Synthesis of Novel Tricyclic 4-Chloro-7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-ones

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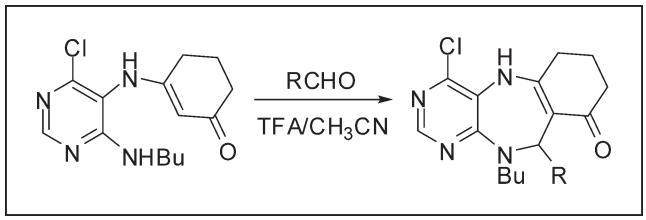

A series of tricyclic 7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-ones were prepared in moderate to high yields using TFA-promoted iminium-cyclization reactions of 3-(6-(butylamino)-4-chloropyrimidin-5-ylamino)cyclohex-2-enones and various aldehydes.

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INTRODUCTION

Benzodiazepines have long been associated with interesting biological activities. For example, clozapine is used to treat schizophrenia; pirenzepine acts selectively as a muscarinic receptor (M1) antagonist; and apafant acts as the platelet activating factor inhibitors [1]. Consequently, syntheses of benzodiazepine derivatives or diazepine-containing heterocycles are of interest to organic and medicinal chemists. Thus, dibenzo[b,e][1,4]-diazepines and other tricyclic systems with a 1,4-diazepine moiety are well documented in the literature [2–9].

As part of our program to prepare heterocyclic libraries, we developed a series of methodologies to rapidly access various heterocyclic scaffolds with benzodiazepine as the core [10–15]. These methodologies entail Bischler–Napieralski cyclization reactions and iminium cyclization reactions as the key transformation steps. To expand the scope of the iminium-cyclization reaction, we envisioned that enaminones **1** could be reacted with various aldehydes to prepare 7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-ones [16], as depicted in Scheme 1. Although syntheses of dibenzo [b,e][1,4]diazepines are frequently reported, there is few report of aminopyrimidines as substrates for such cyclization reactions [16]. Given the large structural differences between a pyrimidine and benzene, optimization of the cyclization reaction was investigated. Herein, we reported the development of this method to prepare 7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-ones.

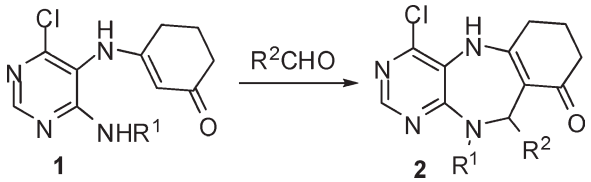
RESULTS AND DISCUSSION

The desired enaminones **1** were readily prepared *via* condensation of **3** [17] with 1,3-cyclohexandione in acetic acid in 78% yields, as depicted in Scheme 2.

To identify the optimal reaction conditions, the formation of the pyrimido-benzodiazepine nucleus was initially studied using benzaldehyde as the substrate, and results are summarized in Table 1.

The standard conditions of AcOH-EtOH are often reported for similar type of cyclization reactions of anilines leading to dibenzo[b,e][1,4]diazepines [2,4]. Therefore, these conditions were studied initially. No desired product was detected at room temperature (entry 1, Table 1) and only trace amount was isolated after prolonged heating (entry 2, Table 1). The lower reactivity of pyrimidines **1** compared to standard anilines is likely because of the large structural differences between pyrimidine and benzene. It is possible that the pyrimidine ring nitrogens are protonated under the acidic reaction conditions, which decreased the propensity of the n-butylamino group toward imine formation. It was reasoned that a stronger acid, such as TFA might help to promote the key imine formation step. Thus, switching the acid from acetic acid to stronger acids, such as TFA and sulfuric acid led to low yields of desired product **2**, entries 3–5, Table 1. The conditions of TFA-acetonitrile proved to be productive in other iminium cyclization reactions, therefore they were investigated next. Treatment of pyrimidine **1** and benzaldehyde in the presence of TFA at room temperature led to product **2** in 22% yield (entry 6, Table 1). On the hand, moderate heating at 60°C produced the desired product **2** in 56% yield. The reaction temperature to reflux shortened the reaction time to 18 h, producing compound **2** in 59% yield (entry 8, Table 1). To test the solvent effect of acetonitrile, the reaction was repeated using AcOH with CH_3CN (entry 9), and after reflux for 18 h only 11% of the desired product was obtained. Another

Scheme 1



condition investigated was $Py/SOCl_2$-CH_2Cl_2 [18], which was reported for aniline cyclization reactions. Reflux for 78 h, the desired product was isolated in 40% yield (entry 10). Thus, the TFA-acetonitrile conditions (entry 8, Table 1) were identified as optimal, which were applied to other aldehydes and results are summarized in Table 2.

