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# One-pot, three-component synthesis of highly functionalized pyrimidone derivatives and access to indole fused pyrimidones via palladium-catalyzed intramolecular Heck reaction

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ABSTRACT

A simple and facile approach to highly functionalized pyrimidone derivatives and indole fused pyrimidones has been developed. The synthesis of substituted pyrimidone derivatives in moderate to good yields involves [4+2] cycloaddition of 1,4-dipoles generated from α,β-unsarurated imines and dimethyl acetylenedicarboxylate (DMAD) with isocyanates as dipolarophiles. Furthermore, the pyrimidones resulted from 2-bromophenyl isocyanate could be transformed into various indole fused pyrimidones via intramolecular palladium-catalyzed Heck reaction under different conditions.



## 1. Introduction

Multi-component reactions are defined as a kind of reactions involving at least three different substrates to form products via a tandem process. These methodologies allow molecular complexity and diversity to be created by the facile formation of several new covalent bonds in one-pot manner without isolation of the intermediates, which combine two major principles of organic synthesis, convergence and atom economy. Consequently, these classes of reactions have found extensive applications in organic, combinatorial, and medicinal chemistry for fast generation of compound libraries.[1]

The pyrimidone skeletons exist in the core structure of several biologically active compounds, such as PPAR agonist,[2] calcium receptor (CaR) antagonist,[3] methaqualone,[4] GnRH receptor antagonist,[5] angiotensin II (A II) receptor antagonist.[6] Evodiamine, a major quinazolinocarbolin alkaloid isolated from the fruit of *Evodia rutaecarpa* Bentham, has been reported exhibiting vasorelaxant[7] and cardiotonic effects.[8] Furthermore, indole fused pyrimidones derivatives, such as tryptanthrin and phaitanthrin E, possess various bioactivities, such as anticancer, antimalarial, antibacterial, antifungal and antileishmanial, respectively.[9,10] Recently, biologically potent alkaloids have been isolated from the roots of *Isatis indigotica*, which is commonly used in traditional Chinese medicine to help overcome various diseases, especially for treating influenza, cold, fever, and infections (Fig. 1).[11] Therefore, it is highly desirable to develop efficient synthetic methods for this class of compound and expand their structure diversity for current medicinal chemistry demands. Although several methods for

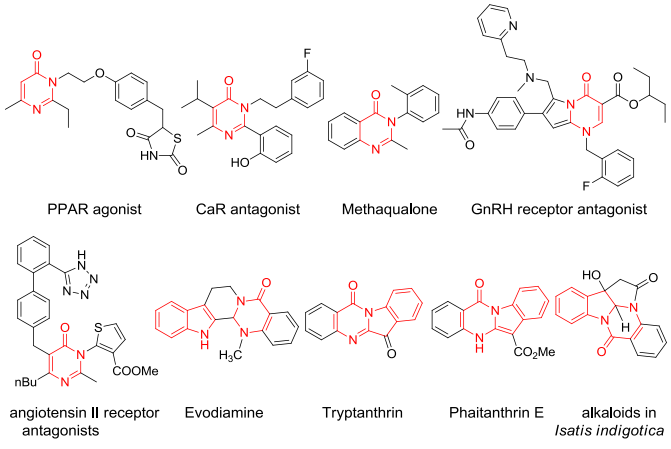


**Fig. 1.** Some pyrimidone derivatives.

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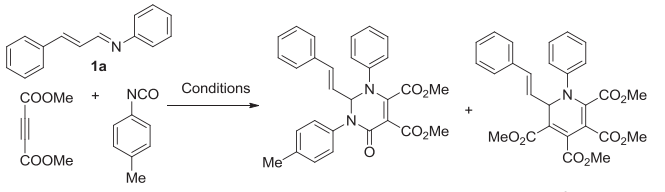
synthesis of pyrimidone and indole fused pyrimidones derivatives have been developed,[3,12] most of these protocols suffer from tedious procedures, poor precursor scopes, and/or low efficiency. Therefore the development of the facile methodologies for the generation of highly functionalized pyrimidone derivatives library is still challenging in organic synthetic chemistry and medicinal chemistry.

Our previous work had successfully demonstrated that the 1,4-dipoles generated from α,β-unsaturated imines and DMAD could react efficiently with benzylaldehyde dipolarophiles in one-pot [4+2] annulations resulting in the diversity oriented synthesis of 1,3-oxazine derivatives in good to excellent yields.[13] Therefore, we envisioned that the α,β-unsaturated imine-DMAD dipole would react with isocyanates to afford pyrimidone derivatives bearing styryl moiety. Moreover, those pyrimidones resulted from 2-bromine phenyl isocyanate could be further transformed into indole fused pyrimidones via intramolecular palladium-catalyzed Heck reaction.[14,15] These protocols well extend our ongoing research on constructing diverse heterocycle compounds. Herein, we would like to report the detailed results of our investigation.

## 2. Results and discussion

With the above idea in mind, we investigated the model reaction of imine (**1a**), DMAD (**2a**), 4-methyl phenyl isocyanate (**3a**) in 1:1:1 ratio on a 0.5 mmol scale in acetonitrile. Fortunately, we found that after 24 h at room temperature, the expected compound **4a** accompanied with byproduct (*E*)-1-phenyl-6-styryl-1,6-dihydropyridine-2,3,4,5-tetracarboxylic acid tetramethyl ester (**9**) were obtained in 51% (Table 1, entry 1) and 15% isolated yield, respectively.

**Table 1**
Optimization of reaction conditions




2a 3a 4a 9

| Entry[a] | **1a**:**2a**:**3a**[b] | Solvent | Temp (°C) | Time (h) | Yield[c] (%) |
|---|---|---|---|---|---|
| 1 | 1:1:1 | $CH_3CN$ | rt | 24 | 51 |
| 2 | 1:1:1.1 | $CH_3CN$ | rt | 24 | 55 |
| 3 | 1:1:1.2 | $CH_3CN$ | rt | 24 | 52 |
| 4 | 1.1:1.1:1 | $CH_3CN$ | rt | 24 | 52 |
| 5 | 1.2:1.2:1 | $CH_3CN$ | rt | 24 | 60 |
| 6 | 1.2:1.2:1 | THF | rt | 24 | 44 |
| 7 | 1.2:1.2:1 | DCM | rt | 24 | 41 |
| 8 | 1.2:1.2:1 | Toluene | rt | 24 | 33 |
| 9 | 1.2:1.2:1 | Dioxane | rt | 24 | 24 |
| 10 | 1.2:1.2:1 | DMF | rt | 24 | Trace |
| 11 | 1.2:1.2:1 | EtOH | rt | 24 | Trace |
| 12 | 1.2:1.2:1 | $CH_3CN$ | 0 | 24 | 52 |
| 13 | 1.2:1.2:1 | $CH_3CN$ | 30 | 24 | 58 |
| 14 | 1.2:1.2:1 | $CH_3CN$ | 50 | 24 | 55 |
| 15 | 1.2:1.2:1 | $CH_3CN$ | Reflux | 24 | 54 |
| 16 | 1.2:1.2:1 | $CH_3CN$ | rt | 12 | 60 |
| 17 | 1.2:1.2:1 | $CH_3CN$ | rt | 10 | 54 |

[a] 0.5 mmol scale in 2 mL of solvent.
[b] Molar ratio.
[c] Isolated yields of **4a** based on **3a**.

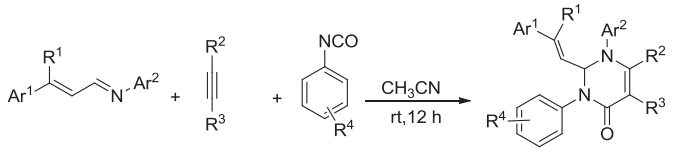
In order to optimize the reaction conditions, a series of reactions of **1a**, **2a**, and **3a** were conducted and the results were shown in Table 1. Increasing the amount of **3a** failed to improve the yield significantly (Table 1, entries 2 and 3), while adding more **1a** and **2a**, from 1.1:1.1:1 to 1.2:1.2:1, better yields were obtained under the same reaction condition (Table 1, entries 4 and 5). When the solvent was changed to THF, DCM, methylbenzene, and dioxane, the yields decreased significantly (Table 1, entries 6–9). In DMF or ethanol, only trace amount of **4a** were detected by TLC (Table 1, entries 10 and 11). When altering the reaction temperature to 0 °C, 30 °C, 50 °C, and under reflux, the yields decreased slightly as compared with at room temperature (Table 1, entries 12–15). The yield was still maintained in 60% when the reaction time was shortened to 12 h (Table 1, entry 16). However, the yield decreased to 54% as the time was reduced to 10 h (Table 1, entry 17). In all these cases, byproduct **9** was observed, which generated from the side reaction of 1,4-dipolar intermediate with DMAD. Even under the optimized reaction conditions **9** was still obtained in 12% yield, which is consistent with our previous observation.[16] In general, in 1.2:1.2:1 M ratio of **1a**, **2a**, and **3a**, at room temperature in acetonitrile for 12 h, the reaction could give best yield in 60%.

