A New Synthesis of 2-Benzazepines

Alan R. Katritzky,* Rexiat Maimait, Yong-Jiang Xu, Rena G. Akhmedova

Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, Florida 32611–7200, USA
Fax +1(352)3929551; E-mail: katritzky@chem.ufl.edu

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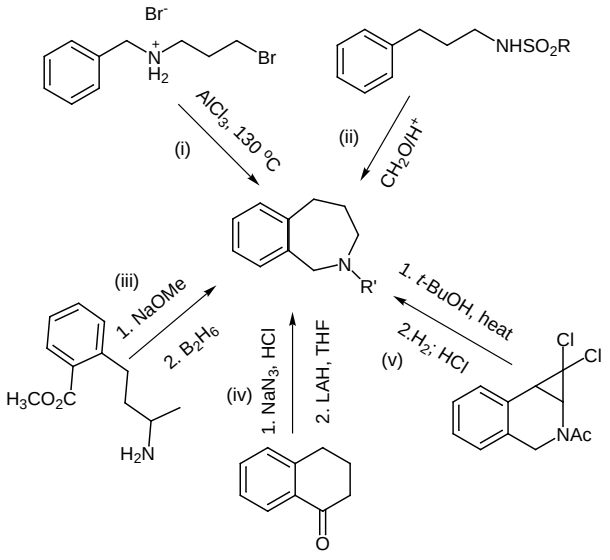
Abstract: $AlCl_3$-mediated intramolecular cyclization of *N,N*-bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-3-phenyl-1-propanamine (**5**) gave 2-benzotriazolylmethyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (**6**). Subsequent nucleophilic substitution of the benzotriazolyl group in **6** with Grignard reagents, triethyl phosphite and sodium borohydride afforded 2,3,4,5-tetrahydro-1*H*-2-benzazepines **1a**–**e**, **2** and **3**. Similarly, $TiCl_4$-mediated cyclization of **8** and **10** gave 5,6,7,13b-tetrahydro-9*H*-isoindolo[1,2-*a*][2]benzazepin-9-one (**9**) and 1,2,5,6,7,11b-hexahydro-3*H*-pyrrolo[2,1-*a*][2]benzazepin-3-one (**11**), respectively.

Key words: benzotriazole, 2-benzazepine, cyclization, synthesis

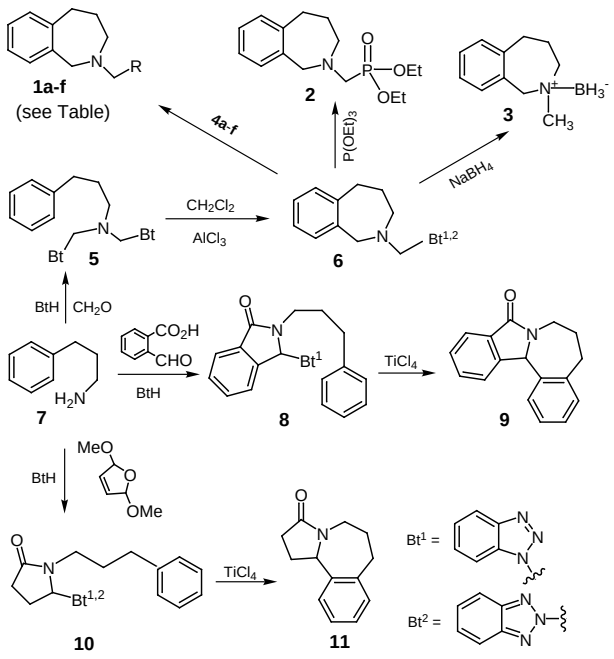
2-Benzazepines[1] are of considerable interest due to their diverse pharmacological properties.[2a–c] Known routes to 2-benzazepines include (Scheme 1): (i) cyclization of *N*-(3-bromopropyl)arylamine hydrobromides with aluminum chloride at 130 °C in decalin;[3] (ii) cyclization of 3-arylpropylsulfonamides with formaldehyde and acid to the *N*-sulfonyl-2-benzazepine;[4] (iii) cyclization of 3-(2-methoxycarbonylaryl)propylamines with sodium methoxide to 2-benzazepin-1-ones and subsequent reduction;[5] (iv) Beckman[6] or Schmidt rearrangements of 3,4-dihydro-1(*2H*)-naphthalenone;[7,8] and (v) ring enlargement of 2-acetyl-7,8-dichloro-1,2-dihydroisoquinolines.[9]



Scheme 1

Recently, we reported the syntheses of 1,4-benzothiazepines and 1,4-benzoxazepines from $ArX(CH_2)_2NRCH_2Bt$ (Bt = benzotriazole) using benzotriazole methodology.[10] In the present work, we now report an analogous approach to 2-benzazepines and explore the possibility of introducing different functional groups onto the benzazepine moiety.

