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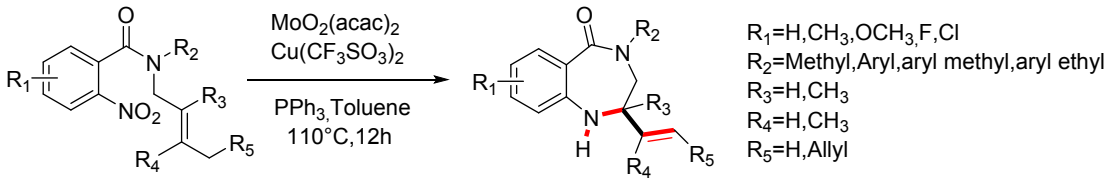
One-Pot Synthesis of Seven-membered Heterocyclic Derivatives of Diazepines Involving Copper-Catalyzed Rearrangement Cascade Allyl-Amination

Yuepeng Chen,[a] Xinglei Liu,[a] Wei Shi,[a] Shilong Zheng,[b] Guangdi Wang,[b] Ling He[a]*

[a] Key Laboratory of Drug-Targeting and Drug Delivery System of the Education Ministry and Sichuan Province, Sichuan Engineering Laboratory for Plant-Sourced Drug and Sichuan Research Center for Drug Precision Industrial Technology, West China School of Pharmacy, Sichuan University, Chengdu 610041, China.[b] RCMI Cancer Research Center and Department of Chemistry, Xavier University of Louisiana, New Orleans, LA 70125, USA

Yuepeng Chen: cyp610327@sina.com
Xinglei Liu: xinleiliu-CHN@outlook.com
Wei Shi: 1098465897@qq.com
Shilong Zheng: szheng@xula.edu
Guangdi Wang: gwang@xula.edu
Ling He: heling2012@scu.edu.cn



- One-pot synthesis of 1,4-benzodiazepine-5-one derivatives
- Strategy via nitrene formation, C-H insertion, C-N formation and C=C rearrangement
- 27 samples, moderate to high yields (up to 90%)

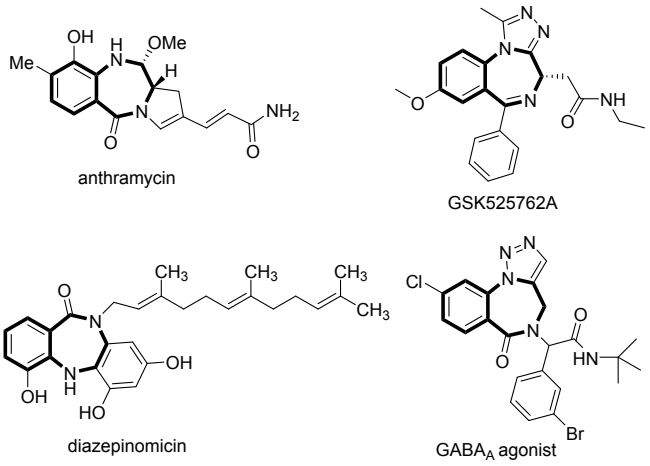
ABSTRACT: A novel and efficient method has been proposed for the synthesis of 1,4-benzodiazepine-5-ones from *o*-nitrobenzoic *N*-allylamides by using molybdenyl acetylacetonate and copper(II) trifluoromethanesulfonate as catalysts, in the presence of triphenylphosphine. This synthesis process involves nitrene formation, C-H bond insertion, C=C bond rearrangement and C-N bond formation cascade reactions via copper and molybdenum-catalyzed mediation. The method features a wide substrate scope and a moderate to high yield (up to 90%), exhibiting the possibility for practical applications.

INTRODUCTION

The construction of 1,4-benzodiazepine-5-one derivatives has practical application value in the development of new drugs.[1] Compounds containing benzodiazepine nucleus are of great significance in the study of pharmacochemistry,[2] attracting the attention of many scientists.[3] In the past few decades, these compounds have explicitly exhibited fascinating biological activities, such as anti-HIV,[5] anti-bacteria,[6,7] anti-anxiety,[8,9] anti-thrombosis,[10] anti-oxidation,[11]

anti-hypertension,[12] and they are also used in the treatment of ischemic injury,[13] muscle relaxant,[14] and diabetes insipidus.[15] In recent years, more attractive molecules including broad-spectrum antitumor antibiotics (e.g. anthramycin[16,17] and diazepinomicin[18]), BRD4 inhibitors (e.g. GSK525762A[19]), and anticonvulsant agent (e.g. $GABA_A$ agonist[20]) have been discovered (**Figure 1**).

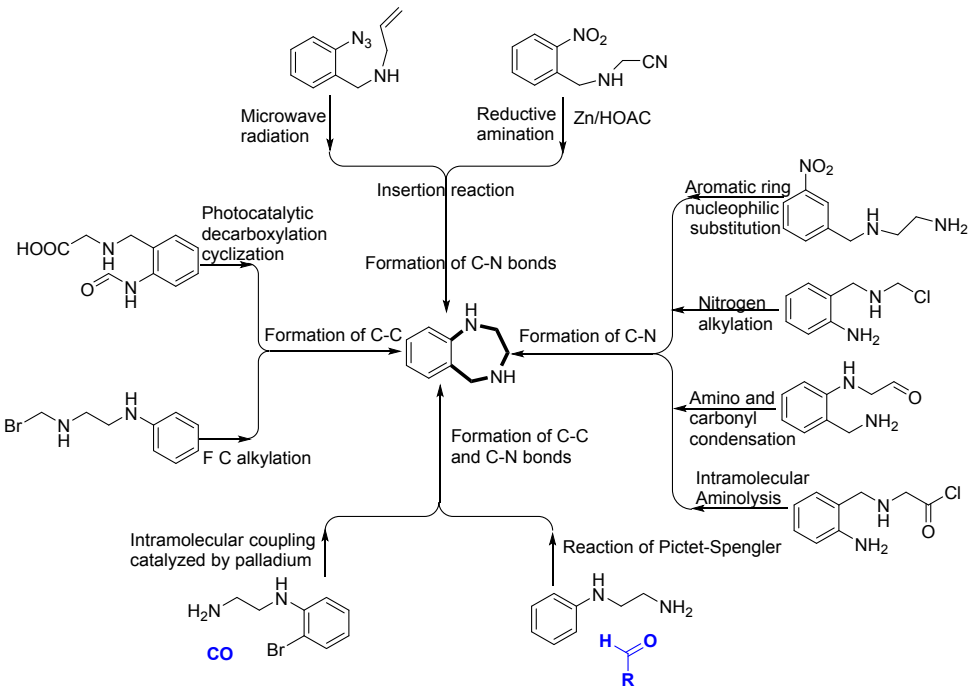
Figure 1. **Bioactive molecules containing benzodiazepine nucleus**



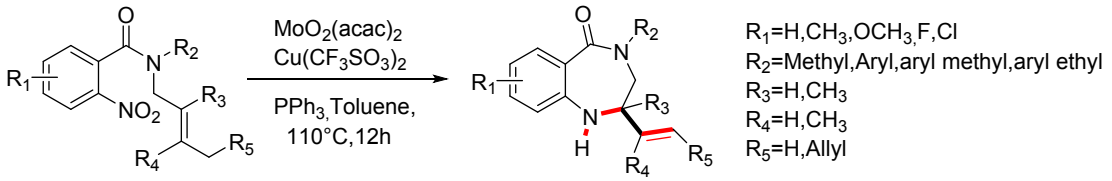
Over the past decades, some synthesis of benzodiazepine skeleton have been reported. (**Scheme 1, previous work**). The first method of constructing seven-membered heterocycles was through C-C bond formation by photocatalytic decarboxylation of the substrate, and intramolecular C-C coupling containing carbonyl groups.[21] The C-C bond was formed by the electrophilic substitution of benzene ring by Fischer alkylation or acylation, and the coupling reaction catalyzed by palladium was carried out under CO atmosphere. The second method was through C-N formation, such as the nucleophilic substitution reaction of amino p-benzene ring,[22] or the intramolecular S_N2 nucleophilic substitution reaction of amino group to halogenated alkyl group.[23] The C-N bond could also be constructed by the condensation reaction between amino group and carbonyl group,[24] such as Liu Carter-like-condensation reaction between amine group and carboxylic acid derivatives,[25] and Pictet-Spengler-like reaction[26] of phenylalkylamine derivatives and aldehydes.[24] For example, Broggini group achieved regioselective formation of seven-membered diazepinone rings by intramolecular Pd-catalyzed amination of N-allyl-anthranilamides and C-H activation method.[27]

Scheme 1 Synthesis of benzodiazepine derivatives

Previous work



This work



Wolfe group synthesized saturated 1,4-benzodiazepines via Pd-catalyzed carboamination reactions with constructing C-C and C-N bonds simultaneously.[28] Grunewald team prepared a series of benzodiazepinone derivatives which acted as selective inhibitors of EC 2.1.1.28 enzyme from 2,3-dihydroquinolin-4(1*H*)-one by means of azide insertion.[29] Vincenzo Santagada group developed microwave enhanced solution synthesis of 1,4-benzodiazepin-5-ones from aromatic primary amines or azides and olefins.[30] Doemling group developed diverse 1,4-benzodiazepine scaffolds by Ugi-four-component reactions.[31] As part of our interest in the synthesis of seven-membered heterocyclic derivatives of diazepines, we herein report the one-pot synthesis of 1,4-benzodiazepine-5-ones with wide substrate scope and moderate to high yields (**Scheme 1, this work**).

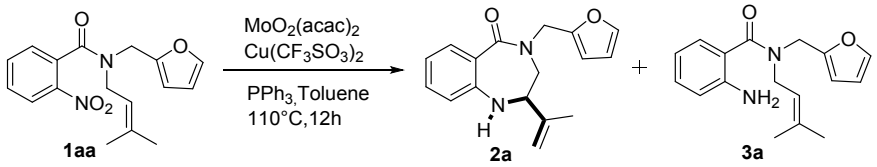
RESULTS AND DISCUSSION

Initially, we began to investigate the best reaction conditions by using N-(furan-2-ylmethyl)-N-(3-methylbut-2-en-1-yl)-2-nitrobenzamide **1aa**, PPh_3 and $MoO_2Cl_2(dmf)_2$ under the condition of toluene refluxing (**Table 1**). To our delight, the target compound 4-(furan-2-ylmethyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5*H*-benzo[e][1,4]diazepin-5-one **2a** could be obtained, but the yield was only 20%, and the majority of aniline derivative **3a** was produced as by-product (**entry 2**). Next, we screened a series of Mo catalysts and found that Mo acetylacetone may be the most effective catalyst (**entry 3**). At the same time, the Mo-group-metal catalysts, tungsten hexacarbonyl and chromium acetylacetone were examined, they could not initiate the

formation of target product (**entry 14-15**). Subsequently, we expanded the screening range of the catalysts including bis(2,4-pentanedionic acid) platinum(II), bis(triphenylphosphine) nickel chloride, iron acetate, $Pd(OAc)_2$, $CuCl_2$, $Ru_3(CO)_{12}$, $Rh(CO)_2(C_5H_7O_2)$ respectively, but could not deliver the target compound (**entry 7-13**). To increase the yield, we used two catalysts to promote the reactions. When $MoO_2Cl_2(dmf)_2$ and $CuCl_2$ were used together, the yield of the target product was increased to 45% (**entry 16**). Fortunately, when we combined $MoO_2(acac)_2$ with $Cu(CF_3SO_3)_2$, the yield of the target product was increased to 90% (**entry 1**), and only trace of the aniline derivative detected. With the optimal catalyst in hand, we investigated the solvent effect on this reaction and different solvents including dichloromethane, tetrahydrofuran, acetone, acetonitrile, N,N-dimethylformamide, dimethyl sulfoxide have been compared with refluxing in the presence of $MoO_2(acac)_2$, $Cu(CF_3SO_3)_2$ and PPh_3. The experimental results showed that the reaction didn't occur in them (**entry 18-22**). Therefore, we decided to use $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$ as catalysts, anhydrous toluene as solvent in the atmosphere of N_2 at 110 °C, then we screened reductants, the yield of target product was 90% by using PPh_3 (**entry 1**). Regretfully, its yields were only 43% and 51% when using S-(-)-BINAP and xantphos, respectively (**entry 24,25**). The reaction did not occur by applying trimethylphosphine or no reductant (**entry 23,26**). In addition the reaction temperature and time were also investigated, using $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$ as catalysts, anhydrous toluene as solvent and PPh_3 as reductant under N_2 atmosphere. When reaction temperature varied from 30 °C to 60 °C, no desired product appeared (**entry 27-28**). The desired compound was produced when the temperature reached 80 °C (**entry 29**), the yield of the product was over 85% when temperature raised to 110 °C or 140 °C (**entry 29-30**). Furthermore, we found that prolonging reaction time could increase the yields, but the yield was almost same when the other reaction conditions unchanged from 12 h to 16 h (**entry 31-33**). Finally, the reaction was completed well at 110 °C for 12 h using substrate **1aa** (0.16 mmol), $MoO_2(acac)_2$ (10mol%), $Cu(CF_3SO_3)_2$ (10mol%), PPh_3 (2.5 equiv), toluene (2 mL) respectively.

