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SYNTHESIS OF 4-AMINO-6-ARYL-6*H*-PYRROLO[1,2-*a*][1]BENZAZEPINE-5-CARBONITRILES FROM 1-(2-BROMOPHENYL)-1*H*-PYRROLES AND ARYLIDENEMALONONITRILES

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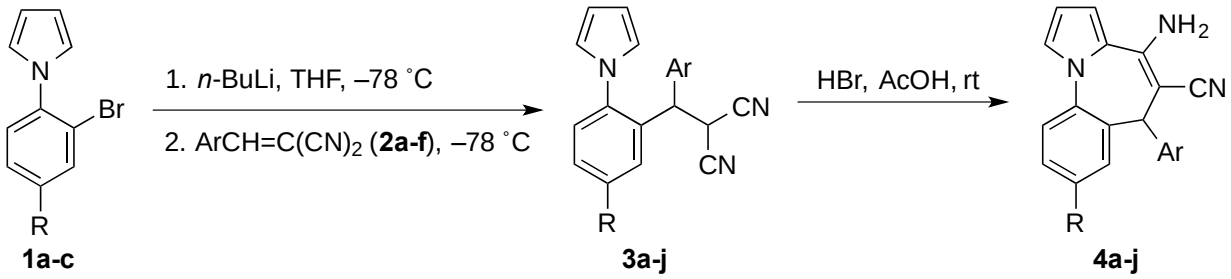
Abstract – A convenient method for the preparation of 4-amino-6-aryl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitriles has been developed. The method is based on the hydrogen bromide-mediated cyclization reaction of 2-{aryl[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitriles, produced by the treatment of 2-(1*H*-pyrrol-1-yl)phenyllithiums with arylidenemalononitriles. The lithium compounds can be easily generated by the bromine/lithium exchange between 1-(2-bromophenyl)-1*H*-pyrroles and butyllithium.

Several compounds with the 6*H*-pyrrolo[1,2-*a*][1]benzazepine skeleton have been reported to be useful because of their biological activities.[1] For example, some work as selective peripheral type benzodiazepine receptor (PBR)[1b] and some are effective for the treatment of cancer[1a] or hypercholesterolemia and hyperlipemia.[1c] However, only a few studies have been done to develop useful synthetic routes to 6*H*-pyrrolo[1,2-*a*][1]benzazepines. Soriano *et al*. have reported a method utilizing a Pt-catalyzed cyclization of 1-(2-allenylphenyl)-1*H*-pyrroles.[2] An efficient method reported by Lee *et al*. involves acid-assisted cyclization of Morita-Baylis-Hillman adducts of 2-(1*H*-pyrrol-1-yl)benzaldehydes with methyl acrylate or methyl vinyl ketone.[3] However, these methods require the use of unordinary and expensive reagents and/or multiple synthetic steps to accomplish the overall process. Accordingly, we became interested in developing a novel method for preparing 6*H*-pyrrolo[1,2-*a*][1]benzazepine derivatives, and envisioned that 2-{aryl[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitriles (**3**) could be

prepared from 1-(2-bromophenyl)-1*H*-pyrroles (**1**) and arylidenemalononitriles (**2**), and they would give 4-amino-6-aryl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitriles (**4**) on treatment with an appropriate acid. In this paper we would like to present the results of our investigation, which provide a facile method for the synthesis of a new type of 6*H*-pyrrolo[1,2-*a*][1]benzazepines utilizing an easily operated two-step procedure.

Our synthesis of **4** from **1** and **2** was conducted according to the sequence illustrated in Scheme 1. The starting materials (**1**) can easily be prepared from commercially available 2-bromobenzenamines by the procedure reported previously.[1c,4,5] As the first step of the sequence, 2-(1*H*-pyrrol-1-yl)phenyllithiums,[6] generated by the bromine/lithium exchange between **1** and butyllithium, were allowed to react with arylidenemalononitriles (**2**), which are commercially available or readily prepared by the literature methods,[7–9] in THF at –78 ˚C. The 1,4-addition of the anions to the acceptors proceeded immediately at this temperature to provide, after protonation by aqueous work up, 2-{aryl[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitriles (**3**) in generally fair to good yields (Table 1, Entries 1–8). However, the use of 1-(2-bromo-4-chlorophenyl)-1*H*-pyrrole (**1c**) gave rather complicated mixtures of the products, from which only low to moderate yields of the desired adducts (**3i**) and (**3j**) were obtained (Entries 9 and 10). This may be attributed to the accompanying lithiation at the 3-position ortho to both the chloro and bromo substituents, which is possible to result in the formation of benzyne intermediates.