Condensation of 3-phenyl-1-propylamine (**7**), benzotriazole and formaldehyde in methanol–water at 20 °C gave pure *N,N*-bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-3-phenyl-1-propanamine (**5**). Compound **5** on heating with 4 equivalents of $AlCl_3$ in anhydrous CH_2Cl_2 under reflux for 8–10 h gave **6** in 70% yield (Scheme 2). Although the starting material **5** was only Bt^1 (benzotriazol-1-yl) isomer, equilibration occurred during the cyclization and product **6** was obtained as a mixture of $Bt^1$and Bt^2 (benzotriazol-2-yl) isomers, in which Bt^1 isomer predominated. Preliminary attempts to separate the $Bt^1$and Bt^2 isomers failed. Since both $Bt^1$and Bt^2 can be substituted by nucleophiles, the mixture was used as such in the subsequent reactions. We have reported the ^1H and ^{13}C NMR data of the major Bt^1 isomer in the experimental section. The ratio of $Bt^1$and Bt^2 isomers was determined by ^1H NMR spectrum to be 4.4:1. The aliphatic region in the ^1H NMR spectrum of **5** showed one strong singlet ascribed to two $BtCH_2N$ at



Scheme 2

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5.63 ppm. After the cyclization, two singlets were observed at 4.00 ppm and 5.42 ppm in the ^{1}H NMR spectrum of **6**, which were ascribed to $ArCH_2N$ and $BtCH_2N$ fragments, respectively.

The benzotriazole moiety in **6** could, as expected,[11] be replaced by various nucleophiles. Thus, reactions of **6** with the corresponding Grignard reagents **4a**–**f** gave compounds **1a**–**f**, respectively, in 40–70% yields (Scheme 2). The results are listed in the Table.

Table Reaction of **6** with Grignard Reagents

Product **1**	Nucleophile	R	Yield (%)
a	*p*-$MeOC_6H_4MgCl$	*p*-$MeOC_6H_4$	70
b	*p*-ClC_6H_4MgCl	*p*-ClC_6H_4	47
c	$C_6H_5C{\equiv}CMgCl$	$C_6H_5C{\equiv}C$	43
d	EtMgBr	Et	71
e	BuMgBr	Bu	69
f	*p*-MeC_6H_4MgCl	*p*-MeC_6H_4	78

Treatment of compound **6** with triethyl phosphite in the presence of $ZnBr_2$ in THF at 0 °C replaced the benzotriazolyl group to give the expected product diethyl 1,3,4,5-tetrahydro-2*H*-2-benzazepin-2-ylmethylphosphonate (**2**) in 87% yield (Scheme 2).

The reduction of **6** with sodium borohydride in methanol failed; however, compound **6** was reduced in THF using sodium borohydride in 4 hours at 20 °C to give 2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine borane complex **3** in 83% yield (Scheme 2).

Heating 3-phenyl-1-propylamine (**7**), benzotriazole and phthalaldehydic acid with a catalytic amount of *p*-toluenesulfonic acid monohydrate using a Dean–Stark apparatus gave 3-(1*H*-1,2,3-benzotriazol-1-yl)-2-(3-phenylpropyl)-1-isoindolinone (**8**) in 89% yield (Scheme 2). Heating **8** with aluminum chloride in CH_2Cl_2 gave traces of product **9**, but $TiCl_4$ (1.7 M solution CH_2Cl_2) afforded the desired 5,6,7,13b-tetrahydro-9*H*-isoindolo[1,2-*a*][2]benzazepin-9-one (**9**) in 83% yield at 20 °C (Scheme 2). Compound **9** was previously prepared by the cyclization of 3-(3-phenylpropylamine)phthalide in polyphosphoric acid at 95 °C in 30% yield.[12]

In a slightly different procedure from the above, 3-phenyl-1-propylamine (**7**) was heated with benzotriazole and 2,5-dimethoxy-2,5-dihydrofuran in acetic acid at 60–70 °C for 48 hours to give **10** as mixed Bt^1 and Bt^2 isomers in 56% yield. Separation by column chromatography afforded the Bt^1 isomer of **10** in 47% yield and the Bt^2 isomer of **10** in 9% yield (Scheme 2). However, the unseparated mixture was used in the subsequent reaction.