As disclosed in Table 2, both aliphatic and aromatic aldehydes are compatible for the current reactions, producing the expected 7,8,10,11-tetrahydro-5*H*-benzo[*e*]-pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-ones **2** in moderate to good yields. The reactions with aliphatic aldehydes (entries 1–3) proceeded at room temperature to generate the desired products in moderate yields. Various functional groups ranging from electron-donating (methyl or methoxy; entries 4–6) to electron-withdrawing groups (halo, cyano, or nitro; entries 8–14) were tolerated under the reaction conditions. The Results presented in Table 2 seem to suggest that both electronic and steric effects may affect the yields when benzaldehydes were used. For example, electron-withdrawing groups tend to give higher yields (entries 11–14) compared to electron-donating groups (entries, 4–6). The presence of an ortho substituent (entries 3 and 8) led to lower yields compared to the corresponding meta- and para-substituted analogs (entries 4 and 9), which suggests steric hindrance may lead to lower yields.

In summary, a novel heterocyclic scaffold entailing 7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-one was prepared efficiently from *N*-substituted pyrimidinediamine and aldehydes. The standard AcOH-EtOH conditions commonly used to prepare dibenzo[b,e][1,4]diazepines proved to unsuitable for aminopyrimidines. Thus, a new TFA-acetonitrile condition was successfully developed to produce the desired 4-chloro-7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-ones in moderate to excellent yields.

Scheme 2

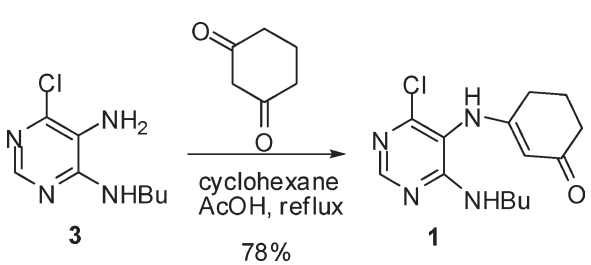
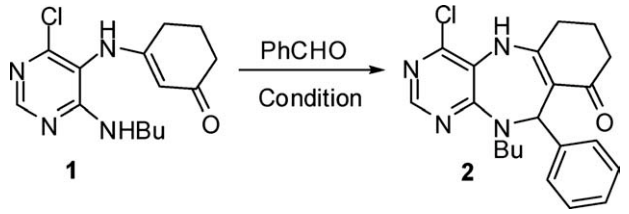


Table 1



Entry	Solvent	Acid	Temp (°C)	Time (h)	Yield (%)
1	EtOH	AcOH	24	24	NR[b]
2	EtOH	AcOH	reflux	43	5[c]
3	EtOH	TFA	24	24	2[c]
4	EtOH	TFA	reflux	43	10
5	EtOH	H_2SO_4	reflux	95	8
6	CH_3CN	TFA	24	24	22[c]
7	CH_3CN	TFA	60	52	56
8	**CH_3CN**	**TFA**	**reflux**	**18**	**59**
9	CH_3CN	AcOH	reflux	18	11[c]
10	DCM	$Py/SOCl_2$	reflux	78	40

[a] Yields are isolated products and the reaction was monitored by LC-MS.
[b] NR denotes no reaction, all starting materials remained.
[c] Some starting material **1** was recovered.