Based on the optimized conditions, the scope and generality of a series of 1,4-benzodiazepine-5-one derivatives were then evaluated. As shown in **Table 2**, the reaction could proceed well to afford corresponding products in moderate to high yields. The structure was further ambiguously confirmed by single crystal X-ray synthesis of compound **2z** (**Figure 2**).

Table 1. Screening Optimal Conditions [a]



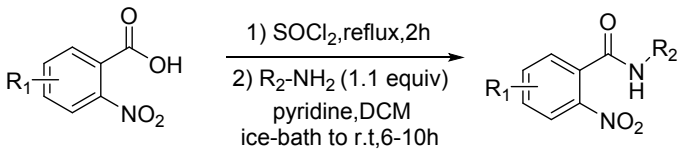
Entry	Variation from the standard conditions	**2a** Yield [b]	**3a** Yield [b]
1	none	90%	-
2	$MoO_2Cl_2(dmf)_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	20%	35%
3	$MoO_2(acac)_2$ without $Cu(CF_3SO_3)_2$	52%	20%
4	$Mo(CO)_6$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	40%	trace
5	$CoMoO_4$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	11%	trace
6	$Pt(acac)_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	trace	-
7	$Ni(PPh_3)_2Cl_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.[c]	-

8	$Fe(OAc)_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
9	$Pd(OAc)_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
10	$CuCl_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
11	$Cu(CF_3SO_3)_2$ without $MoO_2(acac)_2$	N.R.	-
12	$Ru_3(CO)_{12}$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
13	$Rh(CO)_2(C_5H_7O_2)$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
14	$W(CO)_6$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
15	$Cr(acac)_3$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	N.R.	-
16	$MoO_2Cl_2(dmf)_2$, $CuCl_2$ instead of $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$	45%	-
17	$MoO_2Cl_2(dmf)_2$ instead of $MoO_2(acac)_2$	66%	10%
18	CH_2Cl_2 instead of toluene	N.R.	-
19	THF instead of toluene	N.R.	-
20	CH_3CN instead of toluene	N.R.	-
21	DMF instead of toluene	N.R.	-
22	DMSO instead of toluene	N.R.	-
23	$(CH_3)_3P$ instead of PPh_3	N.R.	-
24	S-(-)-BINAP instead of PPh_3	43%	-
25	Xantphos instead of PPh_3	51%	-
26	no PPh_3	N.R.	-
27	30 °C instead of 110 °C	N.R.	-
28	60 °C instead of 110 °C	N.R.	-
29	80 °C instead of 110 °C	5%	-
30	140 °C (xylene)instead of 110 °C	87%	-
31	4 h instead of 12 h	53%	-
32	8 h instead of 12 h	80%	-
33	16 h instead of 12 h	90%	-

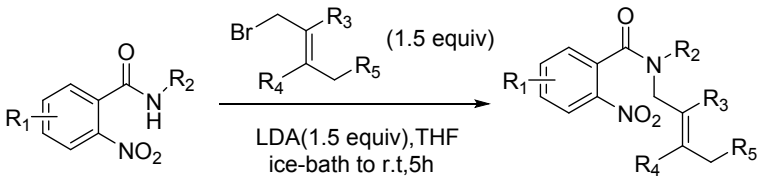
[a]Reaction conditions: **1aa** (0.16 mmol), $MoO_2(acac)_2$ (10mol%), $Cu(CF_3SO_3)_2$ (10mol%), PPh_3 (2.5 equiv), toluene (2 mL) under N_2 at 110 °C for 12 h. [b]Isolated yield. [c]No reaction

Table 2. The formation of diazepines derivatives from the aromatic nitro derivatives [a]

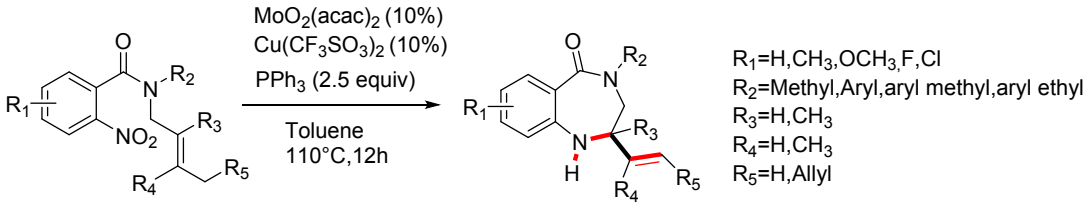
Procedure A:

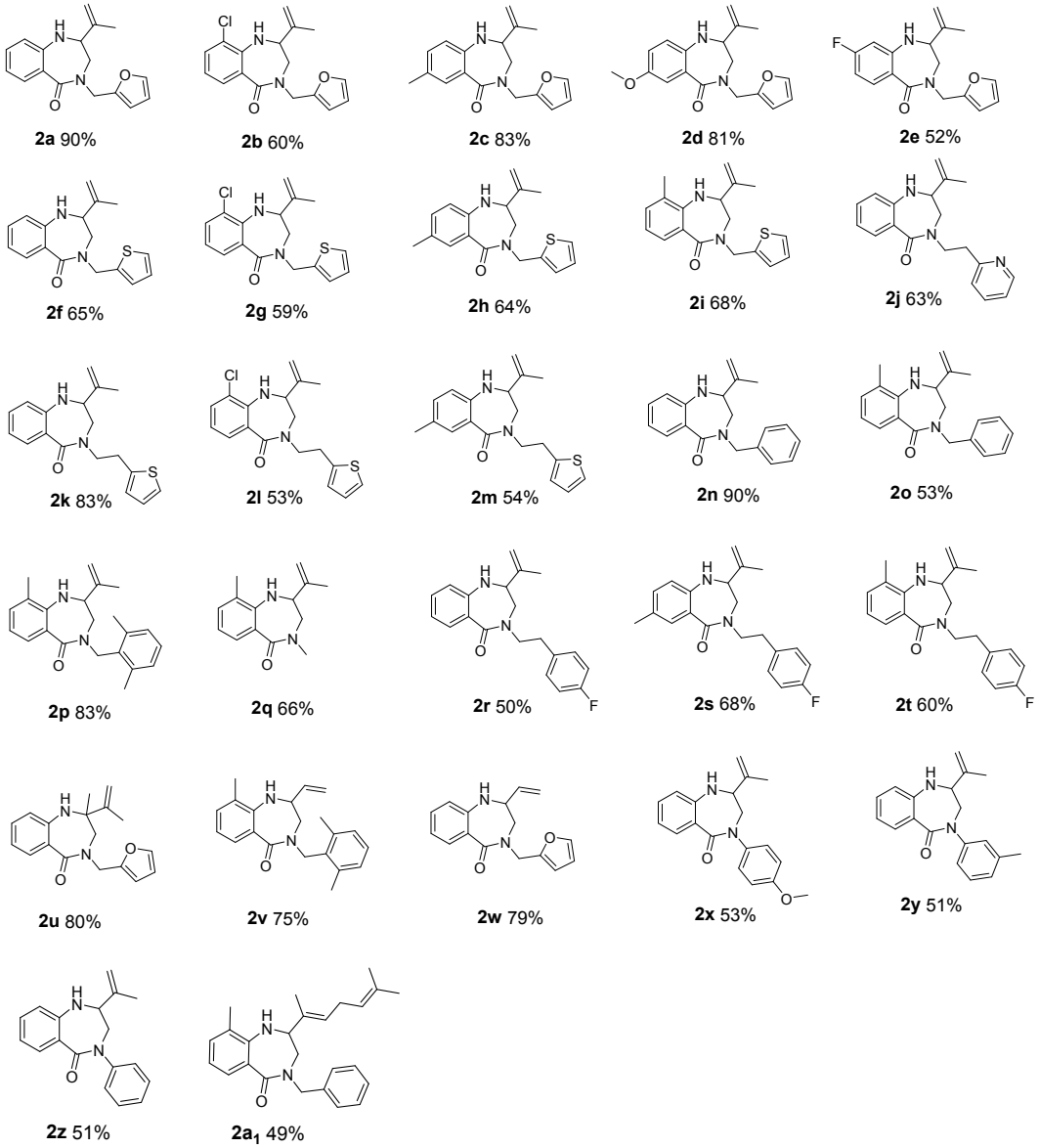


Procedure B:



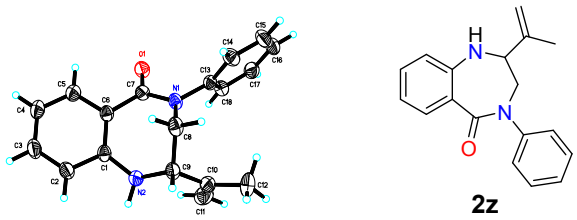
Procedure C:





[a] Reaction conditions: substrate (1 equiv)/ $MoO_2(acac)_2$ (10%)/ $Cu(CF_3SO_3)_2$ (10%)/ PPh_3 (2.5 equiv)/ toluene under N_2 at 110 °C for 12 h.

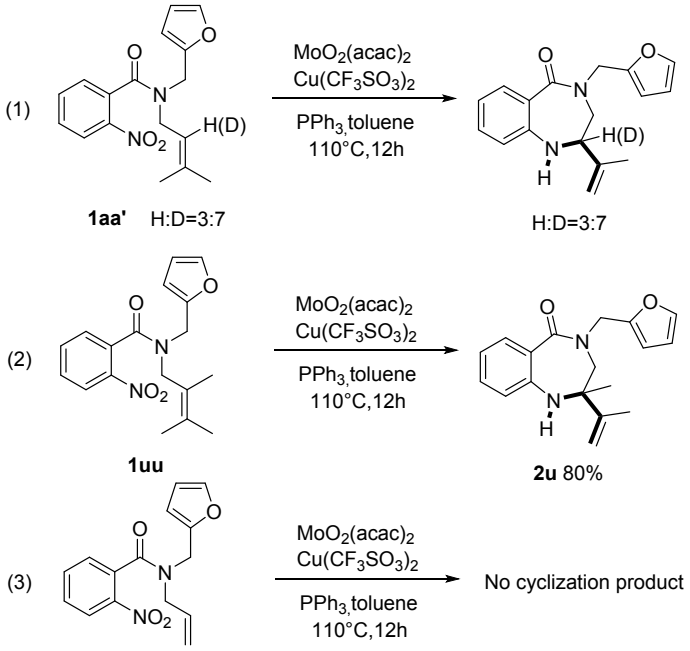
Figure 2. X-ray crystal structure of compound 2z



Ellipsoids are shown at the 50% probability level for the ORTEP diagram of the structure.

To comprehend the reaction well, we performed a series of experiments to observe the special effects of different substrates on the synthesis (**Scheme 2**). The effect of C-H activation with rearrangement of the double bond on the reaction was first investigated. Under standard reaction condition, the ratio of hydrogen to deuterium between the corresponding product obtained by the reaction and the starting material of the reaction remained unchanged (**Scheme 2, reaction 1**). Meanwhile, in the presence of methyl on the side chain alkene, the reaction could still obtain a yield of 80% (**reaction 2**). The results showed that the carbon-hydro activation of alkene hydrogen was not necessary. It could also suggest that the double bond migration occurred prior to the C-N bond formation. To confirm this point, reaction 3 was tested (**Scheme 2, reaction 3**). The reaction could not occur and the corresponding cyclization products could not be detected.