With the optimized reaction conditions in hand, the scope and limitations of this methodology have been examined using various α,β-unsaturated imines **1**, **2** and substituted isocyanates **3** on a 0.5 mmol scale and the results are summarized in Scheme 1. The results revealed that the aniline moiety of α,β-unsaturated imines bearing electron-donating groups tend to result in higher yield (Scheme 1, **4s**) than those bearing electron-withdrawing group (Scheme 1, **4b** and **4c**). However, the electronic effect on cinnamaldehyde part of α,β-unsaturated imines are not significant and resulted 54–67% yields (Scheme 1, **4d**–**h**). The steric effect of substituent on the carbon of α,β-unsaturated imine is significant and decrease the yield to 30% (Scheme 1, **4i**).

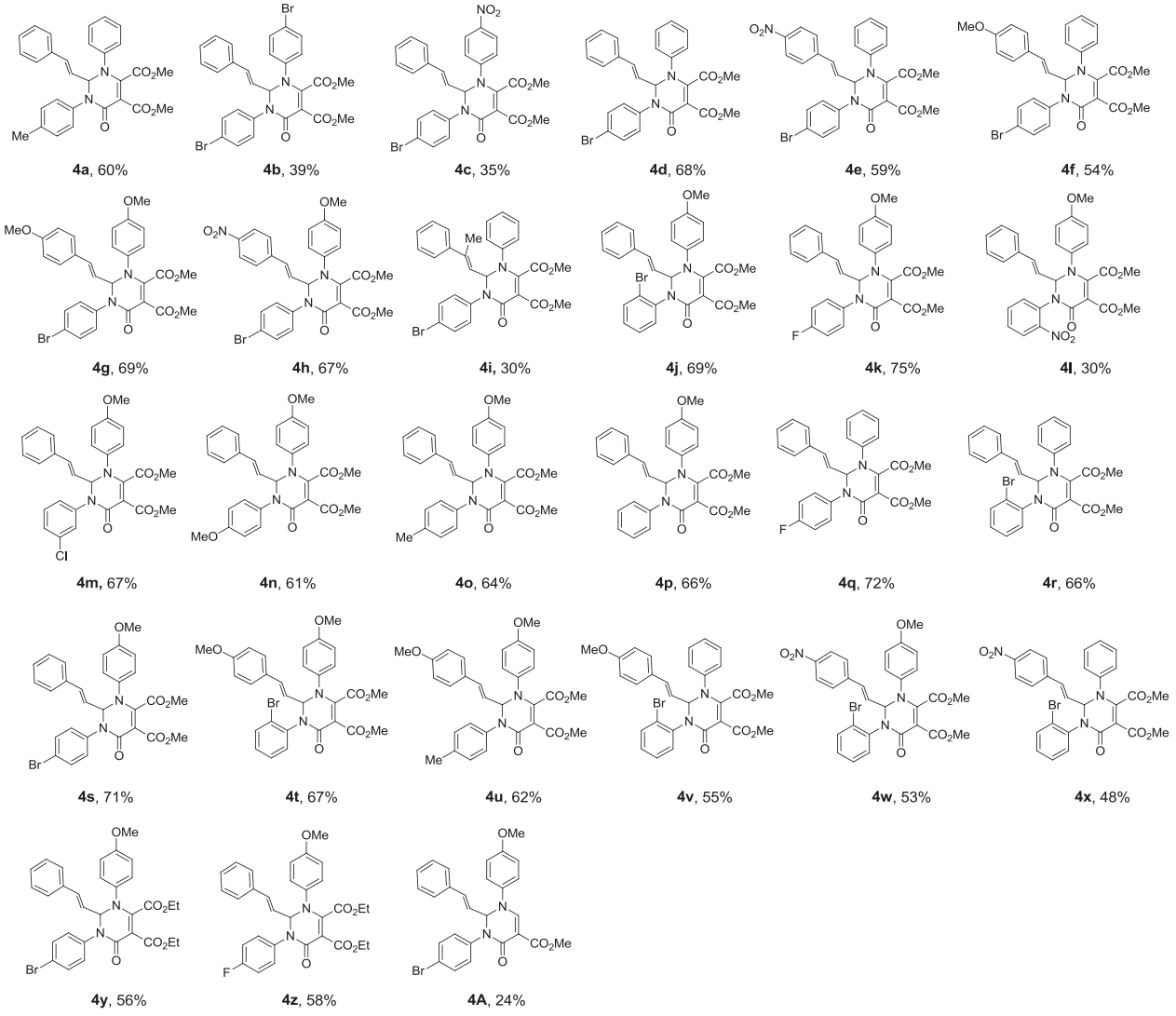
Isocyanates with various functional groups are well tolerated and those bearing electron-withdrawing groups (Scheme 1, **4j**, **4k**, and **4m**), which facilitate the nucleophilic attack to DMAD exhibited better activity than those bearing electron-donating groups (Scheme 1, **4n**–**p**). Unexpectedly, low yield (30%) is observed for 2-nitro phenyl isocyanate, which is likely due to its poor solubility (Scheme 1, **4l**). Furthermore, we studied other combinations of the three kinds of substrate and found that all of these reactions proceeded smoothly in moderate to good yields (Scheme 1, **4q**–**z**). While, in the case of methyl propiolate (**2c**), the loss of one of the electron-withdrawing carboxylate groups led to lower activity and afforded the product **4A** in only 24% yield (Scheme 1, **4A**). The structure of compound **4r** has been confirmed by single crystal X-ray analysis (Fig. 2).

On the basis of the above results, a plausible mechanism of this reaction is illustrated in Scheme 2.[15,17] The reaction may be considered for via the initial formation of the 1,4-dipolar intermediate **I**, which is generated through nucleophilic attack of α,β-unsaturated imines **1** to the electron-deficient triple bond of **2**. Then **I** was trapped by isocyanates **3**, presumably by the process of [4+2] cycloaddition to give the final products **4**.

In order to access indole fused pyrimidones, we further expand the scope of our methodology, in which compound **4j** was chosen to proceed intramolecular Heck reaction. Various catalytic systems were tested and the results were summarized in Table 2. When we used 10 mol % $Pd(OAc)_2$ as catalyst, 40 mol % $PPh_3$ as ligand, 2.5 equiv of $K_2CO_3$ as the base in DMF under $N_2$ at 100 °C for 4 h, the expected products **5a** and **6a** were isolated in 40% and 5% yields, respectively and accompanied with trace amount of decarboxylation product **7a** (Table 2, entry 1). We also observed that compound **5a** could be transformed to **6a** via the base-mediated isomerization in presence of $K_2CO_3$ in DMF at 100 °C. When using $Et_3N$ as base in DMF or toluene, the products could be obtained in yields of close level (Table 2, entries 2 and 3). In $CH_3CN$ at 80 °C for 72 h, the reaction afforded **5a** as a sole product in 35% yield with 58% recovery of **4j** (Table 2, entry 4). While in toluene at 100 °C for same time, only 11% of **4j** was recovered in almost same




1 2 3 4




[a] 0.5 mmol scale based on **3** in 2 mL of $CH_3CN$ at room temperature for 12 h.
[b] Isolated yields of **4** based on **3**.

**Scheme 1.** Synthesis of pyrimidone derivatives by the [4+2] cycloaddition[a,b].

level of product yield (Table 2, entry 3). So substrate **4j** may be not stable under high temperature. Other bases, such as CsF, DBU, and $Cs_2CO_3$, were also been examined for $Pd(OAc)_2$–$PPh_3$ system, these reaction afforded **7a** as major product but in low yields and selectivity (Table 2, entries 5–7). Thus, we speculated that strong base and high temperature could able to promote the decarboxylation to generate **7a**. It is ineffective when water was added as co-solvent to improve the solubility of $K_2CO_3$ (Table 2, entry 8), while adding *n*-$Bu_4NCl$ (1 equiv) as an additive could give **7a** as major product in 51% yield with trace amount of **5a** and **6a** (Table 2, entry 9). When the ligand was changed to dppf, **5a** was obtained as major product in low yield and selectivity (Table 2, entry 10). Furthermore, other palladium sources, such as $PdCl_2(PPh_3)_2$, $PdCl_2$, and $Pd(PPh_3)_4$, combined with various bases and solvents, were screened (Table 2, entries 11–21) and the highest yield of **5a** for this reaction is 66% (Table 2, entry 13). When toluene-$H_2O$ was used as solvent, $Pd(PPh_3)_4$ as catalyst and $K_2CO_3$ as base, no **5a** was observed and afforded **7a** in 28% yield (Table 2, entry 22). Herein, structures of compounds **5a**, **6a**, and **7a** were confirmed by single crystal X-ray analysis (Fig. 3).