EXPERIMENTAL

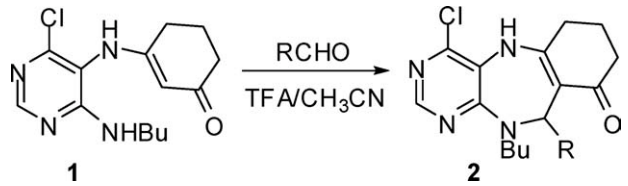
Acetonitrile (CH_3CN) was dried with CaH_2 and distilled. All other commercial reagents were used as received without purification. Melting points were uncorrected. Mass spectra and HPLC data were recorded on a LC/MS system with ELSD detection. The ^1H and ^{13}C NMR data were obtained on a Varian 300 (300 and 75 MHz, respectively) spectrometer with TMS as the internal standard and $CDCl_3$ as the solvent unless otherwise stated. Multiplicities are indicated as the following: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doubled doublet; br, broad. Coupling constants (*J* values) are quoted in Hertz.

3-(6-(Butylamino)-4-chloropyrimidin-5-ylamino)cyclohex-2-enone (1). A solution of 5-amino-4-chloro-6-(butylamino)-pyrimidine **3** (1.5 g, 7.5 mmol), 1,3-cyclohexandione (0.84 g, 7.5 mmol), and a catalytic amount of acetic acid (30 μL, 0.52 mmol) in cyclohexane (40 mL) was heated in an azeotropic distillation apparatus for 2 days. The solvent was removed *in vacuo* to give the crude product, which was recrystallized from acetone to give 1.71 g (78%) of **1**, mp 190–192°C.^1H NMR: 8.29 (s, 1H), 5.74 (s, 1H), 5.32 (s, 1H), 4.93 (s, 1H), 3.47 (q, 2H, $J = 6.9$ Hz), 2.51 (t, 2H, $J = 5.4$ Hz), 2.35 (t, 2H, $J = 6.3$ Hz), 2.10–2.02 (m, 2H), 1.61–1.29 (m, 2H), 1.41–1.29 (m, 2H), 0.92 (t, 3H, $J = 7.2$ Hz). MS (ESI): *m*/*z* 295.3 [M+H$^+$].

General procedure for the synthesis of 4-chloro-7,8,10,11-tetrahydro-5*H*-benzo[*e*]pyrimido[4,5-*b*][1,4]diazepin-9(6*H*)-one (2). To a solution of 3-(6-(butylamino)-4-chloropyrimidin-5-ylamino)cyclohex-2-enone **1** (150 mg, 0.51 mmol) and an aldehyde (0.612 mmol) in 4 mL acetonitrile was added TFA (20 μL, 0.27 mmol). The mixture was stirred for corresponding time at ambient temperature or 80°C. After cooling to

Table 2

Synthesis of 4-chloro-7,8,10,11-tetrahydro-SH-benzo[e]pyrimido[4,5-6][1,4]diazepin 9(6H)-ones.[a]



1 **2**

Entry	R	Compd.	Time	Yield (%)
1	$CH_3CH_2CH_2$	**2.1**	7h	34
2	$CH_3CH_2CH_2$	**2.1**	3d[b]	51
3	CH_3CH_2	**2.2**	3d[b]	62
4	*o*-$MeOC_6H_4$	**2.3**	9h	13
5	*p*-$MeOC_6H_4$	**2.4**	20h	22
6	*p*-MeC_6H_4	**2.5**	20h	57
7	Ph	**2.6**	18h	59
8	*o*-ClC_6H_4	**2.7**	20h	41
9	2′,4′-di-ClC_6H_3	**2.8**	20	45
10	3′,4′-di-ClC_6H_3	**2.9**	22h	65
11	*p*-FC_6H_4	**2.10**	22h	68
12	*p*-CNC_6H_4	**2.11**	18h	80
13	*m*-$NO_2C_6H_4$	**2.12**	17h	87
14	*p*-$NO_2C_6H_4$	**2.13**	18h	87

[a] All reactions were conducted at 80°C unless noted, yields are based on isolated products.
[b] Reaction was carried out at 25°C.

room temperature, the solvent was removed *in vacuo* to give the crude product. Purification by flash chromatography (Petroleum ether/EtOAc = 5:1 or 2:1) afforded the desired products.