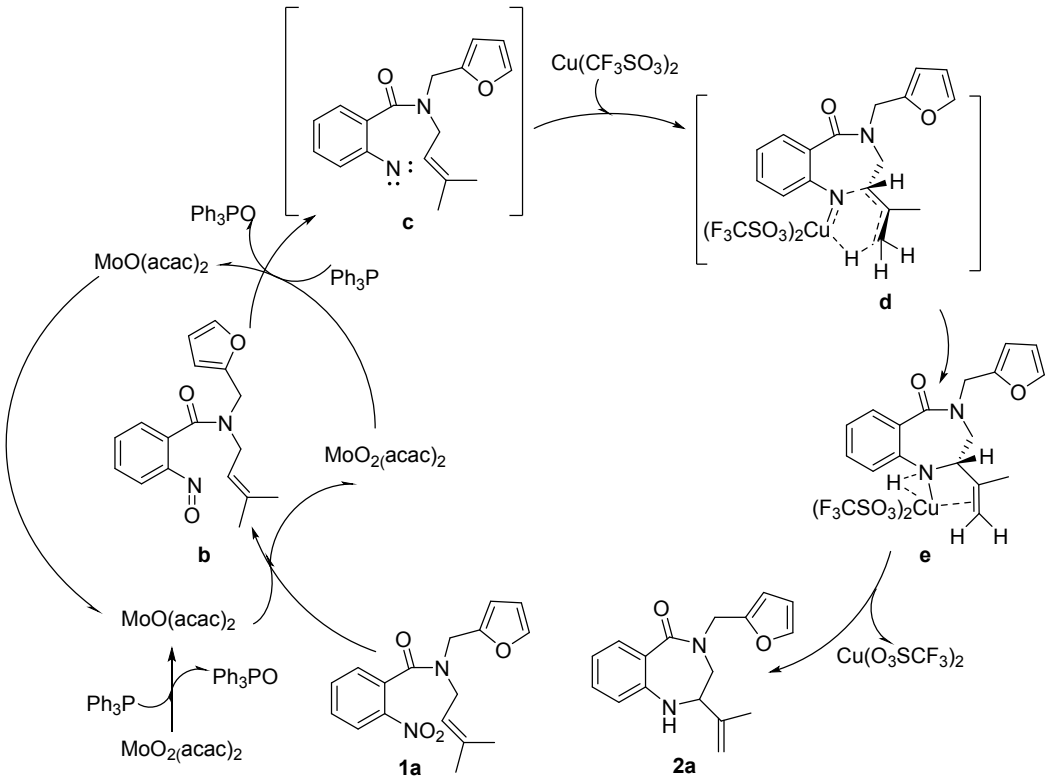
Scheme 2 Exploration of reaction mechanism



On the basis of our experimental results and the previous mechanism investigations, it is speculated that $MoO_2(acac)_2$ is necessary for the reaction, $Cu(CF_3SO_3)_2$ can significantly increase the yield of the reaction. Therefore, a plausible mechanism is suggested that starting from substrate **1a,** $MoO_2(acac)_2$ interacts with PPh_3 to reduce nitro group of the substrate **1a** to the nitrene intermediate **c**, and with the participation of $Cu(CF_3SO_3)_2$ to form N-Cu bond. Next, with double bond carbon and allyl hydrogen to form a cyclohexanic intermediate **d.** Then the allyl

hydrogen was removed, the double bond was rearranged at the same time and to form N-H bond and to give the intermediate **e.** Finally get the target compound **2a** and release catalyst $Cu(CF_3SO_3)_2$. In short, we postulated the mechanism as shown in **Scheme 3**. The novel diazepines synthesis possibly occurred via reduction of nitro group, followed by the removal of allyl-hydrogen in the presence of divalent copper Cu (II), rearrangement of double bond.

Scheme 3 Postulated mechanism



CONCLUSIONS

In summary, we have successfully developed an efficient one-pot strategy for the construction of 1,4-benzodiazepine-5-ones from the derivatives of *N*-(3-methylbut-2-en-1-yl)-2- nitrobenzamide by using $MoO_2(acac)_2$ and $Cu(CF_3SO_3)_2$ as co-catalyst. The tandem annulation procedure involves the reduction of nitro group, the formation of nitrene, C − H activation and the formation of cyclohexanic intermediate, and followed by the removal of allyl-hydrogen in the presence of divalent copper Cu (II), rearrangement of the double bond, a subsequent intramolecular cyclization process. This catalytic system exhibits good functional group tolerance. We have preliminarily explored the antineoplastic activity of these compounds, which could be important intermediates in the synthesis of some biologically active seven-membered nitrogen heterocycles compounds, and further research is underway. We expect that this approach could be widely used in the formation of various heterocyclic frameworks in our future research.

EXPERIMENTAL SECTION

General Methods. NMR experiments were accomplished on a 400 MHz or 600 MHz

spectrometer. Column chromatography was performed on silica gel H. ESI mass spectra analyses were completed on a Thermo Fisher Scientific LTQ FT Ultra mass spectrometer. *o*-Nitrobenzoic acid including its substituted derivatives and all solvents were obtained from commercial sources and were used as received or after drying and re-distillation. All *o*-nitrobenzoic *N*-allylamides were prepared according to the literature. Chromatographic separation was performed on a silica gel H column using petroleum ether (PE)/ethyl acetate (EA) as a mobile phase. All reactions were carried out under a nitrogen atmosphere.

General procedure A: Preparation of *N*-(furan-2-ylmethyl)-2-nitrobenzamide[32] (**1a**). The preparation strategies of the other derivatives were consistent with its preparation strategy. *o*-Nitrobenzoic acid (500 mg, 2.99 mmol) was placed in a 250 mL clean anhydrous round-bottom flask under nitrogen atmosphere. Sulfoxide dichloride (4 mL) was added into the flask, and the mixture was stirred at 80 °C for 2 hours. After completing the reaction, the redundant sulfoxide dichloride was removed under reduced pressure to obtain *o*-nitrobenzoyl chloride. Furamethylamine (0.32 mL, 3.3 mmol) was placed in another 250 mL dried round-bottom flask with stirring under anhydrous condition and nitrogen atmosphere. Anhydrous CH_2Cl_2 (20 mL) and pyridine (3 mL) were injected into the flask by a syringe. Then the prepared *o*-nitrobenzoyl chloride was added under the ice bath. After completing the above operation, the flask was placed at room temperature with stirring for 10 hours. TLC plate monitored the end of the reaction, quenched by adding saturated sodium bicarbonate solution (50 mL) and extracted by using ethyl acetate (30 mL × 2), washed with saturated sodium chloride solution (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification was done by column chromatography on silica gel H with petroleum ether/ethyl acetate (3:1) as eluent to give the pure white solid (664 mg).

N-(Furan-2-ylmethyl)-2-nitrobenzamide (1a, 1u, 1w). Prepared from *o*-nitrobenzoic acid (500 mg, 2.99 mmol) with furfurylamine (0.32 mL, 3.3 mmol) purifued following general procedure A; afforded 664 mg (90% yield) of the title compound as a off-white solid: R_f = 0.32 (2:1 PE/EA), mp 108-109 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.67 (td, *J* = 7.5, 1.3 Hz, 1H), 7.58 (td, *J* = 8.0, 1.6 Hz, 1H), 7.52 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.38 (t, *J* = 1.2 Hz, 1H), 6.35 (d, *J* = 1.2 Hz, 2H), 6.21 (s, 1H), 4.65 (d, *J* = 5.5 Hz, 2H); Literature data[33]: White solid; mp 108–110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.56 (2H, d, *J* = 5.7 Hz), 6.29 (1H, dd, *J* = 3.3 Hz, *J* = 0.9 Hz), 6.32 (1H, dd, *J* = 1.8 Hz, *J* = 3.3 Hz), 6.42 (1H, m, *J* = 5.7 Hz), 7.34 (1H, dd, *J* = 1.8 Hz, *J* = 0.9 Hz), 7.44-7.47 (1H, m), 7.50-7.56 (1H, m), 7.59-7.65 (1H, m), 7.98-8.01 (1H, m); ^{13}C { ^{1}H } NMR (75 MHz, $CDCl_3$) δ 37.1, 107.9, 110.5, 124.5, 128.7, 130.5, 132.4, 133.7, 142.3, 146.1, 150.3, 166.2.

3-Chloro-N-(furan-2-ylmethyl)-2-nitrobenzamide (1b). Prepared from 3-chloro-2-nitrobenzoic acid (500 mg, 2.49 mmol) with furfurylamine (0.27 mL, 2.81 mmol) purifued following general procedure A; afforded 610 mg (87% yield) of the title compound as a white solid: R_f = 0.5 (2:1 PE/EA), mp 121-122 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.9 Hz, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.37 (s, 1H), 6.44 (s, 1H), 6.34 (d, *J* = 2.9 Hz, 1H), 6.30 (d, *J* = 2.9 Hz, 1H), 4.56 (d, *J* = 5.4 Hz, 2H).

N-(Furan-2-ylmethyl)-5-methyl-2-nitrobenzamide (1c). Prepared from 5-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with furfurylamine (0.3 mL, 3.12 mmol) purifued following general procedure A; afforded 665 mg (93% yield) of the title compound as a off-white solid: R_f = 0.3 (2:1 PE/EA); mp 135-137 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.38 (s, 1H),

7.34 (d, J = 8.3 Hz, 1H), 7.29 (s, 1H), 6.35 (s, 2H), 6.18 (s, 1H), 4.63 (d, J = 5.4 Hz, 2H), 2.44 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-d) δ 166.6, 150.4, 145.4, 143.9, 142.4, 132.7, 130.9, 129.3, 124.7, 110.6, 108.0, 37.2, 21.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{13}O_4N_2$, 261.0870; found, 261.0868.

N-(Furan-2-ylmethyl)-5-methoxy-2-nitrobenzamide (1d). Prepared from 5-methoxy-2-nitrobenzoic acid (500 mg, 2.54 mmol) with furfurylamine (0.28 mL, 2.87 mmol) purifued following general procedure A; afforded 668 mg (95% yield) of the title compound as a brown solid: R_f = 0.4 (2:1 PE/EA), mp 131-133 ^{o}C; ^{1}H NMR (600 MHz, Chloroform-d) δ 8.11 (d, J = 9.1 Hz, 1H), 7.37 (s, 1H), 6.97 (dd, J = 9.1, 1.8 Hz, 1H), 6.93 (d, J = 1.8 Hz, 1H), 6.35 (s, 2H), 6.15 (s, 1H), 4.64 (d, J = 5.4 Hz, 2H), 3.90 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-d) δ 166.4, 163.7, 150.3, 142.3, 138.7, 135.1, 127.1, 115.0, 113.9, 110.6, 108.0, 56.2, 37.2.

4-Fluoro-N-(furan-2-ylmethyl)-2-nitrobenzamide (1e). Prepared from 4-fluoro-2-nitrobenzoic acid (500 mg, 2.70 mmol) with furfurylamine (0.38 mL, 3.05 mmol) purifued following general procedure A; afforded 509 mg (71% yield) of the title compound as a white solid: R_f = 0.38 (2:1 PE/EA), mp 115-117 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.20 (t, J = 5.7 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 5.7 Hz, 2H), 7.61 (s, 1H), 6.43 (s, 1H), 6.34 (s, 1H), 4.43 (d, J = 5.5 Hz, 2H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 164.8, 162.1 (d, J = 249.0 Hz), 151.9, 148.7 (d, J = 9.0 Hz), 142.7, 131.7 (d, J = 9.0 Hz), 128.8 (d, J = 3.0 Hz), 120.8 (d, J = 22.5 Hz), 112.5 (d, J = 27.0 Hz), 111.0, 107.5, 36.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{10}O_4N_2F$, 265.0619 ; found, 265.0626.

2-*Nitro-N-(thiophen-2-ylmethyl)benzamide (1f).* Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with thiophen-2-ylmethanamine (0.4 mL, 3.4 mmol) purifued following general procedure A; afforded 670 mg (86% yield) of the title compound as a off-white solid: R_f = 0.3 (2:1 PE/EA), mp 117-119 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.05 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.3 Hz, 1H), 7.52 (d, J = 7.4 Hz, 1H), 7.25 (d, J = 4.3 Hz, 1H), 7.07 (d, J = 3.0 Hz, 1H), 6.98 (dd, J = 4.8, 3.6 Hz, 1H), 6.24 (s, 1H), 4.81 (d, J = 5.6 Hz, 2H).

