# Synthesis of 2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepines and 11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indoles

**Alan R. Katritzky*, Ritu Jain, Rena Akhmedova, and Yong-Jiang Xu**

*Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, Florida 32611- 7200*
*katritzky@chem.ufl.edu*

**Dedicated to Professor (Mrs.) A. Chatterjee on her 85th anniversary**

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**Abstract**

3-(Pyrrol-1-yl)-1-propylamine (1) and 3-(3-methyl-indol-1-yl)-propylamine (7) were condensed with (1-hydroxymethyl)benzotriazole to give 2-(1*H*-1,2,3-benzotriazol-1-yl-methyl)-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (2) (55%) and 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indole (8) (51%) respectively. Nucleophilic substitutions of the benzotriazolyl group in 2 and 8 with Grignard reagents, sodium borohydride, sodium cyanide and triethyl phosphite gave novel 2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepines (3-6) and 11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indoles (9-11) in good yields.

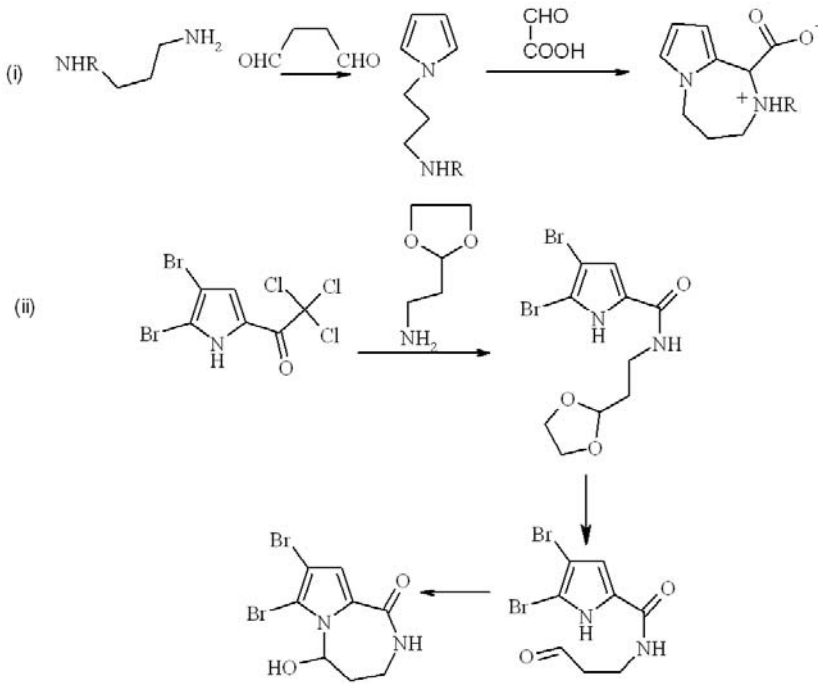
**Keywords:** Pyrrolodiazepines, tetrahydro[1,4]diazepino[1,2-*a*]indoles, benzotriazole

## Introduction

Pyrrolodiazepines have CNS depressant, anti-convulsant, anti-inflammatory and anti-histamine activity.[1] They are inhibitors of enzyme promoted prostaglandin synthesis, and protectors against the convulsive shock induced by metrazol in mice.[2] They act as antitumor antibiotics with sequence selective DNA binding ability,[3] and antagonists of arginine vasopressin.[4]

