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Gold-Catalyzed Tandem Dual Heterocyclization of Enynones with 1,3,5-Triazines: Bicyclic Furan Synthesis and Mechanistic Insights

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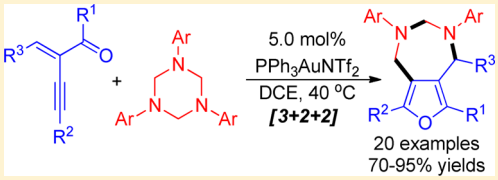
Supporting Information

ABSTRACT: A general and unprecedented gold-catalyzed tandem dual heterocyclization reaction of enynones with 1,3,5-triazines has been developed, which provides bicyclic fused furans in high to excellent yields under mild reaction conditions. In addition, mechanistic studies indicate that the reaction goes through a stepwise [3+2+2]-cycloaddition of furanyl gold intermediate, which is generated from gold-catalyzed cyclization of enynone, with two molecules of formaldimines derived in situ from 1,3,5-triazine, instead of formal [4+3]-cycloaddition.

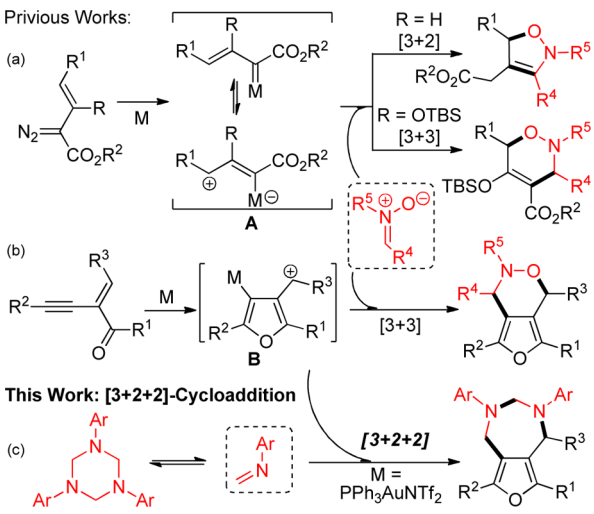


INTRODUCTION

Metal carbene, as a highly reactive species, has shown broad applications in modern synthetic organic chemistry.[1] Among these, the catalytically generated vinylcarbenes serve as 1,3-dipoles in various types of [3+*n*]-cycloadditions or annulations, which become a powerful method for the direct construction of heterocycles with structural diversity,[2] including [3+2]-,[3] [3+3]-,[4] [4+4]-,[5] and [3+5]-cycloadditions.[6] For example, [3+2]- and [3+3]-cycloadditions of vinylcarbene intermediates (Scheme 1, **A**) with nitrones have been well explored by Davies[3] and Doyle,[4] respectively (Scheme 1a). Subsequently, the expansion in this context with 1,5-dipole for [3+5]-cycloadditions is reported by Yoo recently.[6] On the other hand, the intermediate **B**, formed in situ from gold-catalyzed cyclization of enynone,[7] has emerged as a complementary reactive 1,3-dipole species since the early work reported by Larock et al. in 2004.[8] Extensive investigation in this context is disclosed by J. Zhang[9] and others,[10] which represents a general and atom-economic access to highly substituted furans. For example, [3+3]-cycloaddition of the in situ formed electrophilic intermediate **B** with nitrone directly provides the bicyclic fused furans with excellent enantioselectivity (Scheme 1b).[9a,b] Tremendous efforts have been concentrated on the discovery of novel cycloaddition reactions involving trapping of these active intermediates (**A** and **B**) with a broad spectrum of compatible dipolar adducts.[2,7] However, most of these studies focus on the two-component reactions, and so far only limited examples have been developed in the pattern of [3+*m*+*n*]-cycloadditions.[11] The development of efficient and selective annulation that involves trapping of these active dipoles with two molecular of dipolarophiles remains a challenge.

1,3,5-Triazine, which is conveniently prepared through the condensation of paraformaldehyde with aromatic amines, is well-known as the corresponding *N*-aryl formaldimine precursor.[12] Recently, this compound was used in hydroaminomethylation and Mannich addition by Krische[13] and Feng,[14] respectively. Unlike these works via addition with formaldimine, a novel gold-catalyzed formal [4+1]/[4+3]-cycloaddition with diazo ester has been reported by Sun and co-workers, in which the triazine is directly employed for the annulations as the nucleophile.[15] Inspired by these works and as a continuation of our research interests in cycloaddition reactions,[16] herein we report an unprecedented Au-catalyzed [3+2+2] cycloaddition of enynones with 1,3,5-triazines, which goes through trapping the reactive 1,3-dipole intermediate **B** by

Scheme 1. Cycloaddition Patterns Involving Reactive 1,3-Dipoles



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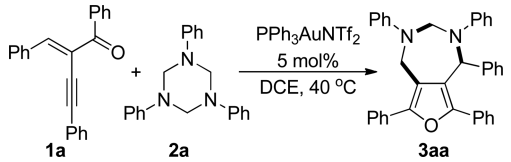
two molecules of formaldimines, which is in situ generated from 1,3,5-triazine (Scheme 1c).

RESULTS AND DISCUSSION

Initially, we employed 2-(1-alkynyl)-2-alken-1-one (**1a**) and 1,3,5-triazine (**2a**) as model substrates for the condition optimization (Table 1). Fortunately, in the presence of

Table 1. Condition Optimization[a]

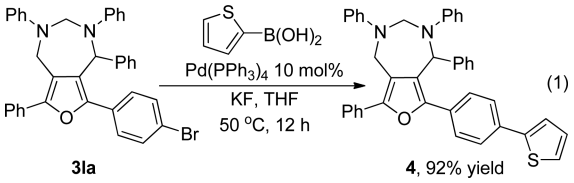


entry	deviation from the optimal reaction conditions	yield (%)[b]
1		88
2	60 °C	86
3	25 °C	83
4	5.0 mol % $AuCl_3$	40
5	1.0 mol % $Rh_2(OAc)_4$	nr[c]
6	5.0 mol % $PdCl_2$	trace[c]
7	5.0 mol % $Cu(OTf)_2$	nr[c]
8	1.0 mol % PPh_3AuNTf_2	75

[a]Optimal reaction conditions: **1a** (0.20 mmol), **2a** (0.24 mmol), and PPh_3AuNTf_2 (5.0 mol %) in DCE (2.0 mL) at 40 °C for 10 h. [b]Isolated yield. [c]Most of the starting materials were recovered. DCE = 1,2-dichloroethane; nr = no reaction.