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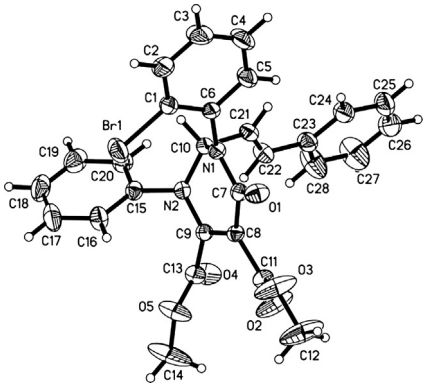
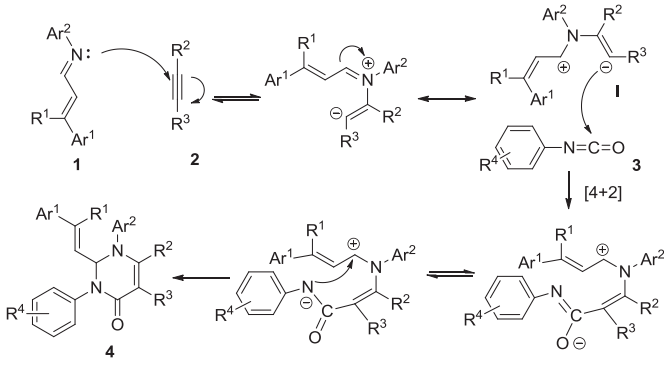



**Fig. 2.** X-ray structure of compound **4r**.



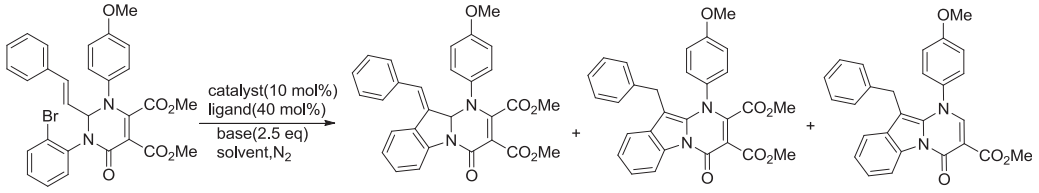

**Scheme 2.** Plausible reaction mechanism.

Originally, we believed that the generation of **7a** may be involved with Pd-mediated coupling. To testify our guess, we used 4-methphenylboronic acid to trap the intermediate generated from **6a**, expecting to afford compound **8**. However, the result revealed that **6a** was transformed to **7a** rather than coupling with 4-methphenyl. On the other hand, **7a** could be obtained without $Pd(OAc)_2$ and ligand (Scheme 3). So we speculated that **6a** may undergo base-induced decarboxylation and the result demonstrated that *n*-$Bu_4NCl$ plays crucial role as phase transfer catalyst in this process resulting **7a** as major product (Table 2, entries 9, 15 and 22). In addition, in DMF at 100 °C and in presence of 2.5 equiv $K_2CO_3$, **5a** could transform to 7a in 95% isolated yield within 4 h (Scheme 4).

With the optimized reaction conditions in hand, the scope and limitation of this transformation were further explored. Several pyrimidone derivatives were investigated using $Pd(PPh_3)_4$ (10 mol %) and $K_2CO_3$ (2.5 equiv) in DMF under 100 °C. The results in Table 3 show that various substituted groups are compatible with the reaction conditions, providing the desired **5a**–**d** as major product in moderate to good yields (Table 3, entries 1–4). While for substrates **4w** and **4x**, decarboxylation products **7e** and **7f** were obtained as major product in low yields, 35% and 30%, respectively, under the same condition (Table 3, entries 5 and 6). The low yields may be relevant to the strong electron-withdrawing nitro group.

We also examined the condition for transformation of the above pyrimidone derivatives to the corresponding decarboxylation products and the results shown in Table 4. For **4j**, **4t**, **4v**, and **4r**, using $Pd(OAc)_2$, *n*-$Bu_4NCl$, $K_2CO_3$, $PPh_3$ in DMF, corresponding decarboxylation products **7a**–**d** were obtained as major product in 45–59% yields (Table 4, entries 1–4). While for substrates **4w** and

**Table 2**
Optimization of intramolecular Heck conditions[a]




| Entry | Catalyst | Ligand | Additive | Base | Solvent | *T* (°C) | Time (h) | Yield (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | **5a** | **6a** | **7a** |
| 1 | $Pd(OAc)_2$ | $PPh_3$ | | $K_2CO_3$ | DMF | 100 | 4 | 40 | 5 | Trace |
| 2 | $Pd(OAc)_2$ | $PPh_3$ | | $Et_3N$ | DMF | 120 | 4 | 39 | Trace | Trace |
| 3[b] | $Pd(OAc)_2$ | $PPh_3$ | | $Et_3N$ | Toluene | 100 | 72 | 37 | Trace | 0 |
| 4[b] | $Pd(OAc)_2$ | $PPh_3$ | | $Et_3N$ | $CH_3CN$ | 80 | 72 | 35 | 0 | 0 |
| 5 | $Pd(OAc)_2$ | $PPh_3$ | | CsF | DMF | 110 | 4 | Trace | 12 | 30 |
| 6 | $Pd(OAc)_2$ | $PPh_3$ | | DBU | *m*-Xylene | 130 | 4 | 0 | Trace | 36 |
| 7 | $Pd(OAc)_2$ | $PPh_3$ | | $CsCO_3$ | DMF | 100 | 4 | Trace | 21 | 42 |
| 8 | $Pd(OAc)_2$ | $PPh_3$ | | $K_2CO_3$ | DMF–$H_2O$ | 100 | 4 | 22 | 4 | 6 |
| 9 | $Pd(OAc)_2$ | $PPh_3$ | *n*-$Bu_4NCl$ | $K_2CO_3$ | DMF | 100 | 4 | Trace | Trace | 51 |
| 10 | $Pd(OAc)_2$ | dppf | | $K_2CO_3$ | DMF | 100 | 4 | 21 | 14 | Trace |
| 11 | $PdCl_2(PPh_3)_2$ | $PPh_3$ | | $K_2CO_3$ | DMF | 100 | 4 | 15 | 11 | Trace |
| 12 | $PdCl_2$ | $PPh_3$ | | $K_2CO_3$ | DMF | 100 | 4 | 57 | 11 | Trace |
| 13 | $Pd(PPh_3)_4$ | | | $K_2CO_3$ | DMF | 100 | 4 | 66 | 14 | Trace |
| 14 | $Pd(PPh_3)_4$ | | | $Et_3N$ | DMF | 100 | 76 | 41 | 0 | 0 |
| 15 | $Pd(PPh_3)_4$ | | *n*-$Bu_4NCl$ | $K_2CO_3$ | DMF | 100 | 4 | Trace | Trace | 19 |
| 16 | $Pd(PPh_3)_4$ | | | $K_2CO_3$ | Toluene-$H_2O$ | 100 | 10 | 52 | 7 | 0 |
| 17 | $Pd(PPh_3)_4$ | | | DIEA | DMF | 100 | 72 | 43 | 0 | 0 |
| 18 | $Pd(PPh_3)_4$ | | | $Na_2CO_3$ | DMF | 100 | 12 | 31 | 3 | Trace |
| 19 | $Pd(PPh_3)_4$ | | | NaOAc | DMF | 100 | 18 | 5 | Trace | 34 |
| 20 | $Pd(PPh_3)_4$ | | | $K_3PO_4$ | DMF | 100 | 18 | 4 | Trace | 28 |
| 21[b] | $Pd(PPh_3)_4$ | | | $K_2CO_3$ | DMF | 80 | 72 | 41 | 11 | Trace |
| 22 | $Pd(PPh_3)_4$ | | *n*-$Bu_4NCl$ | $K_2CO_3$ | Toluene–$H_2O$ | 100 | 6 | 0 | 3 | 28 |

[a] Unless otherwise stated, all reactions have been carried out on a 0.25 mmol scale in 2 mL solvent.
[b] The reactions performed incompletely with recovery of **4j** in 58%, 11%, 35%, respectively.