1a-c **3a-j** **4a-j**

Scheme 1

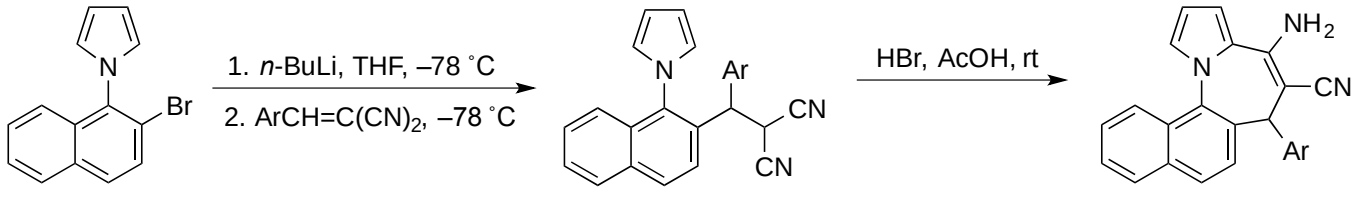
Table 1. Preparation of 4-amino-6-aryl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitriles (**4**)

Entry	**1**	R	**2**	Ar	**3**	Yield/%[a]	**4**	Yield/%[a]
1	**1a**	H	**2a**	Ph	**3a**	88	**4a**	73
2	**1a**	H	**2b**	4-MeC_6H_4	**3b**	77	**4b**	74
3	**1a**	H	**2c**	4-ClC_6H_4	**3c**	78	**4c**	72
4	**1a**	H	**2d**	4-$MeOC_6H_4$	**3d**	75	**4d**	80
5	**1a**	H	**2e**	3,4-$Cl_2C_6H_3$	**3e**	71	**4e**	86
6	**1b**	Me	**2a**	Ph	**3f**	78	**4f**	80
7	**1b**	Me	**2b**	4-MeC_6H_4	**3g**	86	**4g**	67
8	**1b**	Me	**2d**	4-$MeOC_6H_4$	**3h**	64	**4h**	90
9	**1c**	Cl	**2a**	Ph	**3i**	49	**4i**	63
10	**1c**	Cl	**2f**	3,4-$(MeO)_2C_6H_3$	**3j**	21	**4j**	67

[a] Yields of isolated products.

The transformation of thus obtained adducts (**3**) into the desired pyrrolobenzazepines (**4**) was then performed by treating them with an equivalent of hydrogen bromide in acetic acid at room temperature. The cyclization took place quickly, yielding the desired products after aqueous work up and the subsequent purification by column chromatography on silica gel. The yields of the products were generally good as compiled in Table 1 as well. It is necessary to point out that an equivalent of the acid was needed to realize the good yields of the products. The use of catalytic amounts of the acid caused somewhat or rather decreased yields of the products. This may be ascribed to the decomposition of the products during the prolonged reaction times due to the sluggishness under these conditions.

We next attempted to synthesize a new ring system, 6*H*-naphtho[2,1-*f*]pyrrolo[1,2-*a*]azepine from 1-(2-bromonaphthalen-1-yl)-1*H*-pyrrole (**5**).[7] When the procedure described in Scheme 1 was adapted to **5**, it provides an easy route to 4-amino-6-aryl-6*H*-naphtho[2,1-*f*]pyrrolo[1,2-*a*]azepine-5-carbonitriles (**7**) as outlined in Scheme 2. Thus, compound (**5**) was successively treated with butyllithium and arylidenemalononitriles (**2**) under conditions described for the preparation of **3** to afford 2-{aryl[1-(1*H*-pyrrol-1-yl)naphthalen-2-yl]methyl}propanedinitriles (**6**) in relatively good yields. These adducts (**6**) were similarly treated with hydrogen bromide to furnish the corresponding desired products (**7**) in good to excellent yields. Isolation of **7** could be accomplished much more easily than that of **4**. The products precipitated immediately from the reaction mixture after treatment of **6** with the acid. After filtration and washing with water under reduced pressure, spectroscopic pure products could be obtained.



