d, 10-CH), 147.4 (s, 11a-C), 141.8 (d, 8-CH), 135.1 (s, 3a-C), 132.7 (d, 6-CH), 132.7 (d, 3-CH), 132.2 (d, 4-CH), 130.7 (s, 11b-C), 129.0 (d, 1-CH), 127.9 (d, 5-CH), 127.8 (d, 2-CH), 127.7 (s, 11c-C), 126.0 (d, 9-CH), 102.8 (s, 7a-C), 101.6 (s, 6a-C).

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: 329.9780.

7-Benzyl-7*H*-naphtho[1,8-*bc*][1,5]naphthyridine (7) and 7-Benzyl-7*H*-benzo[*e*]pyrido[3,2-*b*]indole (9)
$Pd_2(dba)_3$ (34 mg, 0.04 mmol), Xanthphos (64 mg, 0.11 mmol), and Cs_2CO_3 (850 mg, 2.61 mmol) were added to a suspension of **6a**/**6b** (400 mg, 0.93 mmol) in toluene. After stirring for 5 min, $BnNH_2$ (120 mg) was added and the mixture was stirred overnight at 110 °C. Chromatography (PE–EtOAc, 4:1) gave pure **7** (155 mg, 53% from **6a**) as a yellowish solid and the second product **9** (17 mg, ca. 60%) as a yellow-greenish solid.

7-Benzyl-7*H*-naphtho[1,8-*bc*][1,5]naphthyridine (7)
Mp 148–149 °C.

IR (neat, ATR): 3057, 2924, 1619, 1590, 1570, 1445, 1433, 1380, 1261, 1152, 1026, 905, 767, 725, 695 cm^{-1}.

^1H NMR, COSY, HSQC (400 MHz, 100.6 MHz, $CDCl_3$): δ = 8.27 (dd, *J* = 7.4, 1.2 Hz, 1 H, 1-CH), 8.20 (dd, *J* = 4.5, 1.6 Hz, 1 H, 10-CH), 7.60 (dd, *J* = 8.2, 1.2 Hz, 1 H, 3-CH), 7.50 (m, 1 H, 2-CH), 7.36 (m, 2 H, CH_{Ph}), 7.30 (m, 3 H, CH_{Ph}), 7.17 (m, 2 H, 4-CH, 5-CH), 7.05 (dd, *J* = 8.2, 4.3 Hz, 1 H, 9-CH), 6.98 (dd, *J* = 8.4, 1.4 Hz, 1 H, 8-CH), 6.34 (m, 1 H, 6-CH), 5.02 (s, 2 H, CH_2).

^{13}C NMR, HSQC(100.6 MHz, 400 MHz, $CDCl_3$): δ = 141.7 (d, 10-CH), 140.8 (s, 11a-C), 139.7 (s, 6a-C), 137.5 (s, 7a-C), 135.3 (s, 2′-

C),135.2 (s, 3a-C), 130.9 (s, 11b-C), 129.1 (d, 4′-CH), 127.5 (d, 2-CH), 127.5 (d, 5′-CH), 127.2 (d, 5-CH), 126.2 (d, 3-CH), 126.0 (d, 3′-CH), 125.7 (s, 11c-C), 124.0 (d, 9-CH), 120.1 (d, 8-CH), 118.0 (d, 4-CH), 116.4 (d, 1-CH), 103.9 (d, 6-CH), 50.8 (t, 1′-CH_2).

FD-MS: *m*/*z* (%) = 308.1 (100) [M^+]

Anal. Calcd for $C_{22}H_{16}N_2$: C, 85.79; H, 5.23; N, 9.09. Found: C, 85.46; H, 5.02; N, 9.30.

7-Benzyl-7*H*-benzo[*e*]pyrido[3,2-*b*]indole (9)
Mp 133–134 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.66 (d, *J* = 8.5 Hz, 1 H, 1-CH), 8.77 (dd, *J* = 4.6, 1.6 Hz, 1 H, 10-CH), 8.01 (d, *J* = 8.0 Hz, 1 H), 7.92 (d, *J* = 8.8 Hz, 1 H), 7.83 (t, *J* = 8.6 Hz, 1 H), 7.69 (dd, *J* = 8.8 Hz, 1 H), 7.57–7.53 (m, 2 H), 7.34 (dd, 1 H), 7.28–7.23 (m, 3 H, Ph), 7.07 (dd, 2 H), 5.59 (s, 2 H, CH_2).

^{13}C NMR, (100.6 MHz, $CDCl_3$): δ = 142.9, 142.6, 139.2, 136.6, 132.8, 129.5 (C_q), 129.2 (CH), 128.9 (2 CH), 128.9, 128.5, 127.8, 127.7 (CH), 126.2 (2 CH), 124.8, 123.8, 118.5, 116.2 (CH), 114.3 (C_q), 110.6 (CH), 436.5 (CH_2).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{17}N_2$: 309.1392; found: 309.1401.

7*H*-Naphtho[1,8-*bc*][1,5]naphthyridine (8)
KO*t*-Bu (200 mg, 2.6 mmol) was added to a solution of **7** (80 mg, 0.36 mmol) in DMSO (2 mL) and at 25 °C, air was bubbled through the solution; the mixture turned deeply violet. After 10 min, aq NH_4Cl was added and the product extracted with EtOAc (3 ×), dried, concentrated, and purified by chromatography (PE–EtOAc, 1:1) to give **8** (76 mg, 98%) as a yellowish solid; mp 193 °C (dec).