PPh_3AuNTf_2 (5.0 mol %), the desired product **3aa** was obtained in 88% yield when the reaction was performed in DCE at 40 °C for 10 h (entry 1). Investigation of the reaction temperature could not enhance the yields (entries 2 and 3). Various metal catalysts were also investigated, including $AuCl_3$, $Rh_2(OAc)_4$, $PdCl_2$, and $Cu(OTf)_2$; however, only inferior results were obtained (entries 4–7). A reduced catalyst loading resulted in lower yield (entry 8, 1.0 mol %, 75% yield). The furo[3,4-*e*][1,3]diazepine framework of the obtained product **3aa** is confirmed by single-crystal X-ray diffraction analysis (Figure 1), and the configurations of other compounds were tentatively assigned by analogy.[17]

With the optimal reaction conditions in hand, the scope of enynones was explored (Table 2). All other tested enynone derivatives were well tolerated under these conditions and produced the bicyclic fused furans in 84%–95% yields. Either aryl ketones (R^1 = Ph, **1a**–**1c**) or alkyl ketones (R^1 = Me, **1d**–**1g**) gave the addition products in high yields (>84%, **3aa**–**3ga**). In addition, the electronic property of aryl groups (either R^2 or R^3) on the enynones has little impact on the yield of the transformation, and comparably high yields were obtained for both electron-donating and electron-withdrawing group substituted enynones (**3ha**–**3la**). In addition, the bromo-substituted product **3la** could be subjected to the Suzuki coupling reaction and lead to the corresponding derivative in 92% yield (eq 1).



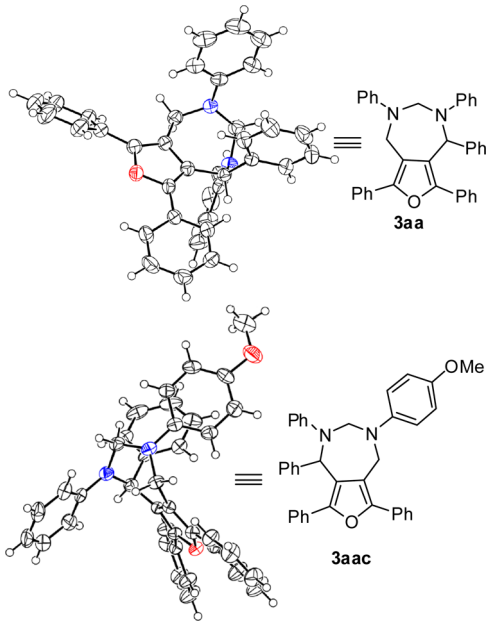
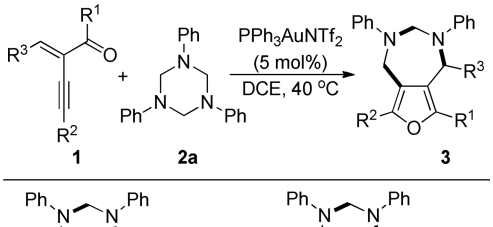
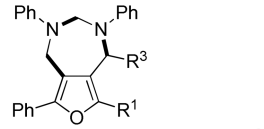


Figure 1. X-ray crystal structures of **3aa** and **3aac** (displacement ellipsoids are drawn at the 50% probability level).

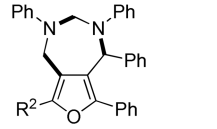
Table 2. Substrate Scope of Enynones 1[a,b]



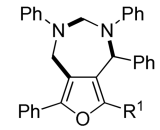


R^1 = Ph
R^3 = Ph, **3aa**, 88%
R^3 = 4-ClC_6H_4, **3ba**, 85%
R^3 = 4-BrC_6H_4, **3ca**, 84%
R^3 = 4-$NO_2C_6H_4$, **3da**, 80%

R^1 = Me
R^3 = Ph, **3ea**, 92%
R^3 = 4-MeC_6H_4, **3fa**, 84%
R^3 = 4-ClC_6H_4, **3ga**, 89%
R^3 = 4-BrC_6H_4, **3ha**, 93%



R^2 = 4-MeC_6H_4, **3ia**, 86%
R^2 = 4-$MeOC_6H_4$, **3ja**, 95%
R^2 = 4-ClC_6H_4, **3ka**, 85%



R^1 = 4-$MeOC_6H_4$, **3la**, 94%
R^1 = 4-BrC_6H_4, **3ma**, 84%

[a]Reaction conditions: **1** (0.20 mmol), **2** (0.24 mmol), and PPh_3AuNTf_2 (5.0 mol %) in DCE (2.0 mL) at 40 °C for 10 h. [b]Isolated yields.

Subsequently, to further investigate the potential of this catalytic system, 1,3,5-triazines **2** derived from substituted aromatic amines were employed (Table 3). To our delight, there is little effect of the substitution on the reaction, and all of these triazines performed smoothly under the optimized conditions to give the cycloaddition products in high to excellent yields (entries 1–7). Additionally, the reaction was found to perform well on a gram-scale, and 1.47 g of pure product **3ac** was obtained in 85% yields (note c). However, for 1,3,5-triazine derived from *m*-methoxyaniline, due to the inherent lower stability of this 1,3,5-triazine, only the corresponding formal N–H insertion product **5** was isolated in 73% yield in the reaction with *m*-methoxyaniline (entry 8).