Cyclization of **10** was more difficult than that of **8** using 1.7 M solution of $TiCl_4$, and only a small amount of **10** was converted; however, $TiCl_4$ (4 equiv) in CH_2Cl_2 for 36 hours at 20 °C cyclized **10** into the novel 1,2,5,6,7,11b-hexahydro-3*H*-pyrrolo[2,1-*a*][2]benzazepin-3-one (**11**) in 52% yield (Scheme 2). No previous examples of the ring system of **11** could be located.

In conclusion, we have developed a new approach to 2-benzazepines via cyclization of *N*,*N*-bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-3-phenyl-1-propanamine (**5**), 3-(1*H*-1,2,3-benzotriazol-1-yl)-2-(3-phenylpropyl)-1-isoindolinone (**8**), and 5-(benzotriazolyl)-2-(3-phenylpropyl)-2-pyrrolidinone (**10**). A series of *N*-substituted 2-benzazepines were obtained by nucleophilic substitution of benzotriazolyl moiety in **6** using different nucleophiles.

Melting points were determined on a Koefler hot stage apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, in $CDCl_3$ referenced to Me_4Si for the ^{1}H spectra and $CDCl_3$ for the ^{13}C spectra. THF was distilled under N_2 from sodium-benzophenone immediately before use. CH_2Cl_2 was distilled over CaH_2 under N_2. Column chromatography was performed on silica gel (200–425 mesh, Fisher Scientific). All reactions with moisture-sensitive compounds were carried out under dry argon.

_N,N_-Bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-3-phenyl-1-propanamine (5)

To a solution of 3-phenyl-1-propylamine (5 g, 37 mmol) and benzotriazole (9.6 g, 81.2 mmol) in MeOH (60 mL) and H_2O (15 mL) was added formaldehyde (6.47 g, 81.4 mmol, 37% aq solution). The reaction mixture was stirred for 24 h at 20 °C. Then, the white precipitates were filtered and washed with Et_2O to give the desired product (9.2 g, 62%), which was directly used in the subsequent reaction without further purification. Pale yellow prisms (from EtOAc–hexane); yield: 62%; mp 84–86 °C.

^{1}H NMR ($CDCl_3$): δ = 1.89 (quintet, 2 H, *J* = 7.2 Hz), 2.50 (t, 2 H, *J* = 7.2 Hz), 2.87 (t, 2 H, *J* = 7.2 Hz), 5.63 (s, 4 H), 7.01 (d, 2 H, *J* = 6.3 Hz), 7.14–7.26 (m, 3 H), 7.41 (dt, 2 H, *J* = 0.9, 7.5 Hz), 7.51 (dt, 2 H, *J* = 0.9, 6.9 Hz), 7.62 (d, 2 H, *J* = 8.4 Hz), 8.10 (d, 2 H, *J* = 8.4 Hz).

^{13}C NMR ($CDCl_3$): δ = 29.1, 32.8, 50.1, 64.4, 109.7, 120.0, 124.2, 126.0, 127.9, 128.2, 128.4, 133.2, 141.1, 146.0.

Anal. Calcd for $C_{23}H_{23}N_7$: C, 69.50; H, 5.83; N, 24.67. Found: C, 69.56; H, 5.88; N, 25.02.

2-(Benzotriazolylmethyl)-2,3,4,5-tetrahydro-1*H*-2-benzazepine (6)

$AlCl_3$ (0.53 g, 16 mmol) was placed in a dry flask under argon with a stirring bar, and a solution of the starting material **5** (1.59 g, 4 mmol) in anhyd CH_2Cl_2 (80 mL) was added and stirred. This mixture was refluxed for 8–10 h, then cooled to r.t. and quenched with 2 M NaOH solution (10 mL). The organic layer was separated and washed with 2 M NaOH solution and H_2O. The organic layer was collected and dried ($MgSO_4$). Removal of the solvent gave a pale yellow oil (0.23 g, 70%), which was used in the next step without purification.