11-Butyl-4-chloro-10-propyl-7,8,10,11-tetrahydro-5H-benzo[e]-pyrimido[4,5-b] [1,4]diazepin-9(6H)-one (2.1). 51%. mp: 83–85°C. ^{1}H NMR: 8.05 (s, 1H), 6.45 (s, 1H), 4.87 (t, 1H, J = 8.1 Hz), 4.32–4.22 (m, 1H), 3.10–3.01 (m, 1H), 2.72–2.59 (m, 1H), 2.56–2.42 (m, 3H), 2.12–1.91 (m, 2H), 1.65–1.45 (m, 4H), 1.33–1.15 (m, 4H). 0.92–0.83 (m, 6H). ^{13}C NMR: 194.4, 155.5, 154.4, 149.5, 144.3, 119.1, 116.7, 55.2, 51.7, 36.3, 35.5, 31.6, 29.8, 20.9, 19.93, 19.86, 13.8, 13.7. MS (ESI): *m*/*z* 349.1 [M+H$^+$].

11-Butyl-4-chloro-10-ethyl-7,8,10,11-tetrahydro-5H-benzo[e]-pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.2). 62%. oil. ^{1}H NMR: 8.03 (s, 1H), 7.29 (s, 1H), 4.78 (t, 1H, J = 8.1 Hz), 4.34–4.25 (m, 1H), 3.09–2.97 (m, 1H), 2.68–2.59 (m, 1H), 2.52 (t, 1H, J = 5.1 Hz), 2.48–2.41 (m, 2H), 2.10–1.94 (m, 2H), 1.74–1.48 (m, 4H), 1.30–1.23 (m, 2H), 0.91–0.80 (m, 6H). ^{13}C NMR: 193.9, 154.8, 154.2, 149.6, 144.8, 119.2, 116.5, 56.7, 51.8, 35.8, 31.6, 29.8, 27.1, 21.0, 19.9, 13.7, 11.1. MS (ESI): *m*/*z* 335.1 [M+H$^+$].

11-Butyl-4-chloro-10-(2-methoxyphenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.3). 13%. mp: 168–169°C. ^{1}H NMR: 7.97 (s, 1H), 7.18–7.13 (m, 1H), 6.99 (d, 1H, J = 6.3 Hz), 6.82–6.73 (m, 2H), 6.25 (s, 1H), 6.23 (s, 1H), 4.36–4.26 (m, 1H), 3.78 (s, 3H), 3.33–3.24 (m, 1H), 2.70–2.61 (m, 1H), 2.57–2.42 (m, 3H), 2.12–1.91 (m, 2H), 1.68–1.50 (m, 2H). 1.37–1.24 (m, 2H), 0.90 (t, 3H, J = 7.5 Hz). ^{13}C NMR: 193.4, 157.1, 155.7, 155.6, 149.8, 145.1, 128.6, 128.1, 126.8, 120.2, 119.8, 116.7, 111.0, 55.14, 55.11, 51.8, 35.9, 31.6, 30.2, 20.8, 20.1, 13.8. MS (ESI): *m*/*z* 413.1 [M+H$^+$].

11-Butyl-4-chloro-10-(4-methoxyphenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.4). 22%. mp: 167–169°C. ^{1}H NMR: 8.04 (s, 1H), 7.09 (d, 2H, J = 8.7 Hz), 6.73 (d, 2H, J = 8.7 Hz), 6.30 (s, 1H), 6.09 (s, 1H), 4.50–4.41 (m, 1H), 3.74 (s, 3H), 3.23–3.14 (m, 1H), 2.73–2.59 (m, 1H), 2.55–2.43 (m, 3H), 2.16–1.95 (m, 2H), 1.73–1.53 (m, 2H). 1.38–1.26 (m, 2H), 0.91 (t, 3H, J = 7.5 Hz). ^{13}C NMR: 194.0, 158.4, 156.2, 155.3, 149.8, 145.2, 133.0, 127.2, 119.4, 118.3, 113.9, 57.8, 55.1, 52.4, 35.8, 31.7, 30.1, 20.9, 20.0, 13.8. MS (ESI): *m*/*z* 413.1 [M+H$^+$].

