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Lewis Acid-Promoted Three-Component Reactions of Propargylic Alcohols with 2-Butynedioates and Secondary Amines

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Supporting Information

ABSTRACT: We report herein a three-component reaction of propargylic alcohols with 2-butynedioates and secondary amines, which furnished functionalized dihydroazepines. In the cases where benzylmethylamine and benzyl-*i*-propylamine were used as the secondary amine, the reaction afforded 2,5-dihydro-1*H*-pyrroles and 2,3-dihydro-1*H*-pyrroles, respectively, as the major product along with the desired dihydroazepines. The reaction mode depends on the electronic and steric effect of the substitutents on the secondary amines used. A tentative mechanism for this cascade process is postulated. The key intermediate is ascribed to 1,3,4-pentatrien-1-amine, which is formed by trapping the in situ generating allenic carbocation with enamine. Because of the reactivity of 1,3,4-pentatrien-1-amine formed, different products were thus formed.

INTRODUCTION

Dihydroazepine and its analogues represent an important class of heterocyclic compounds because of their bioactivities and pharmaceutical applications.[1]Three examples of the clinically used drugs containing the dihydroazepine ring are Imipramine, Carbamazepine, and Oxcarbazepine. In addition, a number of natural products contain this structural unit.[2] Therefore, a number of methodologies have been developed for the construction of these heterocyclic seven-membered rings.[3] Classical approaches include the insertion of nitrenes, cyclization of diene-conjugated nitrile ylides,[4] and intramolecular Heck reaction.[5] Recently, transition metal-catalyzed cyclizations,[6] [4+3] cycloadditions,[7] [5+2] cycloadditions,[8] and ring-closing methathesis[9] have been reported. The known biological properties and the huge potential in drug discovery of these heterocyclic compounds still need the development of facile and efficient methodologies for their selective and diverse synthesis.

Because of the easy generation and the prosperous reactions, allenes have attracted much attention in organic synthesis, especially in the synthesis of heterocycles and carbocycles with high complexity.[10] A practical way to form allenes is using suitable nucleophiles to trap the allenic carbocation intermediates, which could be generated in situ by the Meyer−Schuster rearrangement of propargylic alcohols.[11] Either Brønster acids or Lewis acids could efficiently catalyze this rearrangement. Using this strategy, a number of substituted allenes[12] and allenamides[13] were synthesized. The substituted indenes,[14] methylenecyclobutenes,[15] and thiazoles were also constructed via a cascade process from propargylic alcohols.[16]

In our efforts to develop a cascade process, we wondered whether the allenic carbocation generated in situ from propargylic alcohols could be trapped by enamine to give a cascade reaction product. The enamine bearing two ester groups was derived from butynedioate and a secondary amine and is believed to be able to decrease its nucleophilicity.

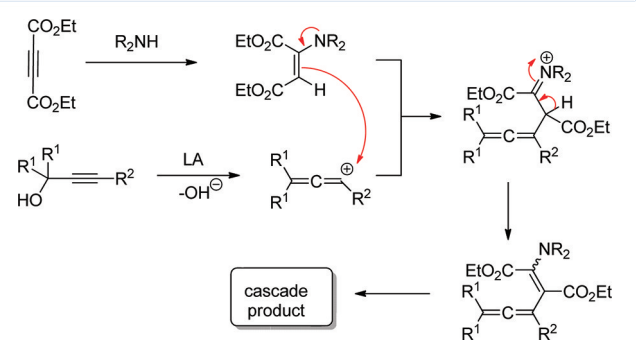

Figure 1. Design blueprint for trapping the allenic carbocation.

A detailed description of the proposal is shown in Figure 1. Herein, we report the realization of this goal leading to a convenient method for the construction of dihydroazepines.

RESULTS AND DISCUSSION

To test this new process, we began by choosing 1,1,3-triphenylprop-2-yn-1-ol (**3a**) and diethyl 2-(diethylamino)-maleate[17] as the coupling partners. The later was formed in situ in an exclusive *E*-configuration by the reaction between diethyl but-2-ynedioate (**1a**) and diethylamine (**2a**). To our delight, dihydroazepine **4a** was constructed in 73% yield when $AlCl_3$ was used as a catalyst (Table 1, entry 1). The structure of **4a** was determined by X-ray single-crystal analysis.[18]

Enlightened by this result, we optimized the reaction conditions for the formation of **4a**, and the results are summarized in Table 1. When the catalyst was changed to $ZnCl_2$, $FeCl_3$, or I_2, **4a** was obtained in a yield of 41, 76, or 49%, respectively (Table 1, entries 2−4). Boron trifluoride etherate gave the best

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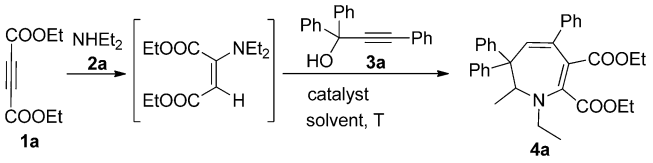
Table 1. Screening for Reaction Conditions[a]



entry	catalyst	solvent	temp	time (h)	yield (%)[b]
1	$AlCl_3$	DCM	reflux	1	73
2	$ZnCl_2$	DCM	reflux	1	41
3	$FeCl_3$	DCM	reflux	1	76
4	I_2	DCM	reflux	2	49
5	$BF_3{\cdot}Et_2O$	DCM	reflux	1	83
6	$BF_3{\cdot}Et_2O$ (10 mol %)	DCM	reflux	8	trace
7	$FeCl_3$ (20 mol %)	DCM	reflux	12	40
8	$BF_3{\cdot}Et_2O$	toluene	50 °C	1	72
9	$BF_3{\cdot}Et_2O$	CH_3CN	50 °C	1	69
10	$BF_3{\cdot}Et_2O$	THF	50 °C	1	12
11	$BF_3{\cdot}Et_2O$	DMF	50 °C	1	trace
12	$BF_3{\cdot}Et_2O$	DCE	80 °C	1	78
13	$BF_3{\cdot}Et_2O$	DCM	rt	5	60
14[c]	$BF_3{\cdot}Et_2O$	DCM	reflux	1	65

[a]Reaction conditions: **1a** (1 mmol), **2a** (1 mmol), solvent (3 mL), rt, 10 min; **3a** (1 mmol), 4 Å molecular sieves (0.4 g), catalyst (1 mmol). [b]Isolated yield. [c]Without 4 Å molecular sieves.

yield among these catalysts (Table 1, entries 1–5). After the loading amount of boron trifluoride etherate had been decreased to 10 mol %, only a trace amount of **4a** was detected by thin layer chromatography (Table 1, entry 6). Similarly, after the amount of $FeCl_3$ had been decreased to 20 mol %, **4a** was isolated in a relatively lower yield in comparison with the use of an equivalent molar amount of $FeCl_3$ (Table 1, entries 3 and 7). Changing the solvent to toluene, acetonitrile (CH_3CN), or tetrahydrofuran (THF) also decreased the yield of **4a** (Table 1, entries 8–10). *N*,*N*-Dimethylformamide (DMF) did not work for this transformation (Table 1, entry 11). Either increasing or decreasing the reaction temperature influenced the isolated yield (Table 1, entries 12 and 13). The presence of a 4 Å molecular sieve would be beneficial for the reaction (Table 1, entry 14). Thus, the optimized reaction condition was established (Table 1, entry 5).

As the next step, we tested the substrate scope. As shown in Figure 2, propargylic alcohols, synthesized from *para*-substituted phenylacetylenes and symmetrical benzophenones, afforded the corresponding dihydroazepine derivatives **4b–e** in good yields (76–85%). The effect of the substituent on the *para* position of phenyl acetylene was not apparent no matter if it was electron-withdrawing (**4d**) or electron-donating (**4e**) . A propargylic alcohol derived from aliphatic alkyne and benzophenone produced **4f** in 55% yield, while 1,1-diphenylprop-2-yn-1-ol afforded **4g** in 40% yield only.