3-Chloro-2-nitro-N-(thiophen-2-ylmethyl)benzamide (1g). Prepared from 3-chloro-2-nitrobenzoic acid (500 mg, 2.49 mmol) with thiophen-2-ylmethanamine (0.33 mL, 2.81 mmol) purifued following general procedure A; afforded 672 mg (91% yield) of the title compound as a off-white solid: R_f = 0.28 (2:1 PE/EA), mp 164-165 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.59 (dd, J = 7.7, 1.0 Hz, 1H), 7.44-7.51 (m, 2H), 7.25 (d, J = 1.7 Hz, 1H), 7.02 (d, J = 1.7 Hz, 1H), 6.96 (t, J = 4.2 Hz, 1H), 6.38 (s, 1H), 4.73 (d, J = 5.6 Hz, 2H).

5-Methyl-2-nitro-N-(thiophen-2-ylmethyl)benzamide (1h). Prepared from 5-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with thiophen-2-ylmethanamine (0.37 mL, 3.12 mmol) purifued following general procedure A; afforded 668 mg (88% yield) of the title compound as a brown solid: R_f = 0.32 (2:1 PE/EA), mp 138-139 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.96 (d, J = 8.4 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.27 (d, J =1.1 Hz, 1H), 7.25 (dd, J = 5.1, 1.2 Hz, 1H), 7.06 (d, J = 2.9 Hz, 1H), 6.97 (dd, J = 5.1, 3.5 Hz, 1H), 6.23 (s, 1H), 4.79 (d, J = 5.6 Hz, 2H), 2.44 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-d) δ 166.4, 145.4, 143.8, 139.8, 132.6, 130.8, 129.2, 127.0, 126.5, 125.5, 124.6, 38.8, 21.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{13}O_3N_2S$, 277.0641; found, 277.0639.

3-Methyl-2-nitro-N-(thiophen-2-ylmethyl)benzamide (1i). Prepared from 3-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with thiophen-2-ylmethanamine (0.37 mL, 3.12 mmol) purifued following general procedure A; afforded 679 mg (89% yield) of the title compound as a

white solid: R_f = 0.3 (2:1 PE/EA), mp 135-136 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (s, 3H), 7.24 (d, *J* = 4.7 Hz, 1H), 7.03 (d, *J* = 3.0 Hz, 1H), 6.96 (dd, *J* = 4.7, 3.6 Hz, 1H), 6.41 (s, 1H), 4.73 (d, *J* = 5.6 Hz, 2H), 2.37 (s, 3H).

2-Nitro-N-(2-(pyridin-2-yl)ethyl)benzamide (1j). Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with 2-(pyridin-2-yl)ethan-1-amine (0.42 mL, 3.4 mmol) purifued following general procedure A; afforded 720 mg (89% yield) of the title compound as a yellow solid: R_f = 0.56 (EA), mp 102-103 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 (dd, *J* = 4.5, 0.4 Hz, 1H), 8.00 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.64 (td, *J* = 7.6, 1.6 Hz, 2H), 7.54 (td, *J* = 8.0, 1.4 Hz, 1H), 7.49 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.27-7.24 (m, 1H), 7.22 (s, 1H), 7.17-7.12 (m, 1H), 3.87 (q, *J* = 6.0 Hz, 2H), 3.12 (t, *J* = 6.2 Hz, 2H).

2-Nitro-N-(2-(thiophen-2-yl)ethyl)benzamide (1k). Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with 2-(thiophen-2-yl)ethan-1-amine (0.44 mL, 3.4 mmol) purifued following general procedure A; afforded 740 mg (90% yield) of the title compound as a yellow waxy solid: R_f = 0.3 (2:1 PE/EA); mp 88-90 °C; ^{1}H NMR (600 MHz, Chloroform-d) δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 4.8 Hz, 1H), 6.94 (d, *J* = 4.5 Hz, 1H), 6.91 (s, 1H), 5.99 (s, 1H), 3.74 (q, *J* = 6.2 Hz, 2H), 3.19 (t, *J* = 6.4 Hz, 2H).

2-Chloro-2-nitro-N-(2-(thiophen-2-yl)ethyl)benzamide (1l). Prepared from 3-chloro-2-nitrobenzoic acid (500 mg, 2.49 mmol) with 2-(thiophen-2-yl)ethan-1-amine (0.36 mL, 2.81 mmol) purifued following general procedure A; afforded 698 mg (90% yield) of the title compound as a yellow solid: R_f = 0.3 (2:1 PE/EA), mp 134-136 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.8 Hz, 1H), 7.48-7.43 (m, 2H), 7.18 (d, *J* = 5.0 Hz, 1H), 6.97 (t, *J* = 4.1 Hz, 1H), 6.89 (d, *J* = 2.4 Hz, 1H), 6.18 (s, 1H), 3.67 (q, *J* = 6.3 Hz, 2H), 3.13 (t, *J* = 6.5 Hz, 2H).

5-Methyl-2-nitro-N-(2-(thiophen-2-yl)ethyl)benzamide (1m). Prepared from 5-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with 2-(thiophen-2-yl)ethan-1-amine (0.4 mL, 3.12 mmol) purifued following general procedure A; afforded 705 mg (88% yield) of the title compound as a off-white solid: R_f = 0.33 (2:1 PE/EA); mp 100-102 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 8.3 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.22 (s, 1H), 7.16 (d, *J* = 4.8 Hz, 1H), 6.95 (t, *J* = 4.8 Hz, 1H), 6.91 (s, 1H), 5.99 (s, 1H), 3.73 (q, *J* = 6.4 Hz, 2H), 3.18 (t, *J* = 6.4 Hz, 2H), 2.43 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-*d*) δ 166.9, 145.3, 143.8, 141.0, 132.9, 130.7, 129.1, 127.1, 125.6, 124.6, 123.9, 41.3, 29.5, 21.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{15}O_3N_2S$, 291.0798; found, 291.0794.

N-Benzyl-2-nitrobenzamide (1n). Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with phenylmethanamine (0.37 mL, 3.4 mmol) purifued following general procedure A; afforded 637 mg (83% yield) of the title compound as a off-white solid: R_f = 0.38 (2:1 PE/EA), mp 123-124 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.1 Hz, 1H), 7.65 (td, *J* = 7.8, 0.4 Hz, 1H), 7.56 (td, *J* = 7.5,0.7 Hz, 1H), 7.51 (dd, *J* = 7.5, 0.6 Hz,1H), 7.39–7.34 (m, 4H), 7.31-7.29 (m, 1H), 6.20 (s, 1H), 4.62 (d, *J* = 5.6 Hz, 2H). Literature data[34]: Light brown solid; mp 121-122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.21 (t, *J* = 5.7 Hz, 1H), 8.04 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.80 (td, *J* = 7.4, 1.1 Hz, 1H), 7.72-7.64 (m, 2H), 7.36 (m, 4H), 7.27 (m, 1H), 4.46 (d, *J* = 6.0 Hz, 2H).

N-Benzyl-3-methyl-2-nitrobenzamide (1o, 1a$_1$). Prepared from 3-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with phenylmethanamine (0.34 mL, 3.12 mmol) purifued following general procedure A; afforded 680 mg (91% yield) of the title compound as a off-white solid: R_f = 0.3 (3:1 PE/EA), mp 137-138 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42–7.27 (m, 8H), 6.31 (s, 1H), 4.57 (d, *J* = 5.7 Hz, 2H), 2.38 (s, 3H).

N-(2,6-Dimethylbenzyl)-3-methyl-2-nitrobenzamide (1p,1v). Prepared from 3-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with (2,6-dimethylphenyl)methanamine (0.43 mL, 3.12 mmol) purifued following general procedure A; afforded 734 mg (89% yield) of the title compound as a white solid: R_f = 0.3 (3:1 PE/EA), mp 153-154 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40–7.33 (m, 3H), 7.16-7.12 (m, 1H), 7.07 (d, *J* = 7.4 Hz, 2H), 5.78 (s, 1H), 4.62 (d, *J* = 4.6 Hz, 2H), 2.41 (s, 6H), 2.37 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-*d*) δ 165.1, 149.2, 137.7, 133.5, 133.1, 131.0, 130.4, 129.9, 128.4, 128.0, 125.8, 38.8, 19.6, 17.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{19}O_3N_2$, 299.1390; found, 299.1394.

N,3-Dimethyl-2-nitrobenzamide (1q). Prepared from 3-methyl-2-nitrobenzoic acid (542 mg, 2.99 mmol) with iodomethane (0.49 mL, 3.4 mmol) purifued following general procedure A; afforded 478 mg (82% yield) of the title compound as a yellow solid: R_f = 0.12 (3:1 PE/EA), mp 133-135 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43-7.36 (m, 3H), 6.18 (s, 1H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.36 (s, 3H).

N-(4-Fluorophenethyl)-2-nitrobenzamide (1r). Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with 2-(4-fluorophenyl)ethan-1-amine (0.48 mL, 3.4 mmol) purifued following general procedure A; afforded 795 mg (92% yield) of the title compound as a off-white solid: R_f = 0.33 (2:1 PE/EA), mp 103-104 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.64 (td, *J* = 7.5, 1.2 Hz, 1H), 7.55 (td, *J* = 8.0, 1.5 Hz, 1H), 7.41 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.24–7.20 (m, 2H), 7.02–6.97 (m, 2H), 5.88 (s, 1H), 3.70 (q, *J* = 6.9 Hz, 2H), 2.94 (t, *J* = 6.9 Hz, 2H).

N-(4-Fluorophenethyl)-5-methyl-2-nitrobenzamide (1s). Prepared from 5-methyl-2-nitrobenzoic acid (500 mg, 2.76 mmol) with 2-(4-fluorophenyl)ethan-1-amine (0.44 mL, 3.12 mmol) purifued following general procedure A; afforded 778 mg (93% yield) of the title compound as a brown solid: R_f = 0.35 (3:1 PE/EA), mp 125-127 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.69 (t, *J* = 4.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.34–7.26 (m, 3H), 7.13 (t, *J* = 8.8 Hz, 2H), 3.43 (q, *J* = 6.8 Hz, 2H), 2.82 (t, *J* = 7.2 Hz, 2H), 2.41 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 166.0, 161.3 (d, *J* = 241.5 Hz), 144.9, 135.8 (d, *J* = 3 Hz), 133.3, 131.0, 130.9 (d, *J* = 7.5 Hz), 130.3, 129.7, 124.5, 115.4 (d, *J* = 21.0 Hz), 41.0, 34.2, 21.1.

N-(4-Fluorophenethyl)-3-methyl-2-nitrobenzamide (1t). Prepared from 3-methyl-2-nitrobenzoic acid (542 mg, 2.99 mmol) with 2-(4-fluorophenyl)ethan-1-amine (0.48 mL, 3.4 mmol) purifued following general procedure A; afforded 802 mg (89% yield) of the title compound as a off-white solid: R_f = 0.35 (3:1 PE/EA), mp 105-106 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (t, *J* = 5.3 Hz, 1H), 7.56 (d, *J* = 5.2 Hz, 2H), 7.48–7.41 (m, 1H), 7.28 (dd, *J* = 8.3, 5.8 Hz, 2H), 7.12 (t, *J* = 8.8 Hz, 2H), 3.41 (q, *J* = 6.9 Hz, 2H), 2.80 (t, *J* = 7.1 Hz, 2H), 2.29 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 164.6, 161.1 (d, *J* = 240.1 Hz), 149.2, 135.6 (d, *J* = 2.1 Hz), 133.7, 130.7 (d, *J* = 4.2Hz), 130.6, 130.4, 129.9, 126.3, 115.2 (d, *J* = 20.9 Hz), 40.9, 34.0, 17.0.

N-(4-Methoxyphenyl)-2-nitrobenzamide (1x). Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with 4-methoxyaniline (0.42 mL, 3.4 mmol) purifued following general procedure A; Afforded 787 mg (97% yield) of the title compound as a off-white solid: R_f = 0.46 (2:1 PE/EA), mp 169-170 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.54 (s, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.86 (t, *J* = 7.5 Hz, 1H), 7.78–7.72 (m, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 3.75 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 163.8, 155.9, 146.8, 134.2, 133.0, 132.2, 131.1, 129.5, 124.4, 121.4, 114.1, 55.4. Literature data[35]: yellow needles; mp 168-169 °C.

2-Nitro-N-(m-tolyl)benzamide (1y). Prepared from 2-nitrobenzoic acid (500 mg, 2.99 mmol) with m-toluidine (0.37 mL, 3.4 mmol) purifued following general procedure A; afforded 652 mg (85%

yield) of the title compound as a brown solid: R_f = 0.16 (3:1 PE/EA); mp 141-143 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.1 Hz, 1H), 7.72-7.58 (m, 3H), 7.44 (s, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 6.99 (m, 1H), 6.63–6.50 (m, 1H), 2.35 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 164.5, 139.0, 137.2, 133.8, 132.8, 130.5, 128.8, 128.5, 125.9, 124.5, 121.1, 119.7, 117.5, 21.4. Literature data[36]: mp 145-147 °C.