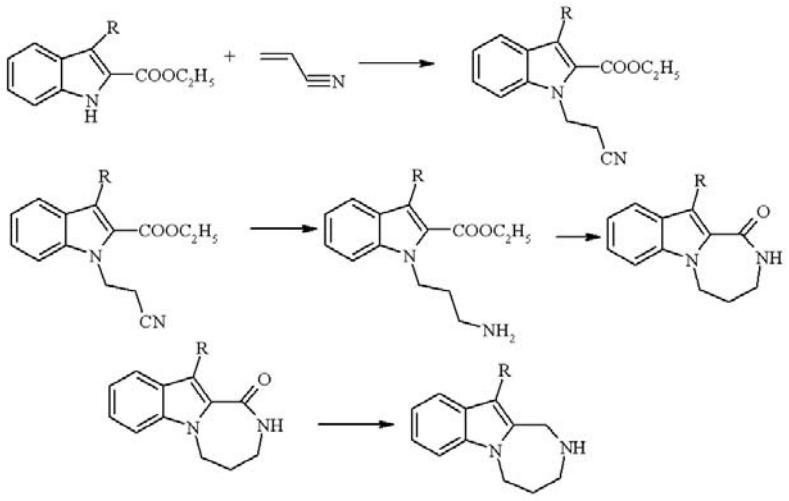
Syntheses of 1,4-diazepines fused with five and six membered heterocyclic rings,[5-7] and octahydropyrrolopyrazines[8-9] are well explored. Two reports address the synthesis of tetrahydropyrrolodiazepines (Scheme 1): (i) Okawara *et al*[10] synthesized 2-substituted-1-carboxy-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepines by the reaction of 3-(pyrrol-1-yl)-1-propylamine with the glyoxalic acid hydrate in ethanol; (ii) bromopyrrolodiazepines (isolated from marine sponges) were synthesized by Marchais *et al*[11] via regioselective intramolecular cyclization of 2-substituted pyrroles.



**Scheme 1**

Tetrahydro[1,4]diazepino[1,2-*a*]indoles are 5-HT antagonists, CNS depressants, anti-allergic agents and muscle relaxants.[12a–e] Some lower the blood pressure[13] and dilate pulmonary vessels.[12e] Available syntheses of tetrahydro[1,4]diazepino[1,2-*a*]indoles start from ethyl-3-phenylindole-2-carboxylates by lactam formation (Scheme 2).[12e, 14–15]



**Scheme 2**

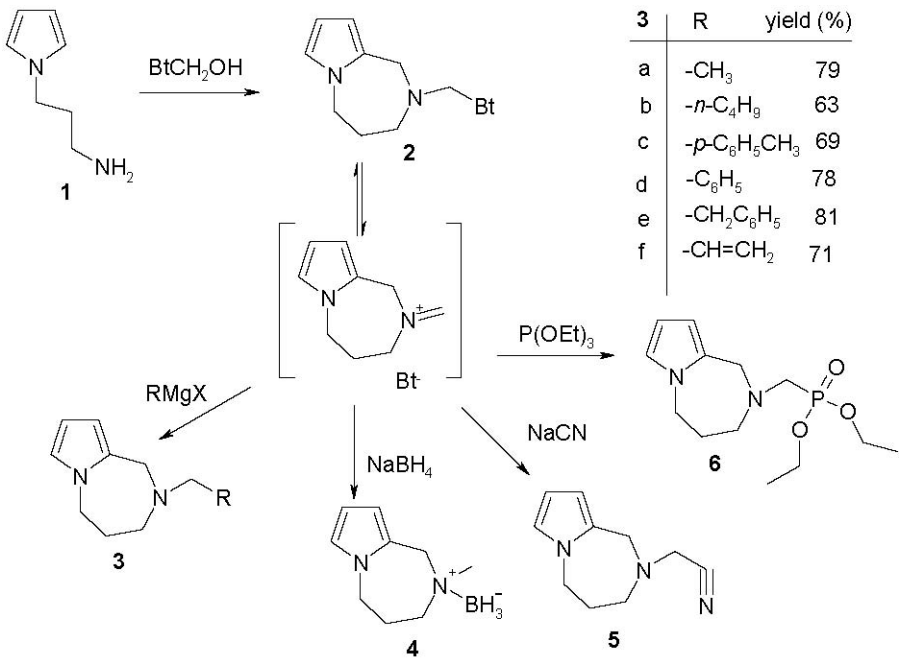
We now report a direct and convenient approach for the synthesis of 2-(1*H*-1,2,3-benzotriazol-1-yl-methyl)-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (**2**) and 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indole (**8**) by the condensation of 3-(pyrrol-1-yl)-1-propylamine (**1**) and 3-(3-methyl-indol-1-yl)-propylamine (**7**) respectively with (1-hydroxymethyl)benzotriazole, followed by the substitution of the benzotriazole residue by a variety of nucleophiles.

