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Palladium-Catalyzed [5+2] Oxidative Annulation of *N*-Arylhydrazones with Alkynes through C-H Activation to Synthesize Benzo[*d*][1,2]diazepines.

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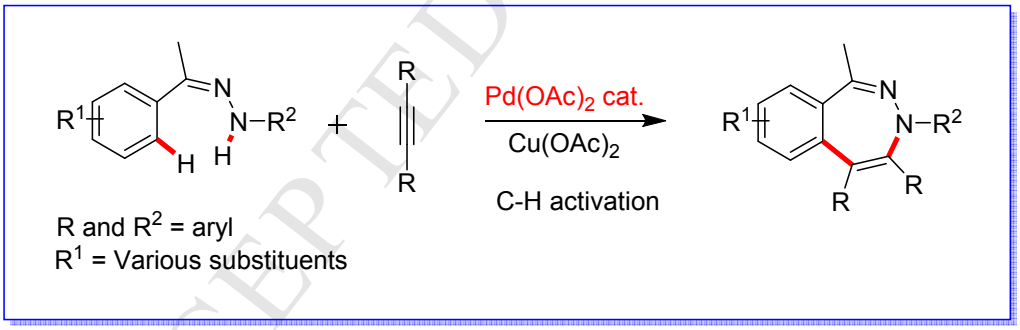
Abstract

An efficient and novel method using palladium catalyst for the synthesis of benzo[*d*][1,2]diazepines by [5+2] annulation of *N*-arylhydrazones with alkynes has been developed. This methodology undergoes through eight membered palladacycle serving as a backbone for the formation of C-C/C-N bond to provide benzodiazepine derivatives in moderate to good yield.

Keywords: Pd catalyst, [5+2] annulation, C-H activation, Alkyne, Palladacycle.

Graphical Abstract:



1. Introduction

In the light of history *N*-Heterocyclic compounds have emerged as an important motif to construct wide range of reactive intermediates, drugs, and bioactive molecules[1a-c]. Particularly, benzodiazepines have been recognized as versatile scaffold due to their promising biological and pharmacological activities[2a-e]. These moieties are found to be important tools in drug discovery as well as they are potent antitumor[3a-d], anti-HIV[4a,b], anti inflammatory[5a,b] and central nervous

system (CNS) agents[6] (Figure 1). Moreover, 1,2-diazapine analogs are important scaffolds in organic synthesis as it provides the pathway to synthesize other cyclic compounds[7].

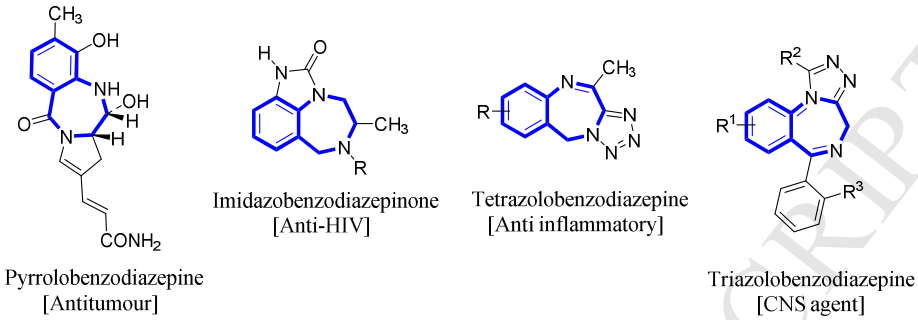


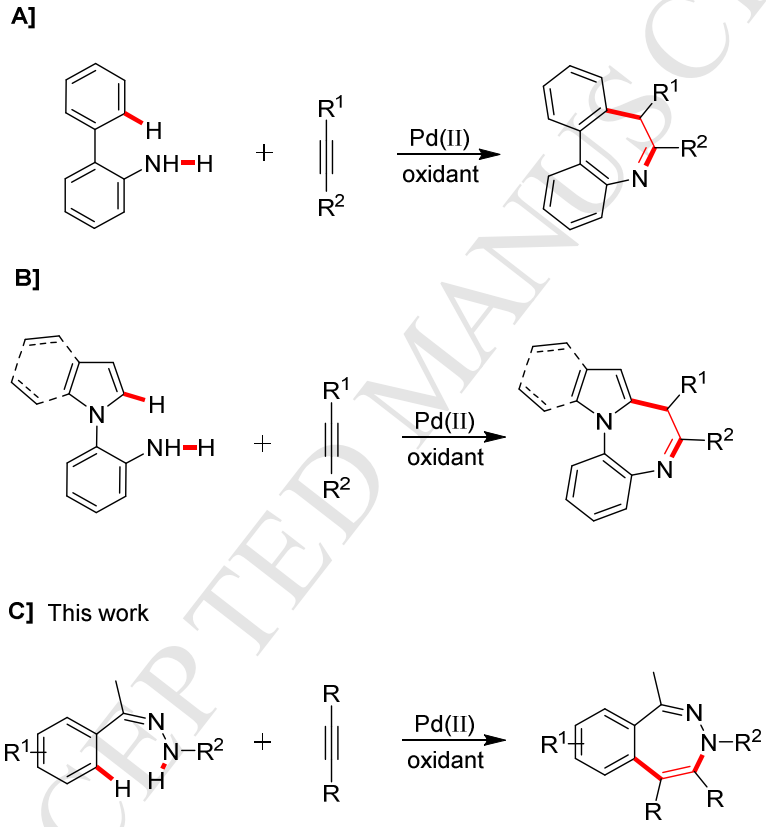
Figure 1 Potent biologically active Benzodiazepine core.