2-Nitro-N-phenylbenzamide (1z). Prepared from 2-nitrobenzoic acid (200 mg, 1.2 mmol) with aniline (0.13 mL, 1.35 mmol) purifued following general procedure A; afforded 236 mg (81% yield) of the title compound as a brown solid: R_f = 0.52 (1:1 PE/EA), mp 154-156 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.73–7.56 (m, 6H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H).

General procedure B: Synthesis of *N*-(furan-2-ylmethyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide[18] (**1aa**). N-(furan-2-ylmethyl)-2-nitrobenzamide (246 mg, 1 mmol) (**1a**) was placed in a 100 mL clean anhydrous round-bottom flask under nitrogen atmosphere, anhydrous THF (15 mL) was injected by a 20 mL syringe. Then the flask was placed in an ice bath, and LDA (ca. 2.0 M, 0.75 mL, 1.5 mmol) was added with stirring for 15 minutes. 3,3-dimethylallyl bromide (220 mg, 1.5 mmol) was slowly dripped into the flask by a 1 mL syringe. After 3 hours, the reaction was monitored by TLC plate, quenched by adding saturated ammonium chloride solution (40 mL), extracted with ethyl acetate(25 mL × 2), washed with saturated sodium chloride solution (20 mL × 2), dried over Na_2SO_4 and concentrated under reduced pressure. Purification was done by column chromatography on silica gel H with petroleum ether/ethyl acetate (4:1) as eluent to give the light yellow oily liquid (266.9 mg). The synthesis process of these compounds was the same method, the polarity of the products is also similar, all belonging to oily substances. Compound **1pp** and **1zz** were identified by ^{1}H/^{13}C NMR and HMRS. The reaction solutions of the rest of the compounds were separated by rapid chromatographic column and went directly into the general procedure C.

N-(2,6-Dimethylbenzyl)-3-methyl-N-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (1pp). Prepared from N-(2,6-dimethylbenzyl)-3-methyl-2-nitrobenzamide (150 mg, 0.503 mmol) (**1p**) and purifued following general procedure B; afforded 116 mg (63% yield) of the title compound as a yellow oil: R_f = 0.4 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45–7.37 (m, 1H), 7.33 (d, *J* = 7.5 Hz, 1H),7.22 (d, *J* = 7.4 Hz, 1H), 7.14–7.08 (m, 1H), 7.06–7.00 (m, 2H), 5.10 (t, *J* = 7.5 Hz, 1H), 4.89 (s, 2H), 3.56 (d, *J* = 6.0 Hz, 2H), 2.46 (s, 3H), 2.36 (s, 6H), 1.60 (s, 3H), 0.96 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 167.4, 148.0, 138.5, 135.8, 132.4, 132.3, 132.2, 131.8, 131.0, 128.5, 127.8, 125.3, 120.3, 45.3, 42.5, 25.7, 20.0, 19.0, 17.3; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{22}H_{26}O_3N_2Na$, 389.1836; found, 389.1839.

N-(3-Methylbut-2-en-1-yl)-2-nitro-N-phenylbenzamide (1zz). Prepared from 2-nitro-*N*-phenylbenzamide (123 mg, 0.52 mmol) (**1z**) and purifued following general procedure B; afforded 112.8 mg (70% yield) of the title compound as a yellow waxy solid: R_f = 0.4 (2:1 PE/EA), 62-64 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.2 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.19–6.98 (m, 5H), 5.41 (t, *J* = 7.0 Hz, 1H), 4.54 (d, *J* = 7.1 Hz, 2H), 1.71 (s, 3H), 1.51 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 166.6, 145.7, 141.5, 136.9, 133.5, 133.4, 129.4, 129.3, 129.1, 128.2, 127.7, 124.2, 118.6, 47.2, 25.7, 17.8; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{19}O_3N_2$, 311.1390; found, 311.1391.

General procedure C. 4-(Furan-2-ylmethyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5*H*-benzo

[e][1,4]diazepin-5-one **2a** was used as the model product for this reaction. The preparation strategies of the other diazepines were consistent with its preparation strategy. *N*-(furan-2-ylmethyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide **1aa** (30 mg, 0.096 mmol) was placed in a 15 mL test tube with agitator, added with triphenylphosphine (63 mg, 0.24 mmol), molybdenum-acetoacetate (3.1 mg, 0.0096 mmol), and copper(II) trifluoromethane-sulfonate (3.5 mg, 0.0096 mmol) successively. After that, dried toluene (3 mL) was added into the test tube. Then the test tube was placed in an oil bath at 110 °C for 12 h. The whole operation process was carried out without water and oxygen under N_2 atmosphere rigidly. TLC plate was used for monitoring the end of the reaction. The mixture was diluted with ethyl acetate (10 mL) and washed with saturated sodium chloride solution (15 mL × 2), dried over Na_2SO_4 and concentrated under reduced pressure. Purification was done by column chromatography on silica gel H with petroleum ether/ethyl acetate (4 : 1, v/v) as eluent to give the 2a of white solid (24.4 mg).

4-(Furan-2-ylmethyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2a). Prepared from *N*-(furan-2-ylmethyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (30 mg, 0.096 mmol) and purified following the procedure C; afforded 24.4 mg (90% yield) of the product as a white solid: R_f = 0.45 (2:1 PE/EA), mp 120-122 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 7.7 Hz, 1H), 7.37 (s, 1H), 7.26 (t, *J* = 7.6 Hz, 2H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.34 (s, 1H), 5.02 (s, 2H), 4.96 (d, *J* = 15.5 Hz, 2H), 4.53 (d, *J* = 15.4 Hz, 1H), 4.03 (dd, *J* = 8.8, 3.1 Hz, 1H), 3.54 (dd, *J* = 15.2, 8.8 Hz, 1H), 3.41 (dd, *J* = 15.2, 3.1 Hz, 1H), 1.73 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.6, 150.8, 145.4, 144.4, 142.4, 132.4, 132.1, 122.5, 119.6, 119.2, 113.0, 110.6, 109.0, 65.3, 48.6, 43.8, 19.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{19}N_2O_2$, 283.1441; found, 283.1440. Larger scale synthesis: Prepared from N-(furan-2-ylmethyl)-N-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (387 mg, 1.23 mmol) and purified following the procedure C; afforded 208.4 mg (60% yield) of **2a**.

9-Chloro-4-(furan-2-ylmethyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2b). Prepared from 3-chloro-*N*-(furan-2-ylmethyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (36 mg, 0.103 mmol) and purified following the procedure C; afforded 19.6 mg (60% yield) of the product as a light yellow oil: R_f = 0.42 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.46–7.35 (m, 2H), 6.77 (t, *J* = 7.8 Hz, 1H), 6.36 (s, 2H), 5.13 (s, 1H), 5.12 (d, *J* = 15.3 Hz, 1H), 4.96 (s, 1H), 4.59 (s, 1H), 4.43 (d, *J* = 15.3 Hz, 1H), 4.00 (dd, *J* = 8.3, 2.7 Hz, 1H), 3.59 (dd, *J* = 15.2, 8.4 Hz, 1H), 3.42 (dd, *J* = 15.2, 2.7 Hz, 1H), 1.73 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 168.6, 150.4, 144.5, 142.5, 140.5, 132.2, 131.2, 123.2, 122.4, 118.8, 113.6, 110.6, 109.2, 65.2, 48.6, 43.9, 19.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}N_2O_2Cl$, 317.1051; found, 317.1048.

4-(Furan-2-ylmethyl)-7-methyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2c). Prepared from *N*-(furan-2-ylmethyl)-5-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitro-benzamide (29 mg, 0.09 mmol) and purified following the procedure C; afforded 21.7 mg (83% yield) of the product as a light yellow oil: R_f = 0.56 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.40 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.1 Hz, 1H), 6.37 (s, 2H), 5.09 (d, *J* = 15.3 Hz, 1H), 5.08 (s, 1H), 4.92 (s, 1H), 4.48 (d, *J* = 15.3 Hz, 1H), 3.96 (dd, *J* = 8.4, 3.1 Hz, 1H), 3.58 (dd, *J* = 15.1, 8.4 Hz, 1H), 3.42 (dd, *J* = 15.0, 3.1 Hz, 1H), 2.29 (s, 3H), 1.73 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.8, 150.8, 145.7, 142.3, 142.2, 133.2, 131.8, 129.0, 122.7, 119.3, 112.7, 110.5, 108.9, 65.4, 48.6,

43.7, 20.2, 19.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_2$, 297.1598; found, 297.1596.

4-(Furan-2-ylmethyl)-7-methoxy-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2d). Prepared from *N*-(furan-2-ylmethyl)-5-methoxy-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (150 mg, 0.44 mmol) and purified following the procedure C; afforded 111.3 mg (81% yield) of the product as a light yellow oil: R_f= 0.5 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (s, 1H), 7.32 (d, *J* = 3.0 Hz, 1H), 6.87 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.62 (d, *J* = 8.7 Hz, 1H), 6.35 (s, 2H), 5.08 (d, *J* = 15.3 Hz, 1H), 5.04 (s, 1H), 4.90 (s, 1H), 4.47 (d, *J* = 15.3 Hz, 1H), 3.94 (dd, *J* = 8.3, 3.4 Hz, 1H), 3.88 (s, 1H), 3.79 (s, 3H), 3.55 (dd, *J* = 15.1, 8.3 Hz, 1H), 3.40 (dd, *J* = 15.1, 3.5 Hz, 1H), 1.71 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.5, 153.4, 150.7, 145.6, 142.3, 138.4, 124.1, 121.0, 120.3, 114.2, 112.6, 110.5, 108.8, 65.5, 55.6, 48.5, 43.7, 19.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_3$, 313.1547; found, 313.1546. Larger scale synthesis: Prepared from N-(furan-2-ylmethyl)-5-methoxy-N-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (301 mg, 0.88 mmol) and purified following the procedure C; afforded 174.9 mg (64% yield) of **2d**.

8-Fluoro-4-(furan-2-ylmethyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2e). Prepared from 4-fluoro-N-(furan-2-ylmethyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (140 mg, 0.42 mmol) and purified following the procedure C; afforded 65.5 mg (52% yield) of the product as a light yellow oil: R_f= 0.6 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (dd, *J* = 8.7, 6.9 Hz, 1H), 7.39 (s, 1H), 6.55 (td, *J* = 8.6, 2.3 Hz, 1H), 6.35-6.34 (m, 2H), 6.32 (d, *J* = 2.3 Hz, 1H), 5.11 (d, *J* = 15.3 Hz, 1H), 5.03 (s, 1H), 4.94 (s, 1H), 4.40 (d, *J* = 15.3 Hz, 1H), 3.91 (dd, *J* = 8.3, 2.2 Hz, 1H), 3.90 (s, 1H), 3.58 (dd, *J* = 15.1, 8.3 Hz, 1H), 3.43 (dd, *J* = 15.1, 2.2 Hz, 1H), 1.72 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 168.7, 165.4 (d, *J* = 249.0 Hz), 150.6, 146.5 (d, *J* = 11.0 Hz), 145.1, 142.5, 135.0 (d, *J* = 10.0 Hz), 118.0 (d, *J* = 2.0 Hz), 113.2, 110.6, 109.1, 106.8 (d, *J* = 22.0 Hz), 104.7 (d, *J* = 24.0 Hz), 65.0, 48.7, 43.9, 19.3; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}N_2O_2FNa$, 323.1166; found, 323.1169.

2-(Prop-1-en-2-yl)-4-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2f). Prepared from *N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(thiophen-2-ylmethyl)benzamide (39 mg, 0.118 mmol) and purified following the procedure C; afforded 22.9 mg (65% yield) of the product as a light yellow oil: R_f= 0.6 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.26-7.22 (m, 2H), 7.03 (d, *J* = 3.1 Hz, 1H), 6.95 (dd, *J* = 4.9, 3.6 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.14 (d, *J* = 15.1 Hz, 1H), 5.05 (s, 1H), 4.92 (s, 1H), 4.68 (d, *J* = 15.1 Hz, 1H), 4.02 (dd, *J* = 8.3, 3.1 Hz, 1H), 3.52 (dd, *J* = 15.1, 8.3 Hz, 1H), 3.37 (dd, *J* = 15.1, 3.1 Hz, 1H), 1.70 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.6, 145.2, 144.5, 139.7, 132.5, 132.1, 127.0, 126.7, 125.8, 122.3, 119.6, 119.2, 113.2, 65.4, 48.5, 46.1, 19.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{19}N_2OS$, 299.1213; found, 299.1211.