## Results and Discussion

Condensation reaction of (1-hydroxymethyl)benzotriazole with 3-(pyrrol-1-yl)-1-propylamine (**1**)[16] (Scheme 3) and 3-(3-methyl-indol-1-yl)-propylamine (**7**)[17-19] (Scheme 4) in chloroform in the presence of trace amounts of *p*-toluene sulphonic acid formed **2** and **8** in 55% and 51% yield respectively. The product was fully characterized by $^{1}$H and $^{13}$C NMR spectra. The aliphatic region of the $^{1}$H NMR spectra showed two singlets ascribed to $BtCH_2N$ ( $\delta$ = 5.39 ppm) and pyrrole $CH_2N$ ( $\delta$ = 3.91ppm) for **2**, and singlets ascribed to $BtCH_2N$ ( $\delta$ = 5.39 ppm) and indole $CH_2N$ ( $\delta$ = 4.08 ppm) for **8** respectively. Crude **2** and **8** were used as such for the subsequent reactions, without any further purification.

Syntheses of 1,2,3,4-tetrahydropyrrolo[1,2-*a*]diazepines derivatives (**3a-f**, **4**-**6**) were carried out using Grignard reagents, sodium borohydride, sodium cyanide and triethyl phosphite as nucleophiles. The benzotriazole moiety can easily be replaced by a variety of nucleophiles.[20-23] Reaction of compound **2** with different Grignard reagents afforded novel 2-substituted-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepines (**3a-f**) in 63-81% yields. Compounds **3a-f** were fully characterized by $^{1}$H, and $^{13}$C NMR spectra, microanalysis and/or HRMS results (Scheme 3).

Reaction of compound **2** with 2 equiv of $NaBH_4$ in THF at room temperature resulted in the replacement of benzotriazole group with a hydrogen atom and led to the formation of a borane complex **4** in 64%.

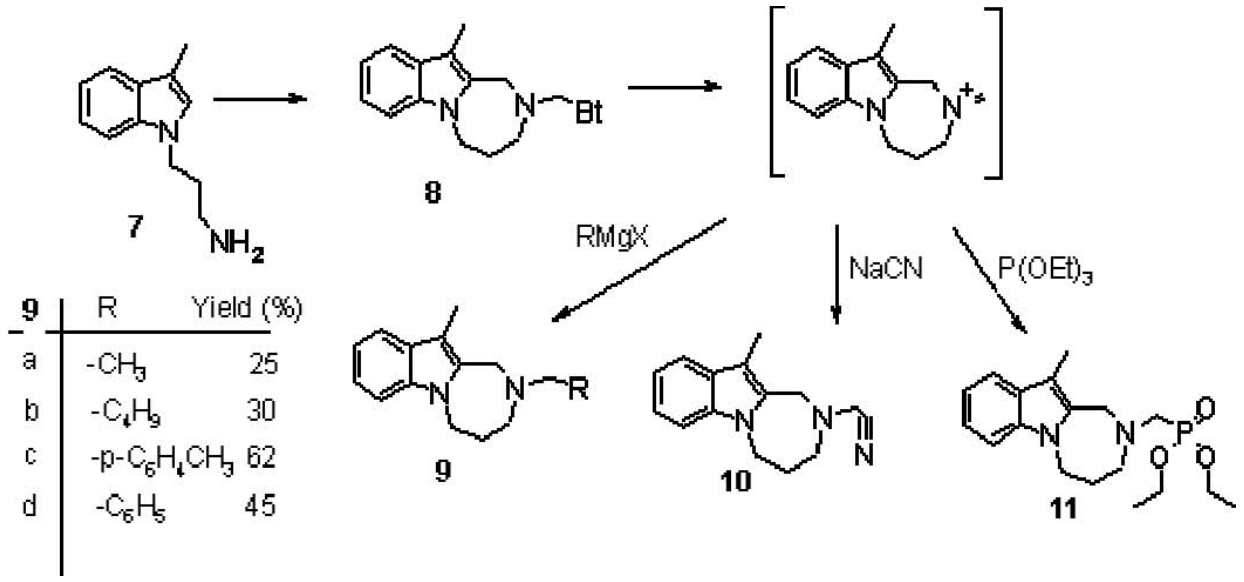



| 3 | R | yield (%) |
|---|---|---|
| a | -$CH_3$ | 79 |
| b | -*n*-$C_4H_9$ | 63 |
| c | -*p*-$C_6H_5CH_3$ | 69 |
| d | -$C_6H_5$ | 78 |
| e | -$CH_2C_6H_5$ | 81 |
| f | -$CH{=}CH_2$ | 71 |

**Scheme 3**

The benzotriazolyl group in **2** can also be substituted by a cyanide anion to give 2-[4,5-dihydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepin-2(3*H*)-yl]acetonitrile (**5**) in 70% yield. The benzotriazolyl group in **2** were also replaced by a triethyl phosphite to give diethyl 4,5-dihydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepin-2(3*H*)-ylmethylphosphonate (**6**) in 55% yield in the presence of $ZnBr_2$ (Scheme 3). The Lewis acid $ZnBr_2$ facilitates the loss of benzotriazolyl anion to form an iminium cation, which is then attacked by the P-nucleophile.