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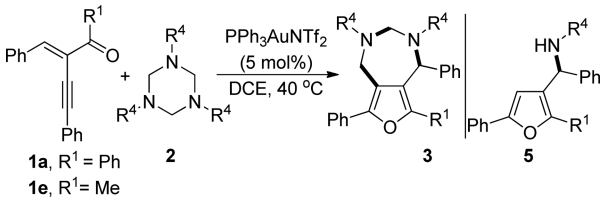
Table 3. Substrate Scope of 1,3,5-Triazines 2[a,b]

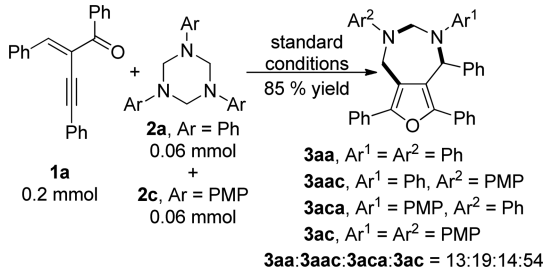


entry	1	R_4	product	yield (%)
1	**1a**	4-MeC_6H_4	**3ab**	85
2[c]	**1a**	4-$MeOC_6H_4$	**3ac**	85
3	**1a**	4-ClC_6H_4	**3ad**	92
4	**1a**	4-BrC_6H_4	**3ae**	94
5	**1a**	4-$CF_3C_6H_4$	**3af**	80
6	**1e**	2-$MeOC_6H_4$	**3eg**	70
7	**1a**	Bn	**3ah**	85
8	**1a**	3-$MeOC_6H_4$	**5**[d]	73

[a]Reaction conditions: **1** (0.20 mmol), **2** (0.24 mmol), and PPh_3AuNTf_2 (5.0 mol %) in DCE (2.0 mL) at 40 °C for 10 h. [b]Isolated yields. [c]The reaction was carried out on the 3.0 mmol scale with 2.0 mol % of PPh_3AuNTf_2. [d]The product **5** was formed with *m*-methoxyaniline derived from the decomposing of the corresponding 1,3,5-triazine.

To gain insight into the details of the reaction mechanism, cross-cycloaddition reaction of **1a** with **2a** and **2c** was conducted (Scheme 2). Notably, different from Sun's protocol

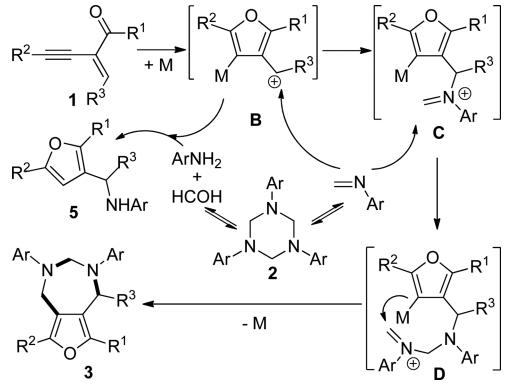
Scheme 2. Cross-Cycloaddition Reaction



in gold-catalyzed formal [4+1]/[4+3]-cycloadditions of metal carbene with triazine,[15] two cross-cycloaddition products were isolated and identified, and one of them, **3aac**, was confirmed by single-crystal X-ray diffraction analysis (Figure 1).[17] On the other hand, control reaction with **2a** and **2c** under standard conditions in the absence of enynone **1a** was performed, and some adducts were formed. However, these compounds were inert to give any cycloaddition product with enynone **1a** under standard conditions, and only decomposition of **1a** was observed (see Figure S1).[18]

On the basis of these results, the proposed catalytic cycle for the tandem dual heterocyclization reaction of enynones with 1,3,5-triazines is shown in Scheme 3. The furanyl gold intermediate **B**, which is generated from gold-catalyzed cyclization of enynone,[8−10] is intercepted by the formaldimine derived in situ from 1,3,5-triazine to give intermediate **C**, and followed by the second addition with another molecule of formaldimine to form **D**. In this reaction, neither 1,5-cyclization product with intermediate **C** nor 2,7-cyclization product with intermediate **D** is observed in this reaction,[9d] and the catalytic cycle is completed via a 1,7-cyclization to produce the [3+2+2]-cycloaddition product **3** and regenerate the gold catalyst. This reaction pathway is also consistent with the results in the cross-

Scheme 3. Proposed Reaction Mechanism



cycloaddition reaction, in which **3ac** was formed in 54% ratio in comparison with the other three products because the nucleophilic formaldimine derived from **2c** shows the priority to addition with both **B** and **C** in the tandem transformations. Also, compound **5** is formed with intermediate **B** in the presence of amine. However, rigorous studies are needed to unambiguously establish the reaction mechanism.

CONCLUSIONS

We have developed a novel gold-catalyzed tandem dual heterocyclization reaction of enynones with 1,3,5-triazines, which provides furo[3,4-*e*][1,3]diazepine derivatives in high to excellent yields under mild reaction conditions. The mechanistic studies indicate that the formaldimine derived in situ from 1,3,5-triazine, instead of 1,3,5-triazine itself, is involved in the cycloaddition. These results represent an unprecedented [3+2+2]-cycloaddition of gold-catalyzed enynone transformation terminated with 1,7-cyclization. Also, neither 1,5-cyclization nor 2,7-cyclization is observed in this reaction. Efforts to expand the scope of the reaction and better understand the mechanism are ongoing in our laboratory.[19]

EXPERIMENTAL SECTION

General. All reactions were carried out in oven-dried glassware. Solvents were dried and degassed by the standard methods. Flash column chromatography was performed using silica gel (300−400 mesh). Analytical thin-layer chromatography was performed using glass plates precoated with 200−300 mesh silica gel impregnated with a fluorescent indicator (254 nm). ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 MHz spectrometer; chemical shifts are reported in ppm with the solvent signal as reference, and coupling constants (*J*) are given in Hertz. The peak information is described as br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (ESI or CI Source). Enynones **1a−1c**,[8a,20] **1d−1g**,[21] **1h−1l**,[8a,20] and 1,3,5-triazines **2**[15] were prepared according to the reported literatures.

General Procedure for the Synthesis of Triazine Compounds 2.[15] To a 100 mL oven-dried flask containing a magnetic stirring bar were added aniline (30 mmol), paraformaldehyde (2.97g, 33 mmol), and toluene (50 mL) in sequence, and the reaction mixture was stirred under refluxing for 2 h. The solvent then was concentrated under reduced pressure (about 5 mL of solvent left), and the solid was precipitated out from the mixture, which was collected by filtration, followed by washing with *n*-hexane, and dried in vacuo to give pure 1,3,5-triazines **2** in >90% yields.

General Procedure for the Tandem Dual Heterocyclization. To a 10 mL oven-dried vial with a magnetic stirring bar were added enynone **1** (0.2 mmol), triazine **2** (0.24 mmol, 1.2 equiv), PPh_3AuNTf_2 (7.4 mg, 5.0 mol %), and anhydrous DCE (2.0 mL) in

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sequence under an atmosphere of argon, and the reaction mixture was stirred at 40 °C for 10 h. When the reaction was completed (monitored by TLC), the crude reaction mixture was purified by flash column chromatography on silica gel (hexanes:EtOAc = 50:1 to 30:1) to give the pure products **3** in high yields.