^{1}H NMR ($CDCl_3$): δ = 1.83 (quintet, 2 H, *J* = 5.1 Hz), 2.89 (t, 2 H, *J* = 5.4 Hz), 3.19 (t, 2 H, *J* = 5.1 Hz), 4.00 (s, 2 H), 5.42 (s, 2 H), 7.10–7.20 (m, 4 H), 7.34–7.56 (m, 2 H), 7.65 (d, 1 H, *J* = 8.1 Hz), 8.09 (d, 1 H, *J* = 8.4 Hz).

^{13}C NMR ($CDCl_3$): δ = 26.7, 35.4, 57.1, 58.2, 68.1, 110.3, 119.9, 123.9, 126.2, 127.3, 127.6, 129.2, 129.7, 133.2, 138.3, 142.5, 146.1.

Anal. Calcd for $C_{17}H_{18}N_4$: N, 20.13. Found: N, 20.49.

HRMS-FAB: *m*/*z* (M – 1) calcd for $C_{17}H_{17}N_4$: 277.1453; found: 277.1430.

2-(4-Methoxybenzyl)-2,3,4,5-tetrahydro-1*H*-2-benzazepine (1a); Typical Procedure

Compound **6** (0.2 g, 0.72 mmol) was dissolved in THF (10 mL) under argon in a round bottom flask containing a stirring bar, and cooled to 0 °C in an ice-water bath. After 10 min, 4-methoxylphenylmagnesium bromide (0.8 mL, 1.0 M, 0.86 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 2 h. This was then warmed up to r.t. and stirred for an additional 10 h. The reaction was quenched with H_2O (10 mL), the organic layer was separated and washed with 2 M NaOH solution. The aqueous layer was back-extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), and concentrated to give a yellow solid. The product was purified by column chromatography on silica gel using 30% Et_2O in pentane as eluent; micro-needles (Et_2O–pentane); yield: 70%; mp 83–85 °C.

^{1}H NMR ($CDCl_3$): δ = 1.75 (quintet, 2 H, *J* = 5.0 Hz), 2.92 (t, 2 H, *J* = 5.1 Hz), 3.10 (t, 2 H, *J* = 5.1 Hz), 3.46 (s, 2 H), 3.81 (s, 3 H), 3.86 (s, 2 H), 6.85 (d, 2 H, *J* = 8.7 Hz), 6.95 (d, 1 H, *J* = 7.2 Hz), 7.00–7.26 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 25.2, 36.2, 55.2, 57.1, 58.7, 59.1, 113.5, 125.8, 127.1, 128.8, 130.0, 130.1, 131.3, 139.4, 143.1, 158.5.

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.43; H, 7.70; N, 5.07.

2-(4-Chlorobenzyl)-2,3,4,5-tetrahydro-1*H*-2-benzazepine (1b)

White needles (EtOAc–hexane); yield: 47%; mp 97–99 °C.

^{1}H NMR ($CDCl_3$): δ = 1.81 (quintet, 2 H, *J* = 5.0 Hz), 2.98 (t, 2 H, *J* = 5.0 Hz), 3.17 (t, 2 H, *J* = 5.0 Hz,), 3.54 (s, 2 H), 3.90 (s, 2 H), 6.96 (d, 1 H, *J* = 7.2 Hz), 7.10–7.24 (m, 2 H), 7.25–7.36 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 25.2, 36.1, 57.0, 58.9, 59.1, 125.8, 127.2, 128.3, 128.8, 129.9, 130.2, 132.5, 137.9, 139.2, 143.0.

Anal. Calcd for $C_{17}H_{18}ClN$: C, 75.13; H, 6.68; N, 5.15. Found: C, 75.32; H, 7.09; N, 5.05.

2-(3-Phenylprop-2-ynyl)-2,3,4,5-tetrahydro-1*H*-2-benzazepine (1c)

Yellow oil; yield: 43%.

^{1}H NMR ($CDCl_3$): δ = 1.80 (quintet, 2 H, *J* = 5.0 Hz), 2.91 (t, 2 H, *J* = 5.0 Hz), 3.20 (t, 2 H, *J* = 5.0 Hz), 3.52 (s, 2 H), 3.98 (s, 2 H), 7.08–7.22 (m, 4 H), 7.27–7.34 (m, 3 H), 7.40–7.50 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 26.3, 35.6, 45.8, 58.9, 59.7, 84.7, 85.5, 123.3, 126.1, 127.4, 128.0, 128.2, 128.8, 129.8, 131.7, 138.7, 142.8.