IR (neat, ATR): 3186, 1629, 1607, 1566, 1444, 1365, 1302, 1249, 1127, 955, 870, 825, 762, 669 cm^{-1}.

^{1}H NMR, COSY, HSQC, HMBC (400 MHz, 100.6 MHz, DMSO-d_6): δ = 9.90 (s, 1 H, NH), 8.05 (dd, *J* = 3.9, 2.0 Hz, 1 H, 10-CH), 7.83 (dd, *J* = 7.2, 1.2 Hz, 1 H, 1-CH), 7.43 (dd, *J* = 8.2, 1.0 Hz, 1 H, 3-CH), 7.34 (m, 1 H, 2-CH), 7.16 (m, 3 H, 9-CH, 8-CH, 5-CH), 6.98 (d, *J* = 7.6 Hz, 1 H, 4-CH), 6.48 (dd, *J* = 7.4, 1.0 Hz, 1 H, 6-CH).

^{13}C NMR, HSQC, HMBC (100.6 MHz, 400 MHz, DMSO-d_6): δ = 141.3 (d, 10-CH), 138.5 (s, 6a-C), 138.0 (s, 11a-C), 135.9 (s, 7a-C), 135.5 (s, 3a-C), 131.8 (s, 11b-C), 127.7 (d, 5-CH), 127.6 (d, 2-CH), 125.1 (d, 3-CH), 124.8 (s, 11c-C), 124.7 (d, 9-CH), 121.4 (d, 8-CH), 115.4 (d, 4-CH), 114.0 (d, 1-CH), 105.5 (d, 6-CH).

MS (FD): *m*/*z* (%) = 218.1 (100) [M^+].

Anal. Calcd for $C_{15}H_{10}N_2$: C, 82.55; H, 4.62; N, 12.84. Found: C, 82.16; H, 4.81; N, 13.00.

7*H*-Benzo[*e*]pyrido[3,2-*b*]indole (10)
Nitro compound **3** (400 mg, 1.60 mmol) was suspended in $P(OEt)_3$ (4 mL) in a microwave tube and irradiated at 300 W and 210 °C for 15 min. After evaporation of excess $P(OEt)_3$, the residue was refluxed in aq 10% HCl. Na_2CO_3 was added until pH 9, the mixture was extracted with toluene (3 ×) and the organic solutions were pooled and concentrated. Crude **10** was purified by chromatography (silica gel, PE–EtOAc, 2:1) to give pure **10** (227 mg, 65%) as an off-white solid; mp 265 °C (dec) (Lit.[14] 244–246 °C).

IR (neat, ATR): 3032, 1622, 1535, 1461, 1355, 1249, 1209, 1138, 1010, 963, 882, 808, 754, 700 cm^{-1}.

^{1}H NMR COSY, HSQC, HMBC (400 MHz, 100.6 MHz, DMSO-d_6): δ = 11.91 (s, 1 H, 7-N*H*), 9.44 (d, *J* = 8.5 Hz, 1 H, 1-CH), 8.63 (dd, *J* = 4.7, 1.6 Hz, 1 H, 10-CH), 8.05 (d, *J* = 8.0 Hz, 1 H, 4-CH), 8.00 (m, 2 H, 8-CH, 5-CH), 7.79 (d, *J* = 8.8 Hz, 1 H, 6-CH), 7.72 (m, 1 H, 2-CH), 7.49, m, 1 H, 3-CH), 7.41 (dd, *J* = 8.2, 4.7 Hz, 1 H, 9-CH).

^{13}C NMR, HSQC, HMBC (100.6 MHz, 400 MHz, DMSO-d_6): δ = 142.3 (s, 11a-C), 142.1 (d, 10-CH), 138.4 (s, 6a-C), 131.6 (s, 7a-C), 128.9 (s, 11c-C), 128.5 (d, 4-CH), 128.4 (d, 5-CH), 128.3 (s, 4a-C), 126.9 (d, 2-CH), 123.8 (d, 1-CH), 123.2 (d, 3-CH), 118.6 (d, 9-CH), 118.4 (d, 8-CH), 113.6 (d, 6-CH), 113.1 (s, 11b-C).

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

X-ray Structure Determination of 7
Enraf–Nonius Turbo-Cad 4, equipped with a rotating anode (CuKα, graphite monochromator; λ = 1.54180 Å). Crystal data: $C_{22}H_{16}N_2$, *M* = 308.4 g mol^{-1}, 0.05 × 0.1 × 0.2 mm^3, monoclinic, $P2_1/n$, *T* = 193 K, unit cell: *a* = 7.603(2) Å, *b* = 17.772(1) Å, *c* = 11.613(2) Å, β = 96.571(10)°, *V* = 1558.8(5) $Å^3$, *z* = 4, d_{calc} = 1.314 g cm^{-3}, absorption μ = 0.6 mm^{-1}, θ range for data collection: 2–70°; index ranges: $-9 \le h \le 0$, $0 \le k \le 21$, $-14 \le l \le 14$. Number of reflections collected: 3301; independent reflections: 2951 [R_{int} = 0.0725]. Direct structure solution: program SIR 97, refinement: SHELXL 97,[17a] full-matrix least squares on 217 parameters, weighted refinement: $w = 1/[\sigma^2(F_o^2) + (0.0826\,P)^2]$ with $P = [\max(F_o^2,0) + 2F_o^2]/3$, H 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* = 1.013, maximal range of parameters: 0.001(e.s.d.), final *R* indices: R_1 = 0.1565, wR_2 = 0.0522, the final difference Fourier map showed minimum and maximum values of 0.23 and –0.23 e $Å^{-3}$, respectively.[17b]

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

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