Over the past decades the synthetic community have witnessed the application of hydrazone in organic synthesis to synthesize plethora of compounds[8a-e]. More conveniently they have been emanated as powerful synthons for constructing diverge range of cyclic compounds through transition metal catalyzed or transition metal free reactions. Some of the reaction of hydrazone includes [3+2] cycloaddition with aryne or alkyne[9a-c], intramolecular cycloaddition with internal olefins[10a,b], transition metal catalyzed intra- and inter- molecular annulation[11a-d] etc. Being an effective precursor for the establishment of five and six membered *N*-heterocyclic compounds the ease of constructing higher member ring still remain unexplored[12a,b].

Metal catalyzed annulation involving C-H activation as a key step has gained lot of interest among researchers all over the world as it provide the elegant protocol to construct diverse range of cyclic compounds as it overshadows the traditional pattern which requires prefunctionalized substrate[13a-i]. The other credential to this strategy is that it offers the shortest possible route, improve atom economy of organic synthesis[14a-c].

In context to this metal catalyzed C-H activation proves to be an efficient protocol in [3+2] or [4+2] cycloaddition reaction to build up cyclic scaffolds which are difficult to synthesize by conventional method[15a-e]. However, very few reports has been documented of [5+2] cycloaddition to construct seven membered ring motif employing palladium catalyst. [5+2] oxidative annulation of o-arylanilines with alkynes to synthesize imine-containing dibenzo[*b*,*d*]azepines with high stereoselectivity through Pd(II) was disclosed by Luan and co-

workers[16] (Scheme 1A). Recently, Thikekar et al. described regioselective synthesis of 1,2-fused-indole diazepines through [5+2] annulation of o-indolo anilines with alkynes employing palladium catalyst[17] (Scheme 1B).. Leading from these examples and our continuing interest in transition metal catalyzed C-H activation[18a-f] herein we report the first Pd(II) catalyzed [5+2] annulations of *N*-arylhydrazones with alkyne to synthesize benzo[*d*][1,2]diazepines through C-H activation under mild condition (Scheme 1C). To the best of our knowledge, no previous synthesis of benzo[*d*][1,2]diazepines have been reported in the literature.



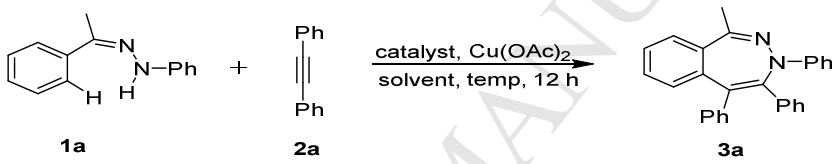
Scheme 1 Pd(II) catalyzed [5+2] annulation of alkynes.

2. Results and discussion

In order to obtain optimized reaction condition *N*-phenylhydrazone **1a** was treated with diphenyl acetylene **2a** in the presence of Pd(II) catalyst and Cu(II) as oxidant (Table 1). It was noted that no desired transformation was observed on employing Ru(II) catalyst under different solvent

system (Table 1, entries 1-3). However, switching over to $PdCl_2$ catalyst afforded the product **3a** in 22% yield in THF and slight increased in yield was recorded when solvent system was changed to 1,4-dioxane (Table 1, entries 4-5). Furthermore, investigation revealed that replacement of $PdCl_2$ with $Pd(OAc)_2$ and using 1,4-dioxane as solvent gave remarkable yield turning out to be optimized condition for the reaction: $Pd(OAc)_2$ catalyst (10 mol %), $Cu(OAc)_2$ oxidant (1 equiv.), at 100 °C in 1,4-dioxane for 12 h (Table 1, entry 6). Changing the solvent or altering the reaction temperature doesn't increase the yield (Table 1, entries 7-11). Moreover, reasonable yield of the expected product was obtained when $CuCl_2$ or dioxygen were used as oxidant and no yield was obtained when the reaction was carried out without catalyst (Table 1, entry 12-14).

Table 1 Optimization of the reaction conditions.[a]