*1,2,4,6,8-Pentaphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]-diazepine (**3aa**).* 90.1 mg, 88% yield. White solid, mp = 80.5−82.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.70 (d, *J* = 7.7 Hz, 2H), 7.54−7.43 (comp, 4H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.25−7.12 (comp, 5H), 7.10−7.00 (comp, 3H), 6.98−6.85 (comp, 4H), 6.82 (t, *J* = 7.5 Hz, 1H), 6.57 (t, *J* = 7.4 Hz, 1H), 6.32 (d, *J* = 7.7 Hz, 2H), 6.22 (s, 1H), 5.12 (d, *J* = 12.1 Hz, 1H), 4.72 (d, *J* = 12.1 Hz, 1H), 4.58 (d, *J* = 16.0 Hz, 1H), 4.43 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.9, 148.3, 147.9, 147.3, 138.6, 131.0, 130.6, 129.5, 129.0, 128.9, 128.9, 128.3, 128.1, 127.7, 127.6, 127.1, 126.3, 125.9, 123.5, 123.5, 119.1, 117.6, 115.8, 113.3, 63.6, 60.0, 45.0; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{31}N_2O$ [M + H]$^+$, 519.2431; found, 519.2442.

*1-(4-Chlorophenyl)-2,4,6,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ba**).* 93.9 mg, 85% yield. White solid, mp = 189.7−191.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.70 (d, *J* = 7.4 Hz, 2H), 7.56−7.42 (comp, 4H), 7.35 (comp, 3H), 7.29−7.21 (comp, 3H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.97 (comp, 4H), 6.85 (comp, 3H), 6.61 (t, *J* = 7.4 Hz, 1H), 6.31 (d, *J* = 8.4 Hz, 2H), 6.17 (s, 1H), 5.10 (d, *J* = 12.1 Hz, 1H), 4.77 (d, *J* = 12.1 Hz, 1H), 4.60 (d, *J* = 16.1 Hz, 1H), 4.41 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.7, 148.3, 147.6, 147.5, 137.0, 132.9, 130.8, 130.4, 129.6, 129.4, 129.0, 129.0, 128.4, 127.8, 127.8, 126.2, 125.8, 123.3, 123.0, 119.4, 117.8, 115.7, 112.9, 63.7, 59.4, 44.8; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{30}ClN_2O$ [M + H]$^+$, 553.2041; found, 553.2051.

*1-(4-Bromophenyl)-2,4,6,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ca**).* 100.1 mg, 84% yield. White solid, mp = 179.2−181.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.74−7.69 (m, 2H), 7.55−7.44 (comp, 4H), 7.42−7.32 (comp, 3H), 7.30−7.21 (comp, 3H), 7.18−7.12 (m, 2H), 7.06−6.92 (comp, 4H), 6.93−6.80 (comp, 3H), 6.63 (t, *J* = 7.3 Hz, 1H), 6.32 (d, *J* = 7.3 Hz, 2H), 6.17 (s, 1H), 5.11 (d, *J* = 12.1 Hz, 1H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.62 (d, *J* = 16.1 Hz, 1H), 4.42 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.7, 148.3, 147.6, 147.5, 137.5, 131.3, 130.8, 130.4, 129.7, 129.6, 129.0, 127.8, 127.8, 126.2, 125.8, 123.3, 122.9, 121.1, 119.4, 117.7, 115.7, 112.9, 63.7, 59.4, 44.8; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{30}BrN_2O$ [M + H]$^+$, 597.1537; found, 597.1539.

*1-(4-Nitrophenyl)-2,4,6,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo-[3,4-e][1,3]diazepine (**3da**).* 90.2 mg, 80% yield. Yellow solid, mp = 58.1−59.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.87 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.36−7.26 (comp, 5H), 7.00−6.90 (comp, 5H), 6.64−6.60 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 2H), 5.86 (s, 1H), 4.90 (s, 2H), 4.45 (d, *J* = 15.2 Hz, 1H), 4.31 (d, *J* = 15.2 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.3, 148.3, 148.1, 147.4, 147.0, 146.7, 130.9, 129.7, 129.0, 128.9, 127.65, 127.60, 125.7, 123.3, 119.7, 119.5, 119.2, 118.1, 115.5, 112.6, 63.3, 59.3, 44.8; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{30}N_3O_3$ [M + H]$^+$, 564.2287; found, 564.2290.

*6-Methyl-1,2,4,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e]-[1,3]diazepine (**3ea**).* 83.9 mg, 92% yield. White solid, mp = 82.3−84.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.59−7.55 (m, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.34−7.26 (comp, 3H), 7.15 (m, 2H), 7.12−7.07 (comp, 3H), 7.01−6.91 (comp, 4H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.59 (t, *J* = 7.3 Hz, 1H), 6.42 (d, *J* = 7.7 Hz, 2H), 5.87 (s, 1H), 5.07 (d, *J* = 13.0 Hz, 1H), 4.82 (d, *J* = 13.0 Hz, 1H), 4.45 (d, *J* = 15.3 Hz, 1H), 4.34 (d, *J* = 15.3 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 150.0, 148.0, 147.6, 146.7, 140.4, 131.2, 129.5, 128.9, 128.9, 128.2, 127.4, 127.3, 126.9, 125.9, 120.9, 120.5, 119.0, 117.5, 115.7, 113.4, 63.2, 59.6, 44.7, 12.2; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{29}N_2O$ [M + H]$^+$, 457.2274; found, 457.2287.

*8-Methyl-2,4,6-triphenyl-1-p-tolyl-2,3,4,5-tetrahydro-1H-furo-[3,4-e][1,3]diazepine (**3fa**).* 79.0 mg, 84% yield. White solid, mp = 87.6−89.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.60−7.54 (m, 2H), 7.44 (m, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.27 (m, 1H), 7.25−7.23 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.95 (comp, 6H), 6.83 (t, *J* = 7.3 Hz, 1H), 6.59 (t, *J* = 7.3 Hz, 1H), 6.42 (d, *J* = 8.0 Hz, 2H), 5.84 (s, 1H), 5.10 (d, *J* = 13.1 Hz, 1H), 4.82 (d, *J* = 13.1 Hz, 1H), 4.40 (dd, *J* = 36.1, 15.3 Hz, 2H), 2.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 150.1, 148.1, 147.5, 146.7, 137.4, 136.6, 131.3, 129.5, 128.9, 128.9, 127.4, 127.3, 126.0, 121.3, 120.6, 118.9, 117.5, 115.8, 113.6, 63.2, 59.4, 44.6, 21.1, 12.2; HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{31}N_2O$ [M + H]$^+$, 471.2431; found, 471.2429.