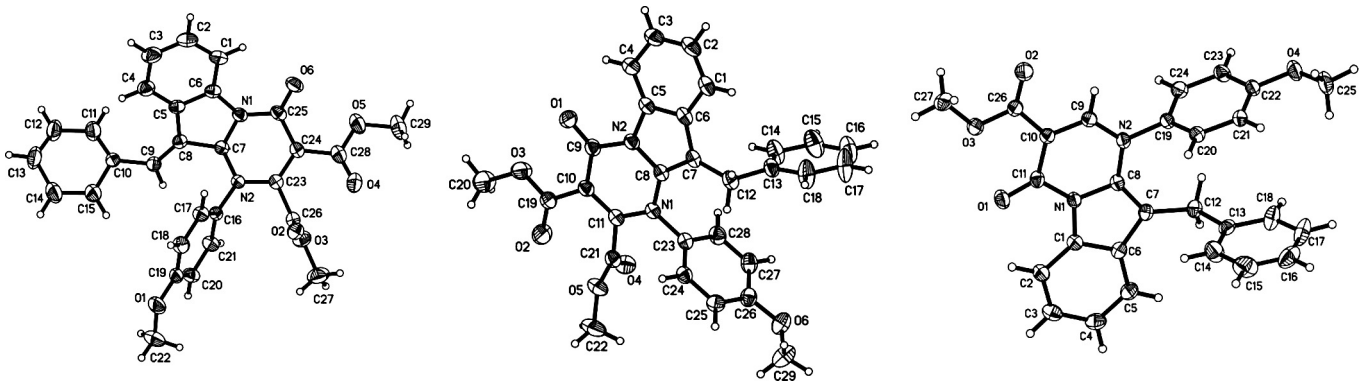
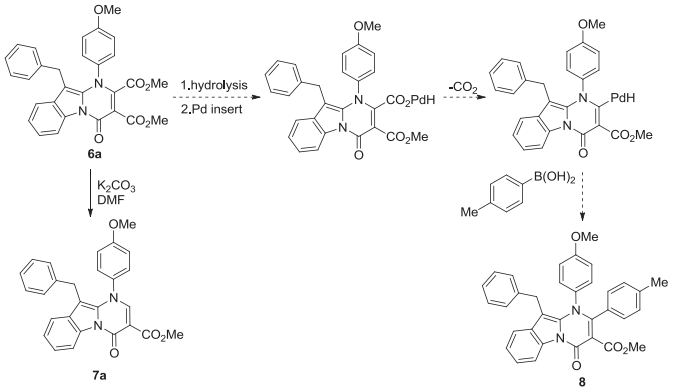
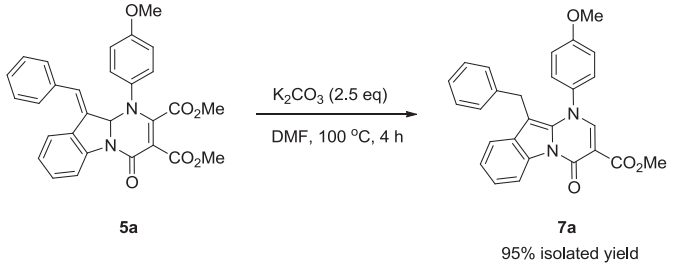


**Fig. 3.** X-ray structure of compound **5a**, **6a**, and **7a**.



**Scheme 3.** Decarboxylation of **6a**.



**Scheme 4.** Transformation of **5a**–**7a**.

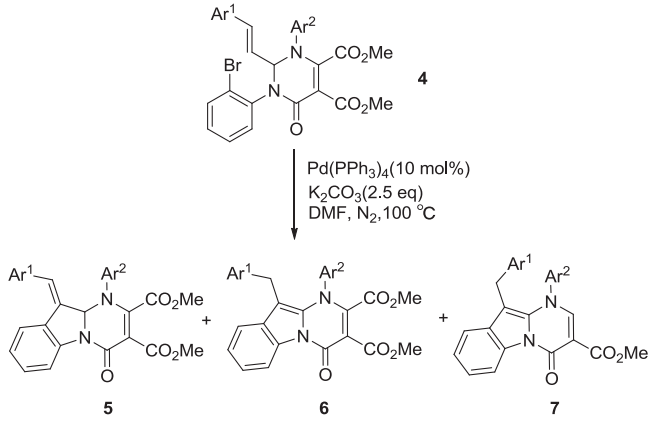
**4x** bearing deactivating group, under the same condition, trace amount of products were observed (Table 4, entries 5 and 6).

The mechanism (Scheme 4) for the formation of **5a** can be regarded as the reductive Heck type reaction involving the intermediate **I**, which might be converted to **6a** via 1,3-H shift. Then **6a** undergoes base-induced decarboxylation to afford **7a**.[18]

## 3. Conclusions

In conclusion, we have developed a facile method for synthesis of highly functionalized pyrimidone derivatives from α,β-unsaturated imines, DMAD and isocyanates via 1,4-dipolar cycloaddition. Various substitutes are tolerated in this reaction, which proceeds smoothly in moderate to good yields. Furthermore, the pyrimidones derived from 2-bromophenyl isocyanate could be transformed to various indole fused pyrimidones when they were subjected to different palladium-catalyzed intramolecular Heck reaction conditions. The mechanisms of the series of transformation also have been proposed. The present method offers direct pathway to the diversified pyrimidone and indole fused pyrimidones compounds, which may possess potential bioactivity.

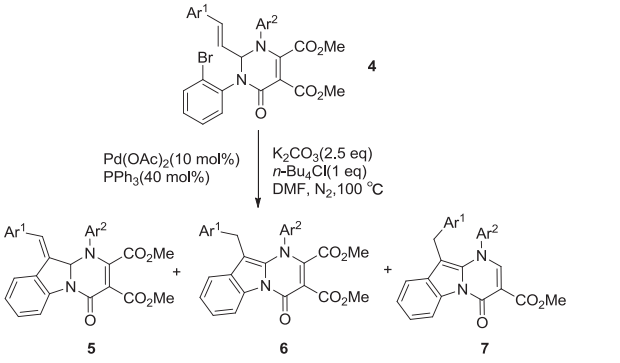
**Table 3**
Palladium-catalyzed intramolecular Heck reaction[a]



| Entry | **4** ($R^1$/$R^2$) | Time (h) | Yield (%) | | |
|---|---|---|---|---|---|
| | | | **5** | **6** | **7** |
| 1 | **4j** | 4 | **5a**:66 | **6a**:14 | **7a**:trace |
| 2 | **4t** | 4 | **5b**:70 | **6b**:trace | **7b**:trace |
| 3 | **4v** | 6 | **5c**:65 | **6c**:trace | **7c**:trace |
| 4 | **4r** | 12 | **5d**:59 | **6d**:trace | **7d**:13 |
| 5 | **4w** | 10 | **5e**:trace | **6e**:trace | **7e**:35 |
| 6 | **4x** | 11 | **5f**:trace | **6f**:trace | **7f**:30 |

[a] Reaction conditions: **4** (0.25 mmol), $Pd(PPh_3)_4$ (10 mol %), $K_2CO_3$ (0.625 mmol), DMF(2 mL), $N_2$, 100 °C.

**Table 4**
Palladium-catalyzed intramolecular Heck reaction[a]



| Entry | **4** ($R^1$/$R^2$) | Time (h) | Yield (%) | | |
|---|---|---|---|---|---|
| | | | **5** | **6** | **7** |
| 1 | **4j** | 4 | **5a**:trace | **6a**:trace | **7a**:51 |
| 2 | **4t** | 6 | **5b**:trace | **6b**:trace | **7b**:45 |
| 3 | **4v** | 7 | **5c**:trace | **6c**:trace | **7c**:47 |
| 4 | **4r** | 12 | **5d**:trace | **6d**:trace | **7d**:59 |
| 5 | **4w** | 11 | **5e**:trace | **6e**:trace | **7e**:trace |
| 6 | **4x** | 11 | **5f**:trace | **6f**:trace | **7f**:trace |

[a] Reaction conditions: 4 (0.25 mmol), $Pd(OAc)_2$(10 mol %), *n*-$Bu_4NCl$ (1 equiv), $K_2CO_3$ (0.625 mmol), $PPh_3$(40 mol %), DMF (2.0 mL), $N_2$, 100 °C.

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Detailed mechanistic study and synthetic application of these methods are underway.