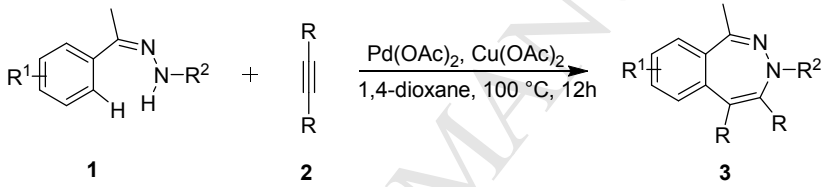
1a **2a** **3a**

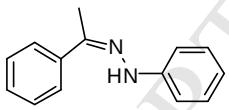
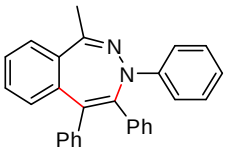
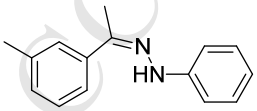
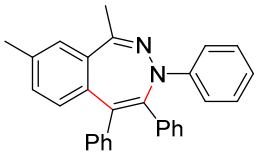
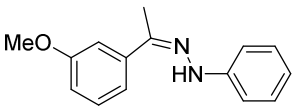
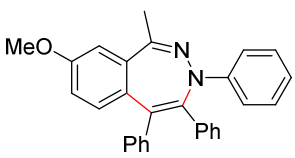
Entry	Catalyst	Solvent	Reaction Temperature (°C)	Yield of 3a[b] (%)
1	$[Ru(p\text{-cymene})Cl_2]_2$	THF	100	0
2	$[Ru(p\text{-cymene})Cl_2]_2$	MeCN	100	0
3	$[Ru(p\text{-cymene})Cl_2]_2$	1,4-dioxane	100	0
4	$PdCl_2$	THF	100	22
5	$PdCl_2$	1,4-dioxane	100	31
6	**$Pd(OAc)_2$**	**1,4-dioxane**	**100**	**76**
7	$Pd(OAc)_2$	THF	100	62
8	$Pd(OAc)_2$	Toluene	100	56
9	$Pd(OAc)_2$	DMF	100	48
10	$Pd(OAc)_2$	1,4-dioxane	rt	19
11	$Pd(OAc)_2$	1,4-dioxane	80	53
12[c]	$Pd(OAc)_2$	1,4-dioxane	100	44
13[d]	$Pd(OAc)_2$	1,4-dioxane	100	57
14	-------	1,4-dioxane	100	0

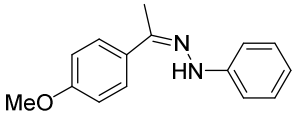
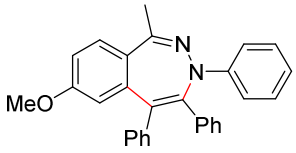
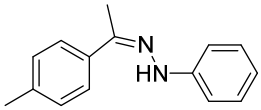
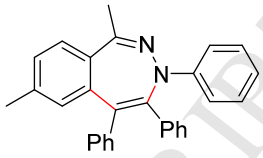
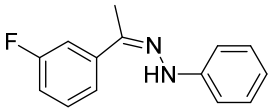
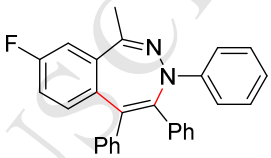
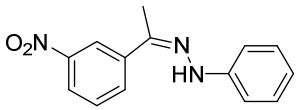
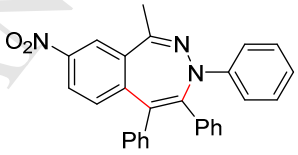
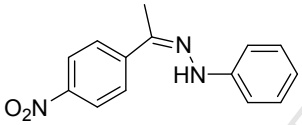
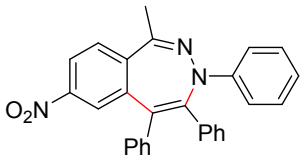
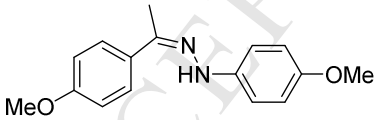
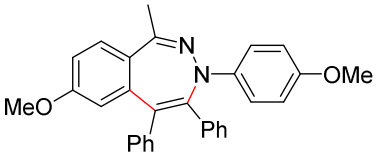
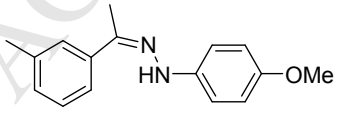
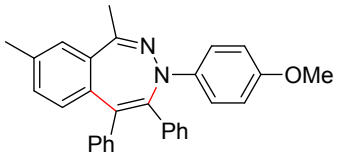
[a]Reaction conditions: **1a** (0.30 mmol, 1 equiv.), **2a** (0.45 mmol, 1.5 equiv.), catalyst (10 mol%), $Cu(OAc)_2$ (0.30 mmol, 1 equiv.), in 3.0 mL of solvent for 12 h at 100 °C. [b]isolated yield. [c] oxidant is $CuCl_2$. [d]oxidant is O_2.

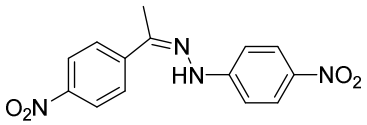
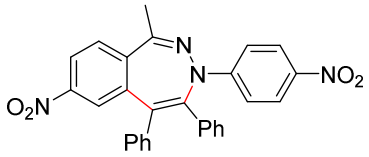
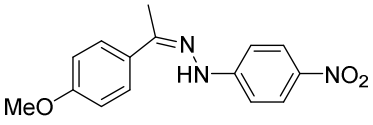
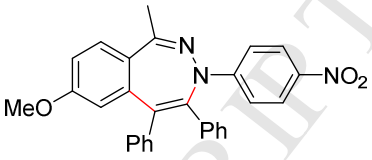
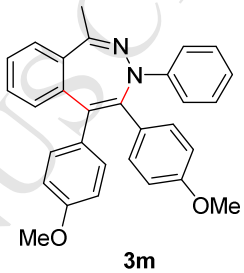
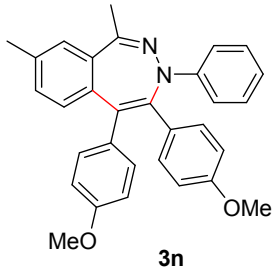
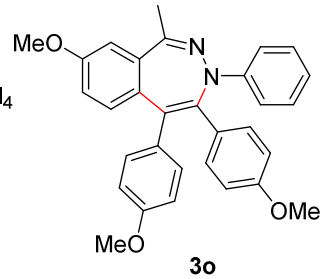
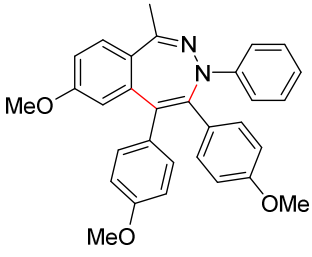
With the optimized condition in hand for unusual [5+2] annulation, the substrate scope of the reaction was explored by employing broad range of hydrazone (**1a-1l**) to react with symmetrical alkyne **2a**. It was observed that reaction proceeded smoothly to afford desired product in good to moderate yield with both electron donating or electron withdrawing groups (Table 2, entries 1-12). In particular, electron donating substituents at substrate **1** gave good yield as compared to electron withdrawing substituents. Moreover, high electronegative atom fluorine on aromatic ring was also well tolerated to give annulated product in 65% yield. The other symmetrical alkyne **2b** was also examined using hydrazone **1a**, **1b**, **1c** and **1d** which produce **3m**, **3n**, **3o** and **3p** product respectively.