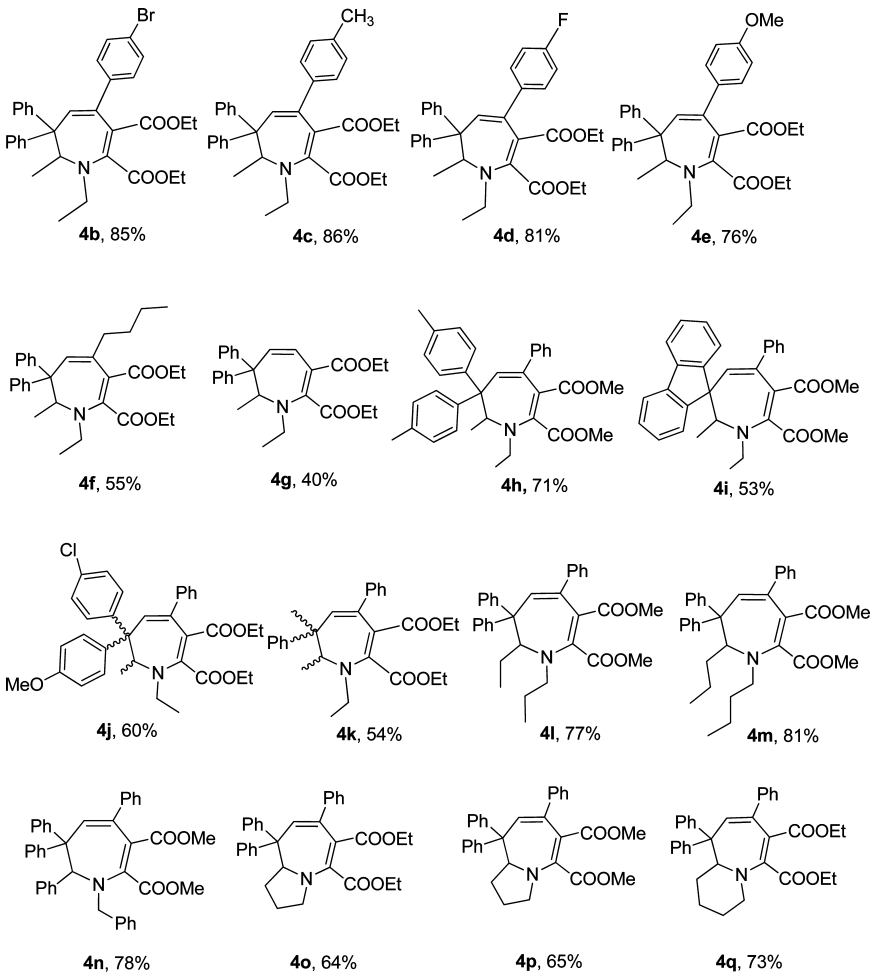


Figure 2. Structures of dihydroazepines **4b–q** and their yields.

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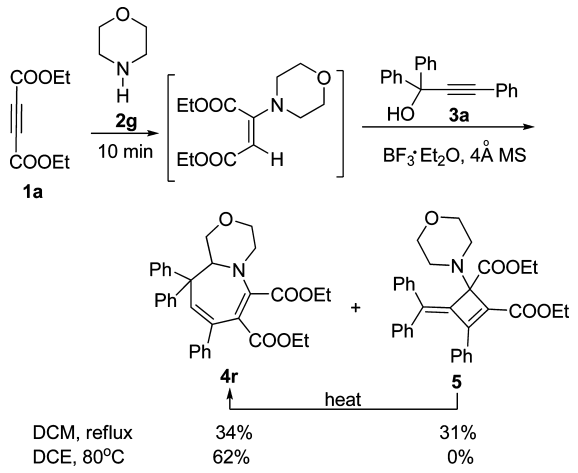
A propargylic alcohol derived from 4,4′-dimethylbenzophenone or fluorenone reacted with enamine generated from dimethyl but-2-ynedioate (**1b**) and diethylamine (**2a**) furnished **4h** and **4i** in 71 and 53% yields, respectively. Propargylic alcohol derived from unsymmetrical ketone also worked for the reaction to give **4j** in 60% yield. An acetophenone-derived alcohol gave **4k** in a slightly lower yield. The enamine component was formed in situ for this cascade reaction. The formation of diethyl 2-(diethylamino)maleate was confirmed by characterizing the isolated enamine from the mixture of diethyl but-2-ynedioate (**1a**) and diethylamine.[19] Dipropylamine (**2b**), dibutylamine (**2c**), dibenzylamine (**2d**), and cyclic secondary amines, such as pyrrolidine (**2e**) and piperidine (**2f**), also worked well for this reaction to afford the corresponding products **4l**–**q** in yields between 64 and 81%.

When morpholine (**2g**) was used, a highly strained molecule **5** (31% yield)[20] was isolated along with the desired product **4r** (34% yield) (Scheme 1). When the reaction temperature was

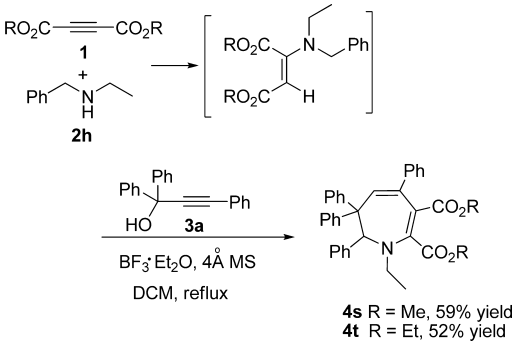
Scheme 1. Formation of 4r and 5



increased to 80 °C, however, **4r** could be obtained as a major product. It was noticed by the varied-temperature NMR that the isolated **5** could be converted to **4r** at higher temperatures (see the Supporting Information).

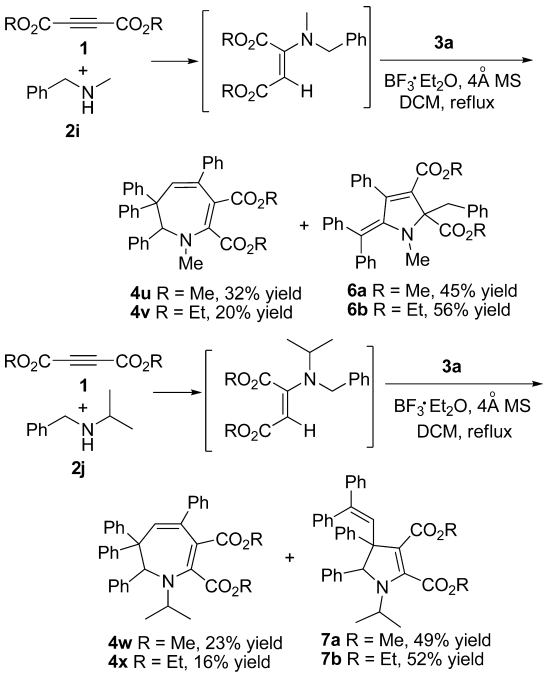
We also examined the amines with two different alkyl groups, such as *N*-benzylethanamine (**2h**), and obtained the expected dihydroazepines **4s** (59% yield) and **4t** (52% yield) (Scheme 2).