## 4. Experimental

### 4.1. General information

All commercially available reagents and solvents were used without further purification unless otherwise stated. TLC was performed using $GF_{254}$ silica gel glass plates and silica gel 60 (300–400 mesh) was used in column chromatography separations. Petroleum ether (PE) refers to the fraction boiling in the 60–90 °C range. Melting points were obtained using a micro melting point apparatus and are uncorrected. Infrared spectra were recorded on a FT-IR spectrometer taken as KBr discs. $^1$H NMR and $^{13}$C NMR spectra were recorded on 400 MHz and 100 MHz or 500 MHz and 125 MHz instruments using $CDCl_3$ solvent with tetramethylsilane as the internal standard. HRMS were recorded using electron spray ionization method.

### 4.2. General procedure for the synthesis of highly functionalized pyrimidone derivatives 4 via three-component cascade reaction

α,β-Unsaturated imines **1** (0.6 mmol), acetylenedicarboxylate **2** (0.6 mmol) and isocyanates **3** (0.5 mmol) were mixed in acetonitrile (2 mL). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the solvent was removed under vacuum, the residue was subject to flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1 to 2:1) to afford pure **4**.

### 4.3. Typical procedure for the synthesis of 5 via intramolecular Heck reaction

Pyrimidone derivatives **4** (0.25 mmol), $Pd(PPh_3)_4$ (28.9 mg, 10 mol %), and $K_2CO_3$ (86.3 mg, 0.625 mmol) were mixed in DMF (2.0 mL). Then the mixture was stirred at 100 °C under nitrogen atmosphere for the indicated time until complete consumption of starting material as monitored by TLC. After completion, the reaction mixture was cooled to room temperature, diluted in ethyl acetate, and washed with brine. The aqueous phase was re-extracted with ethyl acetate for twice. The combined organic phase were dried over anhydrous $Na_2SO_4$ and then concentrated under vacuum, and the resulting residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 4:1 to 2:1) to afford the corresponding product **5**.

*4.3.1. 1-(4-Methyl-phenyl)-6-oxo-3-phenyl-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4a**).* Yellow solid (145 mg, 60%); mp: 87–89 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=7.47–7.31 (m, 10H), 7.21 (d, $J$=8.4 Hz, 2H), 7.16 (d, $J$=8.0 Hz, 1H), 6.78–6.69 (m, 2H), 5.75 (d, $J$=4.0 Hz, 1H), 3.83 (s, 3H), 3.66 (s, 3H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=165.4, 163.3, 159.6, 151.2, 141.5, 137.6, 137.0, 135.0, 134.9, 129.9, 129.0, 128.8, 128.5, 127.2, 126.3, 125.0, 121.6, 102.2, 80.8, 53.1, 52.2, 21.1. IR (KBr): 3056, 2951, 2839, 1742, 1659, 1547, 1508, 1434, 1230, 1158, 1073, 969, 832, 793, 735, 693 cm$^{-1}$; HRMS (ESI): $m/z$ [M] calcd for $C_{29}H_{26}N_2O_5$: 482.1842; found: 482.1841.

*4.3.2. 1,3-Bis-(4-bromo-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4b**).* Yellow solid (122 mg, 39%); mp: 132–134 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=7.53 (d, $J$=8.8 Hz, 2H), 7.46–7.42 (m, 4H), 7.39–7.35 (m, 3H), 7.17 (d, $J$=8.8 Hz, 4H), 6.71 (d, $J$=16.0 Hz, 1H), 6.64 (dd, $J$=16.0, 5.6 Hz, 1H), 5.68 (d, $J$=5.6 Hz, 1H), 3.81 (s, 3H), 3.68 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=165.0, 163.0, 159.2, 150.7, 140.5, 139.0, 135.6, 134.7, 133.2, 132.5, 129.4, 129.0, 128.0, 127.4, 126.7, 122.5, 120.9, 120.8, 103.3, 80.7, 53.5, 52.5; IR (KBr): 3028, 2950, 1742, 1660, 1548, 1488, 1271, 1229, 1194, 1158, 1071, 968, 910, 833, 769, 731, 692 cm$^{-1}$; HRMS (ESI): $m/z$ [M] calcd for $C_{28}H_{22}N_2O_5Br_2$: 623.9895, found: 623.9907.

*4.3.3. 1-(4-Bromo-phenyl)-3-(4-nitro-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4c**).* Yellow solid (102 mg, 35%); mp: 169–171 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=8.28 (d, $J$=8.8 Hz, 2H), 7.49–7.45 (m, 4H), 7.41–7.34 (m, 5H), 7.16 (d, $J$=8.4 Hz, 2H), 6.83 (d, $J$=15.6 Hz, 1H), 6.59 (dd, $J$=16.0, 5.6 Hz, 1H), 5.88 (d, $J$=4.8 Hz, 1H), 3.84 (s, 3H), 3.74 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=164.3, 162.8, 158.7, 147.5, 146.4, 146.1, 138.7, 135.8, 134.7, 132.8, 129.6, 129.2, 127.8, 127.5, 125.8, 123.3, 121.2, 120.9, 110.1, 80.3, 53.9, 52.9; IR (KBr): 3348, 2961, 2924, 2853, 1732, 1589, 1512, 1495, 1435, 1259, 1111, 1012, 958, 853, 750, 733, 698 cm$^{-1}$. HRMS (ESI): $m/z$ [M] calcd for $C_{28}H_{22}N_3O_7Br$: 591.0641, found: 591.0645.

*4.3.4. 1-(4-Bromo-phenyl)-6-oxo-3-phenyl-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4d**).* Yellow solid (186 mg, 68%); mp: 85–86 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=7.45–7.26 (m, 12H), 7.19 (d, $J$=8.4 Hz, 2H), 6.73 (d, $J$=16.0 Hz, 1H), 6.67 (dd, $J$=16.0, 5.2 Hz, 1H), 5.73 (d, $J$=4.8 Hz, 1H), 3.81 (s, 3H), 3.63 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=165.2, 163.1, 159.4, 151.6, 141.3, 139.1, 135.3, 134.8, 132.3, 130.0, 129.2, 128.9, 128.7, 128.0, 127.3, 125.1, 121.1, 120.5, 101.7, 80.6, 53.2, 52.3; IR (KBr): 3028, 2950, 2836, 1745, 1659, 1538, 1488, 1270, 1230, 1070, 968, 910, 809, 758, 731, 695 cm$^{-1}$; HRMS (ESI): $m/z$ [M] calcd for $C_{28}H_{23}N_2O_5Br$: 546.0790, found: 546.0797.

*4.3.5. 1-(4-Bromo-phenyl)-2-[2-(4-nitro-phenyl)-vinyl]-6-oxo-3-phenyl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4e**).* White solid (174 mg, 59%); mp: 207–208 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=8.23 (d, $J$=8.4 Hz, 2H), 7.59 (d, $J$=8.4 Hz, 2H), 7.49–7.37 (m, 5H), 7.29–7.27 (m, 2H), 7.18 (d, $J$=8.4 Hz, 2H), 6.84 (d, $J$=16.0 Hz, 1H), 6.77 (dd, $J$=16.0, 5.2 Hz, 1H), 5.81 (d, $J$=4.8 Hz, 1H), 3.82 (s, 3H), 3.68 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=165.1, 163.2, 159.6, 151.3, 148.1, 141.5, 141.2, 139.0, 132.9, 132.7, 130.3, 129.0, 128.2, 127.9, 126.1, 124.9, 124.4, 120.9, 103.3, 80.1, 53.5, 52.6; IR (KBr): 3062, 2950, 2853, 1742, 1595, 1519, 1489, 1344, 1233, 1070, 972, 833, 756, 741, 696 cm$^{-1}$; HRMS (ESI): $m/z$ [M] calcd for $C_{28}H_{22}N_3O_7Br$: 591.0641, found: 591.0623.

*4.3.6. 1-(4-Bromo-phenyl)-2-[2-(4-methoxy-phenyl)-vinyl]-6-oxo-3-phenyl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4f**).* White solid (156 mg, 54%); mp: 186–188 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=7.45–7.34 (m, 7H), 7.31–7.27 (m, 2H), 7.19 (d, $J$=8.8 Hz, 2H), 6.89 (d, $J$=8.8 Hz, 2H), 6.64 (d, $J$=16.0 Hz, 1H), 6.55 (dd, $J$=16.0, 6.0 Hz, 1H), 5.69 (d, $J$=6.0 Hz, 1H), 3.82 (s, 6H), 3.64 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=165.3, 163.2, 160.5, 159.6, 151.7, 141.4, 139.2, 134.9, 132.3, 130.0, 128.8, 128.7, 128.1, 127.5, 125.3, 120.5, 118.7, 114.3, 101.5, 80.9, 55.5, 53.2, 52.3; IR (KBr): 3003, 2951, 2837, 1746, 1606, 1512, 1488, 1257, 1069, 1011, 968, 910, 828, 731, 696 cm$^{-1}$; HRMS (ESI): $m/z$ [M] calcd for $C_{29}H_{25}N_2O_6Br$: 576.0896, found: 576.0900.