Table 2 Substrate scope.

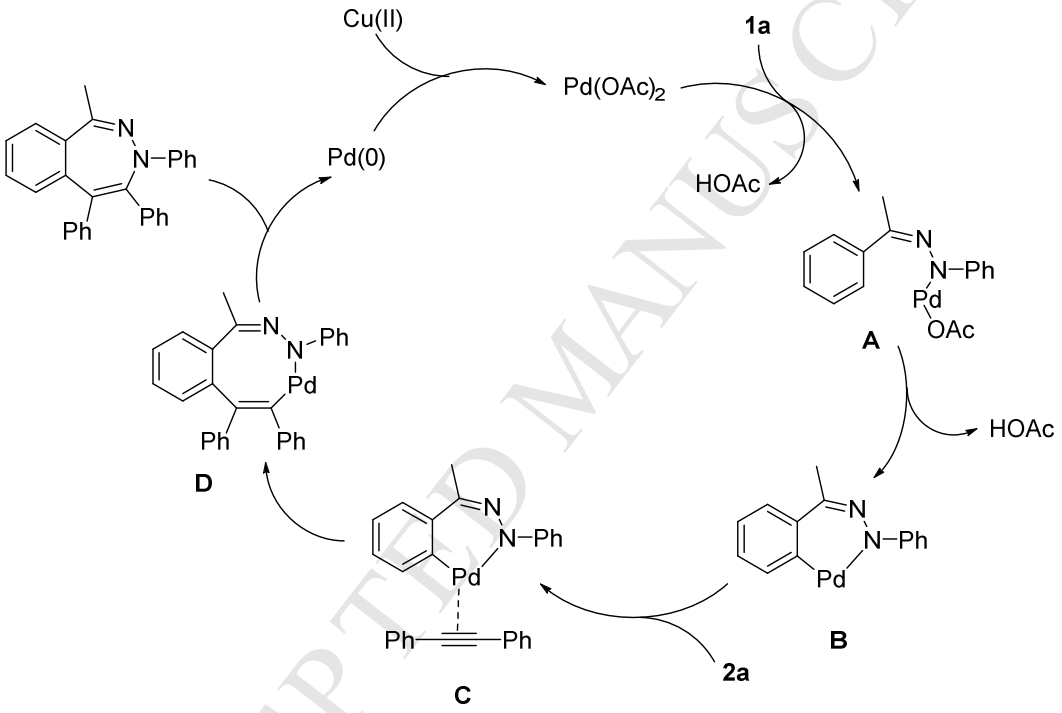


Entry	Hydrazone	Alkyne	Product	Yield(%)
1	 R^1= H, R^2= Ph **1a**	**2a** R = Ph	 **3a**	76
2	 R^1= 3-CH_3, R^2= Ph **1b**	**2a** R = Ph	 **3b**	68
3	 R^1= 3-OCH_3, R^2= Ph **1c**	**2a** R = Ph	 **3c**	74

4	 R^1= 4-OCH_3, R^2= Ph **1d**	**2a** R = Ph	 **3d**	70
5	 R^1= 4-CH_3, R^2= Ph **1e**	**2a** R = Ph	 **3e**	67
6	 R^1= 3-F, R^2= Ph **1f**	**2a** R = Ph	 **3f**	65
7	 R^1= 3-NO_2, R^2= Ph **1g**	**2a** R = Ph	 **3g**	60
8	 R^1= 4-NO_2, R^2= Ph **1h**	**2a** R = Ph	 **3h**	58
9	 R^1= 4-OCH_3, R^2= 4-(OMe)C_6H_4 **1i**	**2a** R = Ph	 **3i**	71
10	 R^1= 3-CH_3, R^2= 4-(OMe)C_6H_4 **1j**	**2a** R = Ph	 **3j**	66

11	 R^1= 4-NO_2, R^2= 4-$(NO_2)C_6H_4$ **1k**	**2a** R = Ph	 **3k**	56
12	 R^1= 4-OMe, R^2= 4-$(NO_2)C_6H_4$ **1l**	**2a** R = Ph	 **3l**	63
13	**1a**	**2b** R= 4-$(OMe)C_6H_4$	 **3m**	75
14	**1b**	**2b** R= 4-$(OMe)C_6H_4$	 **3n**	69
15	**1c**	**2b** R= 4-$(OMe)C_6H_4$	 **3o**	73
16	**1d**	**2b** R= 4-$(OMe)C_6H_4$	 **3p**	64

On the basis of above results and literature survey,[11b,16,17,19a,b] a possible mechanism is proposed in scheme **2**. Initially Pd-N adduct **A** is formed from the reaction of substrate **1a** and Pd(II) catalyst followed by C-H bond activation leading to the formation of six membered palladacycle **B**. Coordination of **2a** with palladacycle **B** resulting in the formation of Pd(II) intermediate **C**. Eight membered palladacycle **D** is formed by migratory insertion of **2a** into Pd-C bond of **C**. Finally, desired product **3a** is formed by C-N bond reductive elimination and Pd(II) catalyst is regenerated by $Cu(OAc)_2$ oxidant completing the catalytic cycle.



