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Total Synthesis of the Marine Pyridoacridine Alkaloid Demethyldeoxyamphimedine

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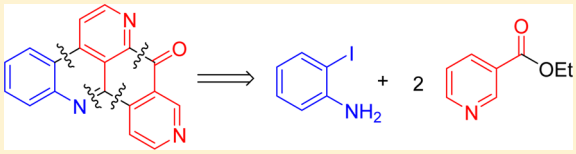
Supporting Information

ABSTRACT: A four-step total synthesis of the marine pyridoacridine alkaloid demethyldeoxyamphimedine (**5**) is presented. With an overall yield of 6.4%, this pentacyclic compound has been synthesized by utilizing only two commercial building blocks, ethyl nicotinate and 2-iodoaniline. The final cyclization step was achieved via a directed remote ring metalation with Knochel–Hauser base (TMPMgCl·LiCl) followed by intramolecular trapping of an ester group.



The pyridoacridine family is a large and growing class of marine alkaloids isolated from sessile organisms like sponges, corals, ascidians, and bryozoa.[1] Meanwhile more than 100 of these polycyclic alkaloids have been isolated, and based on biosynthetic considerations, a number of "undiscovered" alkaloids of this family have been predicted.[2] Many of these alkaloids exhibit significant biological activities, e.g., cytotoxic, antibacterial, antiviral, antifungal, antiparasitic, and insecticidal.[3] The outstanding biological activities have attracted the attention of numerous research groups working toward the total synthesis of members of this class of natural products or analogues thereof.

Among the most prominent types of pentacyclic pyridoacridine alkaloids are the ascidiidemin (**1**) and the amphimedine (**2**) subclasses, which vary particularly in the connection of rings A and B (Figure 1).[2] The amphimedine subclass consists of amphimedine (**2**), neoamphimedine (**3**), deoxyamphimedine (**4**), and demethyldeoxyamphimedine (**5**), which was isolated in 2011 from the marine ascidian *Cystodytes dellechiajei* collected near Catalonia, Spain[4] (Figures 1 and 2). While most of the synthetic strategies leading to ascidiidemin-type

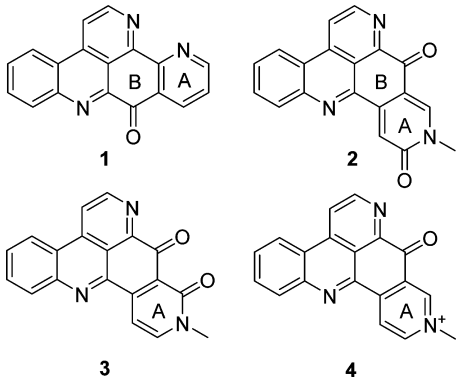


Figure 1. Prominent pentacyclic pyridoacridine alkaloids: ascidiidemin (**1**), amphimedine (**2**), neoamphimedine (**3**), and deoxyamphimedine (**4**).

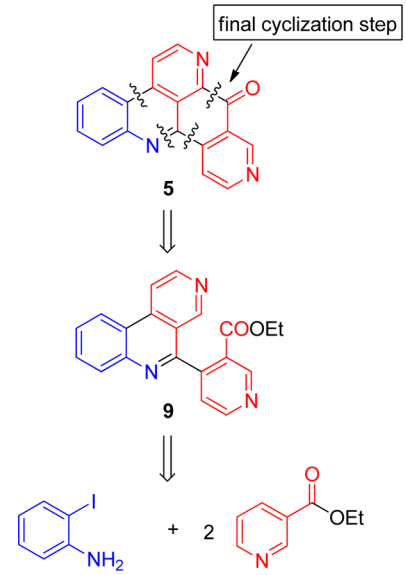


Figure 2. Structure of demethyldeoxyamphimedine (**5**) and retrosynthetic consideration.

structures are based on Bracher's first total synthesis of ascidiidemin (**1**),[5] different synthetic approaches toward the amphimedine scaffold have been developed.[6] The first total synthesis of demethyldeoxyamphimedine (**5**) was accomplished by Delfourne's group[7] in 2002, years before the compound was identified as a natural product. The key step of their multistep synthesis was a hetero-Diels–Alder cycloaddition of isoquinoline-5,8-dione with a 1-azadiene. However, this reaction gave