5

6a Ar = Ph 65%
6b Ar = 4-MeOC$_6$H$_4$ 79%

7a Ar = Ph 95%
7b Ar = 4-MeOC$_6$H$_4$ 76%

Scheme 2

In conclusion, an efficient procedure for the preparation of 4-amino-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitriles, a new type of 6*H*-pyrrolo[1,2-*a*][1]benzazepine derivatives, utilizing the reaction of 2-(1*H*-pyrrol-1-yl)phenyllithiums with arylidenemalononitriles followed by hydrobromic acid-mediated cyclization of the resulting adducts, which starts from readily available 1-(2-bromophenyl)-1*H*-pyrroles, has been developed. The method has been shown to be applicable to the construction of a new ring system, 6*H*-naphtho[2,1-*f*]pyrrolo[1,2-*a*]azepine. The present method is valuable for organic synthesis, because it consists of simple procedures. Moreover, as these products carry an enamino nitrile moiety,

they are able to be elaborated to structurally further complicated polycyclic heterocycles. Further studies are underway to extend this methodology for the preparation of related fused heterocyclic compounds.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a PerkinElmer Spectrum 65 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a Thermo Scientific Exactive spectrometer (DART or ESI). Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. 1-(2-Bromophenyl)-1*H*-pyrroles (**1a**),[4] (**1b**),[5] (**1c**),[1c] arylidenemalononitriles (**2b**),[7] (**2c**),[8] (**2d**),[9] (**2e**),[8] (**2f**),[7] and 1-(2-bromonaphthalen-1-yl)-1*H*-pyrrole (**5**)[10] were prepared according to the reported procedures. *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of 2-{Aryl[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitriles (3) and 2-{Aryl[1-(1*H*-pyrrol-1-yl)naphthalen-2-yl]methyl}propanedinitriles (6). 2-{Phenyl[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3a). To a stirred solution of **1a** (0.22 g, 1.0 mmol) in THF (3 mL) at –78 ˚C was added *n*-BuLi (1.6 M in hexane; 1.0 mmol) dropwise. After 5 min, a solution of PhCH=C(CN)$_2$ (**2a**) (0.15 g, 1.0 mmol) in THF (2 mL) was added and stirring was continued for an additional 15 min before addition of saturated aqueous NH_4Cl (15 mL). The mixture was warmed to room temperature and extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to afford **3a** (0.26 g, 88%); a pale-yellow gum; R_f 0.25 (AcOEt/hexane 1:7); IR (neat) 2256, 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.22 (d, J = 9.2 Hz, 1H), 4.51 (d, J = 9.2 Hz, 1H), 6.36 (br s, 2H), 6.66 (br s, 2H), 7.21 (d, J = 6.9 Hz, 2H), 7.31–7.37 (m, 4H), 7.44 (td, J = 7.4, 1.1 Hz, 1H), 7.51 (td, J = 7.4, 1.1 Hz, 1H), 7.59 (d, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.9, 45.5, 109.9, 111.7, 111.9, 122.7, 127.2, 127.9, 128.7, 128.8, 129.1, 129.25, 129.27, 134.3, 136.4, 140.6. HR-MS (DART, negative). Calcd for $C_{20}H_{14}N_3$ (M–H): 296.1188. Found: *m*/*z* 296.1201.

2-{(4-Methylphenyl)[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3b): a beige solid; mp 112–115 ˚C (hexane/CH_2Cl_2); IR (KBr) 2253 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3H), 4.19 (d, J = 9.2 Hz, 1H), 4.47 (d, J = 9.2 Hz, 1H), 6.36 (br s, 2H), 6.67 (br s, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.35 (dd, J = 8.0, 1.1 Hz, 1H), 7.43 (td, J = 7.4, 1.1 Hz, 1H), 7.50 (ddd, J = 8.0, 7.4, 1.1 Hz, 1H),

7.58 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.1, 29.0, 45.2, 109.9, 111.7, 111.9, 122.8, 127.2, 127.7, 128.7, 129.1, 129.2, 129.9, 133.4, 134.4, 138.7, 140.5. Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.92; H, 5.57; N, 13.49.

2-{(4-Chlorophenyl)[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3c): a pale-yellow solid; mp 143–145 ˚C (hexane/CH_2Cl_2); IR (KBr) 2255, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.19 (d, *J* = 9.2 Hz, 1H), 4.48 (d, *J* = 9.2 Hz, 1H), 6.35 (br s, 2H), 6.62 (br s, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.46 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.53 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.7, 45.1, 110.1, 111.5, 111.6, 122.6, 126.9, 129.0, 129.26, 129.28, 129.45, 129.52, 133.8, 134.8, 134.9, 140.5. Anal. Calcd for $C_{20}H_{14}ClN_3$: C, 72.40; H, 4.25; N, 12.66. Found: C, 72.23; H, 4.13; N, 12.66.