9-Chloro-2-(prop-1-en-2-yl)-4-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2g). Prepared from 3-chloro-*N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(thiophen-2-ylmethyl)benzamide (35 mg, 0.096 mmol) and purified following the procedure C; afforded 18.8 mg (59% yield) of the product as a light yellow oil: R_f= 0.4 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.41 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.28 (s, 1H), 7.05 (d, *J* = 2.9 Hz, 1H), 6.97 (dd, *J* = 4.9, 3.6 Hz, 1H), 6.79 (t, *J* = 7.8 Hz, 1H), 5.20 (d, *J* = 15.1 Hz, 1H), 5.12 (s, 1H), 4.96 (s, 1H), 4.66 (d, *J* = 15.1 Hz, 1H),

4.06 (dd, *J* = 8.2, 2.7 Hz, 1H), 3.56 (dd, *J* = 15.2, 8.2 Hz, 1H), 3.38 (dd, *J* = 15.2, 2.7 Hz, 1H), 1.72 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 167.5, 143.3, 139.5, 138.2, 131.2, 130.2, 126.1, 125.7, 124.9, 122.3, 121.4, 117.9, 112.7, 64.3, 47.5, 45.2, 17.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}N_2OClS$, 333.0823; found, 333.0820.

7-Methyl-2-(prop-1-en-2-yl)-4-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2h). Prepared from 5-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(thiophen-2-ylmethyl)benzamide (36 mg, 0.105 mmol) and purified following the procedure C; afforded 20.9 mg (64% yield) of the product as a light yellow oil: R_f = 0.5 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (s, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.07-7.03 (m, 2H), 6.96 (t, *J* = 8.1 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 5.13 (d, *J* = 15.1 Hz, 1H), 5.08 (s, 1H), 4.91 (s, 1H), 4.68 (d, *J* = 15.1 Hz, 1H), 4.00 (dd, *J* = 8.2, 3.2 Hz, 1H), 3.52 (dd, *J* = 15.1, 8.2 Hz, 1H), 3.36 (dd, *J* = 15.1, 3.2 Hz, 1H), 2.28 (s, 3H), 1.70 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 169.8, 145.5, 142.2, 139.8, 133.3, 131.8, 129.1, 126.8, 126.6, 125.7, 122.7, 119.4, 112.9, 65.5, 48.5, 46.0, 20.3, 19.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}N_2OS$, 313.1369; found, 313.1367.

9-Methyl-2-(prop-1-en-2-yl)-4-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2i). Prepared from 3-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(thiophen-2-ylmethyl)benzamide (31 mg, 0.09 mmol) and purified following the procedure C; afforded 19.1 mg (68% yield) of the product as a light yellow oil: R_f = 0.5 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.25 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 2.9 Hz, 1H), 6.96 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 5.23 (d, *J* = 15.1 Hz, 1H), 5.10 (s, 1H), 4.94 (s, 1H), 4.61 (d, *J* = 15.1 Hz, 1H), 4.02 (dd, *J* = 7.6, 2.9 Hz, 1H), 3.68 (s, 1H), 3.57 (dd, *J* = 15.1, 7.6 Hz, 1H), 3.37 (dd, *J* = 15.1, 2.9 Hz, 1H), 2.19 (s, 3H), 1.71 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 169.9, 145.1, 142.5, 139.8, 133.4, 130.3, 126.9, 126.6, 125.7, 124.7, 122.6, 118.9, 113.3, 65.2, 48.5, 46.2, 19.1, 18.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}N_2OS$, 313.1369; found, 313.1368.

2-(Prop-1-en-2-yl)-4-(2-(pyridin-2-yl)ethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2j). Prepared from *N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(2-(pyridin-2-yl)ethyl)benzamide (49 mg, 0.14 mmol) and purified following the procedure C; afforded 27.9 mg (63% yield) of the product as a light yellow oil: R_f = 0.6 (EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 4.9 Hz, 1H), 7.76 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.63 (td, *J* = 7.6, 1.6 Hz, 1H), 7.29 (s, 1H), 7.23 (td, *J* = 7.6, 1.6 Hz, 1H), 7.16 (t, *J* = 5.0 Hz, 1H), 6.87 (td, *J* = 7.5,1.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.05 (s, 1H), 4.90 (s, 1H), 4.05–4.02 (m, 1H), 3.99 (dd, *J* = 8.3, 3.1 Hz, 1H), 3.88-3.81 (m, 1H),, 3.48 (dd, *J* = 15.0, 8.3 Hz, 1H), 3.29 (dd, *J* = 15.0, 3.1 Hz, 1H), 3.24–3.10 (m, 2H), 1.71 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 168.8, 158.1, 148.1, 144.4, 143.6, 135.8, 131.2, 130.7, 123.0, 122.0, 120.6, 118.6, 118.1, 112.1, 64.8, 49.2, 48.3, 35.7, 18.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{22}N_3O$, 308.1757; found, 308.1755.

2-(Prop-1-en-2-yl)-4-(2-(thiophen-2-yl)ethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2k). Prepared from *N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(2-(thiophen-2-yl)ethyl)benzamide (42 mg, 0.12 mmol) and purified following the procedure C; afforded 31.6 mg (83% yield) of the product as a light yellow oil: R_f = 0.48 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.24 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.16 (d, *J* = 5.1 Hz, 1H), 6.95-6.87 (m, 3H), 6.67 (d, *J* = 8.0 Hz, 1H), 5.08 (s, 1H), 4.93 (s, 1H), 3.99 (dd, *J* = 8.1, 2.8 Hz, 1H), 3.96–3.88 (m, 1H), 3.70-3.63 (m, 1H), 3.46 (dd, *J* = 15.1, 8.1 Hz, 1H), 3.30–3.13 (m, 2H), 3.25 (dd, *J* = 15.1, 2.8 Hz, 1H), 1.72 (s,

3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 168.7, 144.2, 143.6, 140.6, 131.3, 130.7, 126.0, 124.5, 122.8, 122.0, 118.6, 118.1, 112.2, 64.7, 50.5, 49.5, 27.6, 18.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}N_2OS$, 313.1369; found, 313.1367.

9-Chloro-2-(prop-1-en-2-yl)-4-(2-(thiophen-2-yl)ethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2l). Prepared from 3-chloro-*N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(2-(thiophen-2-yl)ethyl)benzamide (51 mg, 0.135 mmol) and purified following the procedure C; afforded 24.8 mg (53% yield) of the product as a light yellow oil: R_f = 0.42 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.17 (dd, *J* = 5.0, 0.8 Hz, 1H), 6.98–6.92 (dd, *J* = 5.0, 3.0 Hz, 1H), 6.88 (d, *J* = 3.0 Hz, 1H), 6.79 (t, *J* = 7.8 Hz, 1H), 5.13 (s, 1H), 4.96 (s, 1H), 4.53 (s, 1H), 4.05 (dd, *J* = 8.1, 2.4 Hz, 1H), 3.98–3.85 (m, 1H), 3.71-3.64 (m, 1H), 3.48 (dd, *J* = 15.2, 8.1 Hz, 1H), 3.30-3.13 (m, 2H), 3.20 (dd, *J* = 15.2, 2.4 Hz, 1H), 1.73 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 167.8, 143.3, 140.4, 139.5, 131.1, 129.8, 126.1, 124.6, 123.0, 122.9, 121.5, 118.1, 112.8, 64.6, 50.7, 49.5, 27.5, 17.9; HRMS (ESI-TOF) m/z:$[M + H]^+$ calcd for $C_{18}H_{20}N_2OClS$, 347.0979; found, 347.0977.

7-Methyl-2-(prop-1-en-2-yl)-4-(2-(thiophen-2-yl)ethyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2m). Prepared from 5-methyl-N-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(2-(thiophen-2-yl)ethyl) benzamide (25 mg, 0.07 mmol) and purified following the procedure C; afforded 12.3 mg (54% yield) of the product as a light yellow oil: R_f=0.4(2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (s, 1H), 7.14 (dd, *J* = 5.0, 0.7 Hz, 1H), 7.05 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.92 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.87 (d, *J* = 2.9 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.06 (s, 1H), 4.90 (s, 1H), 3.98 (dd, *J* = 8.1, 3.1 Hz, 1H), 3.92–3.82 (m, 1H), 3.71-3.64 (m, 1H), 3.41 (dd, *J* = 15.1, 8.3 Hz, 1H), 3.20 (dd, *J* = 15.1, 3.1 Hz, 1H), 3.27-3.11, (m, 2H), 2.27 (s, 3H), 1.69 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 169.8, 144.9, 141.6, 133.1, 131.5, 129.9, 127.0, 125.5, 125.4, 123.8, 119.7, 113.3, 112.5, 65.8, 51.4, 50.4, 28.6, 20.3, 19.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{23}N_2OS$, 327.1526; found, 327.1522.

4-Benzyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2n). Prepared from *N*-benzyl-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (43 mg, 0.133 mmol) and purified following the procedure C; afforded 34.9 mg (90% yield) of the product as a yellow viscous liquid: R_f = 0.5 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.35-7.23 (m, 6H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 5.05 (d, *J* = 14.8 Hz, 1H),5.02 (s, 1H), 4.89 (s, 1H), 4.54 (d, *J* = 14.8 Hz, 1H), 3.95 (dd, *J* = 8.4, 2.9 Hz, 1H), 3.80 (s, 1H), 3.51 (dd, *J* = 15.1, 8.4 Hz, 1H), 3.28 (dd, *J* = 15.1, 2.9 Hz, 1H), 1.65 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 169.9, 145.4, 144.5, 137.2, 132.3, 132.0, 128.7, 128.3, 127.5, 122.6, 119.5, 119.1, 112.9, 65.3, 51.3, 48.6, 19.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{21}N_2O$, 293.1648; found, 293.1646.

4-Benzyl-9-methyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2o). Prepared from *N*-benzyl-3-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (32 mg, 0.095 mmol) and purified following the procedure C; afforded 15.4 mg (53% yield) of the product as a thick yellow oily liquid: R_f= 0.6 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.35–7.28 (m, 5H), 7.20 (d, *J* = 7.7 Hz, 1H), 6.82 (t, *J* = 7.6 Hz, 1H), 5.07 (d, *J* = 14.8 Hz, 1H), 5.06 (s, 1H), 4.91 (s, 1H), 4.54 (d, *J* = 14.8 Hz, 1H), 4.09–3.90 (m, 1H), 3.52 (dd, *J* = 15.0, 8.0 Hz, 1H), 3.27 (dd, *J* = 15.0, 2.8 Hz, 1H), 2.21 (s, 3H), 1.66 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz,

Chloroform-*d*) δ 170.2, 145.1, 142.2, 137.2, 133.4, 130.3, 128.7, 128.4, 127.5, 124.9, 123.0, 119.1, 113.3, 65.1, 51.4, 48.4, 19.1, 18.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{23}N_2O$, 307.1805; found, 307.1803.

5-(2,6-Dimethylbenzyl)-9-methyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2p). Prepared from *N*-(2,6-dimethylbenzyl)-3-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (42 mg, 0.115 mmol) and purified following the procedure C; afforded 31.8 mg (83% yield) of the product as a light yellow oil: R_f= 0.44 (4:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 7.7 Hz, 1H), 7.39–7.31 (m, 1H), 7.19–7.12 (m, 1H), 7.06 (d, *J* = 7.4 Hz, 2H), 6.79 (t, *J* = 7.6 Hz, 1H), 5.23 (d, *J* = 14.6 Hz, 1H), 4.77 (d, *J* = 13.8 Hz, 2H), 4.70 (d, *J* = 14.6 Hz, 1H), 3.69 (dd, *J* = 9.7, 2.8 Hz, 2H), 3.39 (dd, *J* = 14.9, 9.7 Hz, 1H), 2.93 (dd, *J* = 14.9, 2.8 Hz, 1H), 2.38 (s, 6H), 2.18 (s, 3H), 1.41 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 170.0, 146.0, 142.3, 138.5, 133.4, 132.1, 130.4, 128.6, 127.9, 124.5, 122.7, 118.7, 112.6, 65.8, 47.0, 43.8, 20.2, 18.7, 18.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{27}N_2O$, 335.2118; found, 335.2124.

