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Lewis acid-promoted cascade reaction of primary amine, 2-butynedioate, and propargylic alcohol: a convenient approach to 1,2-dihydropyridines and 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*,6*H*)-diones

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ABSTRACT

1,2-Dihydropyridine-5,6-dicarboxylates were efficiently constructed through a cascade reaction of primary amine, 2-butynedioate and propargylic alcohol in the presence of Lewis acid under mild conditions. As exceptional, 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*,6*H*)-diones were approached when the primary amine was methylamine. Possible mechanism for the formation of 1,2-dihydropyridine skeleton is proposed. The process involves 1,3,4-pentatrien-1-amine as a key intermediate that formed in situ by trapping allenic carbocations with enamines.

1. Introduction

1,2-Dihydropyridines and 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*,6*H*)-diones are important substructures of many nitrogen-containing heterocycles with various functionalities.[1] As examples, 1,2-dihydropyridine derivatives have been disclosed to be potential anticancer[2] and antiulcer agents.[3] Beyond of these pharmaceutical values, 1,2-dihydropyridines are useful intermediates for the synthesis of the natural products with bioactivities.[4] The traditional synthetic route to 1,2-dihydropyridines is the reduction of the corresponding pyridines or pyridinium salts with metal complex.[5] However, regioisomeric mixtures from reduction are often obtained. Recent methods include the metal-catalyzed hydroboration[6] and hydrosilylation[7] of pyridines, thermal 6π-aza electrocyclization of 1-azatrienes,[8] and Pt(II)-catalyzed cycloisomerization of aziridinyl propargylic esters,[9] which exhibited high regioselectivities, but required either high temperature or noble metal catalyst.

Previously, we developed an efficient synthesis of dihydroazepine via a cascade reaction of propargylic alcohols, 2-butynedioates and secondary amines in the presence of Lewis acid.[10] During this three-component reaction, the allenic carbocation[11] was ideally formed in situ via Meyer–Schuster rearrangement from propargylic alcohols and was lately trapped by enamine, which was derived from butynedioate and a secondary amine. More recently, when we used primary amines instead of secondary amines to perform this reaction, the products containing 1,2-dihydropyridine skeleton were isolated. Moreover, the fused 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*,6*H*)-diones, which displayed a unique function in pharmaceutical science,[12] were also created when methylamine was used as the primary amine substrate. Herein, we would like to disclose the detail of these results.

2. Results and discussion

Initially, we treated 1,1,3-triphenylprop-2-yn-1-ol (**1a**) with an equivalent amount of dimethyl 2-(*p*-tolylamino)maleate (**2a**) in the presence of $BF_3 \cdot Et_2O$ in DCM at room temperature for 1 h. In this way, **3a** was isolated in 60% yield (Table 1, entry 1). Structure of **3a** was determined by X-ray single-crystal analysis and contained 1,2-dihydropyridine heterocycle.[13] Further optimization of the reaction conditions showed that a slightly decreased temperature (0 °C) would bring about a higher yield (Table 1, entry 2). When the reaction temperature was dropped to −20 °C, **3a** was isolated in 57% yield if the reaction time was extended to 3 h (Table 1, entry 3). Without the existence of 4 Å molecular sieve, **3a** was isolated in 54% yield (Table 1, entry 4). TsOH did not work for this transformation (Table 1, entry 6). Other Lewis acid catalysts, such as $FeCl_3$, $AlCl_3$,

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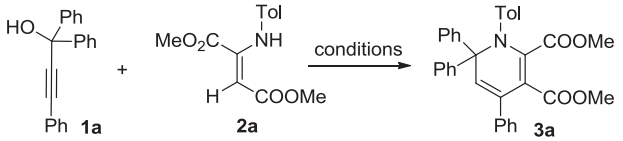
$ZnCl_2$, $Sc(OTf)_3$ and $Zn(OTf)_2$, were subsequently screened (Table 1, entries 5–10). $AlCl_3$ and $ZnCl_2$ afforded **3a** in yields of 52% and 18%, respectively. $FeCl_3$ only gave trace of the desired product. Catalytic amount of $Sc(OTf)_3$ or $Zn(OTf)_2$ did not work with the recovery of the starting materials (Table 1, entries 9–10). Other solvents, such as toluene, acetonitrile and tetrahydrofuran, afforded the desired product in relatively lower yields (Table 1, entries 11–13). Thus, the optimized reaction condition was established (Table 1, entry 2).

Table 1
Screening for the reaction conditions[a]

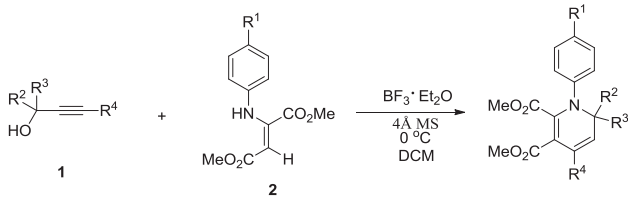


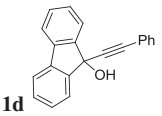
Entry	LA	Solvent	Temp (°C)	Time (h)	Additive	Yield (%)[b]
1	$BF_3\cdot Et_2O$	DCM	rt	1	4 Å MS	60
2	$BF_3\cdot Et_2O$	DCM	0	1	4 Å MS	67
3	$BF_3\cdot Et_2O$	DCM	−20	3	4 Å MS	57
4	$BF_3\cdot Et_2O$	DCM	0	1	—	54
5	$FeCl_3$	DCM	0	2	4 Å MS	Trace
6	TsOH	DCM	0	4	4 Å MS	Trace
7	$AlCl_3$	DCM	0	2	4 Å MS	52
8	$ZnCl_2$	DCM	0	4	4 Å MS	18
9	$Sc(OTf)_3$[c]	DCM	0	12	4 Å MS	nr[d]
10	$Zn(OTf)_2$[c]	DCM	0	12	4 Å MS	nr[d]
11	$BF_3\cdot Et_2O$	Toluene	0	2	4 Å MS	22
12	$BF_3\cdot Et_2O$	CH_3CN	0	2	4 Å MS	40
13	$BF_3\cdot Et_2O$	THF	0	2	4 Å MS	35

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), LA (0.5 mmol), 4 Å MS (0.2 g), solvent (3 mL).
[b] Isolated yield.
[c] LA (0.1 mmol) was used.
[d] No reaction.

With the optimized reaction conditions in hand, we examined the scope of substrates and the results are summarized in Table 2. Propargylic alcohol (**1b**), synthesized from benzophenone and *p*-methyl phenylacetylene, gave a slightly higher yield (Table 2, entry 2) than the propargylic alcohol (**1c**) derived from benzophenone and 3-bromo phenylacetylene (Table 2, entry 3). Fluorenone derived propargylic alcohol (**1d**) also worked for this transformation and afforded **3d** in 62% yield (Table 2, entry 4). Aromatic amine, with the electron-donating substituents, afforded **3f** in 69% yield (Table 2, entry 6).