Scheme 2. Formation of 4s and 4t



However, benzylmethylamine (**2i**) afforded 5-methylene-2,5-dihydro-1*H*-pyrroles **6a** (45% yield) and **6b** (56% yield) in majority except for the desired dihydroazepines **4u** (32% yield) and **4v** (20% yield) (Scheme 3). Other unexpected products were also isolated when *N*-benzylpropan-2-amine (**2j**) was

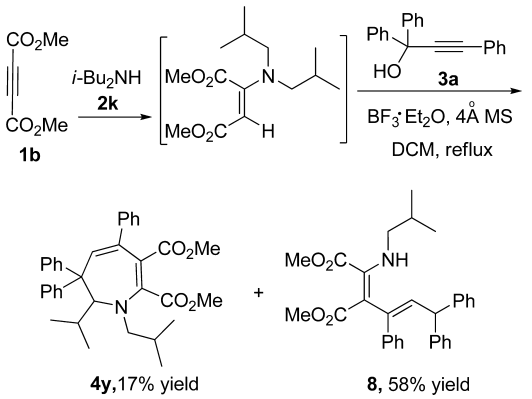
Scheme 3. Formation of 4u–x, 6, and 7



tested. In this case, 2,3-dihydro-1*H*-pyrroles **7a** (49% yield) and **7b** (52% yield) were constructed besides the desired products **4w** (23% yield) and **4x** (16% yield). Structures of **6b**[21] and **7a**[22] were confirmed by X-ray single-crystal diffraction.

In the case where diisobutylamine (**2k**), a bulky secondary amine, was used (Scheme 4), we isolated dihydroazepine **4y**

Scheme 4. Formation of 4y and 8



(17% yield) and a ring-opening dienamine **8** (58% yield).[23] We also observed that the resulting dihydroazepine **4y** was unstable and easily underwent hydrolysis in the presence of a trace amount of water to yield dienamine **8** (see the Supporting Information).

Finally, we examined the enamine[24] derived from methyl propiolate (**1c**) (Scheme 5) and found that it reacted with **3a** to afford 2,4-dienal **9** in 52% yield. Noteworthy is the fact that 2,4-dienals are useful conjugated carbonyl compounds in organic synthesis.[25]

On the basis of these results, we postulated a possible mechanism for the formation of **4**–**8** (Scheme 6). Reaction of **1**

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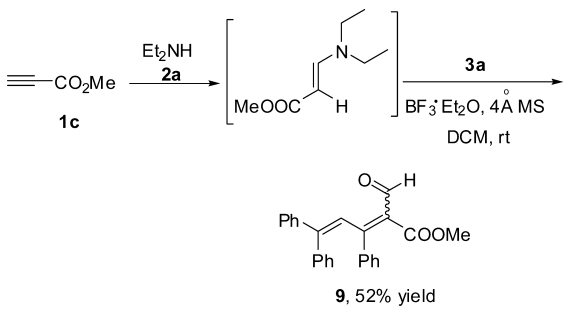
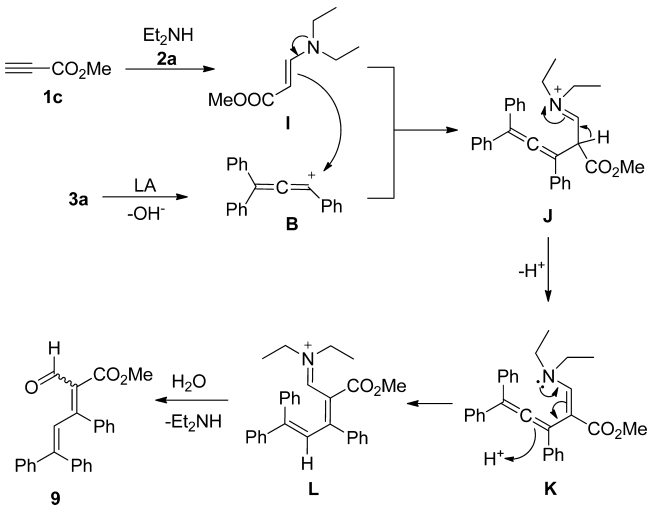
and **2** results in the formation of enamine **A**, which is an electron-deficient enamine in comparison to an alkylated one because of the electron withdrawing nature of two ester groups. **A** suitably traps the allenic carbocation **B** that is formed in situ through the Meyer–Schuster rearrangement of 1,1,3-triphenyl-prop-2-yn-1-ol (**3a**) to generate iminium intermediate **C** with a *β*-hydrogen. Subsequent deprotonation of **C** forms a better-conjugated intermediate **D**, possessing a chain of 1,3,4-pentatrien-1-amine. As electrons flow as indicated in the **D** structure, an azomethine ylide **E**[26] is generated. Intramolecular 1,6-Michael addition of **E**[27] gives dihydroazepine ring **4**, while intramolecular 1,4-Michael addition of **E** forms 2,3-dihydro-1*H*-pyrrole ring **7** in the case of *N*-benzylpropan-2-amine (**2e**). When morpholine is used as a substrate, a four-membered ring **5** is obtained via intermediate **F**, which is the resonance structure of **D**. The reactivity of the iminium of **F** is obvious because of the inductive effect of the oxygen in the morpholine ring,[28] which results in the formation of **5**. **5** is unstable because of the ring strain. It undergoes ring opening under heat and regenerates **F**, which produces the thermodynamically favored **4r**. When benzylmethylamine (**2d**) is used as the substrate, the nitrogen atom of **D** nucleophilically attacks the central carbon of allene to form a zwitterion intermediate **G**. Intramolecular migration of the benzyl group of **G** results in the formation of 2,5-dihydro-1*H*-pyrrole ring **6**. In the case where bulky diisobutylamine (**2f**) is used, **E** can undergo a protonation at its benzylic position to produce imminium **H**. Hydrolysis of **H** leads to the formation of **8** and isobutyl aldehyde.

Formation of **9** could be understood as shown in Scheme 7. 1,3,4-Trienamine **K** is formed from **1c**, **2a**, and **3a** through a pathway similar to that of the formation of **D** in Scheme 6. Compared with enamine **D**, bearing two electron-withdrawing groups, **I** is more electron-rich. Therefore, the central carbon of allene in **K** prefers protonation, resulting in the formation of 2,4-dieniminium **L**, which finally undergoes hydrolysis to form 2,4-dienal **9**.

Scheme 5. Formation of Dienal 9



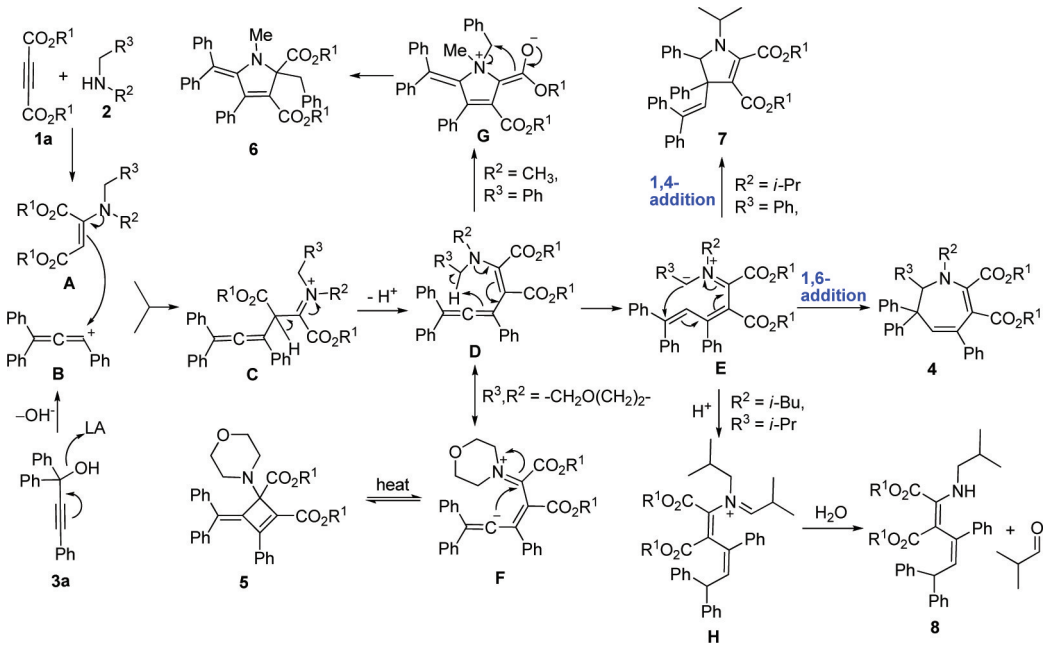
Scheme 7. Postulated Mechanism for the Formation of 9



CONCLUSION

In conclusion, we developed a one-pot reaction of 2-butynedioates with secondary amines and propargylic alcohols in the presence of a Lewis acid. Generally, the reaction furnished functionalized dihydroazepines with a heterocyclic

Scheme 6. Postulated Mechanism for the Formation of 4–8



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seven-membered ring. In some cases, 2,5-dihydro-1*H*-pyrrole, 2,3-dihydro-1*H*-pyrrole, and dienamine were also formed along with the desired dihydroazepines, depending on the electronic effect and the steric effect of the secondary amines. A tentative mechanism for the formation of dihydroazepines and by-products is discussed, and it involves enamine, allenic carbocation, 1,3,4-pentatrien-1-amine, and azomethine intermediates. The key intermediate is ascribed to 1,3,4-pentatrien-1-amine, which is formed by trapping the in situ generating allenic carbocation with enamine.