2-{(4-Methoxyphenyl)[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3d): a white solid; mp 113–116 ˚C (hexane/CH_2Cl_2); IR (KBr) 2262, 1609 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.79 (s, 3H), 4.17 (d, *J* = 9.2 Hz, 1H), 4.45 (d, *J* = 9.2 Hz, 1H), 6.35 (s, 2H), 6.64 (s, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 29.1, 45.0, 55.3, 109.8, 111.8, 112.0, 114.6, 122.7, 127.0, 128.3, 128.8, 129.06, 129.14, 133.4, 134.5, 140.4, 159.7. Anal. Calcd for $C_{21}H_{17}N_3O$: C, 77.04; H, 5.23; N, 12.84. Found: C, 76.82; H, 5.02; N, 12.70.

2-{(3,4-Dichlorophenyl)[2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3e): a pale-yellow gum; R_f 0.37 (AcOEt/hexane 1:5); IR (neat) 2257, 1603 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.21 (d, *J* = 9.2 Hz, 1H), 4.46 (d, *J* = 9.2 Hz, 1H), 6.37 (br s, 2H), 6.61 (br s, 2H), 7.02 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.23 (d, *J* = 2.3 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.47–7.55 (m, 1H), 7.53–7.57 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 28.5, 44.9, 110.3, 111.2, 111.4, 122.6, 126.7, 127.3, 129.1, 129.4 (2 overlapped Cs), 129.8, 129.9, 131.1, 133.3, 133.5, 136.4, 140.6. HR-MS (DART, negative). Calcd for $C_{20}H_{12}Cl_2N_3$ (M–H): 364.0409. Found: *m*/*z* 364.0420.

2-{[5-Methyl-2-(1*H*-pyrrol-1-yl)phenyl](phenyl)methyl}propanedinitrile (3f): a pale-yellow solid; mp 128–130 ˚C (hexane/CH_2Cl_2); IR (KBr) 2255 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.55 (s, 3H), 4.22 (d, *J* = 9.2 Hz, 1H), 4.45 (d, *J* = 9.2 Hz, 1H), 6.34 (br s, 2H), 6.64 (br s, 2H), 7.21 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H), 7.31–7.37 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.5, 28.8, 45.5, 109.7, 111.7, 111.9, 122.9, 127.5, 127.8, 128.6, 128.7, 129.2, 129.9, 134.0, 136.5, 138.0, 139.2. Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.97; H, 5.36; N, 13.48.

2-{(4-Methylphenyl)[5-methyl-2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3g): a white solid; mp 125–127 ˚C (hexane/CH_2Cl_2); IR (KBr) 2253 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 3H), 2.44 (s, 3H), 4.19 (d, *J* = 9.2 Hz, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 6.34 (dd, *J* = 2.3, 1.7 Hz, 2H), 6.65 (br s, 2H), 7.09 (d,

J = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.20 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.33 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.1, 21.4, 28.9, 45.2, 109.7, 111.8, 112.0, 122.9, 127.5, 127.7, 128.5, 129.8, 129.9, 133.5, 134.2, 138.0, 138.6, 139.2. Anal. Calcd for $C_{22}H_{19}N_3$: C, 81.20; H, 5.89; N, 12.91. Found: C, 81.06; H, 5.86; N, 12.89.

2-{(4-Methoxyphenyl)[5-methyl-2-(1*H*-pyrrol-1-yl)phenyl]methyl}propanedinitrile (3h): a pale-yellow solid; mp 137–139 ˚C (hexane/CH_2Cl_2); IR (KBr) 2253, 1611 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 3.79 (s, 3H), 4.17 (d, *J* = 9.2 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 6.33 (t, *J* = 1.7 Hz, 2H), 6.62 (br s, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.33 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.4, 29.1, 44.9, 55.3, 109.7, 111.8, 112.0, 114.5, 122.8, 127.3, 128.4, 128.5, 129.1, 129.8, 134.3, 137.9, 139.2, 159.6. Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31. Found: C, 77.09; H, 5.60; N, 12.21.