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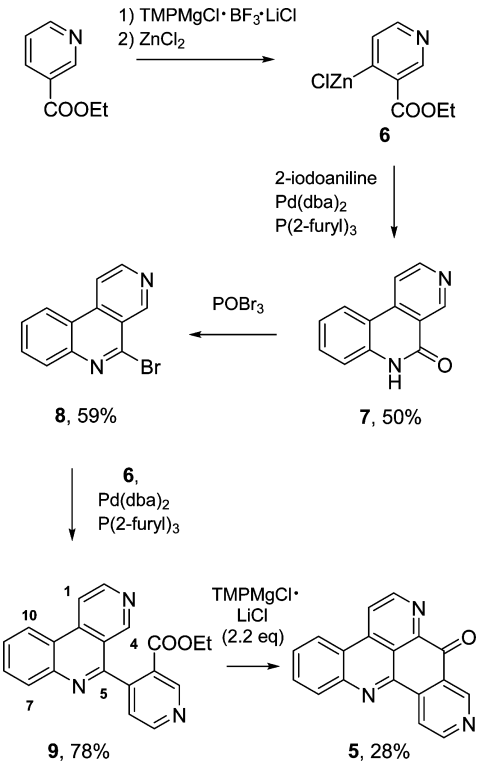
the desired azaanthraquinone in only 0.8% yield, accompanied by a poorly separable regioisomer, rendering the entire total synthesis ineffective. Here, we report on a new, effective four-step total synthesis of the alkaloid demethyldeoxyamphimedine (**5**).

Our synthesis strategy should substantially differ from the above-mentioned total synthesis[7] and lead to a new, general access to pyridoacridine alkaloids. It was inspired by our recent approach to analogues of the alkaloid ascididemin (**1**), in which we prepared 4-arylbenzo[*c*][2,7]naphthyridine building blocks bearing an ester moiety at C-5 and performed ring closure to the pentacycles via superacid-mediated Friedel–Crafts-type intramolecular ring acylation.[8] Since an analogous approach to the target alkaloid **5** through intermediate **9** would have necessitated an acylation of a pyridine ring, the Friedel–Crafts protocol was unpromising here. This prompted us to investigate a cyclization method involving direct metalation at the pertinent ring position, followed by intramolecular trapping of the organometallic functionality by the ester group to give the cyclic ketone. A retrosynthetic analysis led to a strategy which should enable us to prepare the central intermediate **9** from two commercial building blocks, ethyl nicotinate (incorporated twice) and 2-iodoaniline (Figure 2), by extensive utilization of Knochel's work on ring metalation reactions with TMPMgCl·LiCl and related bases, followed by palladium-catalyzed cross-coupling reactions.[9,10]

The first step of our new synthesis was the preparation of benzo[*c*][2,7]naphthyridin-5(6*H*)-one (**7**) in a single operation starting from ethyl nicotinate and 2-iodoaniline. Direct metalation at C-4 of ethyl nicotinate using TMPMgCl·BF_3·LiCl, and subsequent transmetalation with $ZnCl_2$ to **6**,[10] followed by palladium-catalyzed Negishi cross-coupling reaction with 2-iodoaniline led to a biaryl, which underwent lactamization at room temperature to give tricyclic product **7** in 50% yield. This approach is more efficient than previous multistep syntheses.[11] The spectroscopic data of **7** were in full agreement with those reported previously,[11a] thus confirming the high C-4 regioselectivity of the initial metalation step. Intermediate **7** was transferred into 5-bromobenzo[*c*][2,7]-naphthyridine (**8**) in 59% yield using $POBr_3$ at 135 °C.[12] In another Negishi reaction, **8** was coupled with the above-described organozinc intermediate **6** derived from ethyl nicotinate to give the pyridylbenzo[*c*][2,7]naphthyridine **9** in 78% yield. The final cyclization to **5** required regioselective direct metalation at C-4 of the tricycle **9** without affecting the ester group and avoiding undesired nucleophilic addition reactions to the benzo[*c*][2,7]napthtyridine ring system.[8,13] Both of these demands precluded alkyllithium and Grignard reagents as metalating agents. Eventually, ring closure was accomplished by metalation with 2.2 equiv of Knochel's TMPMgCl·LiCl at 0 °C for 2 h and subsequent intramolecular trapping of the ester group at room temperature within 16 h. Negligible conversion took place if only 1 equiv of the base was employed. The alkaloid **5** was obtained in 28% yield (total yield over four steps: 6.4%), side reactions were not observed to a noteworthy extent, but 55% of starting material was recovered. Increasing the amount of metalating agent to 3 equiv did not further improve the yield of **5** (Scheme 1).