Scheme 2 Plausible mechanism for intermolecular [5+2] annulation.

3. Conclusion:

In conclusion, we have developed an efficient and effective method to synthesize benzo[*d*][1,2]diazepines by [5+2] annulation of *N*-arylhydrazones with alkyne via C–H functionalization with a catalytic amount of palladium(II) acetate in the presence of Cu(II) as oxidant. The reaction witnessed the formation of desired compound through eight membered palladacycle as well as tolerance of wide range of functional group.

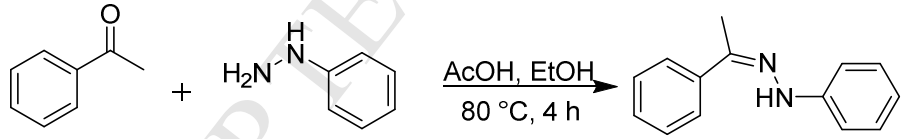
Further, investigation to construct heterocyclic compounds through C-H functionalization is going on in our laboratory.

4. Experimental Section:

4.1. General information:

All the reagents and solvents were purchased from Sigma-Aldrich and Merck and were used as recieved without any further purification. The synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR and elemental analysis. Melting points were determined in open capillaries on a Veego electronic apparatus VMP-D (Veego Instrument Corporation, Mumbai, India) and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz FT NMR, Avance III Bruker model spectrometer using DMSO-d_6 as a solvent and TMS as internal standard. ESI mass spectra were recorded on a Bruker Daltonics MicroTof. NMR chemical shifts are reported as parts per million (ppm) downfield from TMS. The splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Elemental analysis (C, H, N) were performed using a Heraeus CarloErba 1180 CHN analyzer (Hanau, Germany).

4.2 General method for the synthesis of *N*-aryl hydrazone:



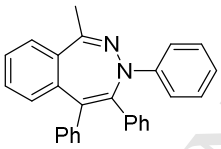
a **b** **1a**

To the mixture of acetophenone **A** (3 g, 25 mmol, 1 equiv.), phenyl hydrazine **B** (2.70 g, 25 mmol, 1 equiv.) in 15 mL of ethanol was added acetic acid in catalytic amount. The mixture was refluxed at 80 °C for 4 h and the progress of the reaction was monitored on TLC. The solvent was evaporated in vacuo and crude was recrystallized from ethanol which afforded **1a** and was used directly for the annulation reaction. All the *N*-arylhydrazone **1b-1l** were synthesized following the same procedure.

4.3 General Procedure To Prepare Benzo[*d*][1,2]diazepines (3) from *N*-Arylhydrazones (1):

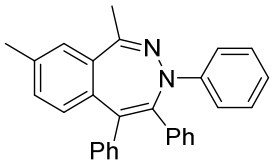
To an oven-dried flat-bottomed flask previously equipped with magnetic stirrer bar was charged with *N*-arylhydrazone **1** (63.0 mg, 0.30 mmol), $Pd(OAc)_2$ (6.7 mg, 10 mol%), $Cu(OAc)_2$ (54.4 mg, 0.30 mmol) in 1,4-dioxane (3.0 mL) followed by alkyne (80.2 mg, 0.45 mmol). The reaction mixture was stirred at 100 °C for 12 h. Upon completion of reaction the mixture was cooled to room temperature, poured into brine, and extracted with EtOAc. The combined extracts were dried over $MgSO_4$ and filtered through pad of Celite eluting with ethyl acetate. The filtrate was concentrated under reduced pressure and was purified by column chromatography (EtOAc/hexane) on silica gel to afford the benzo[*d*][1,2]diazepines **3**.

4.3.1 1-Methyl-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3a).



Yield: 76 %. yellow solid; mp: 164-166 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.53 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.40-7.45 (m, 8H), 7.24-7.26 (m, 6H), 7.10-7.14 (m, 3H), 2.56 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 143.51, 142.28, 137.26, 136.62, 136.34, 131.25, 130.02, 129.74, 129.28, 129.18, 129.03, 128.85, 128.83, 128.78, 126.45, 126.35, 126.27, 121.78, 121.33, 120.34, 20.54. Anal. Calcd. For $C_{28}H_{22}N_2$: C: 87.01; H: 5.74; N: 7.25. Found: C: 87.05; H: 5.72; N: 7.21. MS-EI (*m/z*) 386.63.

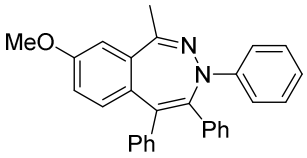
4.3.2 1,8-Dimethyl-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3b).



Yield: 68 %. yellow solid; mp: 143-145 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ, 7.80 (d, *J* = 6.1 Hz, 1H), 7.44-7.46 (m, 6H), 7.29-7.31 (m, 7H), 7.20 (dd, *J* = 7.2 , 2.4 Hz, 1H), 7.13-7.15 (m, 3H), 2.57 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.7, 143.76, 143.51, 137.83, 136.61, 136.34, 133.48, 132.59, 130.03, 129.75, 129.29, 129.14, 129.01, 128.85, 128.83, 128.77,

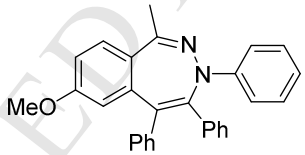
126.47, 126.36, 122.38, 121.78, 120.36, 21.23, 20.57. Anal. Calcd. For $C_{29}H_{24}N_2$: C: 86.97; H: 6.04; N: 6.99. Found: C: 86.11; H: 6.17; N: 6.81. MS-EI (*m/z*) 400.34.