Table 2
Substrate diversity of the transformation[a]

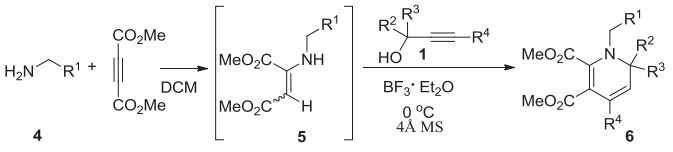


Entry	**1** ($R^2/R^3/R^4$)	**2** (R^1)	**3** (Yield, %)[b]
1	**1a** (Ph/Ph/Ph)	**2a** (Me)	**3a** (67)
2	**1b**(Ph/Ph/4-MeC_6H_4)	**2a**	**3b** (59)
3	**1c** (Ph/Ph/3-BrC_6H_4)	**2a**	**3c** (55)
4	 **1d**	**2a**	**3d** (62)
5	**1a**	**2b** (H)	**3e** (51)
6	**1a**	**2c** (OMe)	**3f** (69)

[a] Reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), $BF_3\cdot Et_2O$ (0.5 mmol), 4 Å MS (0.2 g), DCM (3 mL), 0 °C, 1 h.
[b] Isolated yield.

When benzyl amine (**4a**) was used instead of aromatic amine (**2**), a mixture of dimethyl *cis*- and *trans*-2-(benzylamino)maleates (**5**) was obtained.[14] Without further separation of the *cis*-**5** and *trans*-**5**, propargylic alcohol (**1a**) was added and reacted under the optimized reaction conditions that was established for the formation of **3**. As we expected, 1,2-dihydropyridine (**6a**) was obtained in 73% yield (Table 3, entry 1). Meanwhile, it was noticeable that **6a** could be efficiently formed either from pure *cis*-**5** or pure *trans*-**5**. *cis*-**5** and *trans*-**5** gave **6a** in 72% and 75% yields, respectively. In order to understand the scope of this one-pot two-step approach to 1,2-dihydropyridines, a variety of propargylic alcohols **1** and aliphatic primary amines **4** were examined (Table 3). Propargylic alcohols, synthesized from phenylacetylenes and benzophenones, afforded the corresponding dihydropyridines **6a**–**d** in yields varied from 61% to 73% (Table 3, entries 1–4). 1,1-Diphenylprop-2-yn-1-ol (**1h**) afforded **6e** in 58% yield (Table 3, entry 5). The propargylic alcohol derived from aliphatic alkyne and benzophenone produced **6f** in 40% yield (Table 3, entry 6). 2,4-Diphenylbut-3-yn-2-ol (**1j**) and 2-methyl-4-phenyl but-3-yn-2-ol (**1k**) furnished **6g** (Table 3, entry 7) and **6h** (Table 3, entry 8) in 53% and 35% yields, respectively. No desired product was isolated when the secondary propargylic alcohol **1l** was used as the substrate (Table 3, entry 9). A variety of primary amines **4a**–**g**, including the substituted benzyl amines **4a**–**d**, furan-2-ylmethanamine (**4e**), prop-2-yn-1-amine (**4f**), and butan-1-amine (**4g**), were suitable to this transformation and afforded the corresponding 1,2-dihydropyridines **6i**–**n** in yields varied from 57% to 76% (Table 3, entries 1 and 10–15). Methyl propiolate was also tested, but we obtained **6o** in poor yield (20%) (Scheme 1).[15]

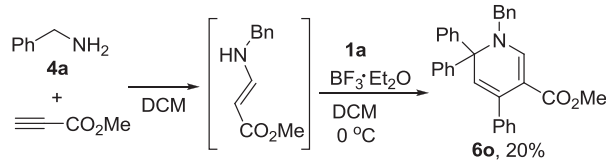
Table 3
Substrate diversity of three-component synthesis of **6**[a]



Entry	**1** ($R^2/R^3/R^4$)	**4** (R^1)	**6** (Yield, %)[b]
1	**1a**	**4a** (Ph)	**6a** (73)
2	**1e** (4-MeC_6H_4/4-MeC_6H_4/Ph)	**4a**	**6b** (66)
3	**1f** (4-ClC_6H_4/4-ClC_6H_4/Ph)	**4a**	**6c** (61)[c]
4	**1g** (4-MeC_6H_4/Ph/Ph)	**4a**	**6d** (70)
5	**1h** (Ph/Ph/H)	**4a**	**6e** (58)
6	**1i** (Ph/Ph/*n*-Bu)	**4a**	**6f** (40)
7	**1j** (Ph/Me/Ph)	**4a**	**6g** (53)
8	**1k** (Me/Me/Ph)	**4a**	**6h** (35)
9	**1l** (Ph/H/Ph)	**4a**	Complex
10	**1a**	**4b** (4-ClC_6H_4)	**6i** (76)
11	**1a**	**4c** (3-$MeOC_6H_4$)	**6j** (64)
12	**1a**	**4d** (3,4-di$MeOC_6H_3$)	**6k** (62)
13	**1a**	**4e** (2-furyl)	**6l** (70)
14	**1a**	**4f** (ethynyl)	**6m** (65)
15	**1a**	**4g** (*n*-Pr)	**6n** (57)

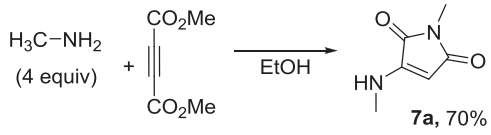
[a] Reaction conditions: Dimethyl but-2-ynedioate (0.5 mmol), **4** (0.5 mmol), **1** (0.5 mmol), $BF_3\cdot Et_2O$ (0.5 mmol), 4 Å MS (200 mg), DCM (3 mL), 0 °C, 1 h.
[b] Isolated yield.
[c] Run at 25 °C.

We then move our attention to the reaction between dimethyl but-2-ynedioate and methylamine in alcohol solution, enamine was isolated in 70% yield as a cyclic form, which was lately identified as 1-methyl-3-(methylamino)-1*H*-pyrrole-2,5-dione (**7a**)



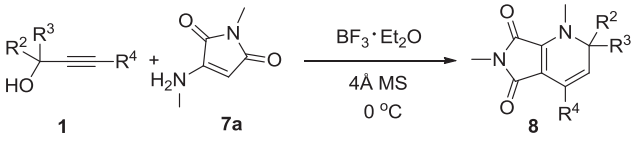
Scheme 1. Formation of **6o** from **4a** and methyl propiolate.