*4.3.7. 1-(4-Bromo-phenyl)-3-(4-methoxy-phenyl)-2-[2-(4-methoxy-phenyl)-vinyl]-6-oxo-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4g**).* Yellow solid (208 mg, 69%); mp: 90–91 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=7.44 (d, $J$=8.8 Hz, 2H), 7.37 (d, $J$=8.8 Hz, 2H), 7.28–7.18 (m, 4H), 6.88 (d, $J$=8.8 Hz, 4H), 6.61–6.53 (m, 2H), 5.58–5.57 (m, 1H), 3.81–3.79 (m, 9H), 3.64 (s, 3H); $^{13}$C NMR (100 MHz, CDCl3): $\delta$=165.3, 163.0, 160.4, 159.8, 159.6, 153.0, 139.1, 135.0, 133.6, 132.2, 128.6, 128.2, 127.5, 127.4, 120.4, 118.4, 114.8, 114.2, 99.1, 81.2, 55.6, 55.4, 53.1, 52.0; IR (KBr):

3003, 2951, 2838, 1742, 1606, 1510, 1488, 1254, 1159, 1029, 969, 910, 831, 795, 730, 645 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{30}H_{27}N_2O_7Br$: 606.1002, found: 606.1007.

*4.3.8. 1-(4-Bromo-phenyl)-3-(4-methoxy-phenyl)-2-[2-(4-nitro-phenyl)-vinyl]-6-oxo-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4h**).* Yellow solid (207 mg, 67%); mp: 184–185 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=8.22 (d, *J*=8.8 Hz, 2H), 7.58 (d, *J*=8.8 Hz, 2H), 7.47 (d, *J*=8.4 Hz, 2H), 7.24 (d, *J*=8.8 Hz, 2H), 7.18 (d, *J*=8.4 Hz, 2H), 6.91 (d, *J*=8.8 Hz, 2H), 6.81 (dd, *J*=16.0, 4.8 Hz, 1H), 6.76 (d, *J*=15.6 Hz, 1H), 5.70 (d, *J*=4.8 Hz, 1H), 3.82–3.81 (m, 6H), 3.67 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.3, 163.2, 160.0, 159.4, 152.7, 148.0, 141.2, 139.0, 133.8, 132.9, 132.6, 128.1, 128.0, 127.2, 125.9, 124.3, 120.8, 115.2, 100.8, 80.5, 55.8, 53.4, 52.4; IR (KBr): 3013, 2951, 2830, 1739, 1596, 1510, 1488, 1344, 1246, 1108, 973, 836, 735, 698 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{24}N_3O_8Br$: 621.0747, found: 621.0775.

*4.3.9. 1-(4-Bromo-phenyl)-6-oxo-3-phenyl-2-(2-phenyl-propenyl)-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4i**).* Yellow solid (83 mg, 30%); mp: 193–195 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.48–7.28 (m, 10H), 7.20–7.16 (m, 4H), 6.45 (s, 1H), 5.68 (s, 1H), 3.81 (s, 3H), 3.63 (s, 3H), 2.15 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.1, 163.2, 159.4, 151.2, 141.7, 139.4, 135.9, 132.4, 132.3, 131.5, 130.0, 129.2, 128.7, 128.5, 128.2, 127.7, 125.6, 120.6, 103.7, 85.2, 53.2, 52.4, 14.3; IR (KBr): 3056, 2950, 2834, 1745, 1660, 1556, 1488, 1434, 1260, 1071, 1011, 923, 830, 792, 758, 697 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{25}N_2O_5Br$: 560.0947, found: 560.0960.

*4.3.10. 1-(2-Bromo-phenyl)-3-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4j**).* Yellow solid (198 mg, 69%); mp: 166–168 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=7.64 (d, *J*=9.0 Hz, 1H), 7.43–7.28 (m, 9H), 7.20–7.17 (m, 1H), 6.86 (d, *J*=9.0 Hz, 2H), 6.79 (dd, *J*=16.0, 8.5 Hz, 1H), 6.48 (d, *J*=16.0 Hz, 1H), 5.37 (d, *J*=9.0 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.64 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.9, 163.3, 159.9, 159.4, 154.5, 138.3, 135.6, 135.0, 133.8, 133.6, 132.9, 129.9, 129.3, 129.0, 128.4, 128.3, 127.3, 122.8, 120.6, 114.7, 97.5, 80.8, 55.7, 53.2, 52.2; IR (KBr): 3030, 2950, 2839, 1746, 1660, 1510, 1474, 1234, 1162, 1076, 1028, 967, 911, 835, 794, 729, 693 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{25}N_2O_6Br$: 576.0896, found: 576.0896.

*4.3.11. 1-(4-Fluoro-phenyl)-3-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4k**).* Yellow solid (193 mg, 75%); mp: 182–183 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.43 (d, *J*=7.2 Hz, 2H), 7.39–7.34 (m, 3H), 7.29–7.24 (m, 4H), 7.02 (t, *J*=8.4 Hz, 2H), 6.89 (d, *J*=8.8 Hz, 2H), 6.73 (dd, *J*=16.0, 7.2 Hz, 1H), 6.60 (d, *J*=16.0 Hz, 1H), 5.56 (d, *J*=6.8 Hz, 1H), 3.82–3.81 (m, 6H), 3.64 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.6, 163.2, 161.4 (d, *J*=246.0 Hz), 159.9, 153.2, 136.1 (d, *J*=2.0 Hz), 135.5, 135.0, 133.8, 129.3, 129.0, 128.9, 128.8, 127.7, 127.4, 121.0, 116.2 (d, *J*=22.0 Hz), 115.0, 99.4, 81.6, 55.7, 53.2, 52.3; IR (KBr): 3029, 2950, 1747, 1667, 1557, 1515, 1428, 1269, 1157, 1072, 968, 911, 815, 794, 733, 695 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{25}N_2O_6F$: 516.1697, found: 516.1694.

*4.3.12. 3-(4-Methoxy-phenyl)-1-(2-nitro-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4l**).* Yellow solid (79 mg, 30%); mp: 120–122 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.98 (d, *J*=8.0 Hz, 1H), 7.60–7.56 (m, 1H), 7.48–7.38 (m, 9H), 6.91–6.86 (m, 3H), 6.56 (d, *J*=16.0 Hz, 1H), 5.58 (d, *J*=8.0 Hz, 1H), 3.80–3.79 (m, 6H), 3.63 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.6, 163.1, 160.1, 160.0, 155.0, 146.9, 136.2, 134.9, 134.0, 133.5, 133.1, 132.9, 129.5, 129.3, 129.1, 128.7, 127.4, 125.6, 120.7, 114.7, 97.0, 81.4, 55.7, 53.2, 52.2; IR (KBr): 3003, 2951, 2840, 1743, 1661, 1531, 1510, 1434, 1233, 1100, 1026, 970, 932, 835, 783, 737, 695 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{25}N_3O_8$: 543.1642, found: 543.1634.

*4.3.13. 1-(3-Chloro-phenyl)-3-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4m**).* Yellow solid (178 mg, 67%); mp: 87–88 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.44 (d, *J*=6.8 Hz, 2H), 7.39–7.33 (m, 4H), 7.27–7.25 (m, 3H), 7.20 (d, *J*=8.0 Hz, 2H), 6.90 (d, *J*=8.8 Hz, 2H), 6.73–6.65 (m, 2H), 5.65 (d, *J*=4.4 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.65 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.4, 163.1, 159.9, 159.6, 153.0, 141.2, 135.5, 134.8, 134.5, 133.7, 130.2, 129.2, 128.9, 127.5, 127.3, 127.1, 126.7, 124.4, 120.9, 115.0, 99.5, 80.9, 55.6, 53.2, 52.2; IR (KBr): 3024, 2951, 2839, 1746, 1660, 1538, 1510, 1434, 1256, 1160, 1073, 968, 910, 836, 793, 730, 691 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{25}N_2O_6Cl$: 532.1401, found: 532.1402.