11-Butyl-4-chloro-10-(4-methylphenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.5). 57%. mp: 144–146°C. ^{1}H NMR: 8.04 (s, 1H), 7.00 (d, 2H, J = 8.1 Hz), 6.86 (d, 2H, J = 7.8 Hz), 6.29 (s, 1H), 6.11 (s, 1H), 4.50–4.41 (m, 1H), 3.23–3.13 (m, 1H), 2.72–2.56 (m, 1H), 2.54–2.41 (m, 3H), 2.26 (s, 3H), 2.16–1.94 (m, 2H), 1.71–1.50 (m, 2H). 1.38–1.26 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz). ^{13}C NMR: 193.9, 156.3, 155.2, 149.6, 145.1, 137.8, 136.4, 129.1, 125.7, 119.2, 118.3, 57.8, 52.3, 35.7, 31.5, 30.0, 20.70, 20.68, 19.9, 13.7. MS (ESI): *m*/*z* 397.2 [M+H$^+$].

11-Butyl-4-chloro-10-phenyl-7,8,10,11-tetrahydro-5H-benzo[e]-pyrimido [4,5-b][1,4]diazepin-9(6H)-one (2.6). 59%. mp: 154–155°C. ^{1}H NMR: 8.04 (s, 1H), 7.24–7.17 (m, 3H), 6.98 (dd, 2H, J_1 = 7.5 Hz, J_2 = 1.8 Hz), 6.28 (s, 1H), 6.15 (s, 1H), 4.52–4.42 (m, 1H), 3.23–3.14 (m, 1H), 2.71–2.42 (m, 4H), 2.16–1.92 (m, 2H), 1.76–1.53 (m, 2H), 1.38–1.25 (m, 2H), 0.91 (t, 3H, J = 7.5 Hz). ^{13}C NMR: 193.9, 156.6, 155.1, 149.5, 145.0, 140.8, 128.4, 126.8, 125.8, 119.1, 118.1, 57.9, 52.3, 35.6, 31.4, 29.9, 20.6, 19.8, 13.6. MS (ESI): *m*/*z* 383.2 [M+H$^+$].

11-Butyl-4-chloro-10-(2-chlorophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.7). 41%. mp: 179–181°C. ^{1}H NMR: 8.04 (s, 1H), 7.34 (d, 1H, J = 7.5 Hz), 7.17–7.05 (m, 3H), 6.27 (s, 1H), 6.24 (s, 1H), 4.33–4.24 (m, 1H), 3.34–3.24 (m, 1H), 2.69–2.35 (m, 4H), 2.09–1.91 (m, 2H), 1.71–1.53 (m, 2H). 1.38–1.26 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz). ^{13}C NMR: 193.6, 156.2, 155.2, 150.2, 145.7, 138.6, 133.6, 130.5, 128.5, 127.3, 126.5, 120.2, 117.7, 56.7, 51.8, 35.7, 31.5, 30.0, 20.3, 20.0, 13.8. MS (ESI): *m*/*z* 417.1 [M+H$^+$].

11-Butyl-4-chloro-10-(2,4-dichlorophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.8). 45%. mp: 152–154°C. ^{1}H NMR: 8.05 (s, 1H), 7.36 (s, 1H), 7.07–6.97 (m, 2H), 6.25 (s, 1H), 6.22 (s, 1H), 4.31–4.22 (m, 1H), 3.31–3.22 (m, 1H), 2.65–2.34 (m, 4H), 2.10–1.92 (m, 2H), 1.69–1.49 (m, 2H). 1.37–1.27 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz). ^{13}C NMR: 193.5, 156.2, 155.0, 150.4, 146.0, 137.4, 134.5, 133.7, 130.3, 128.2, 126.8, 120.1, 117.5, 56.4, 51.9, 35.8, 31.6, 30.1, 20.3, 20.0, 13.8. MS (ESI): *m*/*z* 451.1 [M+H$^+$].

11-Butyl-4-chloro-10-(3,4-dichlorophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.9). 65%. mp: 132–134°C. ^{1}H NMR: 8.07 (s, 1H), 7.28 (s, 1H), 7.06 (dd, 1H, J_1 = 2.1 Hz, J_2 = 0.6 Hz), 6.84–6.80 (m, 1H), 6.33 (s, 1H), 6.09 (s, 1H), 4.50–4.41 (m, 1H), 3.21–3.11 (m, 1H), 2.74–2.44 (m, 4H), 2.18–1.94 (m, 2H), 1.71–1.49 (m, 2H). 1.37–1.26 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz). ^{13}C NMR: 193.9, 156.9, 154.9, 150.0, 145.8, 141.5, 132.6, 131.1, 130.4, 128.2,

125.3, 119.1, 117.6, 57.3, 52.4, 35.6, 31.6, 30.0, 20.7, 19.9, 13.7. MS (ESI): *m*/*z* 451.0 [M+H$^+$].