(Scheme 2). When **7a** was used as nucleophile to react with propargylic alcohols in the presence of Lewis acid under the optimized reaction conditions that was established for the formation of **3**, a series of 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*,6*H*)-diones **8a**–**f** were constructed. Their structures were further confirmed by single-crystal analysis of **8a**.[13] Similar to the formation of **6**, terminal propargylic alcohol (**1h**) could be used as the substrate, but with relatively lower yield in comparison with triaryl substituted propargylic alcohols **1a**, **1c**, **1e**, and **1f** (Table 4, entries 1–5). 2-Methyl-4-phenyl but-3-yn-2-ol (**1k**) also worked for the reaction and produced **8f** in 37% yield (Table 4, entry 6).



Scheme 2. Formation of **7a**.

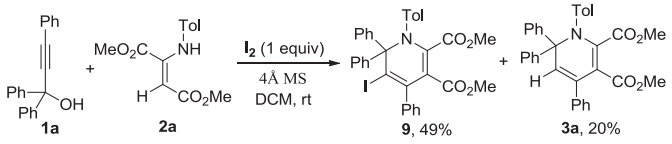
Table 4
Construction of **8** from **1** and **7a**[a]



entry	**1** ($R^2/R^3/R^4$)	**8** (Yield, %)[b]
1	**1a** (Ph/Ph/Ph)	**8a** (70)
2	**1c** (Ph/Ph/3-BrC_6H_4)	**8b** (63)
3	**1e** (4-MeC_6H_4/4-MeC_6H_4/Ph)	**8c** (74)
4	**1f** (4-ClC_6H_4/4-ClC_6H_4/Ph)	**8d** (60)
5	**1h** (Ph/Ph/H)	**8e** (51)
6	**1k** (Me/Me/Ph)	**8f** (37)

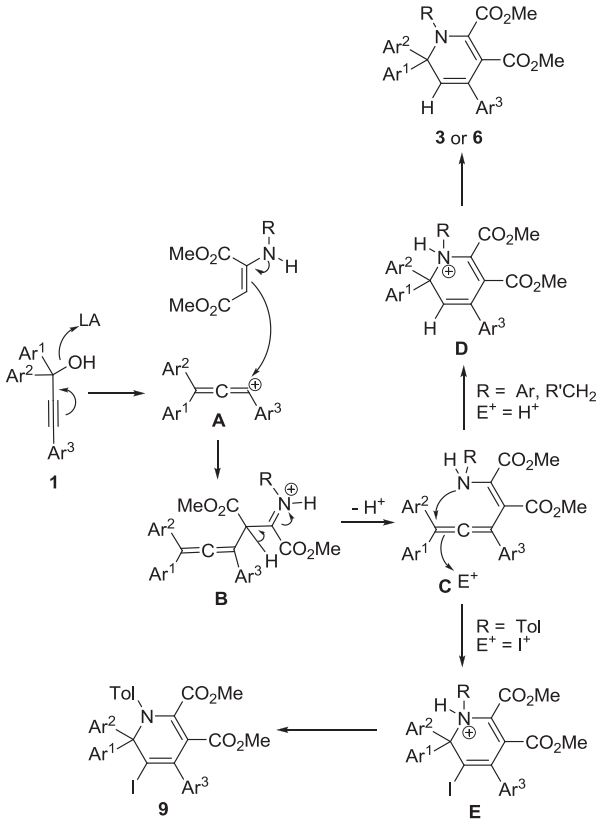
[a] Reaction conditions: **6** (0.5 mmol), **1** (0.5 mmol), $BF_3 \cdot Et_2O$ (0.5 mmol), 4 Å MS (0.2 g), DCM (3 mL), 0 °C, 1 h.
[b] Isolated yield.

In order to have a good insight into the reaction mechanism, iodine was used to trap the possible intermediate. Thus, in the presence of the equivalent molar ratio of iodine to propargylic alcohol, **1a** reacted with **2a** to produce **9** in 49% yield except for the formation of **3a**, which was isolated in yield of 20% (Scheme 3).



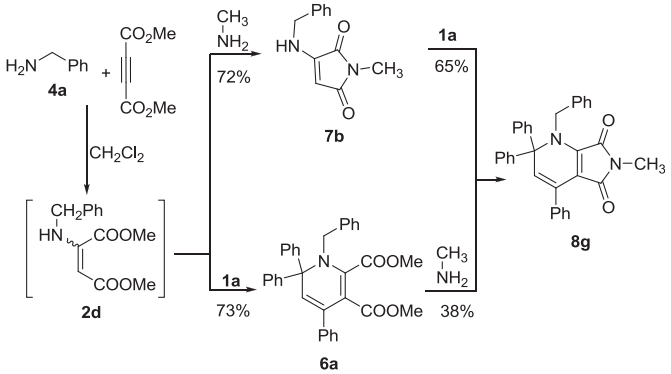
Scheme 3. Formation of 3-iodo-1,2-dihydropyridine (**9**).

Based on the above observations, a plausible mechanism for the formation of **3**, **6**, **8** and **9** is outlined in Scheme 4. The enamine suitably traps the allenic carbocation A, which is formed in situ through the Meyer–Schuster rearrangement of propargylic alcohols in the presence of Lewis acid.[16] Thus, the iminium intermediate **B** is formed with an active hydrogen. Subsequent deprotonation of **B** forms 1,3,4-pentatrien-1-amines **C**. As electrons flow indicated on the **C** structure, the electron-deficient central carbon of allene is attacked by the intramolecular nitrogen. Dihydropyridium **D** is generated, which finally turns to dihydropyridines **3** or **6** via the deprotonation. In the presence of iodine, iodo-substituted dihydropyridium E is formed, furnishing **9**.



Scheme 4. Possible mechanism for the formation of **3**, **6** and **9**.

Promoted by the formation of **8a**–**f**, we then treated **6a** with methylamine at 50 °C for 24 h to obtain **8g** in 38% yield (Scheme 5). Using the alternative way, **8g** was easily prepared from **7b** in 65% yield. It is clear that a relatively lower yield was observed for the



Scheme 5. Alternative formations of **8g**.

rout from **6a** to **8g**. In order to have a good insight into this result, we calculated the alternative ways to construct the five-member rings (Fig. 1). It is observed that the activation energy required for the process from **6a** to **8g** is much higher than that required for the process from **2d** to **7b**. Therefore, a preliminary conclusion could be made that a ring with a higher strain should be constructed prior to the ring with a lower strain. In this case, **8** could be easily formed in a sequence where the pyrrole-2,5-dione ring was constructed first.