*4.3.14. 1,3-Bis-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4n**).* Yellow solid (161 mg, 61%); mp: 100–102 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.43 (d, *J*=7.6 Hz, 2H), 7.39–7.31 (m, 3H), 7.27–7.20 (m, 4H), 6.89–6.84 (m, 4H), 6.73 (dd, *J*=15.6, 6.8 Hz, 1H), 6.60 (d, *J*=15.6 Hz, 1H), 5.55 (d, *J*=6.8 Hz, 1H), 3.81–3.76 (m, 9H), 3.64 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.7, 163.3, 160.0, 159.8, 158.6, 152.9, 135.2, 135.1, 133.9, 133.0, 129.1, 128.9, 128.4, 127.6, 127.3, 121.3, 114.9, 114.5, 99.6, 81.7, 55.7, 55.6, 53.1, 52.2; IR (KBr): 3003, 2951, 2838, 1747, 1660, 1538, 1506, 1434, 1249, 1158, 1073, 968, 911, 836, 794, 730, 693 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{30}H_{28}N_2O_7$: 528.1897, found: 528.1893.

*4.3.15. 3-(4-Methoxy-phenyl)-6-oxo-2-styryl-1-p-tolyl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4o**).* Yellow solid (163 mg, 64%); mp: 143–145 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.43 (d, *J*=7.2 Hz, 2H), 7.38–7.30 (m, 3H), 7.25 (d, *J*=8.4 Hz, 2H), 7.19 (d, *J*=8.4 Hz, 2H), 7.13 (d, *J*=8.0 Hz, 2H), 6.88 (d, *J*=8.8 Hz, 2H), 6.72 (dd, *J*=16.0, 6.4 Hz, 1H), 6.64 (d, *J*=15.6 Hz, 1H), 5.60 (d, *J*=6.4 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.64 (s, 3H), 2.30 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.7, 163.3, 159.8, 159.7, 152.8, 137.7, 137.0, 135.10, 135.06, 134.0, 129.9, 129.1, 128.9, 127.5, 127.3, 126.6, 121.5, 114.9, 99.9, 81.4, 55.7, 53.1, 52.2, 21.2; IR (KBr): 3028, 2950, 2839, 1743, 1660, 1548, 1511, 1434, 1231, 1158, 1073, 968, 911, 837, 794, 731, 693 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{30}H_{28}N_2O_6$: 512.1947, found: 512.1952.

*4.3.16. 3-(4-Methoxy-phenyl)-6-oxo-1-phenyl-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4p**).* Yellow solid (165 mg, 66%); mp: 148–149 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.44 (d, *J*=7.2 Hz, 2H), 7.39–7.30 (m, 7H), 7.26–7.24 (m, 3H), 6.88 (d, *J*=9.2 Hz, 2H), 6.73 (dd, *J*=16.0, 6.4 Hz, 1H), 6.65 (d, *J*=15.6 Hz, 1H), 5.64 (d, *J*=6.4 Hz, 1H), 3.82–3.80 (m, 6H), 3.65 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.7, 163.4, 159.82, 159.79, 152.9, 140.4, 135.2, 135.1, 134.0, 129.3, 129.2, 129.0, 127.6, 127.4, 127.2, 126.7, 121.5, 115.0, 100.0, 81.3, 55.7, 53.2, 52.2; IR (KBr): 3028, 2950, 2839, 1743, 1659, 1538, 1510, 1434, 1232, 1159, 1073, 968, 911, 835, 794, 730, 694 $cm^{-1}$; HRMS (ESI): *m/z* [M] calcd for $C_{29}H_{26}N_2O_6$: 498.1791, found: 498.1798.

*4.3.17. 1-(4-Fluoro-phenyl)-6-oxo-3-phenyl-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4q**).* Yellow solid (175 mg, 72%); mp: 68–70 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.44–7.25 (m, 12H), 7.01 (t, *J*=8.4 Hz, 2H), 6.75–6.67 (m, 2H), 5.74–5.66 (m, 1H), 3.81 (s, 3H), 3.63 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.3, 163.1, 161.3 (d, *J*=245.0 Hz), 159.6, 151.7, 141.3, 136.0 (d, *J*=3.0 Hz), 135.2, 134.8, 129.9, 129.2, 128.9, 128.7 (d, *J*=6.0 Hz), 128.6, 127.3, 125.2, 121.1, 116.1 (d, *J*=23.0 Hz), 101.5, 81.0, 53.2, 52.2; IR (KBr): 3028, 2951, 1747, 1660, 1538, 1506,

1428, 1230, 1157, 1073, 968, 911, 837, 796, 731, 695 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{28}H_{23}N_2O_5F$: 486.1591, found: 486.1589.

*4.3.18. 1-(2-Bromo-phenyl)-6-oxo-3-phenyl-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4r**).* White solid (180 mg, 66%); mp: 192–194 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.63 (d, *J*=8.0 Hz, 1H), 7.44–7.26 (m, 12H), 7.19 (t, *J*=7.6 Hz, 1H), 6.79 (dd, *J*=16.0, 7.6 Hz, 1H), 6.57 (d, *J*=15.6 Hz, 1H), 5.48 (d, *J*=7.6 Hz, 1H), 3.84 (s, 3H), 3.64 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.6, 163.3, 159.3, 153.3, 141.5, 138.4, 135.4, 135.1, 133.7, 132.7, 130.0, 129.8, 129.3, 129.0, 128.9, 128.4, 127.4, 126.1, 122.7, 120.8, 99.5, 80.4, 53.2, 52.3; IR (KBr): 3059, 2950, 1746, 1667, 1556, 1494, 1434, 1278, 1162, 1075, 967, 932, 840, 792, 756, 696 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{28}H_{23}N_2O_5Br$: 546.0790, found: 546.0789.

*4.3.19. 1-(4-Bromo-phenyl)-3-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4s**).* Yellow solid (204 mg, 71%); mp: 99–101 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.45–7.42 (m, 4H), 7.38–7.32 (m, 3H), 7.27–7.24 (m, 2H), 7.20 (d, *J*=8.8 Hz, 2H), 6.89 (d, *J*=8.8 Hz, 2H), 6.71 (dd, *J*=16.0, 6.4 Hz, 1H), 6.64 (d, *J*=16.0 Hz, 1H), 5.61 (d, *J*=6.0 Hz, 1H), 3.81–3.79 (m, 6H), 3.64 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.3, 163.0, 159.8, 159.5, 152.9, 139.1, 135.4, 134.7, 133.6, 132.2, 129.2, 128.9, 128.1, 127.4, 127.2, 120.8, 120.4, 114.9, 99.4, 81.0, 55.6, 53.1, 52.1; IR (KBr): 3024, 2950, 2837, 1743, 1688, 1586, 1538, 1510, 1434, 1234, 1195, 1070, 968, 910, 762, 730, 694 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{29}H_{25}N_2O_6Br$: 576.0896, found: 576.0900.

*4.3.20. 1-(2-Bromo-phenyl)-3-(4-methoxy-phenyl)-2-[2-(4-methoxy-phenyl)-vinyl]-6-oxo-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4t**).* White solid (202 mg, 67%); mp: 194–196 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.63 (d, *J*=7.6 Hz, 1H), 7.37–7.25 (m, 6H), 7.18 (t, *J*=7.6 Hz, 1H), 6.90–6.85 (m, 4H), 6.67 (dd, *J*=16.0, 8.4 Hz, 1H), 6.41 (d, *J*=16.0 Hz, 1H), 5.34 (d, *J*=8.0 Hz, 1H), 3.83–3.82 (m, 6H), 3.79 (s, 3H), 3.63 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.8, 163.2, 160.4, 159.7, 159.3, 154.3, 138.2, 135.1, 133.6, 133.5, 132.8, 129.8, 128.6, 128.3, 128.2, 127.5, 122.6, 118.0, 114.6, 114.3, 97.1, 80.9, 55.6, 55.4, 53.0, 52.1; IR (KBr): 3006, 2951, 2838, 1744, 1660, 1538, 1511, 1434, 1253, 1162, 1076, 968, 911, 832, 794, 731, 682 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{30}H_{27}N_2O_7Br$: 606.1002, found: 606.0998.

*4.3.21. 3-(4-Methoxy-phenyl)-2-[2-(4-methoxy-phenyl)-vinyl]-6-oxo-1-p-tolyl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4u**).* Yellow solid (168 mg, 62%); mp: 87–89 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.38–7.12 (m, 8H), 6.90–6.86 (m, 4H), 6.63–6.54 (m, 2H), 5.57 (d, *J*=4.8 Hz, 1H), 3.81–3.78 (m, 9H), 3.64 (s, 3H), 2.30 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.7, 163.3, 160.3, 159.8, 159.7, 152.8, 137.7, 136.9, 134.6, 133.9, 129.8, 128.6, 127.7, 127.5, 126.5, 119.0, 114.8, 114.2, 99.5, 81.6, 55.6, 55.4, 53.0, 52.1, 21.1; IR (KBr): 3003, 2951, 2838, 1747, 1660, 1538, 1515, 1434, 1257, 1158, 1072, 969, 911, 834, 795, 731, 645 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{31}H_{30}N_2O_7$: 542.2053, found: 542.2050.