Syntheses of 11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indoles (**9a-d**, **10**, **11**) were carried out using Grignard reagents, sodium cyanide and triethyl phosphite as nucleophiles. The methodology used for the reactions of **2** worked for the reactions of **8** also. Similarly, because of the good leaving ability of benzotriazole, it can easily be replaced by a variety of nucleophiles including Grignard reagents, cyano and the triethyl phosphite group (Scheme 4).




| 9 | R | Yield (%) |
|---|---|---|
| a | -$CH_3$ | 25 |
| b | -$C_4H_9$ | 30 |
| c | -p-$C_6H_4CH_3$ | 62 |
| d | -$C_6H_5$ | 45 |

**Scheme 4**

To summarize, we have developed a convenient method for the preparation of 2-substituted-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepines and 11-methyl-2,3,4,5-tetrahydro -1*H*-[1,4] diazepino[1,2-*a*]indoles by the condensation reaction of 3-(pyrrol-1-yl)-1-propylamine (**1**) and 3-(3-methyl-1*H*-indol-1-yl)propylamine (**7**) respectively with (1-hydroxymethyl) benzotriazole followed by the nucleophilic substitution of benzotriazole with Grignard reagents, sodium borohydride, sodium cyanide and triethyl phosphite. Thus various useful functionalities were introduced via nucleophilic substitutions of the benzotriazole group as a synthetic auxiliary.

## Experimental Section

**General Procedures.** Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ with TMS as the internal standard for $^1H$ (300 MHz) or a solvent as the internal standard for $^{13}C$ (75 MHz). Micro elemental analyses were performed on a Carlo Erba EA-1108 elemental analyzer. HRMS were measured on an AEI-30 mass spectrometer using Electron Impact (+ ve mode). Column chromatography was conducted with silica gel 200−425 mesh.

**Procedure for the synthesis of 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (2).** To a solution of 3-(pyrrol-1-yl)-1-propylamine (**1**) (2.48 g, 20 mmol) in $CHCl_3$ (120 ml), $BtCH_2OH$ ( 6 g, 40 mmol) and *p*-TsOH (0.8 g, 4 mmol) were added. After 15 min, molecular sieves (20 g) were added to the resulting mixture. The reaction mixture was stirred at 25 $^oC$ for 24 h, filtered through celite bed and washed with $CHCl_3$ (3x15 ml). The organic solutions were combined and washed with 2 M NaOH (3x20 ml) and dried over $Na_2SO_4$.

The solvent was evaporated in vacuo and the compound obtained was used as such without any further purification. Yellow oil; yield 55%; $^1$H NMR δ 1.87−1.94 (m, 2H), 3.09−3.12 (m, 2H), 3.91 (s, 2H), 3.98−4.01 (m, 2H), 5.39 (s, 2H), 5.99 (t, *J* = 2.7 Hz, 1H), 6.07−6.09 (m, 1H), 6.58 (t, *J* = 2.3 Hz, 1H), 7.25−7.41 (m, 1H), 7.46− 7.52(m, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H); $^{13}$C NMR δ 28.1, 49.0, 50.2, 55.3, 67.1, 106.1, 109.4, 110.2, 118.3, 119.9, 122.3, 123.9, 127.3, 133.2, 146.0.

**General procedure for syntheses of 2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepines 3a–f**

Compound **2** (0.5 g, 2 mmol) was dissolved in dry THF (15 mL) at 0 °C. The corresponding Grignard reagent (3 mmol, 1.5 equiv.) was added dropwise. The mixture was stirred at 0 °C for 2 h and then at room temperature overnight. The reaction was then quenched with water, washed with 2 M aqueous NaOH (2x15 mL) and extracted with ether. After being dried over $MgSO_4$, the solvent was removed in vacuo. The product obtained was further purified by column chromatography on silica gel (eluent: hexanes/EtOAc = 7/1–3/1).