2-{[5-Chloro-2-(1*H*-pyrrol-1-yl)phenyl](phenyl)methyl}propanedinitrile (3i): a white solid; mp 144–146 ˚C (hexane/CH_2Cl_2); IR (KBr) 2255 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.19 (d, *J* = 9.2 Hz, 1H), 4.47 (d, *J* = 9.2 Hz, 1H), 6.38 (br s, 2H), 6.66 (br s, 2H), 7.19 (d, *J* = 7.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.35–7.42 (m, 4H), 7.51 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.6, 45.5, 110.4, 111.3, 111.6, 122.8, 127.4, 127.7, 129.1, 129.48, 129.51, 130.1, 135.0, 135.6, 136.1, 139.1. Anal. Calcd for $C_{20}H_{14}ClN_3$: C, 72.40; H, 4.25; N, 12.66. Found: C, 72.33; H, 4.23; N, 12.62.

2-{[5-Chloro-2-(1*H*-pyrrol-1-yl)phenyl](3,4-dimethoxyphenyl)methyl}propanedinitrile (3j): a pale-yellow solid; mp 137–139 ˚C (hexane/CH_2Cl_2); IR (KBr) 2259, 1604 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.83 (s, 3H), 3.87 (s, 3H), 4.20 (d, *J* = 9.7 Hz, 1H), 4.41 (d, *J* = 9.7 Hz, 1H), 6.38 (br s, 2H), 6.58 (s, 1H), 6.65 (br s, 2H), 6.77 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.52 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 28.6, 45.4, 55.9, 56.0, 110.3, 111.5, 111.56, 111.59, 111.7, 119.5, 122.7, 127.0, 128.0, 129.4, 130.1, 135.0, 136.4, 138.9, 149.3, 149.4. HR-MS (DART, negative). Calcd for $C_{22}H_{17}ClN_3O_2$ (M–H): 390.1010. Found: *m*/*z* 390.1021. Anal. Calcd for $C_{22}H_{18}ClN_3O_2$: C, 67.43; H, 4.63; N, 10.72. Found: C, 67.31; H, 4.54; N, 10.48.

2-{Phenyl[1-(1*H*-pyrrol-1-yl)naphthalen-2-yl]methyl}propanedinitrile (6a): a pale-yellow viscous oil; R_f 0.49 (AcOEt/hexane 1:5); IR (KBr) 2257 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.45 (d, *J* = 9.7 Hz, 1H), 4.56 (d, *J* = 9.7 Hz, 1H), 6.45 (br s, 1H), 6.53 (br s, 1H), 6.59 (br s, 1H), 7.00 (br s, 1H), 7.18 (d, *J* = 8.6 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.29–7.36 (m, 3H), 7.47 (dd, *J* = 8.0, 6.9 Hz, 1H), 7.54 (dd, *J* = 8.0, 6.9 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.6, 45.9, 109.7, 110.2, 111.7, 111.9, 122.7, 123.7, 123.9, 127.5, 127.67, 127.70, 128.1, 128.7, 129.3, 129.9, 132.1, 133.3, 136.5, 136.9. HR-MS (DART, positive). Calcd for $C_{24}H_{18}N_3$ (M+H): 348.1500. Found: *m*/*z* 348.1492.

2-{(4-Methoxyphenyl)[1-(1*H*-pyrrol-1-yl)naphthalen-2-yl]methyl}propanedinitrile (6b): a white amorphous powder; R_f 0.27 (AcOEt/hexane 1:5); IR (KBr) 2256, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.78 (s, 3H), 4.39 (d, *J* = 9.7 Hz, 1H), 4.49 (d, *J* = 9.7 Hz, 1H), 6.43–6.45 (m, 1H), 6.51–6.53 (m, 1H), 6.54–6.57 (m, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.97–6.99 (m, 1H), 7.18 (d, *J* = 8.6 Hz, 3H), 7.47 (dd, *J* = 8.0, 6.9 Hz, 1H), 7.54 (dd, *J* = 8.0, 6.9 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.9, 45.4, 55.3, 109.6, 110.1, 111.8, 114.6, 122.6, 123.7, 123.8, 127.4, 127.7, 128.1, 128.5, 129.0, 129.9, 132.2, 132.4, 133.2, 136.8, 159.6. HR-MS (ESI, positive). Calcd for $C_{25}H_{20}N_3O$ (M+H): 378.1606. Found: *m*/*z* 378.1600.