4,9-Dimethyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2q). Prepared from *N*,3-dimethyl-N-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (60 mg, 0.229 mmol) and purified following the procedure C; afforded 34.8 mg (66% yield) of the product as a yellow solid: R_f= 0.35 (2:1 PE/EA), mp 132-134 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 5.21 (s, 1H), 4.98 (s, 1H), 4.22 (dd, *J* = 6.7, 3.1 Hz, 1H), 3.56 (dd, *J* = 15.0, 6.7 Hz, 1H), 3.42 (dd, *J* = 15.0, 3.1 Hz, 1H), 3.14 (s, 3H), 2.20 (s, 3H), 1.78 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 170.3, 144.9, 142.5, 133.2, 129.9, 124.9, 123.6, 119.2, 113.5, 65.1, 51.1, 36.3, 19.3, 18.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{19}N_2O$, 231.1492; found, 231.1491.

4-(4-Fluorophenethyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2r). Prepared from *N*-(4-fluorophenethyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (150 mg, 0.421 mmol) and purified following the procedure C; afforded 68.3 mg (50% yield) of the product as a thick yellow liquid: R_f= 0.5 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.25-7.18 (m, 3H), 7.00-6.95 (m, 2H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 5.05 (s, 1H), 4.92 (s, 1H), 4.00 (dd, *J* = 8.2, 3.2 Hz, 1H), 3.85-3.78 (m, 1H), 3.64-3.57 (m, 1H), 3.41 (dd, *J* = 15.1, 8.2 Hz, 1H), 3.18 (dd, *J* = 15.1, 3.2 Hz, 1H), 3.00-2.87 (m, 2H), 1.70 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.7, 161.6 (d, *J* = 242.0 Hz), 145.2, 144.5, 134.9 (d, *J* = 3.0 Hz), 132.3, 131.7, 130.4 (d, *J* = 8.0 Hz), 123.2, 119.8, 119.2, 115.4 (d, *J* = 21.0 Hz), 113.3, 65.8, 51.3, 50.5, 33.7, 19.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{22}N_2OF$, 325.1711; found, 325.1708.

4-(4-Fluorophenethyl)-7-methyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2s). Prepared from *N*-(4-fluorophenethyl)-5-methyl-*N*-(3-methylbut-en-1-yl)-2-nitrobenzamide (44 mg, 0.119 mmol) and purified following the procedure C; Afforded 27.3 mg (68% yield) of the product as a light yellow oil: R_f= 0.4 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (s, 1H), 7.21 (dd, *J* = 8.0, 5.6 Hz, 2H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 8.6 Hz, 2H), 6.58 (d, *J* = 8.1 Hz, 1H), 5.07 (s, 1H), 4.90 (s, 1H), 3.97 (dd, *J* = 8.1, 3.2 Hz, 1H), 3.88–3.75 (m, 1H), 3.65-3.57 (m, 1H), 3.40 (dd, *J* = 15.0, 8.1 Hz, 1H), 3.17 (dd, *J* = 15.0, 3.2 Hz, 1H), 3.01-2.88 (m, 2H), 2.28 (s, 3H), 1.70 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.9, 161.6 (d, *J* = 243.0 Hz), 145.4, 142.1, 134.9 (d, *J* = 3.0 Hz), 133.1, 131.5, 130.3 (d, *J* = 8.0 Hz), 129.3, 123.5, 119.4, 115.3 (d, *J* = 21.0 Hz), 113.1, 65.8, 51.2, 50.4,

33.7, 20.3, 19.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{24}FN_2O$, 339.1867; found, 339.1867.

4-(4-Fluorophenethyl)-9-methyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2t). Prepared from *N*-(4-fluorophenethyl)-3-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitro benzamide (140 mg, 0.378 mmol) and purified following the procedure C; afforded 76.7 mg (60% yield) of the product as a light yellow oil: R_f= 0.4 (2:1 PE/EA); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.70–7.61 (m, 1H), 7.56-7.45 (m, 1H), 7.22-7.18 (m, 2H), 6.98 (t, *J* = 8.4 Hz, 2H), 6.80 (t, *J* = 7.5 Hz, 1H), 5.11 (s, 1H), 4.94 (s, 1H), 4.03 (dd, *J* = 7.4, 2.4 Hz, 1H), 3.88-3.84 (m, 1H), 3.59-3.54 (m, 1H), 3.43 (dd, *J* = 15.0, 7.4 Hz, 1H), 3.21 (dd, *J* = 15.0, 2.4 Hz, 1H), 2.99-2.89 (m, 2H), 2.19 (s, 3H), 1.71 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 170.1, 161.6 (d, *J* = 243.0 Hz), 145.0, 142.5, 135.0 (d, *J* = 3.0 Hz), 133.3, 130.3 (d, *J* = 8.0 Hz), 130.0, 125.0, 123.6, 119.2, 115.4 (d, *J* = 21.0 Hz), 113.5, 65.6, 51.3, 50.3, 33.7, 19.1, 18.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{24}N_2OF$, 339.1867; found, 339.1868.

4-(Furan-2-ylmethyl)-2-methyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2u). Prepared from *N*-(2,3-dimethylbut-2-en-1-yl)-*N*-(furan-2-ylmethyl)-2-nitrobenzamide (47 mg, 0.143 mmol) and purified following the procedure C; afforded 33.9 mg (80% yield) of the product as a light yellow oil: R_f= 0.43 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (dd, *J* =7.8, 1.2 Hz, 1H), 7.34 (d, *J* = 1.2 Hz, 1H), 7.29–7.17 (m, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 7.7 Hz, 1H), 6.32-6.27 (m, 2H), 5.36 (s, 1H), 5.10 (d, *J* = 15.4 Hz, 1H), 5.00 (s, 1H), 4.30 (d, *J* = 15.4 Hz, 1H), 3.46 (d, *J* = 15.3 Hz, 1H), 3.28 (d, *J* = 15.3 Hz, 1H), 1.85 (s, 3H), 1.29 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-*d*) δ 169.8, 151.1, 147.1, 142.2, 132.1, 131.6, 124.5, 120.6, 120.3, 114.1, 110.4, 108.6, 67.2, 52.1, 43.8, 24.9, 19.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_2$, 297.1598; found, 297.1595.

4-(2,6-Dimethylbenzyl)-9-methyl-2-vinyl-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2v). Prepared from *N*-(2,6-dimethylbenzyl)-3-methyl-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (70 mg, 0.199 mmol) and purified following the procedure C; afforded 47.7 mg (75% yield) of the product as a light yellow oil: R_f= 0.4 (4:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.13 (d, *J* = 7.0 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 2H), 6.89 (t, *J* = 7.5 Hz, 1H), 5.66-5.57 (m, 1H), 5.21 (d, *J* = 14.6 Hz, 1H), 5.02–4.95 (m, 2H), 4.73 (d, *J* = 14.5 Hz, 1H), 3.74 (br, 1H), 3.24 (dd, *J* = 15.0, 9.8 Hz, 1H), 2.96 (dd, *J* = 15.0, 3.6 Hz, 1H), 2.39 (s, 6H), 2.20 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-*d*) δ 170.4, 138.9, 138.1, 133.5, 132.8, 129.9, 128.9, 128.9, 128.2, 126.3, 125.8, 120.5, 117.0, 64.6, 47.9, 44.0, 20.6, 18.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{25}N_2O$, 321.1961; found, 321.1969.

4-(Furan-2-ylmethyl)-2-vinyl-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2w). Prepared from (*E*)-*N*-(but-2-en-1-yl)-*N*-(furan-2-ylmethyl)-2-nitrobenzamide (41 mg, 0.137 mmol) and purified following the procedure C; afforded 28.9 mg (79% yield) of the product as a light yellow oil: R_f=0.42 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.37 (s, 1H), 7.29-7.20 (m, 2H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 6.34 (s, 1H), 5.80 (td, *J* = 17.0, 10.2 Hz, 1H), 5.27 (d, *J* = 17.0 Hz, 1H), 5.16 (d, *J* = 10.2 Hz, 1H), 5.01 (d, *J* = 15.3 Hz, 1H), 4.54 (d, *J* = 15.3 Hz, 1H), 4.06 (q, *J* = 5.8 Hz, 1H), 3.46 (d, *J* = 5.8 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.5, 150.8, 142.9, 142.3, 136.8, 132.3, 131.8, 123.8, 120.7, 120.0, 117.3, 110.6, 108.9, 62.9, 49.5, 44.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_2$, 269.1285; found, 269.1292.

4-(4-Methoxyphenyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2x). Prepared from *N*-(4-methoxyphenyl)-*N*-(3-methylbut-2-en-1-yl)-2-nitrobenzamide (130 mg, 0.382 mmol) and purified following the procedure C; afforded 62.4 mg (53% yield) of the product as a white solid: R_f = 0.5 (2:1 PE/EA), mp 165-167 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.31-7.28 (m, 3H), 6.94-6.92 (m, 3H), 6.84 (d, *J* = 6.4 Hz, 1H), 5.15 (s, 1H), 4.95 (s, 1H), 4.32 (dd, *J* = 8.3, 3.0 Hz, 1H), 3.99 (dd, *J* = 14.9, 8.3 Hz, 1H), 3.82 (s, 3H), 3.76 (dd, *J* = 14.9, 3.0 Hz, 1H), 1.64 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.8, 158.1, 145.1, 144.7, 136.6, 132.6, 132.2, 127.8, 123.0, 119.8, 119.2, 114.5, 113.4, 65.6, 55.5, 52.4, 19.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{21}O_2N_2$, 309.1598; found, 309.1595.

2-(Prop-1-en-2-yl)-4-(m-tolyl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2y). Prepared from *N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-(m-tolyl)benzamide (38 mg, 0.117 mmol) and purified following the procedure C; afforded 17.5 mg (51% yield) of the product as a light yellow oil: R_f = 0.4 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 7.7 Hz, 1H), 7.31-7.28 (m, 2H), 7.17-7.13 (m, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.92 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 5.13 (s, 1H), 4.93 (s, 1H), 4.32 (dd, *J* = 8.6, 2.7 Hz, 1H), 4.02 (dd, *J* = 14.9, 8.6 Hz, 1H), 3.78 (dd, *J* = 14.9, 2.7 Hz, 1H), 2.37 (s, 3H), 1.64 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, Chloroform-*d*) δ 169.6, 145.0, 144.4, 143.4, 139.1, 132.6, 132.1, 129.0, 127.6, 127.3, 123.5, 123.0, 119.9, 119.3, 113.5, 65.5, 52.1, 21.4, 19.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{21}N_2O$, 293.1648; found, 293.1651.

4-Phenyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2z). Prepared from *N*-(3-methylbut-2-en-1-yl)-2-nitro-*N*-phenylbenzamide (29 mg, 0.094 mmol) and purified following the procedure C; afforded 13.3 mg (51% yield) of the product as a white solid: R_f = 0.43 (2:1 PE/EA), mp 167-169 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 7.2 Hz, 2H), 7.31–7.25 (m, 2H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.15 (s, 1H), 4.93 (s, 1H), 4.30 (dd, *J* = 8.2, 3.0 Hz, 1H), 4.04 (dd, *J* = 14.9, 8.2 Hz, 1H), 3.93 (s, 1H), 3.82 (dd, *J* = 14.9, 3.0 Hz, 1H), 1.62 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.7, 145.0, 144.7, 143.5, 132.7, 132.2, 129.2, 126.7, 126.6, 122.9, 119.8, 119.2, 113.6, 65.5, 52.0, 19.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}ON_2$, 279.1492; found, 279.1490.

(E)-4-Benzyl-9-methyl-2-(6-methylhepta-2,5-dien-2-yl)-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (2a$_1$). Prepared from (E)-*N*-benzyl-*N*-(3,7-dimethylocta-2,6-dien-1-yl)-3-methyl-2-nitrobenzamide (37 mg, 0.091 mmol) and purified following the procedure C; afforded 16.7 mg (49% yield) of the product as a light yellow oil: R_f = 0.6 (2:1 PE/EA); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 7.1 Hz, 1H), 7.34-7.28 (m, 5H), 7.18 (d, *J* = 7.1 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 5.42 (t, *J* = 7.0 Hz, 1H), 5.06 (t, *J* = 7.1 Hz, 1H), 4.96 (d, *J* = 14.7 Hz, 1H), 4.60 (d, *J* = 14.8 Hz, 1H), 3.98 (dd, *J* = 8.4, 2.7 Hz, 1H), 3.55 (dd, *J* = 15.0, 8.4 Hz, 1H), 3.21 (dd, *J* = 15.0, 2.7 Hz, 1H), 2.69 (t, *J* = 7.0 Hz, 2H), 2.18 (s, 3H), 1.70 (s, 3H), 1.63 (s, 3H), 1.55 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, Chloroform-*d*) δ 170.3, 142.8, 137.3, 134.8, 133.3, 132.4, 130.3, 128.6, 128.3, 127.5, 126.8, 124.7, 122.7, 121.9, 118.7, 66.9, 51.3, 48.7, 26.7, 25.7, 18.3, 17.8, 13.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{31}N_2O$, 375.2431; found, 375.2438.