**2-Ethyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (3a).** Brown oil; yield 79%; $^1$H NMR δ 1.07 (t, *J* = 7.2 Hz, 3H), 1.76−1.83 (m, 2H), 2.40 (q, *J* = 7.2 Hz, 2H), 3.06−3.09 (m, 2H), 3.81 (s, 2H), 3.98−4.01 (m, 2H), 5.94−5.96 (m, 1H), 5.99−6.00 (m, 1H), 6.53−6.55 (m, 1H) ; $^{13}$C NMR δ 12.7, 26.4, 46.4, 49.5, 50.3, 57.1, 105.6, 109.2, 121.6, 131.2. Anal. Calcd for $C_{10}H_{16}N_2$: N, 17.06. Found: N, 17.14.

**2-Pentyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (3b).** Brown oil; yield 63%; $^1$H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.23−1.32 (m, 4H), 1.42−1.52 (m, 2H ), 1.75−1.84 (m, 2H), 2.28−2.33 (m, 2H), 3.05−3.08 (m, 2H), 3.80 (s, 2H), 3.98−4.01 (m, 2H), 5.94−5.96 (m, 1H), 5.97−5.99 (m, 1H), 6.54 (t, *J* = 2.2 Hz, 1H) ; $^{13}$C NMR δ 14.0, 22.6, 26.3, 27.3, 29.6, 49.6, 50.7, 52.3, 57.5, 105.6, 109.2, 121.6, 131.6. HRMS calcd for $C_{13}H_{22}N_2$ (M) 206.1783, found 206.1777.

**2-(4-Methylbenzyl)-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (3c).** Yellow-brown oil; yield 69%; $^1$H NMR δ 1.78−1.82 (m, 2H), 2.33 (s, 3H), 3.03−3.06 (m, 2H), 3.47 (s, 2H), 3.76 (s, 2H), 3.98−4.01 (m, 2H), 5.90−5.92 (m, 1H), 5.97 (t, *J* = 3.0 Hz, 1H), 6.56 (t, *J* = 2.2 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.19 (d, *J* = 7.8 Hz, 2H) ; $^{13}$C NMR δ 21.1, 26.7, 49.6, 50.7, 56.7, 57.1, 105.6, 109.4, 121.6, 128.8, 128.9, 131.7, 135.9, 136.4. Anal. Calcd for $C_{16}H_{20}N_2$: C, 79.96; H, 8.39; N, 11.66. Found: C, 79.65; H, 8.50; N, 11.38.

**2-Benzyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (3d).** Yellow-brown oil; yield 78%; $^1$H NMR δ 1.78−1.85 (m, 2H), 3.05−3.08 (m, 2H), 3.51 (s, 2H), 3.76 (s, 2H), 3.99−4.02 (m, 2H), 5.90−5.92 (m, 1H), 5.97 (t, *J* = 3.0 Hz, 1H), 6.57 (t, *J* = 2.2 Hz, 1H), 7.20−7.33 (m, 5H); $^{13}$C NMR δ 26.7, 49.6, 50.7, 56.9, 57.2, 105.6, 109.4, 121.7, 126.9, 128.1, 129.0, 131.6, 139.0. Anal. Calcd for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.35; H, 8.01; N, 12.49.

**2-Phenethyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (3e).** Yellow-brown oil; yield 81%; $^1$H NMR δ 1.79 (br s, 2H), 2.54−2.60 (m, 2H), 2.76−2.81 (m, 2H), 3.13 (br s, 2H), 3.90 (s, 2H), 3.99−4.02 (m, 2H), 5.97 (br s, 1H), 6.04 (br s, 1H), 6.55 (br s, 1H), 7.15−7.28 (m,

5H); $^{13}$C NMR δ 26.3, 34.4, 49.5, 50.4, 54.0, 57.7, 105.8, 109.4, 121.8, 125.9, 128.3, 128.7, 131.2, 140.3. Anal. Calcd for $C_{16}H_{20}N_2$: C, 79.76; H, 8.39; N, 11.66. Found: C, 79.27; H, 8.20; N, 11.74.