4.3.3 8-Methoxy-1-methyl-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3c).



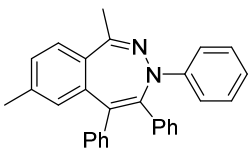
Yield: 74 %. yellow solid; mp: 155-158 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, *J* = 6.1 Hz, 1H), 7.44-7.46 (m, 6H), 7.24-7.26 (m, 6H), 7.10- 7.13 (m, 4H), 6.91 (dd, *J* = 6.8 , 1.9 Hz, 1H), 3.79 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 157.26, 146.20, 143.51, 136.61, 136.34, 132.21, 131.65, 130.02, 129.78, 129.18, 129.28, 129.02, 128.85, 128.83, 126.47, 126.33, 121.78, 120.33, 115.16, 107.35, 56.05, 20.55. Anal. Calcd. For $C_{29}H_{24}N_2O$: C: 83.63; H: 5.81; N: 6.73; O: 3.84. Found: C: 83.34; H: 5.87; N: 6.83; O: 3.85. MS-EI (*m/z*) 416.46.

4.3.4 7-Methoxy-1-methyl-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3d).



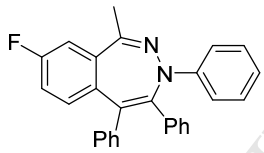
Yield: 70 %. yellow solid; mp: 187-191 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.44-7.46 (m, 7H), 7.36 (m, 1H), 7.26-7.29 (m, 6H), 7.13-7.16 (m, 3H), 6.89 (dd, *J* = 7.2, 2.4 Hz, 1H), 3.80 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.01, 161.01, 143.56, 138.97, 138.74, 136.65, 136.32, 130.01, 129.73, 129.28, 129.16, 129.02, 128.86, 128.84, 126.49, 126.36, 123.27, 121.36, 120.71, 115.60, 114.24, 56.02, 20.53. Anal. Calcd. For $C_{29}H_{24}N_2O$: C: 83.63; H: 5.81; N: 6.73; O: 3.84. Found: C: 83.65; H: 5.81; N: 6.80; O: 3.62. MS-EI (*m/z*) 416.55.

4.3.5 1,7-Dimethyl-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3e).



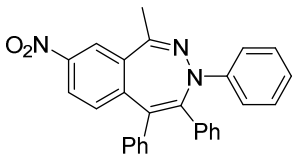
Yield: 67 %. yellow solid; mp: 102-105 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63 (m, 1H) 7.49 (d, *J* = 6.1 Hz, 1H), 7.44-7.46 (m, 6H), 7.26-7.29 (m, 6H), 7.13-7.16 (m, 4H), 2.56 (s, 3H),2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.87, 143.51, 142.23, 139.33, 137.12, 136.65, 136.31, 132.50, 130.04, 129.74, 129.25, 129.16, 129.02, 128.85, 128.83, 126.50, 126.32, 125.64, 121.51, 121.32, 120.68, 21.23, 20.56. Anal. Calcd. For $C_{29}H_{24}N_2$: C: 86.97; H: 6.04; N: 6.99. Found: C: 86.95; H: 6.01; N: 6.85. MS-EI (*m/z*) 400.64.

4.3.6 8-Fluoro-1-methyl-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3f).



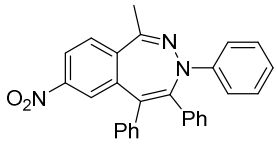
Yield: 65 %. yellow solid; mp: 194-197 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.86 (m, 1H), 7.44-7.46 (m, 6H), 7.26-7.31 (m, 7H), 7.13-7.18 (m, 4H), 2.59 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.12, 163.24, 144.52, 143.51, 136.64, 136.32, 133.33, 132.58, 130.02, 129.71, 129.28, 129.13, 129.03, 128.83, 128.80, 126.46, 126.33, 121.79, 120.34, 114.61, 107.97, 20.54. Anal. Calcd. For $C_{28}H_{21}FN_2$: C: 83.14; H: 5.23; F: 4.70; N: 6.93. Found: C: 83.25; H: 5.21; F: 4.67; N: 6.86. MS-EI (*m/z*) 404.43.

4.3.7 1-Methyl-8-nitro-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3g).



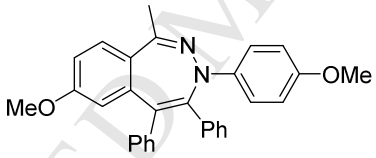
Yield: 60 %. yellow solid; mp: 206-208 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05 (m, 1H), 7.94 (dd, *J* = 6.8, 1.9 Hz, 1H), 7.63 (d, *J* = 6.0 Hz, 1H), 7.42-7.43 (m, 6H), 7.30-7.32 (m, 6H), 7.10-7.15 (m, 3H), 2.60 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.51, 144.31, 143.52, 143.50, 140.36, 136.65, 136.32, 130.04, 129.77, 129.28, 129.13, 129.11, 129.02, 128.87, 128.82, 126.47, 126.38, 124.91, 121.74, 120.34, 116.56, 20.54. Anal. Calcd. For $C_{28}H_{21}N_3O_2$: C: 77.94; H: 4.91; N: 9.74; O: 7.42. Found: C: 77.90; H: 4.81; N: 9.80; O: 7.39. MS-EI (*m/z*) 431.61.