EXPERIMENTAL SECTION

General Methods. Infrared spectra were recorded with a FTIR spectrometer. ^{1}H NMR spectra were recorded at 400 or 500 MHz using TMS as an internal standard and ^{13}C NMR spectra at 75, 100, or 125 MHz using $CDCl_3$ as an internal standard. The following abbreviations are used to describe peak patterns where appropriate: b, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants are reported in hertz. HRMS data were obtained using EI ionization. Melting points were measured with a micro melting point apparatus.

The propargylic alcohols were prepared according to the published methods.[29] Dichloromethane (DCM) was distilled from CaH_2 under a N_2 atmosphere. Molecular sieves (4 Å) were activated by being baked in a muffle oven. Other materials were purchased from common commercial sources and used without additional purification.

General Procedure for the Preparation of Dihydroazepines 4–8. To a solution of secondary amine **2** (0.5 mmol) in dry dichloromethane (3 mL) was added 2-butynedioate **1** (0.5 mmol), and the solution was stirred for 10 min at room temperature. Then, propargylic alcohol **3** (0.5 mmol), 4 Å molecular sieves (200 mg), and $BF_3{\cdot}Et_2O$ (0.5 mmol) were added in sequence. After being stirred at reflux temperature for 1 h, the mixture was evaporated under vacuum. The product was isolated by silica gel column chromatography with a hexane/EtOAc/Et_3N mixture (10:1:0.1, v/v/v).

*Diethyl 1-ethyl-7-methyl-4,6,6-triphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4a**):* yellow solid; 83% yield; mp 158–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.9 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.32–7.22 (m, 4H), 7.21–7.11 (m, 6H), 7.07 (t, J = 6.8 Hz, 1H), 6.06 (s, 1H), 4.64 (q, J = 6.2 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.82–3.54 (m, 2H), 2.96–2.53 (m, 2H), 1.29 (t, J = 6.9 Hz, 3H), 1.24–1.15 (m, 6H), 0.74–0.66 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 166.2, 149.0, 147.4, 146.0, 142.2, 140.9, 132.1, 128.3, 127.93, 127.86, 127.8, 127.6, 126.5, 126.2, 125.93, 125.86, 102.9, 62.6, 61.7, 61.6, 60.1, 53.0, 19.2, 16.1, 13.6, 13.3; IR (KBr) ν 2980, 1733, 1691, 1597, 1546, 1444, 1371, 1256, 1089, 704 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{35}NO_4$ 509.2566, found 509.2567.

*Diethyl 4-(4-bromophenyl)-1-ethyl-7-methyl-6,6-diphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4b**):* white solid; 85% yield; mp 157–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.33 (m, 4H), 7.30 (t, J = 7.6 Hz, 4H), 7.21–7.14 (m, 3H), 7.13–7.04 (m, 3H), 6.03 (s, 1H), 4.65 (q, J = 6.2 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.91–3.55 (m, 2H), 3.02–2.55 (m, 2H), 1.29 (t, J = 7.0 Hz, 3H), 1.23–1.13 (m, 6H), 0.78 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 166.0, 148.8, 147.8, 145.0, 142.0, 140.0, 132.4, 130.9, 128.4, 128.2, 127.8, 127.7, 126.03, 125.98, 119.9, 102.2, 62.7, 61.7, 61.6, 60.2, 53.1, 19.2, 16.1, 13.6, 13.5; IR (KBr) ν 1281, 1733, 1690, 1544, 1446, 1367, 1255, 1142, 1091, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{34}BrNO_4$ 587.1671, found 587.1678.

*Diethyl 1-ethyl-7-methyl-6,6-diphenyl-4-(p-tolyl)-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4c**):* yellow solid; 86% yield; mp 142–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.1 Hz, 2H), 7.33–7.26 (t, J = 8.1 Hz, 4H), 7.21–4.11 (m, 5H), 7.11–7.03 (m, 3H), 6.04 (s, 1H), 4.63 (q, J = 6.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.87–3.55 (m, 2H), 3.03–2.50 (m, 2H), 2.31 (s, 3H), 1.29 (t, J = 6.9 Hz, 3H), 1.24–1.12 (m, 6H), 0.73 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 166.3, 149.1, 147.2, 143.1, 142.3, 140.7, 135.7, 131.7, 128.5, 128.3, 128.0, 127.8, 127.6, 126.4, 125.9, 125.8, 103.1, 62.6, 61.7, 61.6, 60.1, 53.0, 21.0, 19.2, 16.1, 13.6, 13.4; IR (KBr) ν 2976, 1741, 1686, 1547, 1445, 1258, 1220, 1088, 1025, 707 cm^{-1}; HRMS (EI) m/z calcd for $C_{34}H_{37}NO_4$ 523.2624, found 523.2631.

*Diethyl 1-ethyl-4-(4-fluorophenyl)-7-methyl-6,6-diphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4d**):* yellow solid; 81% yield; mp 164–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.33 (m, 4H), 7.30 (t, J = 7.7 Hz, 2H), 7.21–7.04 (m, 6H), 6.95 (t, J = 8.6 Hz, 2H), 6.02 (s, 1H), 4.65 (q, J = 6.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.88–3.55 (m, 2H), 3.01–2.55 (m, 2H), 1.29 (t, J = 7.0 Hz, 3H), 1.23–1.12 (m, 6H), 0.78 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 166.1,161.6 (d, J = 243 Hz), 148.9, 147.5, 142.1, 142.0 (d, J = 3.1 Hz), 139.9, 132.0, 128.4, 128.0, 127.9, 127.74, 127.66, 126.0 (d, J = 5.3 Hz), 114.6 (d, J = 21.2 Hz), 102.7, 62.7, 61.63, 61.59, 60.2, 53.1, 19.2, 16.1, 13.6, 13.5; IR (KBr) ν 2983, 1735, 1710, 1553, 1504, 1444, 1266, 1219, 1085, 755, 706 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{34}FNO_4$ 527.2472, found 527.2464.

*Diethyl 1-ethyl-4-(4-methoxyphenyl)-7-methyl-6,6-diphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4e**):* white solid; 76% yield; mp 120–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 6H), 7.21–7.10 (m, 5H), 7.07 (t, J = 6.7 Hz, 1H), 6.80 (d, J = 8.6 Hz, 2H), 6.01 (s, 1H), 4.64 (q, J = 6.2 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.86–3.57 (m, 5H), 2.99–2.54 (m, 2H), 1.28 (t, J = 7.0 Hz, 3H), 1.23–1.08 (m, 6H), 0.78 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 166.2, 158.3, 149.1, 147.0, 142.3, 140.3, 138.6, 131.2, 128.3, 128.0, 127.8, 127.6, 127.5, 125.9, 125.8, 113.2, 103.2, 62.7, 61.6, 60.1, 55.3, 53.0, 19.2, 16.1, 13.6; IR (KBr) ν 2978, 1735, 1690, 1610, 1547, 1510, 1255, 1219, 1089, 1035, 768 cm^{-1}; HRMS (EI) m/z calcd for $C_{34}H_{37}NO_5$ 539.2672, found 539.2681.