**2-Allyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine (3f).** Yellow-brown oil; yield 71%; $^1$H NMR δ 1.75−1.80 (m, 2H), 2.99−3.04 (m, 4H), 3.76 (s, 2H), 3.96−4.00 (m, 2H), 5.11−5.18 (m, 2H), 5.78−5.93 (m, 1H), 5.93−5.97 (m, 2H), 6.53 (t, *J* = 2.1 Hz, 1H) ; $^{13}$C NMR δ 26.9, 49.4, 50.9, 56.5, 57.2, 105.6, 109.1, 117.6, 121.6, 131.3, 135.8. Anal. Calcd for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15. Found: C, 74.92; H, 9.66.

**Procedure for the synthesis of 2-methyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepine borane complex (4).** Compound **2** (0.54 g, 2 mmol) and $NaBH_4$ (0.15 g, 4 mmol) were stirred at 20 °C overnight in dry THF (20 mL). Then THF was removed in vacuo. The residue was dissolved in EtOAc, washed with 2 M aqueous NaOH (2x15 mL), water and the organic layer was dried over anhydrous $Na_2SO_4$. After the removal of EtOAc in vacuo, the crude product obtained was purified by column chromatography on silica gel (eluent: hexane/ EtOAc = 9/1–4/1). Yellow oil; yield 64%; $^1$H NMR δ 1.30−2.20 (br s, 3H, $BH_3$), 1.91−2.01 (m, 2H), 2.32 (s, 3H), 3.24−3.28 (m, 2H), 4.02−4.10 (m, 4H), 6.00−6.02 (m, 1H), 6.12−6.15 (m, 1H), 6.61 (t, *J* = 2.1 Hz, 1H); $^{13}$C NMR δ 25.7, 44.2, 48.1, 58.1, 64.0, 106.8, 112.9, 123.0, 125.2. Anal. Calcd for $C_9H_{17}BN_2$: C, 65.89; H, 10.44; N, 17.08. Found: C, 66.05; H, 10.54; N, 16.82.

**Procedure for the synthesis of 2-[4,5-dihydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepin-2(3*H*)-yl]acetonitrile (5).** Compound **2** (0.54g, 2 mmol) and NaCN (0.20 g, 4 mmol) were stirred in DMSO (10 mL) at 20 °C for 24 h. The mixture was washed with water and extracted with $CH_2Cl_2$ and dried over anhydrous $Na_2SO_4$. After removal of the solvent in vacuo, the residue was purified by flash chromatography using basic $Al_2O_3$ (eluent: hexane/ EtOAc = 10/1–4/1). Yellow oil; yield 70%; $^1$H NMR δ 1.75−1.82 (m, 2H), 2.99 (t, *J* = 5.2 Hz, 2H), 3.36 (s, 2H), 3.74 (s, 2H), 3.92−3.95 (m, 2H), 5.89 (t, *J* = 3.0 Hz, 1H), 5.96−5.99 (m, 1H), 6.49 (t, *J* = 2.1 Hz, 1H); $^{13}$C NMR δ 27.5, 43.3, 48.7, 51.4, 56.9, 106.1, 109.6, 115.7, 122.3, 129.1. Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.87; H, 7.79; N, 24.37.

**Procedure for the synthesis of diethyl 4,5-dihydro-1*H*-pyrrolo[1,2-*a*][1,4]diazepin-2(3*H*)-ylmethylphosphonate** (**6**)**.** To a solution of **2** (0.54 g, 2 mmol) in dry $CH_2Cl_2$ (20 mL) at 0 °C $ZnBr_2$ (0.22 g, 1 mmol) and triethyl phosphite (0.34 ml, 2.0 mmol) were added respectively. The reaction mixture was stirred at 0 °C for 2 h and at room temperature overnight. The reaction mixture was washed with 1 M aqueous NaOH and brine. The aqueous layer was then extracted with $CH_2Cl_2$, and dried over anhydrous $MgSO_4$. After removal of the solvent in vacuo, the desired product was purified by column chromatography on silica gel (eluent: hexanes/EtOAc = 7/1–2/1). Yellow oil; yield 55%; $^1$H NMR δ 1.30−1.36 (m, 6H), 1.76 (br s, 2H), 2.73 (d, *J* = 10.8 Hz, 2H), 3.23 (br s, 2H), 3.95 (s, 2H), 3.99−4.03 (m, 2H), 4.09−4.18 (m, 4H), 5.95 (t, *J* = 2.9 Hz, 1H), 6.03−6.05 (m, 1H), 6.56 (t, *J* = 2.0 Hz, 1H); $^{13}$C NMR δ 16.4, 25.5, 46.4 (d, *J* = 168.5 Hz), 49.4, 52.2 (d, *J* = 9.0 Hz), 58.2 (d, *J* = 9.0 Hz), 61.9, 62.7, 105.6, 110.3, 122.1, 130.3. HRMS calcd for $C_{13}H_{24}N_2O_3P$ (M+1) 287.1525, found 287.1527.