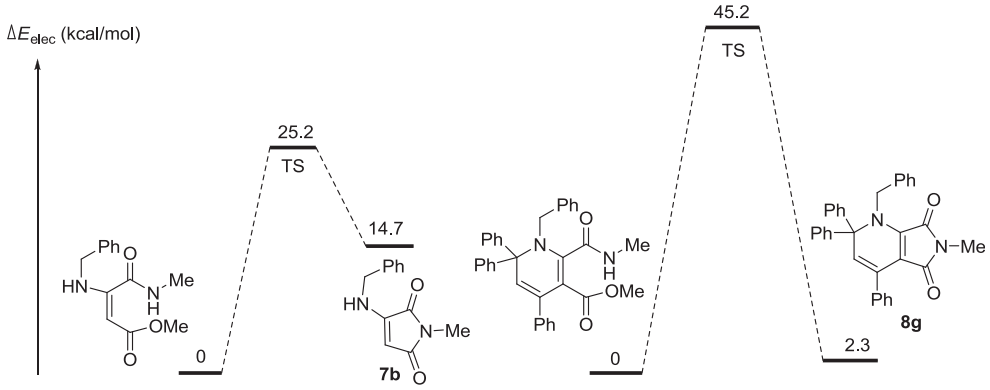


Fig. 1. Alternative ways to form five-member rings **7b** (left) and **8g** (right), calculated using Gaussian 03.

3. Conclusion

In conclusion, we developed a Lewis acid-promoted cascade synthesis of 1,2-dihydropyridines and 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*,6*H*)-diones from propargylic alcohols, 2-butynedioates and primary amines. Thus, the enamines in situ generated from primary amines and 2-butynedioates reacted with propargylic alcohols in the presence of Lewis acid to give 1,2-dihydropyridine-5,6-dicarboxylates. As exceptional, 1*H*-pyrrolo[3,4-*b*]pyridine-5,7(2*H*, 6*H*)-diones were approached when the primary amine was methylamine. It is believed that the cascade process involves 1,3,4-pentatrien-1-amine as a key intermediate derived in situ by trapping the active allenic carbocations with enamines. Compared with the published methods, the present procedure furnished 1,2-dihydropyridines under mild conditions and with commercially available starting materials.

4. Experimental section

4.1. General

Infrared spectra were obtained on a FTIR spectrometer. NMR spectra were recorded for ^{1}H NMR at 400 or 500 MHz, using TMS as internal standard and ^{13}C NMR at 100 or 125 MHz using $CDCl_3$ as 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 (Hz). HRMS were obtained using EI ionization. Melting points were measured with micro melting point apparatus.

The propargylic alcohols were prepared according to the published methods.[17] Dichloromethane (DCM) was distilled from CaH_2 under N_2 atmosphere. 4 Å MS was activated by baking in a muffle oven. Other materials were purchased from common commercial sources and used without additional purification.

Energies reported are Gibbs free energies in gas phase, involving zero-point vibrational energy corrections and thermal corrections at 298 K. Vibrational frequencies were calculated for all optimized structures to confirm the nature of the stationary points. All calculations were performed using Gaussian 03.[18]

4.2. General procedure for the preparation of dihydropyridines 3

To a solution of propargylic alcohol **1** (0.5 mmol), enamine **2** (0.5 mmol) and 4 Å molecular sieve (200 mg) in dry dichloromethane (3 mL) was added $BF_3\cdot Et_2O$ (0.5 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h and then evaporated on vacuum. The product was isolated by silica gel column chromatography with hexane–EtOAc–Et_3N (10:1:0.1, v/v/v) as eluent.

*4.2.1. Dimethyl 4,6,6-triphenyl-1-(p-tolyl)-1,6-dihydropyridine-2,3-dicarboxylate (**3a**).* White solid, mp 162–163 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J=7.4 Hz, 4H), 7.34–7.10 (m, 11H), 6.85 (d, J=7.9 Hz, 2H), 6.75 (d, J=7.9 Hz, 2H), 5.71 (s, 1H), 3.55 (s, 3H), 3.33 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.7, 146.9, 143.3, 140.5, 138.4, 136.9, 135.1, 129.4, 129.0, 128.3, 127.9, 127.6, 127.4, 127.2, 126.9, 124.4, 104.4, 72.4, 52.3, 50.8, 20.9. IR (KBr) ν 3025, 1738, 1694, 1510, 1434, 1235, 1096, 751, 701 cm^{-1}. HRMS (EI) m/z calcd for $C_{34}H_{29}NO_4$ 515.2097, found: 515.2095.

*4.2.2. Dimethyl 6,6-diphenyl-1,4-di-p-tolyl-1,6-dihydropyridine-2,3-dicarboxylate (**3b**).* Yellow solid, mp 150–151 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J=7.5 Hz, 4H), 7.30–7.14 (m, 8H), 7.10 (d, J=7.7 Hz, 2H), 6.84 (d, J=7.9 Hz, 2H), 6.74 (d, J=7.9 Hz, 2H), 5.69 (s, 1H), 3.54 (s, 3H), 3.36 (s, 3H), 2.34 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 165.8, 146.7, 143.4, 138.5, 137.5, 136.8, 136.5, 135.0, 129.4, 129.0, 128.3, 128.2, 127.8, 127.6, 127.2, 124.2, 104.7, 72.4, 52.3, 50.9, 21.2, 20.9. IR (KBr) ν 2949, 1738, 1694, 1510, 1434, 1236, 1095, 910, 734, 703 cm^{-1}. HRMS (EI) m/z calcd for $C_{35}H_{31}NO_4$ 529.2253, found: 529.2255.

*4.2.3. Dimethyl 4-(3-bromophenyl)-6,6-diphenyl-1-(p-tolyl)-1,6-dihydropyridine-2,3-dicarboxylate (**3c**).* Yellow solid, mp 176–177 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.38 (d, J=7.5 Hz, 5H), 7.30–7.13 (m, 8H), 6.85 (d, J=8.1 Hz, 2H), 6.76 (d, J=8.0 Hz, 2H), 5.70 (s, 1H), 3.56 (s, 3H), 3.37 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.61, 165.55, 147.4, 143.1, 142.7, 138.2, 1371, 134.0, 130.8, 129.9, 129.4, 129.0, 128.9, 128.4, 127.7, 127.4, 126.7, 124.9, 121.5, 103.6, 72.4, 52.4, 50.9, 20.9. IR (KBr) ν 2948, 1738, 1694, 1509, 1234, 910, 733, 702 cm^{-1}. HRMS (EI) m/z calcd for $C_{34}H_{28}BrNO_4$ 593.1202, found: 593.1194.