Anal. Calcd for $C_{19}H_{19}N$: N, 5.36. Found: N, 5.67.

HRMS-FAB: Calcd for $C_{19}H_{20}N$ (M + 1): 262.1596; Found: 262.1601.

2-Propyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (1d)

Yellow oil; yield: 71%.

^{1}H NMR ($CDCl_3$): δ = 0.85 (t, 3 H, *J* = 7.2 Hz), 1.45–1.57 (m, 2 H), 1.72 (quintet, 2 H, *J* = 5.1 Hz), 2.28–2.33 (m, 2 H), 2.89 (t, 2 H, *J* = 5.4 Hz), 3.12 (t, 2 H, *J* = 5.4 Hz), 3.89 (s, 2 H), 7.12 (br s, 4 H).

^{13}C NMR ($CDCl_3$): δ = 11.9, 20.6, 25.0, 36.2, 55.3, 59.0, 59.4, 125.9, 127.1, 128.8, 129.7, 139.3, 142.9.

Anal. Calcd for $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.61; H, 10.45; N, 7.65.

2-Pentyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (1e)

Brown oil; yield: 69%.

^{1}H NMR ($CDCl_3$): δ = 0.87 (t, 3 H, *J* = 7.2 Hz), 1.18–1.34 (m, 4 H), 1.46–1.58 (m, 2 H), 1.71–1.79 (m, 2 H,), 2.36–2.42 (m, 2 H), 2.90 (t, 2 H, *J* = 6.0 Hz), 3.15 (t, 2 H, *J* = 5.4 Hz), 3.95 (s, 2 H), 7.13 (br s, 4 H).

^{13}C NMR ($CDCl_3$): δ = 14.0, 22.6, 25.0, 27.2, 29.7, 36.2, 53.4, 59.1, 59.5, 125.8, 127.1, 128.7, 129.7, 139.4, 142.9.

Anal. Calcd for $C_{15}H_{23}N$: C, 82.89; H, 10.67; N, 6.44. Found: C, 83.20; H, 11.08; N, 6.76.

2-(4-Methylbenzyl)-2,3,4,5-tetrahydro-1*H*-2-benzazepine (1f)

Yellow oil; yield: 78%.

^{1}H NMR ($CDCl_3$): δ = 1.75 (quintet, 2 H, *J* = 5.1 Hz), 2.34 (s, 2 H), 2.91(t, 2 H, *J* = 5.4 Hz), 3.10 (t, 2 H, *J* = 5.1 Hz), 3.49 (s, 2 H), 3.87 (s, 2 H), 6.95 (d, 1 H, *J* = 6.9 Hz), 7.05–7.20 (m, 7 H).

^{13}C NMR ($CDCl_3$): δ = 21.1, 25.2, 29.7, 36.1, 57.5, 58.7, 59.2, 125.8, 127.1, 128.7, 128.8, 128.9, 130.0, 136.1, 136.4, 139.4, 143.1.

Anal. Calcd. for $C_{18}H_{21}N$: C, 86.01; H, 8.42; N, 5.57. Found: C, 86.13; H, 8.37; N, 5.89.

Diethyl 1,3,4,5-Tetrahydro-2*H*-2-benzazepin-2-ylmethylphosphonate (2)

To a solution of **6** (0.1 g, 0.36 mmol) in THF (5 mL), cooled to 0 °C in ice-water bath, was added $ZnBr_2$ (0.08 g, 0.36 mmol, oven dried) followed by triethyl phosphite (0.07 mL, 0.4 mmol). The mixture was stirred overnight, quenched with H_2O, extracted with CH_2Cl_2, and the organic layer was washed with aq 2 M NaOH (2 × 15 mL), and dried ($MgSO_4$). Removal of the solvent gave 0.12 g of oil which was purified using 5% MeOH in $CHCl_3$ as eluent; colorless oil; yield: 90 mg, 87%.

^{1}H NMR ($CDCl_3$): δ = 1.32 (t, 6 H, *J* = 7.2 Hz), 1.64–1.74 (m, 2 H), 2.72 (d, 2 H, *J* = 10.5 Hz), 2.90 (t, 2 H, *J* = 5.1 Hz), 3.27 (t, 2 H, *J* = 5.1 Hz), 4.06 (s, 2 H), 4.06–4.20 (m, 4 H), 7.02–7.20 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 16.5 (d, *J* = 5.7 Hz), 24.4, 36.1, 47.5 (d, *J* = 167.2 Hz), 60.2 (d, *J* = 9.2 Hz), 60.4 (d, *J* = 8.0 Hz), 62.0 (d, *J* = 6.9 Hz), 125.9, 127.4, 129.0, 130.4, 138.4, 143.0.