**Procedure for the synthesis of 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indole (8).** Following the same procedure for the synthesis as that of **2** using 3-(3-methylindol-1-yl)-propylamine (**7**) as the starting material, the title compound **8** was obtained as yellow microcrystals. The product was used as such for the next step without further purification. Yield 51%; mp 69−70 °C; $^1$H NMR δ 1.96−2.05 (m, 2H), 2.30 (s, 3H), 3.26 (t, *J* = 5.2 Hz, 2H), 4.12 (s, 2H), 4.27−4.30 (m, 2H), 5.44 (s, 2H), 7.13−7.18 (m, 1H), 7.24−7.33 (m, 2 H), 7.43−7.50 (m, 1H), 7.56−7.61 (m, 2H), 7.70 (d, *J* = 8.1 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H); $^{13}$C NMR δ 8.7, 28.3, 43.7, 47.4, 55.7, 67.3, 108.4, 109.2, 110.3, 118.3, 118.6, 119.0, 120.0, 121.6, 124.0, 127.4, 127.9, 133.4, 136.1, 146.2.

**General procedure for syntheses of 2-ethyl-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino [1,2-*a*] indole (9a–d)**

Following the same procedure for the synthesis as **3**, using 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*] indole (**8**) as the starting material after column chromatography on silica gel (eluent: hexane/ EtOAc = 7/1–3/1)gave **9a–d** as the pure product.

**2-Ethyl-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-a]indole (9a).** Yellow oil; yield 25%; $^1$H NMR δ 1.01 (t, *J* = 7.1 Hz, 3H), 1.69−1.76 (m, 2H), 2.22 (s, 3H), 2.33 (q, *J* = 7.1 Hz, 2H), 3.04 (t, *J* = 5.2 Hz, 2H), 3.91 (s, 2H), 4.08−4.11 (m, 2H), 6.95−7.00(m, 1H), 7.06−7.16 (m, 2H), 7.42 (d, *J* = 7.7 Hz, 1H); $^{13}$C NMR δ 8.7, 12.9, 26.5, 44.1, 46.5, 48.0, 57.3, 108.3, 108.6, 118.3, 118.6, 121.1, 127.9, 134.6, 135.9.Anal. Calcd for $C_{15}H_{20}N_2$: C, 78.90; H, 8.83; N, 12.27. Found: C, 78.32; H, 9.19; N, 12.26.

**11-Methyl-2-pentyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-a]indole (9b).** Yellow oil; yield 41%; $^1$H NMR δ 0.88 (t, *J* = 7 Hz, 3H), 1.20−1.33 (m, 4H), 1.49 (quin, *J* = 7.4 Hz, 2H), 1.78−1.85 (m, 2H), 2.29 (s, 3H), 2.29−2.34 (m, 2H), 3.14 (t, *J* = 5.2 Hz, 2H), 4.00 (s, 2H), 4.19−4.21 (m, 2H), 7.03−7.08 (m, 1H), 7.14−7.24 (m, 2H), 7.51 (d, *J* = 7.9 Hz, 1H); $^{13}$C NMR δ 8.8, 14.0, 22.6, 26.4, 27.4, 29.6, 44.2, 48.2, 52.3, 57.7, 108.4, 108.7, 118.3, 118.6, 121.1, 127.9, 134.8, 135.9. Anal. Calcd for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.36. Found: C, 79.34; H, 9.87; N, 10.51.