*1-(4-Chlorophenyl)-8-methyl-2,4,6-triphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ga**).* 87.3 mg, 89% yield. White solid, mp = 121.1−123.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.57 (d, *J* = 8.1 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.31 (comp, 3H), 7.00 (comp, 8H), 6.87 (t, *J* = 7.3 Hz, 1H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.40 (d, *J* = 8.1 Hz, 2H), 5.81 (s, 1H), 5.02 (d, *J* = 13.0 Hz, 1H), 4.84 (d, *J* = 13.0 Hz, 1H), 4.39 (dd, *J* = 38.9, 15.3 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.8, 147.8, 147.6, 146.8, 138.9, 132.6, 131.1, 129.6, 129.0, 128.9, 128.7, 128.3, 127.4, 125.9, 120.5, 120.3, 119.2, 117.7, 115.7, 113.1, 63.1, 59.1, 44.6, 12.1; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{28}ClN_2O$ [M + H]$^+$, 491.1885; found, 491.1878.

*1-(4-Bromophenyl)-8-methyl-2,4,6-triphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ha**).* 99.3 mg, 93% yield. White solid, mp = 147.3−148.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.60−7.53 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.34−7.26 (comp, 3H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.02−6.95 (comp, 4H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 8.0 Hz, 2H), 5.78 (s, 1H), 5.01 (d, *J* = 13.0 Hz, 1H), 4.84 (d, *J* = 13.0 Hz, 1H), 4.38 (dd, *J* = 38.0, 15.3 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.8, 147.8, 147.7, 146.9, 139.5, 131.2, 131.1, 129.6, 129.0, 129.0, 128.9, 127.4, 125.9, 120.8, 120.4, 120.3, 119.3, 117.7, 115.7, 113.1, 63.1, 59.1, 44.6, 12.2; HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{28}BrN_2O$ [M + H]$^+$, 535.1380; found, 535.1389.

*1,2,4,8-Tetraphenyl-6-p-tolyl-2,3,4,5-tetrahydro-1H-furo[3,4-e]-[1,3]diazepine (**3ia**).* 91.5 mg, 86% yield. White solid, mp = 149.7−151.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.60 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.36−7.28 (comp, 4H), 7.25−7.14 (comp, 5H), 7.12−7.03 (comp, 3H), 6.98−6.87 (comp, 4H), 6.83 (t, *J* = 7.3 Hz, 1H), 6.58 (t, *J* = 7.3 Hz, 1H), 6.33 (d, *J* = 8.1 Hz, 2H), 6.23 (s, 1H), 5.14 (d, *J* = 12.1 Hz, 1H), 4.73 (d, *J* = 12.1 Hz, 1H), 4.57 (d, *J* = 16.0 Hz, 1H), 4.43 (d, *J* = 16.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 150.0, 147.9, 147.9, 147.6, 138.6, 137.7, 130.7, 129.6, 129.5, 128.9, 128.3, 128.2, 128.1, 127.5, 127.1, 126.2, 125.8, 123.4, 122.8, 119.1, 117.5, 115.8, 113.2, 63.6, 60.0, 44.9, 21.5; HRMS (TOF MS ESI$^+$) calculated for $C_{38}H_{33}N_2O$ [M + H]$^+$, 533.2587; found, 533.2597.

*6-(4-Methoxyphenyl)-1,2,4,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ja**).* 104.2 mg, 95% yield. White solid, mp = 138.7−139.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.65−7.59 (m, 2H), 7.49−7.42 (m, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.20 (comp, 5H), 7.10−7.00 (comp, 5H), 6.92 (comp, 4H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.57 (t, *J* = 7.3 Hz, 1H), 6.32 (d, *J* = 7.5 Hz, 2H), 6.22 (s, 1H), 5.14 (d, *J* = 12.2 Hz, 1H), 4.71 (d, *J* = 12.2 Hz, 1H), 4.52 (d, *J* = 15.9 Hz, 1H), 4.40 (d, *J* = 15.9 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 158.7, 149.4, 147.3, 147.1, 146.9, 138.1, 130.1, 128.9, 128.2, 127.7, 127.5, 127.2, 126.8, 126.5, 125.1, 123.2, 122.7, 121.3, 118.5, 116.9, 115.2, 113.8, 112.6, 63.0, 59.4, 54.9, 44.3; HRMS (TOF MS ESI$^+$) calculated for $C_{38}H_{33}N_2O_2$ [M + H]$^+$, 549.2537; found, 549.2552.

*6-(4-Chlorophenyl)-1,2,4,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ka**).* 93.9 mg, 85% yield. White solid, mp = 185.2−183.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.66−7.60 (m, 2H), 7.47 (comp, 4H), 7.34−7.28 (m, 2H), 7.28−7.25 (m, 1H), 7.21 (m, 2H), 7.18−7.12 (m, 2H), 7.11−7.02 (comp, 3H), 6.94 (m, 2H), 6.89 (d, *J* = 7.9 Hz, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.59 (t, *J* = 7.3 Hz, 1H), 6.30 (d, *J* = 7.9 Hz, 2H), 6.22 (s, 1H), 5.12 (d, *J* = 12.1 Hz, 1H), 4.71 (d, *J* = 12.1 Hz, 1H), 4.55 (d, *J* = 16.0 Hz, 1H), 4.40 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.9, 148.6, 147.8, 146.2, 138.4, 133.5, 130.4, 129.5, 129.4, 129.2, 128.9, 128.3, 128.1, 127.8, 127.4, 127.2, 125.9, 124.1, 123.6, 119.2, 117.7, 115.7, 113.2, 63.7, 60.0, 44.9, 31.7, 22.8, 14.3; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{30}ClN_2O$ [M + H]$^+$, 553.2041; found, 553.2050.