Anal. Calcd. for $C_{15}H_{24}NO_3P$: C, 60.59; H, 8.14; N, 4.71. Found: C, 60.16; H, 8.51; N, 5.07.

2-Methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine Borane Complex (3)

To a solution of **6** (0.28 g, 1 mmol) in THF (20 mL) was added $NaBH_4$ (0.15 g, 4 mmol) and stirred at r.t. for 4 h. The solvent was evaporated, the residue was dissolved in CH_2Cl_2, and washed with 2 M NaOH solution. The organic layer was dried ($MgSO_4$) and concentrated to give yellow solid, which was purified by column chromatography on silica gel using 20% EtOAc in hexane; yellow prisms (EtOAc–hexane); yield: 83%; mp 67.6–68.8 °C.

^{1}H NMR ($CDCl_3$): δ = 1.10–2.10 (m, 5 H), 2.32 (s, 3 H), 2.78–3.10 (m, 2 H), 3.15–3.40 (m, 2 H), 4.00 (d, 1 H, *J* = 14.7 Hz), 4.36 (d, 1 H, *J* = 14.4 Hz), 7.15–7.30 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 23.7, 34.3, 45.2, 65.5, 65.9, 126.8, 128.9, 129.1, 131.6, 132.9, 142.4.

Anal. Calcd. for $C_{11}H_{18}BN$: C, 74.46; H, 10.36; N, 8.00. Found: C, 75.56; H, 10.22; N, 7.95.

3-(1*H*-1,2,3-Benzotriazol-1-yl)-2-(3-phenylpropyl)-1-isoindolinone (8)

3-Phenyl-1-propylamine (0.3 g, 2.2 mmol), BtH (0.28 g, 2.4 mmol), phthalaldehydic acid (0.34 g, 2.2 mmol) and *p*-toluenesulfonic acid monohydrate (0.04 g, 0.24 mmol) were dissolved in toluene (50 mL) and refluxed using a Dean–Stark apparatus. After 24 h, the reaction mixture was cooled. After evaporating the solvent, the residue was dissolved in CH_2Cl_2 and washed with aq 2 M NaOH and brine. The organic layer was dried (Na_2SO_4), and concentrated to give a yellow oil, which was purified by column chromatography on

silica gel using 30% EtOAC in hexane as eluent; yellow flakes (EtOAc–hexane); yield: 89%; mp 92–93 °C.

^{1}H NMR ($CDCl_3$): δ = 1.75 (quintet, 2 H, *J* = 7.5 Hz), 2.25 (dt, 2 H, *J* = 4.2, 2.7 Hz), 2.90–3.40 (m, 1 H), 3.72–3.84 (m, 1 H), 6.40 (d, 1 H, *J* = 8.4 Hz), 7.00 (d, 2H, *J* = 7.2 Hz), 7.06–7.22 (m, 4 H), 7.28–7.36 (m, 2 H), 7.38 (s, 1 H), 7.58 (t, 1 H, *J* = 7.5 Hz), 7.67 (t, 1 H, *J* = 7.5 Hz), 8.04 (d, 1 H, *J* = 7.5 Hz), 8.08 (d, 1 H, *J* = 8.4 Hz).

^{13}C NMR ($CDCl_3$): δ = 29.3, 33.0, 40.1, 72.7, 110.0, 120.5, 123.5, 124.2, 124.7, 125.9, 128.1, 128.2, 128.3, 130.5, 130.9, 132.0, 132.9, 138.9, 140.8, 147.0, 167.2.

Anal. Calcd. for $C_{23}H_{20}N_4O$: C, 74.98; H, 5.47; N, 15.21. Found: C, 75.12; H, 5.70; N, 15.11.