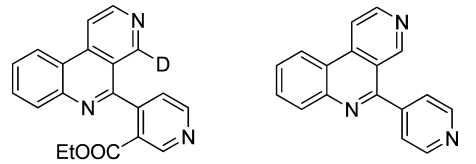
In order to evaluate whether the demand for 2 equiv of metalation agent is due to unproductive complexation of the first equivalent[14] or to additional metalation at another position of the substrate molecule, we performed a D_2O quenching experiment after the metalation period (2 h, 0 °C).[15] In

Scheme 1. Total Synthesis of Demethyldeoxyamphimedine (5)



recovered (about 65%) educt **9-D** deuterium incorporation (about 50–70% in different batches; calculated from the NMR resonance of 4-H) was detected at C-4 (Scheme 2 and

Scheme 2. Outcome of a D_2O Quenching Experiment (9-D) and Model Compound 10



Supporting Information). In cyclized product **5** obtained in this experiment (yield: 5%) no deuterium incorporation was found. The absence of detectable deuteriation at any other position indicates that metalation occurs exclusively at C-4 of the starting material **9**. The surprisingly high amount of deuterium incorporation in **9-D** further demonstrates that cyclization does not occur spontaneously after the metalation step.

This regioselective metalation could eventually proceed via direct metalation next to a pyridine nitrogen, as shown for the employed TMPMgCl·LiCl with isoquinoline[16] and for TMPMgCl·BF_3LiCl with pyridine and quinoline.[10] Alternatively, the ester group could be involved as a directing group in a directed remote metalation (DReM),[17] since in addition to numerous examples for carboxamides, carbamates, and carboxylates showing this ability, few examples for esters as remote directing groups in metalation–cyclization cascades have been published.[18] For this purpose, we prepared 5-(pyridin-4-yl)benzo[*c*][2,7]naphthyridine (**10**, Scheme 2), an analogue of **9** only lacking the ester group, by Suzuki cross-

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coupling of **8** with pyridine-4-boronic acid and subjected it to the metalation protocol as described for the synthesis of alkaloid **5**. Upon quenching with D_2O, virtually no incorporation of deuterium into the recovered compound **10** was observed. This indicates that the ester group contributes to the ring metalation in the conversion of **9** to alkaloid **5** in the sense of a directed remote metalation. Our observation is in contrast to the one on ethyl 2-(pyridin-3-yl)benzoate, where a complexation of the pyridine nitrogen (and not the ester group) with the base (LiTMP) was postulated.[17b,18b]

In summary, the protocol described here allows for a straightforward total synthesis of the marine alkaloid demethyldeoxyamphimedine (**5**) starting from sparsely functionalized, commercial building blocks.

EXPERIMENTAL SECTION

General Information. All reactions were performed under argon atmosphere with flame-dried glassware. Solvents used were of HPLC grade or p.a. grade and/or purified according to standard procedures. Melting points were determined by open tube capillary method apparatus and are uncorrected. NMR spectra were recorded on a 400, 500, or 600 MHz spectrometer with tetramethylsilane as internal standard. NMR spectra were recorded in deuteriated solvents, and chemical shifts are reported in parts per million (ppm). *J* values are given in Hertz. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet. Signal assignments were carried out based on ^{1}H, ^{13}C{^{1}H}, HMBC, HMQC, and COSY spectra. Mass spectra (MS) were by electron impact (EI) at 70 eV. HRMS in EI mode (70 eV) were determined with sector field detectors. Chromatographic purification of products was performed by flash column chromatography (FCC) using silica gel (0.015−0.040 mm) as stationary phase. Purity of all synthesized compounds was >95%, determined by HPLC with a EC-C18 column (3.0 × 100 mm) (except for compound **10**), with acetonitrile/water/THF (700:298:2) eluent and UV detection at 210 and 254 nm.