*Diethyl 4-butyl-1-ethyl-7-methyl-6,6-diphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4f**):* white oil; 55% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 4H), 7.22–7.15 (m, 1H), 7.13 (t, J = 7.5 Hz, 2H), 7.06–6.98 (m, 3H), 5.95 (s, 1H), 4.47 (q, J = 6.2 Hz, 1H), 4.30–4.20 (m, 1H), 4.16–4.00 (m, 3H), 2.83–2.78 (m, 1H), 2.73–2.61 (m, 1H), 2.48–2.34 (m, 1H), 2.29–2.16 (m, 1H), 1.52–1.09 (m, 16H), 0.85 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 166.6, 149.4, 145.2, 143.1, 138.3, 129.3, 128.2, 128.1, 128.0, 127.4, 125.75, 125.74, 104.8, 61.4, 61.3, 60.5, 52.3, 38.4, 33.2, 23.0, 18.7, 15.7, 14.1, 13.9, 13.6; IR (film) ν 2956, 1731, 1704, 1549, 1445, 1369, 1256, 1147, 1086, 749, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{39}NO_4$ 489.2879, found 489.2882.

*Diethyl 1-ethyl-7-methyl-6,6-diphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4g**):* white oil; 40% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.32 (m, 4H), 7.27–7.19 (m, 1H), 7.18–7.02 (m, 4H), 6.89 (d, J = 7.7 Hz, 2H), 6.03 (d, J = 12.2 Hz, 1H), 4.42 (q, J = 6.1 Hz, 1H), 4.29–7.16 (m, 4H), 2.82–2.67 (m, 1H), 2.10–1.89 (m, 1H), 1.36–1.26 (m, 6H), 1.22–1.13 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 166.3, 150.6, 147.6, 145.2, 128.3, 128.1, 127.6, 126.5, 126.3, 126.1, 98.7, 62.0, 61.6, 61.4, 60.4, 51.2, 16.9, 15.1, 14.3, 13.7; IR (film) ν 2982, 1737, 1689, 1543, 1366, 1255, 1194, 1091, 729, 698 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{31}NO_4$ 433.2253, found 433.2250.

*Dimethyl 1-ethyl-7-methyl-4-phenyl-6,6-di-p-tolyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4h**):* white solid; 71% yield; mp 161–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 7.3 Hz, 2H), 7.25 (dd, J_1 = 12.6 Hz, J_2 = 7.6 Hz, 4H), 7.17 (t, J = 7.3 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H), 7.03–6.93 (m, 4H), 6.06 (s, 1H), 4.58 (q, J = 6.2 Hz, 1H), 3.69 (s, 3H), 3.17 (s, 3H), 2.92–2.53 (m, 2H), 2.28 (s, 3H), 2.23 (s, 3H), 1.27 (t, J = 7.0 Hz, 3H), 1.16 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 166.8, 147.0, 146.2, 146.0, 140.4, 139.7, 135.3, 132.7, 129.0, 128.4, 127.9, 127.7, 127.6, 126.3, 126.1, 103.1, 62.1, 61.1, 53.1, 52.5, 51.2, 20.9, 20.8, 19.0, 15.8; IR (KBr) ν 2947, 1738, 1699, 1557, 1431, 1262, 1223, 910, 734, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{35}NO_4$ 509.2566, found 509.2564.

*Dimethyl 1-ethyl-2-methyl-5-phenyl-1,2-dihydrospiro[azepine-3,9′-fluorene]-6,7-dicarboxylate (**4i**):* white solid; 53% yield; mp 114–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J_1 = 16.1 Hz, J_2 = 7.7 Hz, 2H), 7.43–7.31 (m, 4H), 7.31–7.12 (m, 7H), 5.89 (s, 1H), 3.86 (s, 3H), 3.18 (s, 3H), 3.10–2.99 (m, 2H), 2.37–2.20 (m, 1H), 1.35 (d, J = 6.7 Hz, 3H), 1.00 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 167.1, 150.5, 150.0, 146.4, 145.7, 140.1, 139.9, 139.4, 128.3, 127.8, 127.7, 127.6, 127.0, 126.6, 126.3, 126.1, 125.3,

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120.1, 119.6, 106.0, 62.90, 61.92, 52.81, 52.77, 51.5, 17.9, 14.7; IR (KBr) ν 2945, 1740, 1701, 1548, 1492, 1264, 1221, 1096, 756, 737, 704 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{29}NO_4$ 479.2097, found 479.2096.

*Diethyl 6-(4-chlorophenyl)-1-ethyl-6-(4-methoxyphenyl)-7-methyl-4-phenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4j**):* yellow solid; 60% yield; mp 99−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.5 Hz, 2H), 7.31−7.17 (m, 5H), 7.14 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 6.03 (s, 1H), 4.58 (q, J = 6.0 Hz, 1H), 4.19−4.02 (m, 2H), 3.80−3.55 (m, 5H), 3.07−2.58 (m, 2H), 1.35−1.27 (t, J = 6.9 Hz, 3H), 1.23−1.13 (m, 6H), 0.69 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 166.0, 157.5, 147.5, 145.6, 141.1, 131.8, 131.5, 129.4, 128.6, 127.8, 127.6, 126.5, 126.3, 113.8, 102.7, 63.0, 61.7, 60.4, 60.2, 55.2, 53.3, 19.3, 16.2, 13.5, 13.4; IR (KBr) ν 2981, 1738, 1698, 1552, 1510, 1255, 1093, 1037, 832, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{34}H_{36}ClNO_5$ 573.2282, found 573.2285.

*Diethyl 1-ethyl-6,7-dimethyl-4,6-diphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4k**):* white oil; 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.1 Hz, 1H), 7.39−7.14 (m, 9H), 6.14 (s, 0.5H), 5.57 (s, 0.5H), 4.37−4.22 (m, 1H), 4.16−4.01 (m, 1H), 3.76−3.41 (m, 4H), 3.00−2.66 (m, 0.5H), 2.54−2.38 (m, 0.5H), 1.55 (s, 1.5H), 1.44 (s, 1.5H), 1.41−1.31 (m, 3H), 1.24−1.16 (m, 1.5H), 1.16−1.07 (m, 3H), 0.90 (d, J = 6.6 Hz, 1.5H), 0.72−0.58 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 170.0, 166.7, 166.4, 147.6, 146.8, 146.7, 146.6, 146.4, 143.0, 139.9, 137.5, 132.9, 131.7, 128.2, 127.9, 127.8, 126.72, 126.67, 126.5, 126.2, 126.0, 125.9, 103.2, 102.3, 66.4, 65.5, 61.9, 61.5, 60.2, 60.1, 52.6, 52.1, 51.3, 48.9, 30.0, 24.0, 17.4, 17.2, 15.8, 15.4, 13.7, 13.6, 13.3, 13.2; IR (film) ν 2979, 1737, 1698, 1549, 1444, 1258, 1217, 1097, 761, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{28}H_{33}NO_4$ 447.2410, found 447.2406.

*Dimethyl 7-ethyl-4,6,6-triphenyl-1-propyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4l**):* white solid; 77% yield; mp 208−209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.23 (m, 8H), 7.22−7.14 (m, 4H), 7.13−7.07 (m, 1H), 7.07−7.01 (m, 2H), 6.11 (s, 1H), 4.28 (d, J = 9.3 Hz, 1H), 3.70 (d, J = 2.0 Hz, 3H), 3.19 (d, J = 2.1 Hz, 3H), 2.53−2.20 (m, 2H), 1.65−1.24 (m, 4H), 1.16 (t, J = 7.2 Hz, 3H), 0.62 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 166.9, 149.6, 146.5, 146.1, 142.7, 140.0, 133.8, 128.5, 128.3, 128.1, 127.9, 127.7, 126.5, 126.2, 126.0, 106.3, 69.9, 63.3, 60.0, 52.6, 51.5, 24.0, 23.0, 12.2, 11.1; IR (KBr) ν 2969, 1741, 1708, 1553, 1492, 1429, 1260, 1217, 1094, 753, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{35}NO_4$ 509.2566, found 509.2569.