Preparation of deuterated compound 1aa'. See S94 in the SI. Compounds **b**, **c**, **d**, **e**, **f** were obtained according to the referenece.[37] Preparation method of compound **1aa'** was consistent with the procedure of compound **1aa**.

Supporting Information.

Concise list of types of data or files found in the SI: ^{1}H and ^{13}C {^{1}H} NMR Spectra, additional

reaction schemes, X-ray single crystal data and CIF file, larger scale reaction schemes.

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REFERENCES

1.Thakrar, S.; Bavishi, A.; Radadiya, A.; Parekh, S.; Bhavsar, D.; Vala, H.; Pandya, N.; Shah, A. Microwave-Assisted Rapid Synthesis of Novel 1,5-Benzodiazepine Derivatives as Potent Antimicrobial Agent. *J. Heterocycl. Chem.* **2013,** *50*, E73-E79.

2.Al-Said, N.H.; Al-Qaisi, L.S. Total synthesis of asperlicin D. *Tetrahedron Lett.* **2006,** *47*, 693-694.

3.Sternbach, L.H. 1,4-Benzodiazepines Chemistry and Some Aspects of the Structure-Activity Relationship. *Angew. Chem.-Int. Edit.* **1971,** *10*, 34-43.

4.Gourdeau, H.; McAlpine, J. B.; Ranger, M.; Simard, B.; Berger, F.; Beaudry, F.; Falardeau, P. Identification, characterization and potent antitumor activity of ECO-4601, a novel peripheral benzodiazepine receptor ligand. *Cancer Chemoth Pharm.* **2008,** *61*, 911-921.

5.Ellman, J.A. ChemInform Abstract: Design, Synthesis, and Evaluation of Small-Molecule Libraries. *Acc. Chem. Res.* **1996**, *29*, 132-143.

6.Charan, R.D. Diazepinomicin, a New Antimicrobial Alkaloid from a Marine Micromonospora sp. *J. Nat. Prod.* **2004,** *67,* 1431-1433

7.Misra, A.; Sharma, S.; Sharma, D.; Dubey, S.; Mishra, A.; Kishore, D.; Dwivedi, J. Synthesis and molecular docking of pyrimidine incorporated novel analogue of 1,5-benzodiazepine as antibacterial agent. *J. Chem. Sci.* **2018,** *130,* 31-43.

8.Beccalli, E. M.; Broggini, G.; Paladino, G.; Zoni, C. Palladium-mediated approach to dibenzo[b,e][1,4]diazepines and benzopyrido-analogues. An efficient synthesis of tarpane. *Tetrahedron Lett.* **2005,** *61*, 61-68.

9.Cepanec, I.; Litvić, M.; Pogorelic, I. Efficient Synthesis of 3-Hydroxy-1,4-benzodiazepines Oxazepam and Lorazepam by New Acetoxylation Reaction of 3-Position of 1,4-Benzodiazepine Ring. *Org Process Res Dev.* **2006,** *10*, 1192-1198.

10.McDowell, R.S.; Blackburn, B.K.; Gadek, T.R.; McGee, L.R.; Rawson, T.; Reynolds, M.E.; Robarge, K.D.; Somers, T.C.; Thorsett, E.D. The Novel Design of Potent Non-peptidal Inhibitors of Platelet Aggregation Based on a Benzodiazepinedione Scaffold. *J. Am. Chem. Soc.* **1994,** *116,* 5077-5083

11.Sharma, A.; Kishore, D.; Singh, B. An Expedient Method for the Synthesis of 1,2,4-Triazolo-fused 1,5-Benzodiazepine, 1,5-Benzoxazepine, and 1,5-Benzothiazepine Scaffolds: A Novel Seven-membered Ring System of Biological Interest. *J. Heterocyclic Chem.* **2018,** *55*, 586-592.

12.Ming-Fu, C. Practical synthesis of potential endothelin receptor antagonists of 1,4-benzodiazepine-2,5-dione derivatives bearing substituents at the C3-, N1- and N4-positions. *Org. Biomol.Chem***. 2006,** *3,* 510-518.

13. Ferraris, D.; Ficco, R. P.; Dain, D.; Ginski, M.; Lautar, S.; Lee-Wisdom, K.; Liang, S.; Lin, Q.; Lu, M. X. C.; Morgan, L.; Thomas, B.; Williams, L. R.; Zhang, J.; Zhou, Y.; Kalish, V. J.

Design and synthesis of poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors. part 4: Biological evaluation of imidazobenzodiazepines as potent PARP-1 inhibitors for treatment of ischemic injuries. *Bioorgan Med Chem.* **2003,** *11*, 3695-3707.

14.Zellou, A.; Cherrah, Y.; Essassi, E. M.; Hassar, M. Synthesis and pharmacological study of 1,5-benzodiazepine-2,4-dithiones and alkyl derivatives. *Ann Pharm Fr.* **1998,** *56*, 175-80.

15.Failli, A. A.; Shumsky, J. S.; Steffan, R. J.; Caggiano, T. J.; Williams, D. K.; Trybulski, E. J.; Ning, X.; Lock, Y.; Tanikella, T.; Hartmann, D.; Chan, P. S.; Park, C. H. Pyridobenzodiazepines: A novel class of orally active, vasopressin V2 receptor selective agonists. *Bioorg. Med. Chem. Lett*. **2006,** *16*, 954-959.

16..Puvvada, M.S. Inhibition of bacteriophage T7 RNA polymerase in vitro transcription by DNA-binding pyrrolo(2,1-c)(1,4)benzodiazepines. *Biochemistry*. **1997,** *9,* 2478-2484.

17..Annor-Gyamfi, J.; Jarrett, J.; Osazee, J.; Bialonska, D.; Whitted, C.; Palau, V.; Shilabin, A. Synthesis and biological activity of fused tetracyclic Pyrrolo[2,1-c][1,4] benzodiazepines. *Heliyon.* **2018,** *4,* 539-557.

18.Takahashi, Y.; Hirokawa, T.; Watanabe, M.; Fujita, S.; Ogura, Y.; Enomoto, M.; Shigefumi, K. First synthesis of BU-4664L. *Tetrahedron Lett.* **2015**, *56,*5670-5672.

19..Liu, Z.; Wang, P.; Chen, H.; Wold, E.; Tian, B.; Brasier, A.; Zhou, J. Drug Discovery Targeting Bromodomain-Containing Protein 4 (BRD4). *J. Med. Chem.* **2017,** *60*, 4533−4558.

20.Shafie, A.; Mohammadi-Khanaposhtani, M.; Asadi, M.; Rahimi, N.; Ranjbar, P. R.; Ghasemi, J. B.; Larijani,B.; Mahdavi,M.; Shafaroodi,H.; Dehpour,A.R. Novel fused 1,2,3-triazolo-benzodiazepine derivatives as potent anticonvulsant agents: design, synthesis, in vivo, and in silico evaluations. *Molecular Diversity.* **2019,** 1-11.

21.Griesbeck, A.; Kramer, W.; Lex, J. Diastereo- and Enantioselective Synthesis of Pyrrolo[1,4]benzodiazepines Through Decarboxylative Photocyclization. *Angew. Chem.-Int. Edit.* **2001,** *40*, 577-579.

22..Dong-Hui, L. Highly efficient and enantioselective biotransformations of racemic azetidine-2-carbonitriles and their synthetic applications. *J.Org. Chem.* **2009,** *16,* 6077–6082.

23.Cuny, G.; Bois-Choussy, M.; Zhu, J. Palladium- and Copper-Catalyzed Synthesis of Medium- and Large-Sized Ring-Fused Dihydroazaphenanthrenes and 1,4-Benzodiazepine-2,5-diones. Control of Reaction Pathway by Metal-Switching. *J. Am. Chem. Soc.* **2004,** *126*, 14475-84.

24.Webb, R. R.; Barker, P. L.; Baier, M.; Reynolds, M. E.; Robarge, K. D.; Blackburn, B. K.; Tischler, M. H.; Weese, K. J. Mono-N-alkylation of anthranilamides via quinazolinones. An efficient synthesis of G5598, a benzodiazepine dione gpIIbIIIa antagonist. *Tetrahedron Lett.* **1994,** *35*, 2113-2116.

25.Eleftheriadis, N.; Neochoritis, C. G.; Tsoleridis, C. A.; Stephanidou-Stephanatou, J.; Iakovidou-Kritsi, Z. One-pot microwave assisted synthesis of new 2-alkoxycarbonylmethylene-4-oxo-1,5-benzo-, naphtho-, and pyridodiazepines and assessment of their cytogenetic activity. *Eur. J. Med. Chem.* **2013,** *67*, 302-309.

26.Siddiqui, I.; Srivastava, A.; Singh, A.; Shamim, S.; Rai, P. $MoO_2Cl_2(DMF)_2$ Catalyzed Microwave Assisted Reductive Cyclization of Nitroaromatics into Dibenzodiazepines. *RSC Adv.* **2014,** *5,* 5256-5260.

27.Egle, M, B. Regioselective formation of six- and seven-membered ring by intramolecular Pd-catalyzed amination of N-allyl-anthranilamides. *J.Org. Chem*. **2004,** *17*, 5627-5630

28..Neukom,J.D. Synthesis of saturated 1,4-benzodiazepines via Pd-catalyzed carboamination reactions. *Org. Lett*. **2011,** *9,* 2196-2199

29.Grunewald,G.L. Effect of ring size or an additional heteroatom on the potency and selectivity of bicyclic benzylamine-type inhibitors of phenylethanolamine N-methyltransferase. *J. Med. Chem.* **1996**, *39*, 3539-3546.

30.Santagada, V.; Perissutti, E.; Fiorino, F.; Vivenzio, B.; Caliendo, G. Microwave enhanced solution synthesis of 1,4-benzodiazepin-5-ones. *Tetrahedron Lett*. **2001,** *42*, 2397-2400.

31.Huang, Y.; Khoury, K.; Chanas, T.; Domling, A. ChemInform Abstract: Multicomponent Synthesis of Diverse 1,4-Benzodiazepine Scaffolds. *Org. Lett*. **2012**, *14*, 5916-5919

32.Bruneau, P. Indazolinones, a new series of redox-active 5-lipoxygenase inhibitors with built-in selectivity and oral activity. *J.Med. Chem.* **1991,** *34*, 1028-1036.

33.Butin, A.; Nevolina, T.; Shcherbinin, V.; Trushkov, I.; Cheshkov, D.; Krapivin, G. ChemInform Abstract: Furan Ring Opening-Pyrrole Ring Closure: A New Synthetic Route to Aryl(heteroaryl)-Annulated Pyrrolo[1,2-a][1,4]diazepines. *Org. Biomol.Chem.* **2010,** *8*, 1416-1418.

34.Zhichkin, P.; Kesicki, E.; Treiberg, J.; Bourdon, L.; Ronsheim, M.; Ooi, H.; White, S.; Judkin, S; Fairfax, D. A Novel Highly Stereoselective Synthesis of 2,3-Disubstituted 3H-Quinazoline-4-one Derivatives. *Org. Lett*. **2007,** *9*, 1415-1418.

35.Clark, C.; Lin, C.; Sansom, R. Anticonvulsant activity of 2- and 3-aminobenzamides. *J. Med. Chem.***1986,** *29*, 1534-1537.

36.Hey, D.; Leonard, J.; Moynehan, T.; Rees, C. Internuclear cyclisation Part XVI. Abnormal reactions of diazonium salts from N-alkyl-2-amino-2?- and -4-methoxybenzanilides. A new dienone phenol rearrangement. *J. Chem. Soc.* **1961,** 232-238.

37.Thulasiram,H.V. Synthesis of deuterium-labeled derivatives of dimethylallyl diphosphate. *J. Org. Chem.* **2006**, *71,* 1739-1741.