Typical Procedure for the Preparation of 6*H*-Pyrrolo[1,2-*a*][1]benzazepines (4). 4-Amino-6-phenyl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4a). To a stirred solution of **3a** (0.14 g, 0.47 mmol) in AcOH (3 mL) at rt was added HBr (33% in AcOH; 0.47 mmol) and stirring was continued for 15 min. The mixture was poured into H_2O (20 mL) and extracted with AcOEt (3 × 10 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 (AcOEt/hexane 1:3) to afford **4a** (0.10 g, 73%); a white solid; mp 169–171 ˚C (hexane/CH_2Cl_2); IR (KBr) 3476, 3357, 3236, 2175, 1627 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.63 (br s, 2H), 4.78 (s, 1H), 6.13 (br s, 1H), 6.51 (br s, 1H), 6.92 (d, *J* = 6.3 Hz, 2H), 6.97 (br s, 1H), 7.01–7.04 (m, 3H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.38–7.42 (m, 2H), 7.46 (d, *J* = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 47.8, 78.3, 110.1, 111.3, 121.5, 124.8, 125.4, 126.0, 126.3, 127.4, 127.6, 127.8, 128.4, 130.1, 137.2, 137.8, 140.2, 149.2. HR-MS (DART, positive). Calcd for $C_{20}H_{16}N_3$ (M+H): 298.1344. Found: *m*/*z* 298.1334. Anal. Calcd for $C_{20}H_{15}N_3$: C, 80.78; H, 5.08; N, 14.13. Found: C, 80.55; H, 5.11; N, 14.00.

4-Amino-6-(4-methylphenyl)-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4b): a white solid; mp 174–177 ˚C (hexane/CH_2Cl_2); IR (KBr) 3450, 3338, 3233, 2175, 1637 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.16 (s, 3H), 4.62 (br s, 2H), 4.74 (s, 1H), 6.15 (br s, 1H), 6.52 (br s, 1H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.99 (br s, 1H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.45 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.8, 47.7, 78.5, 110.1, 111.2, 121.6, 124.7, 125.4, 125.9, 127.3, 127.7, 128.3, 128.5, 130.1, 135.7, 137.1, 137.3, 137.9, 149.1. HR-MS (DART, positive). Calcd for $C_{21}H_{18}N_3$ (M+H): 312.1500. Found: *m*/*z* 312.1490. Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.71; H, 5.43; N, 13.42.

4-Amino-6-(4-chlorophenyl)-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4c): a white solid; mp 148–151 ˚C (hexane/CH_2Cl_2); IR (KBr) 3471, 3431, 3370, 3339, 3236, 2183, 1642, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.67 (br s, 2H), 4.72 (s, 1H), 6.16 (br s, 1H), 6.53 (br s, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.98 (br s, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 7.4 Hz, 1H),

7.45 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 47.3, 77.8, 110.4, 111.5, 121.3, 124.9, 125.6, 127.4 (2 overlapped Cs), 127.5, 127.9, 128.6, 130.0, 132.0, 137.1, 137.4, 138.9, 149.3. HR-MS (DART, positive). Calcd for $C_{20}H_{15}ClN_3$ (M+H): 332.0954. Found: *m*/*z* 332.0949. Anal. Calcd for $C_{20}H_{14}ClN_3$: C, 72.40; H, 4.25; N, 12.66. Found: C, 72.10; H, 3.89; N, 12.54.

4-Amino-6-(4-methoxyphenyl)-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4d): a white solid; mp 64–67 ˚C (hexane/CH_2Cl_2); IR (KBr) 3436, 3339, 3236, 2174, 1619 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.66 (s, 3H), 4.62 (br s, 2H), 4.73 (s, 1H), 6.15 (br s, 1H), 6.53 (br s, 1H), 6.56 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.99 (br s, 1H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.35–7.41 (m, 2H), 7.45 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 47.3, 55.1, 78.5, 110.2, 111.3, 113.2, 121.6, 124.8, 125.5, 127.1, 127.3, 127.7, 128.3, 130.0, 132.1, 137.2, 138.0, 149.1, 157.9. HR-MS (DART, positive). Calcd for $C_{21}H_{18}N_3O$ (M+H): 328.1450. Found: *m*/*z* 328.1443.