*Dimethyl 1-butyl-4,6,6-triphenyl-7-propyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4m**):* white solid; 81% yield; mp 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.22 (m, 8H), 7.18 (t, J = 7.2 Hz, 4H), 7.12−7.01 (m, 3H), 6.11 (s, 1H), 4.36 (d, J = 9.5 Hz, 1H), 3.68 (s, 3H), 3.19 (s, 3H), 2.54−2.27 (m, 2H), 1.87−1.69 (m, 1H), 1.59−1.31 (m, 4H), 1.29−1.13 (m, 1H), 1.05−0.85 (m, 5H), 0.78 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 166.8, 149.6, 146.6, 146.2, 142.7, 140.0, 133.8, 128.5, 128.3, 128.1, 127.9, 127.7, 126.4, 126.2, 126.1, 126.0, 106.3, 68.5, 63.3, 58.1, 52.5, 51.4, 33.5, 31.6, 20.8, 19.9, 14.5, 13.6; IR (KBr) ν 2960, 1738, 1696, 1547, 1444, 1253, 1202, 1093, 758, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{35}H_{39}NO_4$ 537.2879, found 537.2876.

*Dimethyl 1-benzyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4n**):* white solid; 78% yield; mp 153−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.6 Hz, 2H), 7.40−7.12 (m, 13H), 7.11−6.93 (m, 6H), 6.80 (t, J = 4.0 Hz, 2H), 6.75 (d, J = 7.6 Hz, 2H), 6.51 (s, 1H), 5.47 (s, 1H), 4.35 (d, J = 15.3 Hz, 1H), 4.10 (d, J = 15.3 Hz, 1H), 3.82 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 167.6, 151.0, 144.8, 144.3, 143.8, 140.1, 139.8, 134.1, 130.4, 128.6, 128.5, 128.3, 128.2, 128.1, 127.7, 127.4, 127.3, 127.1, 126.6, 126.3, 126.2, 126.0, 101.4, 74.6, 56.2, 55.9, 52.7, 50.7; IR (KBr) ν 2980, 1727, 1694, 1553, 1492, 1444, 1356, 1261, 1142, 759, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{41}H_{35}NO_4$ 605.2566, found 605.2563.

*Diethyl 7,9,9-triphenyl-2,3,9,9a-tetrahydro-1H-pyrrolo[1,2-a]-azepine-5,6-dicarboxylate (**4o**):* white solid; 64% yield; mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.28 (m, 4H), 7.28−7.12 (m, 11H), 6.06 (s, 1H), 4.52 (t, J = 6.7 Hz, 1H), 4.37−4.23 (m, 2H), 3.72−3.53 (m, 2H), 3.38 (dd, J_1 = 17.4 Hz, J_2 = 7.6 Hz, 1H), 3.13−3.02 (m, 1H), 2.13−2.03 (m, 2H), 1.64−1.50 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H), 0.91−0.78 (m, 1H), 0.58 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 166.2, 150.7, 146.9, 146.8, 143.4, 138.3, 136.0, 130.2, 128.3, 128.0, 127.8, 127.3, 126.9, 126.7, 126.4, 126.1, 102.3, 71.8, 61.6, 59.6, 51.1, 30.2, 23.1, 13.9, 13.3; IR (KBr) ν 2980, 1727, 1694, 1560, 1261, 1222, 1142, 1095, 759, 701 cm^{-1}; HRMS (EI) calcd for $C_{33}H_{33}NO_4$ 507.2410, found 507.2412.

*Dimethyl 7,9,9-triphenyl-2,3,9,9a-tetrahydro-1H-pyrrolo[1,2-a]-azepine-5,6-dicarboxylate (**4p**):* white solid; 65% yield; mp 187−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.29 (m, 4H), 7.29−7.12 (m, 11H), 6.10 (s, 1H), 4.52 (t, J = 6.6 Hz, 1H), 3.86 (s, 3H), 3.36 (dd, J = 16.5, 8.1 Hz, 1H), 3.14−3.02 (m, 4H), 2.16−1.98 (m, 2H), 1.67−1.53 (m, 1H), 0.95−0.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 166.6, 150.7, 146.8, 146.6, 143.3, 138.4, 135.8, 130.1, 128.3, 128.0, 127.8, 127.3, 126.7, 126.54, 126.48, 126.1, 101.9, 71.8, 59.4, 52.6, 51.2, 50.8, 30.2, 23.0; IR (KBr) ν 2948, 1735, 1701, 1560, 1442, 1271, 1225, 1143, 760, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{29}NO_4$ 479.2097, found 479.2098.

*Diethyl 8,10,10-triphenyl-1,2,3,4,10,10a-hexahydropyrido[1,2-a]-azepine-6,7-dicarboxylate (**4q**):* white solid; 73% yield; mp 191−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.40 (m, 6H), 7.36−7.20 (m, 5H), 7.20−7.09 (m, 3H), 7.05 (t, J = 7.0 Hz, 1H), 6.72 (s, 1H), 4.73 (d, J = 8.7 Hz, 1H), 4.32−4.06 (m, 2H), 3.71−3.52 (m, 3H), 3.13 (t, J = 11.8 Hz, 1H), 1.86 (s, 1H), 1.79−1.55 (m, 5H), 1.27 (t, J = 7.0 Hz, 3H), 0.64 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 166.6, 149.9, 146.2, 144.6, 144.2, 141.1, 133.4, 128.6, 127.9, 127.7, 126.8, 126.6, 126.2, 125.9, 125.8, 100.3, 72.5, 61.4, 58.9, 54.5, 54.0, 31.4, 27.4, 25.2, 13.9, 13.6; IR (KBr) ν 2935, 1729, 1691, 1547, 1492, 1445, 1256, 1117, 1040, 746, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{34}H_{35}NO_4$ 521.2566, found 521.2568.

*Dimethyl 1-ethyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4s**):* white solid; 59% yield; mp 175−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.8 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H), 7.33−7.16 (m, 6H), 7.15−7.05 (m, 4H), 7.04−6.93 (m, 4H), 6.81 (d, J = 7.6 Hz, 2H), 6.52 (s, 1H), 5.61 (s, 1H), 3.78 (s, 3H), 3.42−3.11 (m, 2H), 3.05 (s, 3H), 1.11 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 166.9, 150.6, 145.1, 144.5, 144.2, 141.1, 140.2, 133.3, 129.9, 128.8, 128.1, 128.0, 127.8, 127.6, 127.3, 127.1, 126.5, 126.34, 126.29, 126.0, 100.9, 57.0, 52.5, 50.6, 50.4, 14.4; IR (KBr) ν 2947, 1738, 1698, 1557, 1266, 1445, 1126, 910, 725, 699 cm^{-1}; HRMS (EI) m/z calcd for $C_{36}H_{33}NO_4$ 543.2410, found 543.2411.

*Diethyl 1-ethyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4t**):* white solid; 52% yield; mp 165−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 7.5 Hz, 2H), 7.33−7.16 (m, 6H), 7.15−7.06 (m, 4H), 7.05−6.95 (m, 4H), 6.83 (d, J = 7.4 Hz, 2H), 6.48 (s, 1H), 5.62 (s, 1H), 4.22 (q, J = 7.0 Hz, 2H), 3.54 (q, J = 7.1 Hz, 2H), 3.44−3.10 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H), 0.57 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 166.4, 150.7, 145.1, 144.8, 144.3, 141.3, 140.5, 133.0, 129.9, 128.8, 128.2, 127.9, 127.8, 127.5, 127.3, 127.1, 126.4, 126.3, 126.1, 101.0, 77.7, 61.5, 59.2, 57.0, 50.3, 14.5, 13.8, 13.4; IR (KBr) ν 2977, 1734, 1690, 1554, 1493, 1441, 1257, 1220, 1132, 700 cm^{-1}; HRMS (EI) m/z calcd for $C_{38}H_{37}NO_4$ 571.2723, found 571.2716.