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*8-(4-Methoxyphenyl)-1,2,4,6-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3la**).* 103.1 mg, 94% yield. White solid, mp = 154.6−156.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.70 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.45−7.29 (comp, 3H), 7.26−7.13 (comp, 4H), 7.13−7.01 (comp, 3H), 6.97−6.78 (comp, 7H), 6.58 (t, *J* = 7.4 Hz, 1H), 6.34 (d, *J* = 8.0 Hz, 2H), 6.17 (d, *J* = 7.7 Hz, 1H), 5.14 (d, *J* = 12.2 Hz, 1H), 4.74 (d, *J* = 12.2 Hz, 1H), 4.58 (d, *J* = 16.0 Hz, 1H), 4.44 (d, *J* = 16.0 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 159.2, 150.0, 148.5, 147.9, 146.7, 138.8, 131.1, 129.5, 128.9, 128.9, 128.3, 128.1, 127.5, 127.4, 127.1, 126.1, 123.5, 123.3, 121.8, 119.1, 117.5, 115.7, 114.4, 113.3, 63.6, 59.9, 55.4, 45.0; HRMS (TOF MS ESI$^+$) calculated for $C_{38}H_{33}N_2O_2$ [M + H]$^+$, 549.2537; found, 549.2547.

*6-(4-Bromophenyl)-1,2,4,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ma**).* 100.2 mg, 84% yield. White solid, mp = 166.8−168.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.76−7.63 (m, 2H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.45−7.35 (comp, 3H), 7.35−7.30 (m, 2H), 7.23 (m, 2H), 7.17−7.00 (comp, 5H), 6.98−6.79 (comp, 5H), 6.58 (t, *J* = 7.3 Hz, 1H), 6.30 (d, *J* = 8.0 Hz, 2H), 6.16 (s, 1H), 5.12 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 16.1 Hz, 1H), 4.42 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.9, 147.8, 147.7, 147.2, 138.1, 132.1, 130.7, 129.6, 129.4, 129.0, 128.9, 128.4, 128.1, 127.9, 127.3, 127.2, 126.3, 124.3, 123.9, 121.6, 119.3, 117.6, 115.7, 113.2, 63.6, 60.1, 44.8; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{30}BrN_2O$ [M + H]$^+$, 597.1536; found, 597.1556.

*1,6,8-Triphenyl-2,4-dip-tolyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ab**).* 92.8 mg, 85% yield. White solid, mp = 87.2−88.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.65 (d, *J* = 7.3 Hz, 2H), 7.46−7.41 (comp, 4H), 7.33−7.28 (m, 2H), 7.24 (m, 1H), 7.18 (comp, 3H), 7.09−7.02 (comp, 3H), 6.96 (d, *J* = 8.5 Hz, 2H), 6.74 (comp, 4H), 6.24 (d, *J* = 8.5 Hz, 2H), 6.16 (s, 1H), 5.02 (d, *J* = 12.2 Hz, 1H), 4.59 (d, *J* = 12.2 Hz, 1H), 4.44 (dd, *J* = 34.2, 15.9 Hz, 2H), 2.20 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 148.2, 147.9, 147.3, 146.0, 139.1, 131.1, 130.7, 130.0, 129.4, 128.9, 128.8, 128.8, 128.4, 128.3, 128.2, 127.7, 127.5, 127.1, 126.9, 126.3, 125.9, 123.8, 123.7, 116.0, 114.0, 64.6, 60.2, 45.6, 31.7, 22.8, 20.5, 20.4, 14.3; HRMS (TOF MS ESI$^+$) calculated for $C_{39}H_{35}N_2O$ [M + H]$^+$, 547.2744; found, 547.2736.

*2,4-Bis(4-methoxyphenyl)-1,6,8-triphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ac**).* In 3.0 mmol scale, 1.47 g, 85% yield. White solid, mp = 85.3−86.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.68 (d, *J* = 7.3 Hz, 2H), 7.51−7.43 (comp, 4H), 7.38−7.28 (comp, 3H), 7.26−7.23 (comp, 3H), 7.20−7.12 (comp, 3H), 6.82 (d, *J* = 9.1 Hz, 2H), 6.74 (d, *J* = 9.1 Hz, 2H), 6.54 (d, *J* = 9.0 Hz, 2H), 6.35 (d, *J* = 9.0 Hz, 2H), 6.10 (s, 1H), 4.99 (d, *J* = 12.3 Hz, 1H), 4.55 (d, *J* = 12.3 Hz, 1H), 4.47 (s, 2H), 3.72 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 153.2, 152.5, 148.3, 147.5, 144.6, 143.0, 139.4, 131.1, 130.7, 128.9, 128.9, 128.4, 128.3, 127.7, 127.6, 127.2, 126.4, 126.0, 124.2, 123.8, 118.1, 116.2, 114.8, 114.4, 66.5, 60.8, 55.8, 55.8, 46.6; HRMS (TOF MS ESI$^+$) calculated for $C_{39}H_{35}N_2O_3$ [M + H]$^+$, 579.2642; found, 579.2633.

*2,4-Bis(4-chlorophenyl)-1,6,8-triphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ad**).* 107.9 mg, 92% yield. White solid, mp = 113.4−115.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.67 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.30 (comp, 3H), 7.18−7.04 (comp, 7H), 6.85 (d, *J* = 9.0 Hz, 2H), 6.78 (d, *J* = 9.0 Hz, 2H), 6.18 (d, *J* = 9.0 Hz, 2H), 6.12 (s, 1H), 5.08 (d, *J* = 12.4 Hz, 1H), 4.66 (d, *J* = 12.4 Hz, 1H), 4.50 (d, *J* = 16.1 Hz, 1H), 4.38 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 148.6, 148.4, 147.8, 146.3, 138.1, 130.7, 130.3, 129.4, 129.2, 129.0, 129.0, 128.7, 128.5, 128.0, 127.9, 127.5, 126.3, 125.9, 124.2, 122.7, 122.7, 122.4, 117.0, 114.3, 63.8, 60.0, 44.9; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{29}Cl_2N_2O$ [M + H]$^+$, 587.1651; found, 587.1661.

*2,4-Bis(4-bromophenyl)-1,6,8-triphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ae**).* 126.7 mg, 94% yield. White solid, mp = 103.4−105.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.71 (d, *J* = 7.3 Hz, 2H), 7.52 (comp, 4H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.37−7.28 (comp, 5H), 7.19−7.10 (comp, 5H), 7.01 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H), 6.16 (d, *J* = 9.3 Hz, 3H), 5.09 (d, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 4.46 (dd, *J* = 56.0 Hz, 16.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 148.8, 148.6, 147.7, 146.6, 137.9, 132.3, 131.5, 130.6, 130.3, 129.0, 129.0, 128.5, 128.0, 127.9, 127.8, 127.5, 126.3, 125.8, 122.6, 122.6, 117.3, 114.6, 111.4, 109.6, 63.5, 59.9, 44.7; HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{29}Br_2N_2O$ [M + H]$^+$, 675.0641; found, 675.0641.