Benzo[*c*][2,7]naphthyridin-5(6*H*)-one (7). A dry and nitrogen-flushed 100 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with TMPMgCl·LiCl (3.9 mL, 5.09 mmol, 1.3 M in THF) and cooled to −40 °C. Freshly distilled BF_3·Et_2O (0.63 mL, 5.09 mmol) was added dropwise, and the mixture was stirred for 20 min at the same temperature. Ethyl nicotinate (700 mg, 4.63 mmol) was dissolved under nitrogen atmosphere in dry THF (20 mL) and then added dropwise to the reaction mixture. The mixture was stirred at −40 °C for 40 min before anhydrous $ZnCl_2$ (5.1 mL, 5.09 mmol, 1 M in THF) was added. After the mixture was stired for 60 min at the same temperature, $Pd(dba)_2$ (132 mg, 0.23 mmol, 5 mol %) and P(2-furyl)$_3$ (107 mg, 0.46 mmol, 10 mol %), dissolved in dry THF (16 mL), were transferred to the reaction mixture followed by the addition of 2-iodoaniline (810 mg, 3.70 mmol) dissolved in dry THF (6 mL). The reaction mixture was slowly warmed to room temperature and stirred for 44 h at the same temperature. Saturated aqueous NH_4Cl solution (20 mL) and concd NH_3 (2 mL) were then added, and the layers were separated, followed by the extraction with EtOAc (3 × 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by FCC (CH_2Cl_2/MeOH = 95:5) to give **7** (360 mg, 50%) as a white solid: mp 301 °C (lit.[11b] mp 300 °C); ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ (ppm) = 11.91 (s, 1H, 6-H), 9.42 (s, 1H), 8.89 (d, *J* = 5.6 Hz, 1H), 8.44 (d, *J* = 7.3 Hz, 1H), 8.40 (d, *J* = 5.6 Hz, 1H), 7.60 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.38 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.31 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H); ^{13}C NMR (126 MHz, $(CD_3)_2SO$) δ (ppm) = 160.3, 152.0, 150.2, 140.6, 138.2, 131.9, 124.3, 122.6, 120.4, 116.4, 116.2, 115.7; IR (KBr pellet) ν (cm^{-1}) = 3024, 2891, 1682, 1602, 1478, 1419, 1360, 1184, 1041, 1019, 763, 667, 643; MS (EI) *m*/*z* (rel int) = 197 $[M + H]^+$ (12), 196 $[M]^{+\bullet}$ (100), 195 (58), 177 (14), 140 (12); HRMS (EI) *m*/*z* calcd. for $C_{12}H_8N_2O$ $[M]^+$ 196.0637, found 196.0631.

5-Bromobenzo[*c*][2,7]naphthyridine (8). Benzo[*c*][2,7]-naphthyridine-5(6*H*)-one (7, 150 mg, 0.70 mmol) was mixed with $POBr_3$ (1.00 g, 3.50 mmol), and the mixture was then heated under nitrogen atmosphere at 135 °C for 3 h. After the mixture was cooled to room temperature, water (20 mL) was added with cooling on ice. The mixture was neutralized using 6 M NaOH and extracted with $CHCl_3$ (3 × 50 mL). The combined organic layers were washed with brine (50 mL) and water (2 × 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by FCC (EtOAc/isohexane = 2:1) to give **8** (107 mg, 59%) as a white solid: mp 167 °C (lit.[12a] mp 142−144 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 9.66 (s, 1H), 8.99 (d, *J* = 5.7 Hz, 1H), 8.96 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.24 (d, *J* = 5.7 Hz, 1H), 8.07 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.82 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.72 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 153.7, 150.0, 145.6, 143.7, 139.3, 131.8, 129.9, 128.4, 123.0, 122.3, 121.5, 115.1; IR (KBr pellet) ν (cm^{-1}) = 1600, 1550, 1460, 1409, 1281, 1241, 1183, 1056, 1034, 1016, 940, 835, 763, 727, 620; MS (EI) *m*/*z* (rel int) = 260 $[M]^{+\bullet}$ (39), 258 $[M]^{+\bullet}$ (40), 179 (100), 152 (24); HRMS (EI) *m*/*z* calcd for $C_{12}H_7BrN_2$ $[M]^+$ 257.9793, found 257.9786.