*Diethyl 8,10,10-triphenyl-3,4,10,10a-tetrahydro-1H-[1,4]oxazino-[4,3-a]azepine-6,7-dicarboxylate (**4r**):* white solid; 34% yield; mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.39 (m, 6H), 7.36−7.25 (m, 4H), 7.22−711 (m, 3H), 7.07 (t, J = 7.3 Hz, 1H), 6.86 (s, 1H), 4.96 (d, J = 9.0 Hz, 1H), 4.32−4.16 (m, 2H), 3.84 (dd, J_1 = 34.0 Hz, J_2 = 11.1 Hz, 2H), 3.69−3.48 (m, 4H), 3.47−3.32 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H), 0.65 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 166.0, 150.2, 144.6, 144.4, 143.3, 141.9, 133.4, 128.8, 128.0, 127.9, 126.7, 126.4, 126.2, 126.0, 103.6, 73.2, 71.3, 67.4, 61.7, 59.1, 52.2, 13.9, 13.5; IR (KBr) ν 2977, 1735, 1695, 1560, 1365, 1261, 1122, 1075, 748, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{33}NO_5$ 523.2359, found 523.2351.

*Dimethyl 1-methyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4u**):* white solid; 32% yield; mp 194−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.7 Hz, 2H), 7.39 (d, J = 7.5 Hz, 2H), 7.30 (t, J = 7.2 Hz, 4H), 7.25−7.17 (m, 2H), 7.14−7.05

(m, 4H), 7.01 (t, J = 7.5 Hz, 2H), 7.05−6.97 (m, 2H), 6.75 (d, J = 7.5 Hz, 2H), 6.56 (s, 1H), 5.41 (s, 1H), 3.82 (s, 3H), 3.05 (s, 3H), 2.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.8, 151.1, 144.7, 144.6, 144.5, 140.2, 140.0, 133.0, 129.8, 128.8, 128.0, 127.9, 127.72, 127.69, 127.5, 127.2, 126.5, 126.41, 126.37, 126.0, 100.2, 81.2, 56.5, 52.5, 50.6, 41.3; IR (KBr) ν 2947, 1741, 1698, 1558, 1494, 1448, 1270, 1131, 755, 699 cm^{-1}; HRMS (EI) m/z calcd for $C_{35}H_{31}NO_4$ 529.2253, found 529.2250.

*Diethyl 1-methyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4v**):* white solid; 20% yield; mp 170−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 7.7 Hz, 2H), 7.40 (d, J = 7.3 Hz, 2H), 7.34−7.16 (m, 6H), 7.15−7.07 (m, 4H), 7.02 (t, J = 7.5 Hz, 2H), 6.98−6.90 (m, 2H), 6.77 (d, J = 7.5 Hz, 2H), 6.54 (s, 1H), 5.42 (s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.65−3.41 (m, 2H), 2.95 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 0.55 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 166.3, 151.2, 144.8, 144.7, 144.6, 140.5, 140.1, 132.6, 129.8, 127.93, 127.87, 127.7, 127.6, 127.4, 127.2, 126.4, 126.34, 126.28, 126.2, 100.1, 81.3, 61.5, 59.0, 56.4, 41.1, 13.8, 13.4; IR (KBr) ν 2927, 1734, 1695, 1629, 1560, 1266, 1134, 1078, 721, 699 cm^{-1}; HRMS (EI) m/z calcd for $C_{37}H_{35}NO_4$ 557.2566, found 557.2569.

*Dimethyl 1-isopropyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4w**):* white solid; 23% yield; mp 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.8 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H), 7.33−7.01 (m, 12H), 6.95 (t, J = 7.3 Hz, 2H), 6.82 (d, J = 7.8 Hz, 2H), 6.49 (s, 1H), 5.78 (s, 1H), 3.93−3.82 (m, 1H), 3.78 (s, 3H), 3.06 (s, 3H), 1.46 (d, J = 6.4 Hz, 3H), 0.73 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 167.5, 150.7, 145.4, 144.4, 144.1, 142.3, 140.1, 133.7, 130.5, 128.7, 128.1, 128.0, 127.8, 127.5, 127.1, 126.7, 126.4, 126.2, 125.9, 71.7, 57.1, 56.7, 52.4, 50.6, 24.7, 19.9; IR (KBr) ν 2947, 1738, 1669, 1538, 1494, 1431, 1262, 1105, 910, 735, 699 cm^{-1}; HRMS (EI) m/z calcd for $C_{37}H_{35}NO_4$ 557.2566, found 557.2569.

*Diethyl 1-isopropyl-4,6,6,7-tetraphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4x**):* white solid; 16% yield; mp 167−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.4 Hz, 2H), 7.41 (d, J = 7.1 Hz, 2H), 7.35−7.18 (m, 5H), 7.18−7.01 (m, 7H), 6.95 (t, J = 7.3 Hz, 2H), 6.83 (d, J = 7.3 Hz, 2H), 6.46 (s, 1H), 5.79 (s, 1H), 4.33−4.21 (m, 2H), 4.09−3.82 (m, 1H), 3.54 (q, J = 6.2 Hz, 2H), 1.46 (d, J = 6.3 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H), 0.76 (d, J = 6.5 Hz, 3H), 0.59 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 166.9, 151.0, 145.4, 144.7, 144.3, 142.6, 140.5, 133.2, 130.5, 128.8, 128.2, 127.9, 127.8, 127.4, 127.1, 126.7, 126.4, 126.2, 126.1, 101.7, 71.7, 61.4, 59.1, 57.0, 56.2, 24.9, 19.9, 13.7, 13.4; IR (KBr) ν 2981, 1734, 1695, 1546, 1493, 1248, 1222, 1101, 1030, 699 cm^{-1}; HRMS (EI) m/z calcd for $C_{39}H_{39}NO_4$ 585.2879, found 585.2877.

*Dimethyl 1-isobutyl-7-isopropyl-4,6,6-triphenyl-6,7-dihydro-1H-azepine-2,3-dicarboxylate (**4y**):* white solid; 17% yield; mp 137−138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 7.7 Hz, 2H), 7.43 (d, J = 7.3 Hz, 2H), 7.37−7.26 (m, 6H), 7.21 (t, J = 7.3 Hz, 1H), 7.13 (dd, J_1 = 14.9 Hz, J_2 = 7.5 Hz, 3H), 7.02 (t, J = 7.3 Hz, 1H), 6.56 (s, 1H), 4.78 (d, J = 3.4 Hz, 1H), 3.66 (s, 3H), 3.15 (s, 3H), 2.98−2.85 (m, 2H), 2.23−2.09 (m, 1H), 1.72−1.62 (m, 1H), 1.08 (d, J = 7.0 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H), 0.58 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 166.8, 149.7, 148.8, 145.0, 142.0, 140.8, 131.8, 128.29, 128.28, 128.0, 127.6, 126.4, 125.8, 103.3, 72.3, 64.2, 59.9, 52.3, 51.1, 35.4, 26.2, 25.6, 21.3, 20.9, 19.6; IR (KBr) ν 2960, 1741, 1709, 1547, 1256, 1214, 1109, 1088, 750, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{35}H_{39}NO_4$ 537.2879, found 537.2891.