4-Amino-6-(3,4-dichlorophenyl)-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4e): a pale-yellow solid; mp 239–240 ˚C (hexane/CH_2Cl_2); IR (KBr) 3481, 3351, 2177, 1627 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.69 (s, 1H), 4.70 (br s, 2H), 6.19 (br s, 1H), 6.56 (br s, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 6.97 (s, 1H), 7.01 (br s, 1H), 7.09 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.40–7.46 (m, 3H); ^{13}C NMR (DMSO-d_6) δ 45.9, 72.8, 110.0, 112.7, 121.9, 124.9, 125.7, 126.4, 127.3, 127.4, 127.6, 128.4, 128.8, 129.7, 129.9, 130.3, 136.7, 137.2, 142.7, 150.7. HR-MS (DART, positive). Calcd for $C_{20}H_{14}Cl_2N_3$: (M+H): 366.0565. Found: *m*/*z* 366.0559. Anal. Calcd for $C_{20}H_{13}Cl_2N_3$: C, 65.59; H, 3.58; N, 11.47. Found: C, 65.20; H, 3.49; N, 11.33.

4-Amino-8-methyl-6-phenyl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4f): a pale-yellow solid; mp 196–198 ˚C (hexane/CH_2Cl_2); IR (KBr) 3458, 3341, 2172, 1632 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 4.62 (br s, 2H), 4.72 (s, 1H), 6.11 (br s, 1H), 6.49 (br s, 1H), 6.92–6.96 (m, 3H), 7.00–7.04 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.27 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.8, 47.9, 78.3, 109.9, 110.1, 121.6, 124.5, 125.3, 126.0, 126.2, 127.6, 127.8, 128.9, 130.7, 134.9, 137.4, 137.5, 140.3, 149.3. HR-MS (DART, positive). Calcd for $C_{21}H_{18}N_3$ (M+H): 312.1500. Found: *m*/*z* 312.1494. Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.87; H, 5.23; N, 13.44.

4-Amino-8-methyl-6-(4-methylphenyl)-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4g): a pale-yellow solid; mp 210–212 ˚C (hexane/$CHCl_3$); IR (KBr) 3480, 3341, 2181, 1636 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.16 (s, 3H), 2.43 (s, 3H), 4.60 (br s, 2H), 4.68 (s, 1H), 6.13 (br s, 1H), 6.50 (br s, 1H), 6.79 (d, *J* = 7.4 Hz, 2H), 6.83 (d, *J* = 7.4 Hz, 2H), 6.96 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.25 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.8 (2 overlapped Cs), 47.7, 78.5, 109.9, 111.1, 121.7, 124.5, 125.3, 125.9, 127.6, 128.5, 128.8, 130.7, 134.9, 135.7, 137.2, 137.3, 137.6, 149.1. HR-MS (DART, positive).

Calcd for $C_{22}H_{20}N_3$ (M+H): 326.1657. Found: *m*/*z* 326.1651. Anal. Calcd for $C_{22}H_{19}N_3$: C, 81.20; H, 5.89; N, 12.91. Found: C, 80.96; H, 5.89; N, 12.64.

4-Amino-6-(4-methoxyphenyl)-8-methyl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4h): a white solid; mp 170–172 ˚C (hexane/CH_2Cl_2); IR (KBr) 3458, 3349, 2167, 1632 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.66 (s, 3H), 4.60 (br s, 2H), 4.67 (s, 1H), 6.13 (br s, 1H), 6.50 (br s, 1H), 6.56 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.25 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.8, 47.3, 55.1, 78.5, 109.9, 111.1, 113.2, 121.7, 124.5, 125.3, 127.1, 127.6, 128.8, 130.6, 132.3, 134.9, 137.3, 137.7, 149.1, 157.9. HR-MS (DART, positive). Calcd for $C_{22}H_{20}N_3O$ (M+H): 342.1606. Found: *m*/*z* 342.1598. Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31. Found: C, 77.36; H, 5.53; N, 12.30.

4-Amino-8-chloro-6-phenyl-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4i): a pale-yellow solid; mp 217–218 ˚C (hexane/CH_2Cl_2); IR (KBr) 3479, 3350, 2179, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.67 (br s, 2H), 4.72 (s, 1H), 6.14 (br s, 1H), 6.52 (br s, 1H), 6.89–6.93 (m, 3H), 7.02–7.05 (m, 3H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.38 (d, 8.6 Hz, 1H), 7.48 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 47.6, 77.8, 110.5, 111.6, 121.2, 125.0, 125.4, 125.88, 125.93, 126.5, 127.9, 128.3, 129.8, 132.9, 135.8, 139.2, 139.4, 149.2. HR-MS (DART, positive). Calcd for $C_{20}H_{15}ClN_3$ (M+H): 332.0954. Found: *m*/*z* 332.0947. Anal. Calcd for $C_{20}H_{14}ClN_3$: C, 72.40; H, 4.25; N, 12.66. Found: C, 72.36; H, 4.18; N, 12.60.