*1,6,8-Triphenyl-2,4-bis[4-(trifluoromethyl)phenyl]-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3af**).* 104.7 mg, 80% yield. White solid, mp = 49.8−51.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.68−7.66 (m, 2H), 7.53−7.49 (m, 2H), 7.46−7.44 (comp, 4H), 7.41−7.37 (m, 1H), 7.34−7.30 (m, 2H), 7.28−7.24 (m, 1H), 7.12 (d, *J* = 8.8 Hz, 2H), 7.07−6.99 (comp, 4H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.24−6.22 (comp, 3H), 5.21 (d, *J* = 12.4 Hz, 1H), 4.88 (d, *J* = 12.4 Hz, 1H), 4.63 (d, *J* = 16.4 Hz, 1H), 4.35 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 151.8, 149.8, 148.8, 148.0, 137.1, 130.5, 130.1, 129.12, 129.06, 128.6, 128.2, 128.0, 127.9, 127.7, 127.0 (q, *J* = 3.5 Hz), 126.29, 126.24 (q, *J* = 3.7 Hz), 125.8, 123.5 (d, *J* = 3.5 Hz), 122.04, 121.98, 120.9 (d, *J* = 3.5 Hz), 119.2 (d, *J* = 3.5 Hz), 114.5, 111.8, 62.7, 59.4, 44.3; HRMS (TOF MS ESI$^+$) calculated for $C_{39}H_{29}F_6N_2O$ [M + H]$^+$, 655.2184; found, 655.2189.

*2,4-Bis(2-methoxyphenyl)-8-methyl-1,6-diphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3eg**).*[19] 81.0 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.62 (d, *J* = 8.0 Hz, 2H), 7.40−7.35 (comp, 4H), 7.32−7.24 (comp, 4H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.78−6.64 (comp, 5H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 5.61 (d, *J* = 4.0 Hz, 1H), 5.15 (d, *J* = 4.0 Hz, 1H), 4.20 (s, 1H), 4.10 (s, 2H), 3.75 (s, 3H), 3.72 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.7, 148.3, 147.2, 146.9, 142.0, 138.1, 137.4, 130.9, 128.8, 128.6, 127.5, 127.2, 127.1, 126.0, 122.8, 121.3, 117.8, 116.9, 116.7, 110.8, 110.4, 109.3, 109.2, 55.34, 55.31, 53.7, 38.5, 12.7.

*2,4-Dibenzyl-1,6,8-triphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3ah**).*[19] 92.9 mg, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.48 (d, *J* = 9.0 Hz, 2H), 7.38−7.21 (comp, 18H), 7.18−7.15 (comp, 2H), 7.09−7.06 (comp, 3H), 5.19 (s, 1H), 4.09 (d, *J* = 12.0 Hz, 1H), 3.99−3.94 (comp, 2H), 3.88−3.79 (comp, 2H), 3.61 (d, *J* = 12.0 Hz, 1H), 3.49 (d, *J* = 12.0 Hz, 1H), 3.37 (d, *J* = 15.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 150.4, 148.9, 140.9, 139.8, 139.7, 131.2, 130.9, 129.22, 129.19, 128.8, 128.60, 128.57, 128.4, 128.1, 127.5, 127.4, 127.2, 127.1, 126.82, 126.78, 126.3, 123.3, 121.9, 73.7, 59.2, 57.2, 49.1.

Cross-Cycloaddition Reaction (1). To a 10 mL oven-dried vial with a magnetic stirring bar were added enynone **1a** (61.6 mg, 0.2 mmol), triazine **2a** (37.8 mg, 0.12 mmol, 0.6 equiv), triazine **2c** (48.7 mg, 0.12 mmol, 0.6 equiv), PPh_3AuNTf_2 (7.4 mg, 5.0 mol %), and anhydrous DCE (2.0 mL) in sequence under an atmosphere of argon, and the reaction mixture was stirred at 40 °C for 10 h. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo, and the crude reaction mixture was subjected to proton NMR analysis for determination of the ratio of the products (**3aa**:**3aac**:**3aca**:**3ac** = 13:19:14:54). The crude reaction mixture was purified by flash column chromatography on silica gel (hexanes:EtOAc = 50:1 to 30:1) to give the pure product **3aa**, **3aac**, **3aca**, **3ac** in total 85% yields.

*4-(4-Methoxyphenyl)-1,2,6,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3aac**).* White solid, mp = 83.4−85.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.67 (d, *J* = 7.3 Hz, 2H), 7.47 (comp, 4H), 7.37−7.29 (comp, 3H), 7.26−7.21 (comp, 3H), 7.16 (comp, 5H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.56 (d, *J* = 9.0 Hz, 2H), 6.35 (d, *J* = 9.0 Hz, 2H), 6.23 (s, 1H), 5.08 (d, *J* = 12.1 Hz, 1H), 4.60 (d, *J* = 12.1 Hz, 1H), 4.45 (dd, *J* = 33.6, 15.8 Hz, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 152.6, 150.0, 148.4, 147.4, 142.9, 139.0, 131.0, 130.6, 129.4, 128.9, 128.4, 128.2, 127.7, 127.6, 127.2, 126.3, 125.9, 123.8, 123.7, 119.0, 116.1, 115.8, 114.5, 65.5, 59.8, 55.8, 46.6; HRMS (TOF MS ESI$^+$) calculated for $C_{38}H_{33}N_2O_2$ [M + H]$^+$, 549.2537; found, 549.2537.

*2-(4-Methoxyphenyl)-1,4,6,8-tetraphenyl-2,3,4,5-tetrahydro-1H-furo[3,4-e][1,3]diazepine (**3aca**).* Yellow solid, mp = 82.6−84.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.72 (d, *J* = 7.5 Hz, 2H), 7.53−7.45 (comp, 4H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.4 Hz,

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2H), 7.24 (d, J = 7.5 Hz, 1H), 7.22−7.18 (m, 2H), 7.08 (comp, 3H), 6.93 (t, J = 8.0 Hz, 2H), 6.86 (d, J = 9.1 Hz, 2H), 6.78 (dd, J = 9.7, 2.6 Hz, 2H), 6.57 (t, J = 7.2 Hz, 1H), 6.34 (d, J = 8.0 Hz, 2H), 6.10 (s, 1H), 5.05 (d, J = 12.2 Hz, 1H), 4.66 (d, J = 12.2 Hz, 1H), 4.53 (q, J = 16.0 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 155.0, 153.3, 148.2, 148.0, 147.5, 144.5, 138.9, 131.0, 130.6, 128.9, 128.8, 128.3, 128.2, 127.8, 127.6, 127.1, 126.3, 125.9, 123.9, 123.6, 118.1, 117.5, 113.4, 64.7, 61.0, 55.7, 45.1; HRMS (TOF MS ESI$^+$) calculated for $C_{38}H_{33}N_2O_2$ [M + H]$^+$, 549.2537; found, 549.2546.