4.3.8 1-Methyl-7-nitro-3,4,5-triphenyl-3*H*-benzo[*d*][1,2]diazepine (3h).



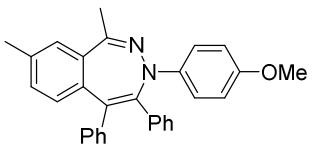
Yield: 58 %. yellow solid; mp: 137-140 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.57 (m, 1H), 8.05 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.81 (d, *J* = 6.1 Hz, 1H), 7.41-7.44 (m, 6H), 7.26-7.29 (m, 6H), 7.12-7.14 (m, 3H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.02, 147.55, 144.09, 143.52, 140.71, 136.65, 136.32, 130.02, 129.76, 129.28, 129.14, 129.03, 128.85, 128.82, 126.47, 126.32, 125.78, 121.39, 121.34, 120.72, 119.54, 20.55. Anal. Calcd. For $C_{28}H_{21}N_3O_2$: C: 77.94; H: 4.91; N: 9.74; O: 7.42. Found: C: 77.89; H: 4.84; N: 9.74; O: 7.49. MS-EI (*m/z*) 431.44.

4.3.9 7-Methoxy-3-(4-methoxyphenyl)-1-methyl-4,5-diphenyl-3*H*-benzo[*d*][1,2]diazepine (3i).



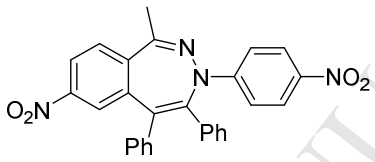
Yield: 71 %. yellow solid; mp: 166-167 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.48 (m, 1H), 7.39-7.41 (m, 4H), 7.25-7.28 (m, 6H), 7.14 (m, 2H), 7.08 (m, 2H), 6.89 (dd, *J* = 7.2, 2.4 Hz, 1H), 6.77 (m, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 2.59 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.11, 161.01, 159.47, 138.99, 138.74, 136.91, 136.67, 136.33, 130.02, 129.74, 129.24, 129.13, 129.02, 128.37, 126.34, 123.27, 121.35, 120.74, 115.57, 114.23, 113.81, 56.01, 20.54. Anal. Calcd. For $C_{30}H_{26}N_2O_2$: C: 80.69; H: 5.87; N: 6.27; O: 7.17. Found: C: 80.65; H: 5.81; N: 6.24; O: 7.11. MS-EI (*m/z*) 446.58.

4.3.10 3-(4-Methoxyphenyl)-1,8-dimethyl-4,5-diphenyl-3*H*-benzo[*d*][1,2]diazepine (3j).



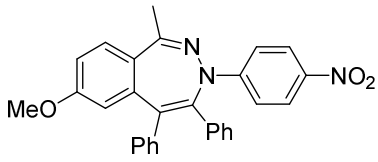
Yield: 66 %. yellow solid; mp: 89-92 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 (d, *J* = 6.1 Hz, 1H), 7.46 (m, 4H), 7.28-7.30 (m, 7H), 7.14-7.18 (m, 3H), 7.04 (m, 2H), 3.78 (s, 3H), 2.57 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.42, 159.48, 143.74, 137.83,136.94, 136.62, 136.33, 133.46, 132.58, 130.02, 129.75, 129.28, 129.13, 129.02, 128.79, 128.35, 126.37, 122.38, 121.77, 120.32, 113.82, 56.01, 21.22, 20.54. Anal. Calcd. For $C_{30}H_{26}N_2O$: C: 83.69; H: 6.09; N: 6.51; O: 3.72. Found: C: 83.64; H: 6.04; N: 6.50; O: 3.72. MS-EI (*m/z*) 430.58.

4.3.11 1-Methyl-7-nitro-3-(4-nitrophenyl)-4,5-diphenyl-3*H*-benzo[*d*][1,2]diazepine (3k).



Yield: 56 %. yellow solid; mp: 215-217 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (m, 1H), 8.34 (m, 2H), 8.05 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.82 (d, *J* = 6.1 Hz, 1H), 7.54 (m, 2H), 7.45 (m, 4H), 7.26-7.28 (m, 4H), 7.13-7.15 (m 2H), 2.60 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.01, 148.47, 147.55, 147.13, 144.09, 140.71, 136.64, 136.32, 130.02, 129.75, 129.26, 129.14, 129.03, 127.19, 126.32, 125.78, 123.64, 121.39, 121.34, 120.72, 119.54, 20.54. Anal. Calcd. For $C_{28}H_{20}N_4O_4$: C: 70.58; H: 4.23; N: 11.76; O: 13.43. Found: C: 70.51; H: 4.22; N: 11.70; O: 13.49. MS-EI (*m/z*) 476.57.

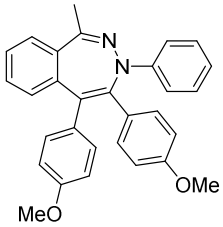
4.3.12 7-Methoxy-1-methyl-3-(4-nitrophenyl)-4,5-diphenyl-3*H*-benzo[*d*][1,2]diazepine (3l).