*4.2.4. Dimethyl 4′-phenyl-1′-(p-tolyl)-1′H-spiro[fluorene-9,2′-pyridine]-5′,6′-dicarboxylate (**3d**).* Yellow solid, mp 230–231 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.79 (m, 2H), 7.52–7.0 (m, 2H), 7.36–7.15 (m, 9H), 6.65 (d, J=8.2 Hz, 2H), 6.57 (d, J=8.2 Hz, 2H), 4.97 (s, 1H), 3.44 (s, 3H), 3.41 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.8, 149.9, 149.0, 141.0, 138.6, 137.7, 136.5, 136.0, 129.5, 129.2, 128.2, 128.1, 127.5, 127.1, 126.7, 126.4, 119.7, 119.1, 99.1, 72.9, 52.1, 50.8, 20.9. IR (KBr) ν 2948, 1744, 1695, 1537, 1509, 1232,

1106, 909, 734, 700 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{34}H_{27}NO_4$ 513.1940, found: 513.1937.

*4.2.5. Dimethyl 1,4,6,6-tetraphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**3e**).* White solid, mp 153–154 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, *J*=7.2 Hz, 1H), 7.29–7.21 (m, 2H), 7.12–6.94 (m, 11H), 6.88 (d, *J*=7.3 Hz, 2H), 6.78 (d, *J*=6.4 Hz, 4H), 5.36 (s, 1H), 3.61 (d, *J*=4.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 160.3, 140.6, 137.8, 137.2, 133.2, 130.3, 129.2, 128.7, 128.6, 128.3, 127.8, 127.2, 126.5, 126.3, 124.3, 123.6, 122.1, 52.0, 51.7, 48.3. IR (KBr) ν 3027, 1722, 1716, 1496, 1268, 1150, 765, 698 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{33}H_{27}NO_4$ 501.1940, found: 501.1940.

*4.2.6. Dimethyl 1-(4-methoxyphenyl)-4,6,6-triphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**3f**).* White solid, mp 172–173 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J*=7.8 Hz, 4H), 7.32–7.12 (m, 11H), 6.90 (d, *J*=7.9 Hz, 2H), 6.47 (d, *J*=8.4 Hz, 2H), 5.71 (s, 1H), 3.63 (s, 3H), 3.56 (s, 3H), 3.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.7, 158.2, 147.2, 143.3, 140.6, 135.1, 133.8, 131.1, 128.9, 127.8, 127.7, 127.4, 127.3, 126.9, 124.0, 112.8, 103.6, 72.6, 55.1, 52.4, 50.8. IR (KBr) ν 3022, 1738, 1694, 1608, 1508, 1235, 1096, 751, 702 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{34}H_{29}NO_5$ 531.2046, found: 531.2045.

4.3. General procedure for the preparation of dihydropyridines 6

To a solution of amine **4** (0.5 mmol) in dry dichloromethane (3 mL) was added 2-butynedioate (0.5 mmol) and the solution was stirred for 10 min at room temperature. Then, propargylic alcohol **1** (0.5 mmol), 4 Å MS (200 mg) and $BF_3{\cdot}Et_2O$ (0.5 mmol) were added in a sequence. After stirred at 0 °C for 1 h, the mixture was evaporated on vacuum. The product was isolated by column chromatography, using silica gel as stationary phase and hexane–EtOAc–Et_3N (10:1:0.1, v/v/v) as eluent.

*4.3.1. Dimethyl 1-benzyl-4,6,6-triphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6a**).* White solid, mp 183–184 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.23 (m, 9H), 7.22–7.11 (m, 6H), 7.09–7.00 (m, 3H), 6.88–6.71 (m, 2H), 5.71 (s, 1H), 4.45 (s, 1H), 3.75 (s, 3H), 3.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 149.5, 143.4, 140.9, 137.7, 135.3, 128.6, 127.83, 127.75, 127.54, 127.50, 127.47, 126.8, 126.6, 126.2, 123.1, 101.6, 71.0, 53.3, 52.8, 50.7. IR (KBr) ν 2949, 1735, 1694, 1617, 1529, 1301, 1217, 1111, 909, 734, 700 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{34}H_{29}NO_4$ 515.2097, found: 515.2097.

*4.3.2. Dimethyl 1-benzyl-4-phenyl-6,6-di-p-tolyl-1,6-dihydropyridine-2,3-dicarboxylate (**6b**).* White solid, mp 155–156 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.21 (m, 5H), 7.16 (d, *J*=6.3 Hz, 4H), 7.06 (s, 3H), 6.98 (d, *J*=6.9 Hz, 4H), 6.79 (s, 2H), 5.68 (s, 1H), 4.43 (s, 2H), 3.72 (s, 3H), 3.29 (s, 3H), 2.27 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.2, 149.5, 141.1, 140.6, 137.8, 137.2, 135.0, 128.5, 127.6, 127.5, 126.7, 126.5, 126.3, 123.3, 101.4, 70.6, 53.2, 52.7, 50.6, 20.9. IR (KBr) ν 2948, 1737, 1693, 1531, 1302, 1216, 910, 733, 703 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{36}H_{33}NO_4$ 543.2410, found: 543.2406.

*4.3.3. Dimethyl 1-benzyl-6,6-bis(4-chlorophenyl)-4-phenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6c**).* White solid, mp 172–173 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.21 (m, 5H), 7.20–7.04 (m, 11H), 6.76 (d, *J*=6.4 Hz, 2H), 5.61 (s, 1H), 4.38 (s, 2H), 3.81 (s, 3H), 3.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.9, 149.3, 141.5, 140.5, 137.3, 136.2, 133.8, 129.9, 128.1, 128.0, 127.6, 127.4, 127.1, 126.9, 126.1, 122.0, 102.0, 69.9, 53.4, 53.0, 50.8. IR (KBr) ν 2949, 1737, 1694, 1530, 1302, 1217, 1093, 733, 701 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{34}H_{27}Cl_2NO_4$ 583.1317, found: 583.1313.

*4.3.4. Dimethyl 1-benzyl-4,6-diphenyl-6-(p-tolyl)-1,6-dihydropyridine-2,3-dicarboxylate (**6d**).* Yellow solid, mp 156–157 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.16 (m, 10H), 7.13 (d, *J*=7.6 Hz, 2H), 7.09–7.01 (m, 3H), 6.96 (d, *J*=7.6 Hz, 2H), 6.78 (d, *J*=4.8 Hz, 2H), 5.70 (s, 1H), 4.54–4.33 (m, 2H), 3.73 (s, 3H), 3.30 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 149.5, 143.6, 141.0, 140.5, 137.8, 137.3, 135.2, 128.7, 128.5, 128.4, 127.8, 127.7, 127.5, 127.4, 126.8, 126.5, 126.2, 123.2, 101.5, 70.8, 53.3, 52.7, 50.6, 20.9. IR (KBr) ν 2948, 1736, 1694, 1529, 1301, 1216, 910, 733, 700 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{35}H_{31}NO_4$ 529.2253, found: 529.2255.