Cross-Cycloaddition Reaction (2). To a 10 mL oven-dried vial with a magnetic stirring bar were added **2a** (18.9 mg, 0.06 mmol, Figure S1, the first spectrum), **2c** (24.4 mg, 0.06 mmol, the second spectrum), PPh_3AuNTf_2 (3.7 mg, 5.0 mol %), and anhydrous DCE (2.0 mL) in sequence under an atmosphere of argon, and the reaction mixture was stirred at 40 °C for 10 h. The reaction mixture then was filtered through a short pad of Celite, and the solid was washed with DCE (2.0 mL × 2). The combined solution was evaporated in vacuo, and the crude reaction mixture was subjected to proton NMR analysis (the third, spectrum). Efforts trying to separate the mixture failed. Also, further work was carried out by adding enynone **1a** (30.8 mg, 0.1 mmol, the fourth spectrum), PPh_3AuNTf_2 (3.7 mg, 5.0 mol %), and anhydrous DCE (2.0 mL) to the above obtained reaction mixture under an atmosphere of argon, and the reaction mixture was stirred at 40 °C for 10 h. The reaction mixture then was filtered through a short pad of Celite, and the solid was washed with DCE (2.0 mL × 2). The combined solution was evaporated in vacuo, and the crude reaction mixture was subjected to proton NMR analysis (the fifth spectrum). These results indicate that a transformation(s) occurred for the mixed triazines solution under standard conditions in the absence of enynone **1a**; however, these formed product(s) did not react with enynone **1a** to give the cycloaddition product(s), and only decomposition of **1a** was observed under standard conditions while the others remained (see Figure S1).[18]

General Procedure of the Gram Scale Synthesis. To a 50 mL oven-dried round-bottom flask with a magnetic stirring bar were added enynone **1a** (0.92 g, 3.0 mmol), triazine **2c** (1.46 g, 3.6 mmol, 1.2 equiv), PPh_3AuNTf_2 (44.4 mg, 2.0 mol %), and anhydrous DCE (20.0 mL) in sequence under an atmosphere of argon, and the reaction mixture was stirred at 40 °C for 10 h. When the reaction was completed (monitored by TLC), most of the solvent was evaporated in vacuo (about 5.0 mL of DCE was left), and the reaction mixture was purified by flash column chromatography on silica gel (hexanes:EtOAc = 50:1 to 30:1) to give 1.47 g of pure **3ac** (85% yield).

Procedure for the Synthesis of 4. To a 10-mL oven-dried vial containing a magnetic stirring bar, **3la** (119.2 mg, 0.2 mmol), KF (58.1 mg, 1.0 mmol), $Pd(PPh_3)_4$ (23.1 mg, 10 mol %), and thiophen-2-yl boronic acid (128.0 mg, 1.0 mmol) was added THF (5.0 mL) under argon atmosphere. The reaction mixture then was stirred at 50 °C for 12 h. After the reaction was completed (monitored by TLC), the reaction mixture was cooled to room temperature and quenched with water (20 mL). The reaction mixture was extracted with EtOAc (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure after filtration. The obtained residue was purified by flash column chromatography on silica gel (hexanes:EtOAc = 50:1 to 30:1) to give 109.6 mg of coupling product **4** as a yellow solid, 92% yield, mp = 103.5−105.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.74−7.68 (m, 2H), 7.52 (comp, 6H), 7.38 (t, J = 7.4 Hz, 1H), 7.29 (m, 1H), 7.28−7.26 (m, 1H), 7.26−7.20 (m, 2H), 7.18−7.13 (m, 2H), 7.13−7.02 (comp, 4H), 6.97−6.87 (comp, 4H), 6.83 (t, J = 7.3 Hz, 1H), 6.57 (t, J = 7.3 Hz, 1H), 6.31 (d, J = 8.0 Hz, 2H), 6.24 (s, 1H), 5.13 (d, J = 12.0 Hz, 1H), 4.72 (d, J = 12.0 Hz, 1H), 4.61 (d, J = 16.1 Hz, 1H), 4.42 (d, J = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm) 149.9, 147.9, 147.4, 143.9, 138.3, 133.4, 130.9, 129.6, 129.5, 129.0, 128.9, 128.4, 128.3, 128.2, 127.8, 127.3, 126.3, 126.2, 126.1, 125.2, 124.0, 123.9, 123.3, 119.2, 117.6, 115.7, 113.2, 63.7, 60.1, 44.9; HRMS (TOF MS ESI$^+$) calculated for $C_{41}H_{33}N_2OS$ [M + H]$^+$, 601.2308; found, 601.2310.

N-[(2,5-Diphenylfuran-3-yl)(phenyl)methyl]-3-methoxyaniline (**5**). 63.0 mg, 73% yield. Dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.70−7.67 (comp, 4H), 7.49−7.47 (m, 2H), 7.43−7.23 (comp, 9H), 7.03 (t, J = 8.0 Hz, 1H), 6.57 (s, 1H), 6.29−6.26 (m, 1H), 6.20−6.17 (m, 1H), 6.11−6.10 (m, 1H), 5.78 (s, 1H), 4.39 (br, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) (δ, ppm) 160.8, 152.8, 149.1, 148.4, 142.1, 130.7, 130.5, 130.1, 129.0, 128.8, 127.9, 127.7, 127.4, 126.3, 125.5, 123.9, 107.7, 106.5, 103.3, 99.4, 55.1, 54.6; HRMS (TOF MS ESI$^+$) calculated for $C_{30}H_{26}NO_2$ [M + H]$^+$, 432.1964; found, 432.1967.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02947.

^{1}H and ^{13}C NMR spectra for all products (PDF)

X-ray analysis data for **3aa** (CIF)

X-ray analysis data for **3aac** (CIF)

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Notes

The authors declare no competing financial interest.

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