Yield: 63 %. yellow solid; mp: 176-178 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (m, 2H), 7.58 (m 2H), 7.51 (d, *J* = 6.1 Hz, 1H), 7.40-7.42 (m, 4H), 7.26-7.27 (m, 4H), 7.13-7.14 (m, 2H), 6.90 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.79 (m, 1H), 3.76 (s, 3H), 2.60 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.24, 161.01, 148.47, 147.13, 138.99, 138.74, 136.67, 136.33, 130.02, 129.74,

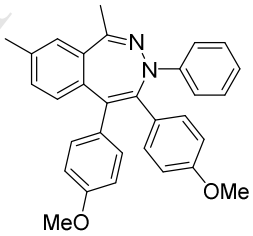
129.28, 129.13, 129.02, 127.17, 126.34, 123.67, 123.26, 121.35, 120.74, 115.57, 114.23, 56.01, 20.54. Anal. Calcd. For $C_{29}H_{23}N_3O_3$: C: 75.47; H: 5.02; N: 9.10; O: 10.40. Found: C: 75.44; H: 5.07; N: 9.12; O: 10.28. MS-EI (*m/z*) 461.47.

4.3.13 4,5-Bis(4-methoxyphenyl)-1-methyl-3-phenyl-3*H*-benzo[*d*][1,2]diazepine (3m).



Yield: 75 %. yellow solid; mp: 110-113 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (d, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 6.8 Hz, 1H), 7.43-7.45 (m, 8H), 7.28 (m, 2H), 7.10 (m, 1H), 6.87-6.89 (m, 4H), 3.78 (s, 6H), 2.55 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ164.33, 159.53, 159.27, 143.54, 142.29, 137.24, 131.92, 131.26, 130.32, 130.21, 129.31, 128.85, 128.83, 128.78, 126.47, 126.28, 121.76, 121.33, 120.37, 114.51, 114.27, 56.02, 20.54. Anal. Calcd. For $C_{30}H_{26}N_2O_2$: C: 80.69; H: 5.87; N: 6.27; O: 7.17. Found: C: 80.65; H: 5.88; N: 6.20; O: 7.25. MS-EI (*m/z*) 446.48.

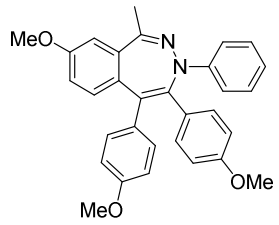
4.3.14 4,5-Bis(4-methoxyphenyl)-1,8-dimethyl-3-phenyl-3*H*-benzo[*d*][1,2]diazepine (3n).



Yield: 69 %. yellow solid; mp: 211-213 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (d, *J* = 6.1 Hz, 1H), 7.43-7.44 (m, 6H), 7.30 (m, 1H), 7.26 (m, 2H), 7.19 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.09 (m, 1H), 6.87-6.89 (m, 4H), 3.79-3.80 (s, 6H), 2.59 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.82, 159.51, 159.26, 143.78, 143.52, 137.80, 133.46, 132.58, 131.93, 130.35, 130.27, 129.30, 128.82, 128.80, 128.78, 126.50, 122.38, 121.78, 120.36, 114.51, 114.21, 56.03,

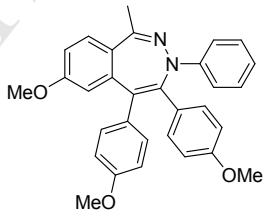
21.20, 20.54. Anal. Calcd. For $C_{31}H_{28}N_2O_2$: C: 80.84; H: 6.13; N: 6.08; O: 6.95. Found: C: 80.80; H: 6.13; N: 6.06; O: 6.89. MS-EI (*m/z*) 460.55.

4.3.15 8-Methoxy-4,5-bis(4-methoxyphenyl)-1-methyl-3-phenyl-3*H*-benzo[*d*][1,2]diazepine (3o).



Yield: 73 %. yellow solid; mp: 199-201 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.69 (d, *J* = 6.1 Hz, 1H), 7.42 (m, 6H), 7.26 (m, 2H), 7.05-7.07 (m, 2H), 6.88-6.90 (m, 5H), 3.79-3.80 (s, 9H), 2.57 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.15, 159.50, 159.25, 157.21, 146.13, 143.55, 132.26, 131.90, 131.62, 130.31, 130.24, 129.33, 128.84, 128.81, 126.46, 121.76, 120.34, 115.18, 114.49, 114.21, 107.34, 56.02, 20.54. Anal. Calcd. For $C_{31}H_{28}N_2O_3$: C: 78.13; H: 5.92; N: 5.88; O: 10.07. Found: C: 78.22; H: 5.84; N: 5.90; O: 10.02. MS-EI (*m/z*) 476.64.

4.3.16 7-Methoxy-4,5-bis(4-methoxyphenyl)-1-methyl-3-phenyl-3*H*-benzo[*d*][1,2]diazepine (3p).



Yield: 64 %. yellow solid; mp: 184-187 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.43-7.44 (m, 7H), 7.35 (m, 1H), 7.26 (m, 2H), 7.09 (m, 1H), 6.87-6.89 (m, 5H), 3.79-3.80 (s, 9H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.78, 161.01, 159.51, 159.26, 143.56, 138.97, 138.73, 131.94, 130.31, 130.25, 129.29, 128.87, 128.85, 126.45, 123.28, 121.36, 120.71, 115.58, 114.51, 114.24, 56.02, 20.54. Anal. Calcd. For $C_{31}H_{28}N_2O_3$: C: 78.13; H: 5.92; N: 5.88; O: 10.07. Found: C: 78.08; H: 5.93; N: 5.86; O: 10.08. MS-EI (*m/z*) 476.51.

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