Ethyl 4-(Benzo[*c*][2,7]naphthyridin-5-yl)nicotinate (9). A dry and nitrogen-flushed 25 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with TMPMgCl·LiCl (0.82 mL, 1.07 mmol, 1.3 M in THF) and cooled to −40 °C. Freshly distilled BF_3·Et_2O (0.13 mL, 1.07 mmol) was added dropwise, and the mixture was stirred for 10 min at the same temperature. Ethyl nicotinate (147 mg, 0.97 mmol) was dissolved under nitrogen atmosphere in dry THF (5 mL) and then added dropwise over 2 min to the reaction mixture. The mixture was stirred at −40 °C for 20 min before anhydrous $ZnCl_2$ (1.07 mL, 1.07 mmol, 1 M in THF) was added. After the mixture was stirred for 30 min at the same temperature, $Pd(dba)_2$ (29 mg, 0.05 mmol, 5 mol %) and P(2-furyl)$_3$ (23 mg, 0.10 mmol, 10 mol %), dissolved in 2 mL of dry THF, were transferred to the reaction mixture, directly followed by the addition of 5-bromobenzo[*c*][2,7]-naphthyridine (**8**, 200 mg, 0.78 mmol), dissolved in dry THF (4 mL). The reaction mixture was slowly warmed to room temperature and stirred for 24 h at this temperature. The reaction mixture was quenched with satd aqueous NH_4Cl solution (10 mL) and concd NH_3 (1 mL), and the layers were separated followed by the extraction with EtOAc (3 × 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by FCC (CH_2Cl_2/MeOH = 95:5) to give **9** (200 mg, 78%) as a pale yellow solid: mp 151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 9.44 (s, 1H), 8.98 (d, *J* = 4.9 Hz, 1H,), 8.96 (m, 2H), 8.64 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.47 (dd, *J* = 5.8, 0.7 Hz, 1H), 8.22 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.91 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.81 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.54 (dd, *J* = 4.9, 0.6 Hz, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 0.80 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 164.6, 158.6, 153.2, 152.0, 151.0, 148.8, 147.1, 144.7, 137.4, 131.4, 130.4, 128.1, 125.9, 124.8, 122.8, 121.9, 120.5, 115.5, 61.4, 13.5; IR (KBr pellet) ν (cm^{-1}) = 1715 (CO), 1606, 1577, 1566, 1544, 1364, 1281, 1217, 1120, 1106, 1048, 1020, 854, 775, 734, 628; MS (EI) *m*/*z* (rel int) = 329 $[M]^{+\bullet}$ (50), 285 (23), 284 (86), 256 (100), 229 (24); HRMS (EI): *m*/*z* calcd for $C_{20}H_{15}N_3O_2$ $[M]^+$ 329.1164, found 329.1155.

8*H*-Benzo[*b*]pyrido[4,3,2-*de*][1,8]phenanthrolin-8-one (Demethyldeoxyamphimedine) (5). A dry and nitrogen-flushed 25 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with TMPMgCl·LiCl (0.64 mL, 0.83 mmol, 1.3 M in THF) and cooled to 0 °C. A solution of ethyl 4-(benzo[*c*][2,7]naphthyridin-5-yl)nicotinate (**9**, 125 mg, 0.38 mmol) in dry THF (6 mL) was added dropwise to the reaction mixture. After being stirred for 2 h at 0 °C, the mixture was warmed to room temperature, and stirring was continued for 16 h. Saturated aqueous NH_4Cl solution (15 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by FCC (CH_2Cl_2/MeOH = 97:3). The product-containing fractions were concentrated under reduced pressure, and the residue was suspended in EtOAc. The suspension was filtered and washed with EtOAc to give

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5 (30 mg, 28%) as yellow powder as filter residue: mp 368 °C (lit.[7] mp >260 °C; lit:[4] no mp given); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 9.72 (s, 1H), 9.38 (d, J = 5.5 Hz, 1H), 9.11 (d, J = 5.3 Hz, 1H), 8.83 (dd, J = 5.3, 0.8 Hz, 1H), 8.71 (d, J = 5.5 Hz, 1H), 8.68 (dd, J = 8.1, 1.0 Hz, 1H), 8.43 (dd, J = 8.4, 0.9 Hz, 1H), 8.02 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.90 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) = 181.7, 154.7, 150.6, 150.4, 147.1, 146.8, 145.5, 141.9, 138.1, 132.1, 131.8, 129.8, 126.4, 123.0, 122.2, 119.8, 119.0, 118.3; IR (KBr pellet) ν (cm^{-1}) = 1676 (CO), 1589, 1562, 1470, 1353, 1312, 1265, 1236, 1192, 949, 878,859, 772, 719; MS (EI) m/z (rel int) = 284 $[M + H]^+$ (21), 283 $[M]^{+\bullet}$ (100), 254 (17); HRMS (EI) m/z calcd for $C_{18}H_9N_3O$ $[M]^+$ 283.0746, found 283.0739.