*4.3.5. Dimethyl 1-benzyl-6,6-diphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6e**).* Yellow solid, mp 139–140 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J*=7.0 Hz, 4H), 7.26–7.12 (m, 6H), 7.10–6.93 (m, 3H), 6.72 (d, *J*=5.6 Hz, 2H), 6.58 (d, *J*=9.7 Hz, 1H), 5.59 (d, *J*=9.7 Hz, 1H), 4.45 (s, 2H), 3.66 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 165.7, 147.9, 143.5, 137.4, 128.5, 128.0, 127.6, 127.5, 126.5, 126.3, 121.9, 119.9, 99.3, 71.0, 53.0, 52.8, 51.2. IR (KBr) ν 2949, 1733, 1698, 1548, 1299, 1244, 909, 732, 702 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{28}H_{25}NO_4$ 439.1784, found: 439.1780.

*4.3.6. Dimethyl 1-benzyl-4-butyl-6,6-diphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6f**).* White solid, mp 107–108 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.31–7.23 (m, 4H), 7.23–7.14 (m, 6H), 7.04 (d, *J*=3.9 Hz, 3H), 6.75 (d, *J*=4.4 Hz, 2H), 5.52 (s, 1H), 4.39 (s, 2H), 3.62 (d, *J*=2.9 Hz, 6H), 2.50 (t, *J*=7.3 Hz, 2H), 1.52–1.42 (m, 2H), 1.36 (dd, J_1=14.6, J_2=7.3 Hz, 2H), 0.93 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 166.4, 148.3, 144.0, 138.0, 133.4, 128.5, 127.8, 127.7, 127.3, 126.5, 126.3, 121.3, 102.6, 70.5, 52.9, 52.5, 51.0, 33.7, 31.7, 22.4, 14.0. IR (KBr) ν 2951, 1733, 1707, 1524, 1297, 1200, 1116, 735, 701 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{32}H_{33}NO_4$ 495.2410, found: 495.2413.

*4.3.7. Dimethyl 1-benzyl-6-methyl-4,6-diphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6g**).* Yellow solid, mp 77–78 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J*=7.4 Hz, 2H), 7.35–7.22 (m, 10H), 7.22–7.17 (m, 1H), 7.15 (d, *J*=7.3 Hz, 2H), 5.16 (s, 1H), 4.51 (q, *J*=17.3 Hz, 2H), 3.70 (s, 3H), 3.33 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.2, 150.1, 145.2, 141.0, 138.5, 134.7, 128.3, 127.5, 127.2, 127.1, 126.7, 126.4, 126.1, 122.6, 100.7, 64.3, 52.6, 51.9, 50.7, 26.7. IR (KBr) ν 2948, 1738, 1694, 1530, 1300, 1221, 1133, 734, 699 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{29}H_{27}NO_4$ 453.1940, found: 453.1936.

*4.3.8. Dimethyl 1-benzyl-6,6-dimethyl-4-phenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6h**).* Yellow solid, mp 133–134 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.18 (m, 10H), 4.90 (s, 1H), 4.50 (s, 2H), 3.78 (s, 3H), 3.38 (s, 3H), 1.32 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 166.4, 150.3, 141.1, 138.9, 135.4, 128.5, 127.6, 127.3, 127.2, 126.7, 126.3, 121.7, 100.7, 58.6, 52.7, 50.6, 50.5, 26.3. IR (KBr) ν 2924, 1739, 1693, 1525, 1434, 1303, 1126, 734, 700 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{24}H_{25}NO_4$ 391.1784, found: 391.1782.

*4.3.9. Dimethyl 1-(4-chlorobenzyl)-4,6,6-triphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6i**).* Yellow solid, mp 156–157 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.22 (m, 9H), 7.21–7.16 (m, 6H), 7.01 (d, *J*=8.4 Hz, 2H), 6.71 (d, *J*=8.4 Hz, 2H), 5.71 (s, 1H), 4.39 (s, 2H), 3.79 (s, 3H), 3.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.1, 149.2, 143.2, 140.8, 136.3, 135.2, 132.4, 128.6, 127.9, 127.8, 127.7, 127.54, 127.51, 127.4, 126.9, 123.1, 101.7, 71.0, 52.9, 52.7, 50.7. IR (KBr) ν 3023, 1736, 1694, 1530, 1493, 1216, 1101, 758, 701 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{34}H_{28}ClNO_4$ 549.1707, found: 549.1704.

*4.3.10. Dimethyl1-(3-methoxybenzyl)-4,6,6-triphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6j**).* White solid, mp 151–152 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.23 (m, 9H), 7.22–7.16 (m, 6H), 6.96 (t, *J*=7.9 Hz, 1H), 6.61 (dd, J_1=8.1, J_2=2.1 Hz, 1H), 6.39 (d, *J*=7.6 Hz, 1H), 6.31 (s, 1H), 5.73 (s, 1H), 4.41 (s, 2H), 3.78 (s, 3H), 3.67 (s, 3H), 3.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 159.1, 149.5, 143.4, 140.9, 139.4, 135.4, 128.8, 128.7, 127.8, 127.53, 127.51, 127.45, 126.8,

123.1, 118.7, 112.6, 111.4, 101.7, 70.9, 55.0, 53.3, 52.8, 50.7. IR (KBr) ν 2949, 1733, 1694, 1601, 1530, 1300, 1215, 1101, 910, 734, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{35}H_{31}NO_5$ 545.2202, found: 545.2200.

*4.3.11. Dimethyl1-(3,4-dimethoxybenzyl)-4,6,6-triphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6k**).* Yellow solid, mp 181–182 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.23 (m, 9H), 7.23–7.16 (m, 6H), 6.58 (d, J=8.3 Hz, 1H), 6.37 (dd, J_1=8.3, J_2=1.8 Hz, 1H), 6.25 (d, J=1.8 Hz, 1H), 5.71 (s, 1H), 4.39 (s, 2H), 3.80 (d, J=2.2 Hz, 6H), 3.72 (s, 3H), 3.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 149.5, 148.2, 147.7, 143, 140.9, 135.4, 130.4, 128.7, 127.8, 127.5, 127.4, 126.8, 123.1, 118.6, 110.6, 109.5, 101.5, 70.8, 55.9, 55.6, 53.0, 52.9, 50.7. IR (KBr) ν 2649, 1737, 1694, 1516, 1263, 1214, 1101, 911, 733, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{36}H_{33}NO_6$ 575.2308, found: 575.2305.