**11-Methyl-2-(4-methylbenzyl)-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-a]indole (9c).** Yellow oil; yield 37%; $^1$H NMR δ 2.00−2.15 (m, 2H), 2.27 (s, 3H), 2.57 (s, 3H), 3.33 (t, *J* = 5.1 Hz, 2H), 3.70 (s, 2H), 4.15 (s, 2H), 4.32−4.40 (m, 2H), 7.28−7.47 (m, 7H), 7.74 (d, *J* = 7.7 Hz, 1H), ; $^{13}$C NMR δ 8.5, 21.0, 26.7, 44.0, 47.9, 56.7, 57.3, 108.3, 108.6, 118.2, 118.6, 121.0, 127.9, 128.7, 128.8, 134.8, 135.7, 135.8, 136.4. HRMS calcd for $C_{21}H_{24}N_2$ (M) 304.1939, found 304.1941.

**2-Benzyl-11-methyl-2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,2-a]indole (9d).** Yellow oil; yield 45%; $^1$H NMR δ 1.60−1.72 (m, 2H), 1.87 (s, 3H), 2.98 (t, *J* = 4.9 Hz, 2H), 3.37 (s, 2H), 3.78 (s, 2H), 4.00−4.02 (m, 2H), 6.95 (t, *J* = 7.1 Hz, 1H), 7.03−7.16 (m, 7H), 7.37 (d, *J* = 7.7 Hz, 1H),; $^{13}$C NMR δ 8.5, 26.7, 44.0, 47.9, 56.9, 57.5, 108.3, 108.6, 118.2, 118.6, 121.0, 126.9, 127.9, 128.1, 128.7, 134.7, 135.8, 138.9. HRMS calcd for $C_{20}H_{22}N_2$ (M) 290.1783, found 290.1776.

**Procedure for synthesis of 2-[11-methyl-4,5-dihydro-1*H*-[1,4]diazepino[1,2-*a*]indol-2(3*H*)-yl] acetonitrile (10).** Following the same procedure for the synthesis as that of **5**, using 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino[1,2-*a*]indole (**8**) as the starting material after column chromatography using basic alumina ((eluent: hexane/ EtOAc = 10/1–4/1) gave **10** as the pure product. Yellow oil; yield 55%; $^1$H NMR δ 1.80−1.88 (m, 2H), 2.31 (s, 3H), 3.13 (t, *J* = 5.3 Hz, 2H), 3.40 (s, 2H), 4.03 (s, 2H), 4.19−4.22 (m, 2H), 7.06−7.10 (m, 1H), 7.17−7.25 (m, 2H), 7.52 (d, *J* = 7.7 Hz, 1H); $^{13}$C NMR δ 8.7, 27.3, 42.9, 43.6, 48.8, 57.3, 108.4, 109.7, 115.9, 118.7, 119.0, 121.8, 127.7, 132.2, 136.0. Anal. Calcd for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16. Found: C, 75.09; H, 7.30.

**Procedure for the syntheses of diethyl [11-methyl-4,5-dihydro-1*H*-[1,4]diazepino[1,2-*a*] indol-2(3*H*)-yl]methylphosphonate (11).** Following the same procedure for the synthesis as **6**, using 2-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-11-methyl-2,3,4,5-tetrahydro-1*H*-[1,4]diazepino [1,2-*a*] indole (**8**) as the starting material after column chromatography on silica gel (eluent: hexane/ EtOAc = 7/1–2/1) gave **11** as the pure product. Yellow oil; yield 71%; $^1$H NMR δ 1.38 (t, *J* = 7.1 Hz, 6H), 1.81−1.86 (m, 2H), 2.38 (s, 3H), 2.74 (d, *J* = 10.6 Hz, 2H), 3.32−3.36 (m, 2H), 4.16−4.27 (m, 8H), 7.11−7.16 (m, 1H), 7.22−7.31 (m, 2H), 7.58 (d, *J* = 7.7 Hz, 1H); $^{13}$C NMR δ 8.3, 16.2 (d, *J* = 5.7 Hz, 1C), 25.8, 43.7, 46.7 (d, *J* = 169.5 Hz, 1C), 49.4 (d, *J* = 7.4 Hz, 1C), 58.7 (d, *J* = 10.3 Hz, 1C), 61.8 (d, *J* = 6.9 Hz, 1C), 108.2, 109.9, 118.1, 118.5, 121.2, 127.5, 133.4, 135.8. HRMS calcd for $C_{18}H_{27}O_3N_2P_1$ (M+1) 351.1838, found 351.1849.

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