5-(Pyridin-4-yl)benzo[*c*][2,7]naphthyridine (10). 5-Bromobenzo[*c*][2,7]naphthyridine (**8**, 175 mg, 0.68 mmol), pyridine-4-boronic acid (100 mg, 0.82 mmol), and $Pd(PPh_3)_4$ (39.3 mg, 0.034 mmol, 5 mol %) were dissolved in THF (15 mL) and K_2CO_3 solution (1.64 mL, 1.64 mmol, 1 M in water). The reaction mixture was stirred for 20 h under nitrogen atmosphere at 80 °C to reflux before it was transferred into water (30 mL) and extracted with EtOAc (4 × 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by FCC (CH_2Cl_2/MeOH = 95:5) to give **10** (65 mg, 37%) as slightly brown solid: mp 142 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 9.42 (s, 1H), 9.00 (d, J = 5.7 Hz, 1H), 8.90−8.87 (m, 2H), 8.64 (dd, J = 8.2, 1.3 Hz, 1H), 8.49 (d, 5.8 Hz, 1H), 8.29 (dd, J = 8.2, 1.3 Hz, 1H), 7.93 (ddd, 8.3, 7.1, 1.3 Hz, 1H), 7.82 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.75−7.70 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 158.1, 151.7 (2C), 150.4, 149.1, 145.9, 145.1, 138.5, 131.6, 130.9, 128.4, 124.6 (2C), 122.8, 122.0, 119.7, 115.7; IR (KBr pellet) ν (cm^{-1}) = 3035, 3023, 1599, 1561, 1541, 1405, 1364, 1353, 1247, 828, 763, 734, 625; MS (EI) m/z (rel int) = 257 $[M]^{+\bullet}$ (100), 229 (10); HRMS (EI) m/z calcd for $C_{17}H_{11}N_3$ $[M]^+$ 257.0953, found 257.0947.

Ethyl 4-(4-[^{2}H]-Benzo[*c*][2,7]naphthyridin-5-yl)nicotinate (9-D). A dry and nitrogen-flushed 10 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with TMPMgCl·LiCl (0.51 mL, 0.51 mmol, 1.0 M in THF/toluene) and cooled to 0 °C. A solution of ethyl 4-(benzo[*c*][2,7]naphthyridin-5-yl)nicotinate (**9**, 75 mg, 0.23 mmol) in dry THF (6 mL) was added dropwise to the reaction mixture. After the mixture was stirred for 2 h at 0 °C, D_2O (0.50 mL) was added, followed by the addition of satd aqueous NH_4Cl solution (2 mL). The mixture was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by FCC (CH_2Cl_2/MeOH = 97:3) to give **9-D** (49 mg, 65%) as a brown solid: mp 146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 9.44 (s, ca. 0.3H), 8.98 (d, J = 4.9 Hz, 1H), 8.95 (m, 2H), 8.64 (dd, J = 8.2, 1.3 Hz, 1H), 8.47 (d, J = 5.9 Hz, 1H), 8.22 (dd, J = 8.2, 1.3 Hz, 1H), 7.91 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.81 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.54 (d, J = 4.9 Hz, 1H), 3.98 (q, J = 7.1 Hz, 2H), 0.80 (td, J = 7.1, 1.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 164.8, 158.8, 153.3, 152.2, 151.1, 149.0, 147.3, 144.9, 137.6, 131.5, 130.6, 128.2, 126.1, 125.0, 122.9, 122.1, 120.6, 115.7, 61.5, 13.7; IR (NaCl film) ν (cm^{-1}) = 1722, 1681, 1603, 1577, 1566, 1548, 1462, 1415, 1362, 1125, 1109, 1073, 1052, 855, 765; MS (EI) m/z (rel int) = 330 $[M]^{+\bullet}$ (61), 329 (35), 286 (22), 285 (85), 284 (100), 258 (61), 257 (81); HRMS (EI) m/z calcd. for $C_{20}H_{14}DN_3O_2$ $[M]^+$ 330.1227, found 330.1240.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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