*Diethyl 4-(diphenylmethylene)-1-morpholino-3-phenylcyclobut-2-ene-1,2-dicarboxylate (**5**):* yellow solid; 31% yield; mp 98−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 3.6 Hz, 2H), 7.34−7.26 (m, 3H), 7.09 (t, J = 6.9 Hz, 3H), 6.99 (t, J = 6.8 Hz, 3H), 6.95−6.82 (m, 4H), 4.27−4.01 (m, 4H), 3.68 (d, J = 3.6 Hz, 4H), 2.85 (s, 4H), 1.22 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 162.4, 161.5, 139.1, 138.7, 136.9, 136.2, 130.9, 130.5, 130.2, 128.4, 128.3, 128.0, 127.6, 127.4, 127.3, 126.9, 78.0, 67.5, 60.9, 60.4, 48.8, 14.03, 13.95; IR (KBr) ν 2925, 1743, 1704, 1444, 1330, 1243, 1177, 1117, 762, 698 cm^{-1}; HRMS (EI) m/z calcd for $C_{33}H_{33}NO_5$ 523.2359, found 523.2366.

*Dimethyl 2-benzyl-5-(diphenylmethylene)-1-methyl-4-phenyl-2,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**6a**):* yellow solid; 45% yield; mp 119−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.31 (m, 3H), 7.22−7.07 (m, 5H), 6.91−6.59 (m, 10H), 6.36 (s, 1H), 6.28 (d, J = 6.0 Hz, 1H), 3.87 (s, 3H), 3.62−3.42 (m, 5H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 163.8, 153.6, 150.5, 143.4, 141.9, 136.3, 134.2, 132.4, 131.6, 130.8, 130.3, 128.8, 128.4, 127.9, 127.5, 126.8, 126.6, 126.5, 125.5, 125.4, 115.1, 79.0, 52.8, 51.4, 37.9, 34.3; IR (KBr) ν 2951, 1730, 1617, 1439, 1366, 1238, 1172, 1106, 758, 697 cm^{-1}; HRMS (EI) m/z calcd for $C_{35}H_{31}NO_4$ 529.2253, found 529.2249.

*Diethyl 2-benzyl-5-(diphenylmethylene)-1-methyl-4-phenyl-2,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**6b**):* yellow solid; 56% yield; mp 114−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.31 (m, 3H), 7.22−7.06 (m, 5H), 6.88−6.59 (m, 10H), 6.36 (s, 1H), 6.28 (d, J = 7.3 Hz, 1H), 4.41−4.25 (m, 2H), 4.02 (q, J = 6.9 Hz, 2H), 3.59 (d, J = 14.4 Hz, 1H), 3.47 (d, J = 14.5 Hz, 1H), 2.43 (s, 3H), 1.37 (t, J = 7.0 Hz, 3H), 0.96 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 163.4, 153.2, 150.9, 143.5, 142.0, 136.5, 134.4, 132.9, 132.3, 131.7, 130.8, 130.3, 128.8, 128.5, 127.9, 127.5, 126.8, 126.5, 125.43, 125.37, 114.6, 79.0, 61.6, 60.2, 37.7, 34.3, 14.4, 13.7; IR (KBr) ν 2983, 1728, 1700, 1617, 1378, 1214, 1175, 1035, 758, 698 cm^{-1}; HRMS (EI) m/z calcd for $C_{37}H_{35}NO_4$ 557.2566, found 557.2574.

*Dimethyl 4-(2,2-diphenylvinyl)-1-isopropyl-4,5-diphenyl-4,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**7a**):* white solid; 49% yield; mp 174−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (t, J = 7.5 Hz, 2H), 7.38 (d, J = 7.8 Hz, 2H), 7.34−7.18 (m, 7H), 7.09−6.95 (m, 5H), 6.89 (s, 2H), 6.76 (s, 2H), 6.20 (s, 1H), 5.49 (s, 1H), 3.99 (s, 3H), 3.53 (s, 3H), 3.01−2.86 (m, 1H), 0.79 (d, J = 7.0 Hz, 3H), 0.59 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 164.9, 153.5, 145.1, 143.2, 142.9, 140.6, 137.0, 136.3, 131.3, 128.8, 128.3, 128.0, 127.9, 127.5, 127.43, 127.38, 127.2, 127.1, 127.0, 125.9, 108.3, 75.0, 58.2, 52.8, 50.9, 48.8, 20.5, 20.2; IR (KBr) ν 2948, 1750, 1685, 1576, 1491, 1222, 1135, 789, 723, 703 cm^{-1}; HRMS (EI) m/z calcd for $C_{37}H_{35}NO_4$ 557.2566, found 557.2565.

*Diethyl 4-(2,2-diphenylvinyl)-1-isopropyl-4,5-diphenyl-4,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**7b**):* white solid; 52% yield; mp 131−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 7.5 Hz, 2H), 7.40 (d, J = 7.3 Hz, 2H), 7.33−7.16 (m, 7H), 7.09−6.96 (m, 5H), 6.91 (s, 2H), 6.76 (s, 2H), 6.23 (s, 1H), 5.46 (s, 1H), 4.45 (q, J = 7.1 Hz, 2H), 4.17−3.89 (m, 2H), 3.04−2.89 (m, 1H), 1.48 (t, J = 7.1 Hz, 3H), 0.99 (t, J = 7.1 Hz, 3H), 0.79 (d, J = 7.0 Hz, 3H), 0.59 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.4, 153.5, 145.3, 143.1, 142.8, 140.6, 137.3, 136.8, 131.3, 128.7, 128.3, 128.0, 127.5, 127.3, 127.2, 127.0, 126.9, 125.8, 108.6, 74.7, 61.9, 59.0, 58.4, 48.9, 20.5, 20.3, 14.3, 14.0; IR (KBr) ν 2980, 1745, 1685, 1588, 1443, 1367, 1219, 1184, 1132, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{39}H_{39}NO_4$ 585.2879, found 585.2880.

*Dimethyl 2-(isobutylamino)-3-[(E)-1,3,3-triphenylprop-1-en-1-yl]-maleate (**8**):* white solid; 58% yield; mp 94−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 5H), 7.10−6.91 (m, 10H), 4.56 (s, 1H), 3.81 (s, 3H), 3.34 (s, 3H), 2.58−2.35 (m, 2H), 2.14 (s, 1H), 1.82−1.68 (m, 1H), 0.93 (t, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 169.1, 149.5, 146.3, 142.2, 140.4, 139.3, 131.6, 130.2, 128.5, 128.2, 128.1, 127.5, 127.4, 127.2, 126.6, 62.2, 55.7, 52.4, 51.3, 28.6, 20.5; IR (KBr) ν 3384, 2958, 1735, 1686, 1581, 1492, 1431, 1252, 757, 700 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{33}NO_4$ 483.2410, found 483.2408.

Procedure for the Preparation of 9. To a solution of diethylamine (**2a**) (1 mmol) in dry dichloromethane (3 mL) was added methyl propiolate (1 mmol), and the solution was stirred at room temperature for 10 min. Then, propargylic alcohol (**3a**) (1 mmol), 4 Å molecular sieves (400 mg), and $BF_3{\cdot}Et_2O$ (1 mmol) were added in sequence. The mixture was stirred for 1 h and then evaporated under vacuum. The residue was purified by silica gel column chromatography with a hexane/EtOAc mixture (10:1, v/v) to afford pure **9** (191 mg, 52% yield).

*(Z)-Methyl 2-formyl-3,5,5-triphenylpenta-2,4-dienoate (**9**):* yellow solid; 52% yield; mp 127−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.40−7.26 (m, 5H), 7.17−6.96 (m, 9H), 6.87 (d, J = 7.3 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 189.8, 167.0, 159.2, 154.2, 141.6, 139.0, 135.3, 134.3, 130.7, 130.4, 129.2, 128.5, 128.3, 128.0, 127.7, 127.4, 126.4, 52.5; IR (KBr) ν 2855, 1729, 1651, 1568, 1329, 1310, 1269, 1147, 775, 702 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{20}O_3$ 368.1412, found 368.1405.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra and crystallographic information (CIF files) for compounds **4a**, **6b**, **7a**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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