*4.3.12. Dimethyl 1-(furan-2-ylmethyl)-4,6,6-triphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6l**).* White solid, mp 162–163 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.15 (m, 15H), 7.09 (s, 1H), 6.10 (s, 1H), 5.68 (d, J=3.1 Hz, 1H), 5.63 (s, 1H), 4.39 (s, 2H), 3.86 (s, 3H), 3.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.09, 166.07, 150.4, 148.2, 143.4, 141.3, 140.8, 134.6, 128.5, 128.0, 127.6, 127.5, 127.4, 126.8, 123.5, 110.3, 107.6, 102.2, 71.2, 52.9, 50.7, 46.1. IR (KBr) ν 2949, 1734, 1695, 1530, 1299, 1203, 1101, 734, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{32}H_{27}NO_5$ 505.1889, found: 505.1889.

*4.3.13. Dimethyl 4,6,6-triphenyl-1-(prop-2-yn-1-yl)-1,6-dihydropyridine-2,3-dicarboxylate (**6m**).* Yellow solid, mp 192–193 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J=7.5 Hz, 4H), 7.39–7.22 (m, 9H), 7.19 (d, J=6.1 Hz, 2H), 5.57 (s, 1H), 3.98 (s, 3H), 3.88 (s, 2H), 3.31 (s, 3H), 2.00 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.9, 147.1, 142.9, 140.6, 134.0, 128.6, 128.2, 127.8, 127.5, 127.4, 126.8, 123.4, 102.2, 78.5, 72.0, 71.5, 53.0, 50.8, 38.7. IR (KBr) ν 3288, 2949, 1733, 1694, 1537, 1213, 909, 733, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{30}H_{25}NO_4$ 463.1784, found: 463.1783.

*4.3.14. Dimethyl 1-benzyl-4-butyl-6,6-diphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**6n**).* White solid, mp 134–135 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.28 (m, 10H), 7.27–7.20 (m, 3H), 7.18 (d, J=7.3 Hz, 2H), 5.52 (s, 1H), 3.99 (s, 3H), 3.28 (s, 3H), 3.11 (t, J=8.2 Hz, 2H), 1.09–0.83 (m, 2H), 0.88–0.62 (m, 2H), 0.51 (t, J=7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.32, 166.27, 149.5, 143.9, 141.2, 134.3, 128.6, 128.1, 127.6, 127.4, 127.3, 126.6, 99.1, 71.3, 52.8, 50.4, 32.1, 19.8, 13.1. IR (KBr) ν 2956, 1739, 1693, 1529, 1299, 1210, 1097, 909, 733, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{31}H_{31}NO_4$ 481.2253, found: 481.2256.

*4.3.15. Methyl 1-benzyl-4,6,6-triphenyl-1,6-dihydropyridine-3-carboxylate (**6o**).* White solid, mp 105–106 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.36 (d, J=7.4 Hz, 4H), 7.33–7.18 (m, 11H), 7.17–7.09 (m, 3H), 6.83–6.68 (m, 2H), 5.26 (s, 1H), 4.40 (s, 2H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 147.4, 143.5, 140.9, 136.9, 133.7, 128.5, 128.3, 128.2, 127.6, 127.5, 127.3, 127.2, 126.6, 121.7, 98.5, 71.6, 55.4, 50.4. IR (KBr) ν 3058, 2946, 1696, 1625, 1559, 1215, 1084, 756, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{32}H_{27}NO_2$ 457.2042, found: 457.2043.

4.4. Procedure for the preparation of 1-methyl-3-(methylamino)-1*H*-pyrrole-2,5-dione (7a)

To a solution of 2-butynedioate (5 mmol, 0.71 g) in EtOH (10 mL) was added CH_3NH_2 (30–33 wt. % in absolute ethanol, 20 mmol, 2 mL) at room temperature. The reaction mixture was stirred at room temperature for 24 h and the solvent was evaporated in vacuo. Pure **7a** was obtained as yellow solid in 70% yield by column chromatography, using silica gel as stationary phase and hexane–EtOAc–Et_3N (2:1:0.1, v/v/v) as eluent. Mp 147–148 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 5.45 (s, 1H), 4.82 (s, 1H), 2.97 (s, 3H), 2.94 (d, J=5.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 167.4, 150.5, 83.8, 30.5, 23.3. IR (KBr) ν 3341, 3109, 1700, 1640, 1450, 988, 689 cm^{-1}. HRMS (EI) m/z calcd for $C_6H_8N_2O_2$ 140.0586, found: 140.0585.

4.5. Procedure for the preparation of 3-(Benzylamino)-1-methyl-1*H*-pyrrole-2,5-dione (7b)

To a solution of 2-butynedioate (5 mmol, 0.71 g) in DCM (10 mL) was added $PhCH_2NH_2$ (5 mmol, 0.54 g) at room temperature. The reaction mixture was stirred at room temperature for 1 h and the solvent was evaporated in vacuo. Then ethanol (10 mL) and CH_3NH_2 (30–33 wt. % in absolute ethanol, 20 mmol, 2 mL) were added. The reaction mixture was stirred at room temperature for 48 h. The resulting yellow solid (0.78 g, 72% yield) was collected by filtration without further purification. Mp 141–142 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58–6.58 (m, 5H), 5.77 (s, 1H), 4.85 (s, 1H), 4.35 (s, 2H), 2.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 167.6, 149.1, 135.7, 129.0, 128.2, 127.7, 85.4, 48.4, 23.4. IR (KBr) ν 3324, 3100, 1696, 1625, 1456, 1124, 703 cm^{-1}. HRMS (EI) m/z calcd for $C_{12}H_{12}N_2O_2$ 216.0899, found: 216.0902.

4.6. General procedure for the preparation of 8

To a solution of propargylic alcohol **1** (0.5 mmol), **7a** (0.5 mmol, 70 mg) and 4 Å molecular sieve (200 mg) in dry dichloromethane (3 mL) was added $BF_3{\cdot}Et_2O$ (0.5 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h and then evaporated on vacuum. The product was isolated by column chromatography using silica gel as stationary phase and hexane–EtOAc–Et_3N (10:1:0.1, v/v/v) as eluent.

*4.6.1. 1,6-Dimethyl-2,2,4-triphenyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione (**8a**).* Red solid, mp 250–251 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47–7.28 (m, 15H), 5.26 (s, 1H), 3.18 (s, 3H), 2.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 165.4, 145.1, 142.2, 136.3, 129.6, 128.5, 128.3, 128.1, 127.9, 127.8, 127.6, 122.7, 98.9, 74.5, 34.3, 23.4. IR (KBr) ν 3058, 1699, 1624, 1449, 1385, 773, 702 cm^{-1}. HRMS (EI) m/z calcd for $C_{27}H_{22}N_2O_2$ 406.1681, found: 406.1678.