11-Butyl-4-chloro-10-(4-fluorophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.10). 68%. mp: 146–148°C. ^{1}H NMR: 8.05 (s, 1H), 6.97–6.86 (m, 4H), 6.31 (s, 1H), 6.10 (s, 1H), 4.50–4.40 (m, 1H), 3.22–3.13 (m, 1H), 2.73–2.44 (m, 4H), 2.19–1.93 (m, 2H), 1.72–1.49 (m, 2H), 1.42–1.23 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz). ^{13}C NMR: 194.0, 163.3, 160.0, 156.7, 155.2, 149.8, 145.3, 136.7, 127.7, 127.6, 119.3, 118.0, 115.6, 115.3, 57.7, 52.4, 35.7, 31.6, 30.1, 20.8, 20.0, 13.8. MS (ESI): *m*/*z* 401.1 [M+H$^+$].

11-Butyl-4-chloro-10-(4-cyanophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.11). 80%. mp: 51–53°C. ^{1}H NMR: 8.08 (s, 1H), 7.51 (d, 2H, J = 8.4 Hz), 7.10 (d, 2H, J = 8.1 Hz), 6.34 (s, 1H), 6.18 (s, 1H), 4.50–4.40 (m, 1H), 3.23–3.14 (m, 1H), 2.74–2.45 (m, 4H), 2.17–2.00 (m, 2H), 1.70–1.54 (m, 2H). 1.36–1.26 (m, 2H), 0.91 (t, 3H, J = 7.5 Hz). ^{13}C NMR: 193.9, 157.2, 154.7, 149.9, 146.6, 145.7, 132.3, 126.7, 118.9, 118.3, 117.5, 110.7, 57.7, 52.4, 35.5, 31.4, 29.9, 20.5, 19.8, 13.6. MS (ESI): *m*/*z* 408.2 [M+H$^+$].

11-Butyl-4-chloro-10-(3-nitrophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.12). 80%. mp: 51–53°C. ^{1}H NMR: 8.08 (s, 1H), 8.04 (d, 1H, J = 7.8 Hz), 7.84 (s, 1H), 7.43–7.33 (m, 2H), 6.34 (s, 1H), 6.21 (s, 1H), 4.56–4.47 (m, 1H), 3.21–3.18 (m, 1H), 2.71–2.47 (m, 4H), 2.19–2.04 (m, 2H), 1.75–1.57 (m, 2H). 1.40–1.26 (m, 2H), 0.93 (t, 3H, J = 6.9 Hz). ^{13}C NMR: 193.9, 157.2, 154.8, 150.0, 148.4, 145.9, 143.4, 132.2, 129.6, 122.1, 121.2, 119.1, 117.1, 57.6, 52.5, 35.6, 31.5, 30.0, 20.7, 19.9, 13.7. MS (ESI): *m*/*z* 428.1 [M+H$^+$].

11-Butyl-4-chloro-10-(4-nitrophenyl)-7,8,10,11-tetrahydro-5H-benzo[e] pyrimido[4,5-b][1,4]diazepin-9(6H)-one (2.13). 80%. mp: 51–53°C. ^{1}H NMR: 8.09 (s, 1H), 8.07 (d, 2H, J = 8.4 Hz), 7.16 (d, 2H, J = 8.4 Hz), 6.34 (s, 1H), 6.23 (s, 1H), 4.51–4.41 (m, 1H), 3.26–3.17 (m, 1H), 2.76–2.47 (m, 4H), 2.20–1.93 (m, 2H), 1.74–1.50 (m, 2H). 1.39–1.24 (m, 2H), 0.90 (t, 3H, J = 7.5 Hz). ^{13}C NMR: 193.9, 157.2, 154.7, 150.0, 148.8, 146.7, 145.8, 126.9, 123.7, 119.0, 117.6, 57.7, 52.4, 35.5, 31.5, 29.9, 20.6, 19.9, 13.7. MS (ESI): *m*/*z* 428.1 [M+H$^+$].

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