4-Amino-8-chloro-6-(3,4-dimethoxyphenyl)-6*H*-pyrrolo[1,2-*a*][1]benzazepine-5-carbonitrile (4j): a white solid; mp 103–105 ˚C (hexane/CH_2Cl_2); IR (KBr) 3458, 3335, 2178, 1634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.60 (s, 3H), 3.66 (s, 3H), 4.62 (br s, 3H), 6.11 (br s, 1H), 6.33 (d, *J* = 8.6 Hz, 1H), 6.36 (br s, 1H), 6.47 (d, *J* = 8.6 Hz, 1H), 6.48 (s, 1H), 6.87 (s, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 1H), 7.40 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 47.4, 55.7, 55.8, 77.8, 109.6, 110.57, 110.62, 111.7, 118.6, 121.2, 125.5, 125.9, 127.7, 128.3, 129.7, 131.9, 132.8, 135.7, 139.2, 147.6, 148.3, 149.2. HR-MS (DART, positive). Calcd for $C_{22}H_{19}ClN_3O_2$ (M+H): 392.1166. Found: *m*/*z* 392.1159. Anal. Calcd for $C_{22}H_{18}ClN_3O_2$: C, 67.43; H, 4.63; N, 10.72. Found: C, 67.26; H, 4.59; N, 10.56.

Typical Procedure for the Preparation of Naphthopyrroloazepines (7). 4-Amino-6-phenyl-6*H*-naphtho[2,1-*f*]pyrrolo[1,2-*a*]azepine-5-carbonitrile (7a). Compound (**6a**) (0.23 g, 0.66 mmol) was treated with HBr in AcOH as described for the preparation of **4a**. After completion of the reaction, the precipitate was filtered under reduced pressure and washed with water. The crude product was recrystallized to give **7a** (0.22 g, 95%); a white solid; mp 130–132 ˚C (hexane/CH_2Cl_2); IR (KBr) 3455, 3383, 2174, 1623 cm^{-1}; ^1H NMR (DMSO-d_6) δ 4.65 (br, 2H), 4.88 (s, 1H), 6.09 (dd, *J* = 3.4, 2.9 Hz, 1H), 6.55 (d, *J* = 2.3 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 7.01 (dd, *J* = 8.0, 7.3 Hz, 2H), 7.14 (br s, 1H), 7.49 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.54 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.6 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), ^{13}C NMR (DMSO-d_6) δ 47.4,

75.0, 108.2, 111.5, 122.0, 122.2, 125.6, 125.9, 126.1, 127.2, 127.60, 127.64, 127.7, 128.3, 128.4, 128.5, 128.6, 131.9, 133.5, 138.7, 141.2, 150.9. HR-MS (ESI, positive). Calcd for $C_{24}H_{18}N_3$ (M+H): 348.1500. Found: *m*/*z* 348.1494. Anal. Calcd for $C_{24}H_{17}N_3$: C, 82.97; H, 4.93; N, 12.10. Found: C, 82.89; H, 5.21; N, 11.81.

4-Amino-6-(4-methoxyphenyl)-6*H*-naphtho[2,1-*f*]pyrrolo[1,2-*a*]azepine-5-carbonitrile (7b): a white solid; mp 150–153 ˚C (hexane/CH_2Cl_2); IR (KBr) 3454, 3365, 2173, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.67 (s, 3H), 3.73 (s, 2H), 4.77 (s, 1H), 6.11 (dd, *J* = 4.0, 2.9 Hz, 1H), 6.53 (dd, *J* = 4.0, 1.7 Hz, 1H), 6.55 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 7.08 (dd, *J* = 2.9, 1.7 Hz, 1H), 7.44 (ddd, *J* = 8.0, 7.4, 1.7 Hz, 1H), 7.49 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 47.7, 55.1, 79.7, 108.5, 110.5, 113.1, 121.5, 122.5, 126.0, 126.9 (2 overlapped Cs), 127.6, 127.8, 128.2, 128.4, 129.0, 129.3, 132.3, 132.4, 133.9, 128.4, 149.8, 157.9. HR-MS (DART, positive). Calcd for $C_{25}H_{20}N_3O$ (M+H): 378.1606. Found: *m*/*z* 378.1599. Anal. Calcd for $C_{25}H_{19}N_3O$: C, 79.55; H, 5.07; N, 11.13. Found: C, 79.36; H, 5.07; N, 10.98.

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