*4.6.2. 4-(3-Bromophenyl)-1,6-dimethyl-2,2-diphenyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione (**8b**).* Red solid, mp 217–218 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.47–7.29 (m, 12H), 7.18 (t, J=7.8 Hz, 1H), 5.25 (s, 1H), 3.17 (s, 3H), 2.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.2, 145.2, 142.0, 138.4, 130.9, 130.8, 129.1, 128.6, 128.4, 128.3, 128.0, 127.0, 123.1, 121.7, 98.3, 74.6, 34.3, 23.4. IR (KBr) ν 2873, 1701, 1624, 1443, 1112, 766, 730, 702 cm^{-1}. HRMS (EI) m/z calcd for $C_{27}H_{21}BrN_2O_2$ 484.0786, found: 484.0796.

*4.6.3. 1,6-Dimethyl-4-phenyl-2,2-di-p-tolyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione (**8c**).* Red solid, mp 130–131 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J=6.5 Hz, 2H), 7.33–7.25 (m, 7H), 7.21 (d, J=7.9 Hz, 4H), 5.22 (s, 1H), 3.17 (s, 3H), 2.96 (s, 3H), 2.37 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 165.4, 145.2, 139.5, 137.6, 136.4, 129.2, 128.3, 128.1, 127.8, 127.6, 122.9, 98.7, 74.2, 34.2, 23.3, 21.0. IR (KBr) ν 2923, 1701, 1625, 1440, 1383, 817, 732 cm^{-1}. HRMS (EI) m/z calcd for $C_{29}H_{26}N_2O_2$ 434.1994, found: 434.1992.

*4.6.4. 2,2-Bis(4-chlorophenyl)-1,6-dimethyl-4-phenyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione (**8d**).* Red solid, mp 155–156 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.36 (m, 4H), 7.36–7.27 (m, 9H), 5.17 (s, 1H), 3.16 (s, 3H), 2.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.1, 144.9, 140.4, 135.8, 134.2, 130.3, 129.6, 128.9, 128.14, 128.06, 127.7, 121.7, 99.4, 73.7, 34.2, 23.4. IR (KBr) ν 2940, 1753, 1701, 1625, 1490, 1384, 1094, 732, 698 cm^{-1}. HRMS (EI) m/z calcd for $C_{27}H_{20}Cl_2N_2O_2$ 474.0902, found: 474.0896.

*4.6.5. 1,6-Dimethyl-2,2-diphenyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione(**8e**).* Red solid, mp 119–120 °C. ^1H NMR

(400 MHz, $CDCl_3$) δ 7.49–7.30 (m, 10H), 6.31 (d, J=9.6 Hz, 1H), 5.30 (d, J=9.6 Hz, 1H), 3.09 (s, 3H), 2.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.9, 143.8, 142.0, 128.5, 128.3, 127.8, 123.7, 113.0, 100.1, 74.2, 33.7, 23.4. IR (KBr) ν 2929, 1699, 1628, 1443, 1376, 1091, 730, 702 cm^{-1}. HRMS (EI) m/z calcd for $C_{21}H_{18}N_2O_2$ 330.1368, found: 330.1368.

*4.6.6. 1,2,2,6-Tetramethyl-4-phenyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione (**8f**).* Red solid, mp 62–63 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 5H), 4.82 (s, 1H), 3.45 (s, 3H), 2.93 (s, 3H), 1.46 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 165.4, 146.3, 136.7, 131.4, 128.0, 127.7, 127.6, 121.7, 99.0, 61.1, 30.0, 27.1, 23.2. IR (KBr) ν 3057, 1711, 1628, 1444, 1381, 1011, 732, 698 cm^{-1}. HRMS (EI) m/z calcd for $C_{17}H_{18}N_2O_2$ 282.1368, found: 282.1364.

*4.6.7. 1-Benzyl-6-methyl-2,2,4-triphenyl-1H-pyrrolo[3,4-b]pyridine-5,7(2H,6H)-dione (**8g**).* Red solid, mp 107–108 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J=5.7 Hz, 2H), 7.37–7.29 (m, 3H), 7.30–7.16 (m, 10H), 7.02 (d, J=2.8 Hz, 3H), 6.64 (s, 2H), 5.56 (s, 1H), 5.16 (s, 2H), 2.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 165.4, 144.9, 143.0, 137.7, 136.2, 130.5, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 126.3, 125.7, 123.5, 101.8, 74.4, 50.3, 23.5. IR (KBr) ν 3059, 1702, 1621, 1445, 1383, 1006, 765, 697 cm^{-1}. HRMS (EI) m/z calcd for $C_{33}H_{26}N_2O_2$ 482.1994, found: 482.1996.

4.7. Preparation of dimethyl 5-iodo-4,6,6-triphenyl-1-(*p*-tolyl)-1,6-dihydropyridine-2,3-dicarboxylate (9)

To a solution of propargylic alcohol **1a** (0.5 mmol, 142 mg), enamine **2a** (0.5 mmol, 125 mg) and 4 Å molecular sieve (200 mg) in dry dichloromethane (3 mL) was added I_2 (0.5 mmol, 127 mg). The mixture was stirred at room temperature for 3 h and then evaporated on vacuum. The product was isolated by column chromatography as a mixture (208 mg) of **9** and **3a**, using silica gel as stationary phase and hexane–EtOAc–Et_3N (10:1:0.1, v/v/v) as eluent. The yields of **9** (49%) and **3a** (20%) were determined according to the ^1H NMR spectra. Pure **9** was obtained by recrystallization as yellow solid. Mp 176–177 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.59–7.45 (m, 4H), 7.35 (t, J=7.3 Hz, 2H), 7.30 (t, J=7.1 Hz, 1H), 7.27–7.18 (m, 6H), 7.15 (d, J=7.2 Hz, 2H), 6.76 (q, J=8.3 Hz, 4H), 3.50 (s, 3H), 3.24 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 145.0, 144.7, 143.2, 142.7, 139.7, 136.7, 130.4, 129.0, 128.9, 128.4, 127.8, 127.6, 127.3, 127.2, 109.3, 97.8, 76.2, 52.4, 51.2, 21.0. IR (KBr) ν 3026, 1735, 1571, 1508, 1433, 1231, 758, 700 cm^{-1}. HRMS (EI) m/z calcd for $C_{34}H_{28}INO_4$ 641.1063, found: 641.1060.

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Supplementary data

Copies of NMR spectra for all synthesized compounds. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.07.076. These data include MOL files and InChiKeys of the most important compounds described in this article.

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