5,6,7,13b-Tetrahydro-9*H*-isoindolo[1,2-*a*][2]benzazepin-9-one (9)

Compound **8** (0.31 g, 0.84 mmol) was dissolved in CH_2Cl_2 (9 mL), $TiCl_4$ (3.3 mmol, 1.7 M in CH_2Cl_2) was added, and the mixture was stirred at r.t. for 10 h. Then, the reaction was quenched with H_2O. The organic layer was separated, washed with aq 2 M NaOH, brine, and dried ($MgSO_4$). Removal of the solvent gave a yellow solid, which was purified by column chromatography on silica gel using 25% EtOAc in hexane as eluent. White micro prisms (EtOAc–hexane); yield: 89%; mp 138–141 °C (Lit.[12] mp 143–145 °C).

^{1}H NMR ($CDCl_3$): δ = 1.84–2.00 (m, 1 H), 2.10–2.28 (m, 1 H), 2.66–2.76 (m, 2 H), 3.31–3.41 (m, 1 H), 4.33–4.40 (m, 1 H), 5.75 (s, 1 H), 7.11–7.14 (m, 1 H), 7.23–7.32 (m, 3 H), 7.45–7.58 (m, 3 H), 7.90 (d, 1 H, *J* = 7.2 Hz).

^{13}C NMR ($CDCl_3$): δ = 25.4, 31.5, 41.0, 65.8, 123.3, 123.8, 126.8, 127.4, 128.3, 128.4, 130.5, 131.4, 132.2, 135.1, 139.9, 144.0, 168.9.

5-(Benzotriazolyl)-1-(3-phenylpropyl)-2-pyrrolidinone (10)

3-Phenyl-1-propylamine (1.37 g, 10 mmol), BtH (2.38 g, 20 mmol), 2,5-dimethoxy-2,5-dihydrofuran (1.43 g, 11 mmol) were dissolved in HOAc (75 mL) and heated at 60-70 °C for 48 h. Then, the reaction mixture was cooled and neutralized with NaOH. The mixture was extracted with CH_2Cl_2, the organic layer was dried (Na_2SO_4), and concentrated to give a yellow oil. The product was separated by column chromatography using 30%–50% EtOAc in hexane as eluent; yellow oil; yield: 56%.

^{1}H NMR ($CDCl_3$): δ = 1.56–1.84 (m, 2 H), 2.34–2.44 (m, 1 H), 2.46–2.72 (m, 5 H), 2.84–2.96 (m, 1 H), 3.54–3.65 (m, 1 H), 6.44 (dd, 1 H, *J* = 7.9, 2.4 Hz), 7.03 (d, 2 H, *J* = 6.9 Hz), 7.10–7.28 (m, 3 H), 7.32–7.54 (m, 3 H), 8.10 (d, 1 H, *J* = 8.1 Hz).

^{13}C NMR ($CDCl_3$): δ = 24.9, 28.0, 29.3, 32.9, 40.4, 72.4, 108.8, 120.5, 124.4, 125.9, 128.0, 128.1, 128.2, 131.2, 140.7, 146.3, 174.3.

Anal. Calcd. for $C_{19}H_{20}N_4O$: N, 17.49. Found: N, 17.02.

HRMS-FAB: *m*/*z* (M + 1) calcd for $C_{19}H_{21}N_4O$: 321.1715; found: 321.1717.

1,2,5,6,7,11b-Hexahydro-3*H*-pyrrolo[2,1-*a*][2]benzazepin-3-one (11)

Compound **10** (0.4 g, 1.25 mmol) was placed in a dry flask, dissolved in anhyd CH_2Cl_2 (50 mL), $TiCl_4$ (0.55 mL, 5 mmol) was added and and the mixture was stirred at 20 °C for 36 h. The reaction was quenched with H_2O. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with aq 2 M NaOH, dried (Na_2SO_4), and concentrated to give 0.13 g of a brown oil (52%) as the product: No further purification was needed.

^{1}H NMR ($CDCl_3$): δ = 1.64–1.82 (m, 1 H), 1.96–2.10 (m, 1 H), 2.12–2.28 (m, 1 H), 2.36–2.55 (m, 3 H), 2.60–2.74 (m, 1 H), 2.87–3.40 (m, 2 H), 4.09–4.17 (m, 1 H), 4.84 (t, 1 H, *J* = 7.2 Hz), 7.10–7.50 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 25.7, 27.9, 31.0, 31.2, 39.6, 64.0, 126.5, 126.7, 127.9, 130.8, 138.6, 139.1, 174.3.

HRMS: *m*/*z* (M + 1) calcd for $C_{13}H_{16}NO$: 202.1232; found: 202.1175

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