*4.3.22. 1-(2-Bromo-phenyl)-2-[2-(4-methoxy-phenyl)-vinyl]-6-oxo-3-phenyl-1, 2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4v**).* Yellow solid (162 mg, 55%); mp: 168–169 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.61 (d, *J*=8.0 Hz, 1H), 7.37–7.26 (m, 9H), 7.18 (t, *J*=7.6 Hz, 1H), 6.89 (d, *J*=8.4 Hz, 2H), 6.67 (dd, *J*=15.6 Hz, 7.6 Hz, 1H), 6.50 (d, *J*=15.6 Hz, 1H), 5.45 (d, *J*=7.6 Hz, 1H), 3.83–3.81 (m, 6H), 3.63 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.4, 163.0, 160.3, 159.1, 153.0, 141.1, 138.1, 134.7, 133.3, 132.4, 129.7, 129.5, 128.6, 128.4, 128.1, 127.3, 125.8, 122.4, 118.0, 114.1, 98.8, 80.4, 55.3, 52.9, 52.0; IR (KBr): 3003, 2950, 2837, 1743, 1661, 1539, 1512, 1435, 1253, 1162, 1074, 968, 911, 829, 793, 733, 696 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{29}H_{25}N_2O_6Br$: 576.0896, found: 576.0897.

*4.3.23. 1-(2-Bromo-phenyl)-3-(4-methoxy-phenyl)-2-[2-(4-nitro-phenyl)-vinyl]-6-oxo-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4w**).* Yellow solid (165 mg, 53%); mp: 207–209 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=8.22 (d, *J*=8.8 Hz, 2H), 7.65 (d, *J*=8.4 Hz, 1H), 7.57 (d, *J*=8.8 Hz, 2H), 7.34–7.19 (m, 5H), 6.93–6.87 (m, 3H), 6.65 (d, *J*=15.6 Hz, 1H), 5.48 (d, *J*=7.2 Hz, 1H), 3.82–3.81 (m, 6H), 3.67 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=165.5, 163.2, 159.9, 159.2, 154.0, 148.0, 141.3, 138.1, 133.81, 133.76, 132.9, 132.6, 130.1, 128.5, 128.0, 127.8, 125.3, 124.3, 122.6, 114.9, 98.6, 79.9, 55.7, 53.3, 52.3; IR (KBr): 3062, 2951, 2834, 1739, 1658, 1545, 1511, 1436, 1343, 1235, 1162, 1028, 969, 840, 790, 754, 730, 690 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{29}H_{24}N_3O_8Br$: 621.0747, found: 621.0745.

*4.3.24. 1-(2-Bromo-phenyl)-2-[2-(4-nitro-phenyl)-vinyl]-6-oxo-3-phenyl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid dimethyl ester (**4x**).* Yellow solid (142 mg, 48%); mp: 156–157 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.23 (d, *J*=8.0 Hz, 2H), 7.64 (d, *J*=8.0 Hz, 1H), 7.58 (d, *J*=8.5 Hz, 2H), 7.42–7.34 (m, 7H), 7.23–7.21 (m, 1H), 6.87 (dd, *J*=16.0, 7.0 Hz, 1H), 6.73 (d, *J*=16.0 Hz, 1H), 5.59 (d, *J*=7.0 Hz, 1H), 3.83 (s, 3H), 3.67 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.4, 163.3, 159.1, 152.9, 148.1, 141.5, 141.4, 138.2, 133.9, 132.7, 132.5, 130.2, 130.0, 128.9, 128.6, 128.1, 125.61, 125.55, 124.4, 122.6, 100.7, 79.6, 53.4, 52.4; IR (KBr): 3071, 2950, 2847, 1734, 1653, 1545, 1512, 1435, 1343, 1232, 1153, 1074, 973, 857, 788, 748, 690 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{28}H_{22}N_3O_7Br$: 591.0641, found: 591.0638.

*4.3.25. 1-(4-Bromo-phenyl)-3-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylic acid diethyl ester (**4y**).* Yellow solid (169 mg, 56%); mp: 76–77 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.45–7.33 (m, 7H), 7.26–7.19 (m, 4H), 6.88 (d, *J*=8.4 Hz, 2H), 6.73 (dd, *J*=15.6, 6.4 Hz, 1H), 6.63 (d, *J*=15.6 Hz, 1H), 5.58 (d, *J*=6.4 Hz, 1H), 4.30–4.25 (m, 2H), 4.09 (q, *J*=7.2 Hz, 2H), 3.80 (s, 3H), 1.32 (t, *J*=7.2 Hz, 3H), 1.06 (t, *J*=7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=164.8, 162.6, 159.8, 159.7, 152.7, 139.3, 135.4, 134.9, 134.0, 132.3, 129.2, 128.9, 128.2, 127.7, 127.3, 121.2, 120.5, 114.9, 100.1, 81.1, 62.5, 61.0, 55.7, 14.3, 13.7; IR (KBr): 3053, 2981, 2838, 1738, 1660, 1538, 1511, 1454, 1257, 1170, 1068, 968, 910, 836, 785, 731, 694 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{31}H_{29}N_2O_6Br$: 604.1209, found: 604.1221.

*4.3.26. 1-(4-Fluoro-phenyl)-3-(4-methoxy-phenyl)-6-oxo-2-styryl-1,2,3,6-tetrahydro-pyrimidine-4,5-dicarboxylic acid diethyl ester (**4z**).* Yellow solid (158 mg, 58%); mp: 67–69 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.44 (d, *J*=6.8 Hz, 2H), 7.39–7.31 (m, 3H), 7.29–7.24 (m, 4H), 7.02 (t, *J*=8.4 Hz, 2H), 6.88 (d, *J*=8.8 Hz, 2H), 6.75 (dd, *J*=16.0, 7.2 Hz, 1H), 6.61 (d, *J*=15.6 Hz, 1H), 5.55 (d, *J*=7.2 Hz, 1H), 4.33–4.22 (m, 2H), 4.09 (q, *J*=7.2 Hz, 2H), 3.80 (s, 3H), 1.32 (t, *J*=7.2 Hz, 3H), 1.06 (t, *J*=7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=164.8, 162.6, 161.3 (d, *J*=246.0 Hz), 160.0, 159.8, 152.7, 136.2 (d, *J*=3.0 Hz), 135.3, 135.0, 134.0, 129.2, 128.93, 128.85 (d, *J*=8.0 Hz), 127.8, 127.3, 121.3, 116.1 (d, *J*=22.0 Hz), 114.8, 99.9, 81.5, 62.4, 61.0, 55.7, 14.3, 13.7; IR (KBr): 3058, 2981, 2839, 1737, 1659, 1547, 1510, 1450, 1227, 1156, 1070, 969, 834, 781, 735, 693 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{31}H_{29}N_2O_6F$: 544.2010, found: 544.2007.

*4.3.27. 3-(4-Bromo-phenyl)-1-(4-methoxy-phenyl)-4-oxo-2-styryl-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid methyl ester (**4A**).* White solid (63 mg, 24%); mp: 98–100 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=8.25 (s, 1H), 7.47 (d, *J*=8.8 Hz, 2H), 7.39–7.31 (m, 5H), 7.23–7.19 (m, 4H), 6.94 (d, *J*=8.8 Hz, 2H), 6.60 (dd, *J*=16.0, 6.4 Hz, 1H), 6.53 (d, *J*=16.0 Hz, 1H), 5.83 (d, *J*=5.6 Hz, 1H), 3.84–3.82 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=166.1, 160.0, 158.8, 150.5,

139.7, 135.6, 135.1, 134.9, 132.4, 129.3, 129.1, 128.8, 127.3, 122.6, 121.3, 120.6, 115.4, 99.3, 79.4, 55.9, 52.0; IR (KBr): 3328, 2949, 2842, 1734, 1616, 1596, 1511, 1438, 1244, 1179, 1033, 826, 745, 691 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{27}H_{23}N_2O_4Br$: 518.0841, found: 518.0844.

*4.3.28. 10-Benzylidene-1-(4-methoxy-phenyl)-4-oxo-1,4,10,10a-tetrahydropyrimido[1,2-a]indole-2,3-dicarboxylic acid dimethyl ester (**5a**).* Yellow solid (82 mg, 66%); mp: 101–103 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.13 (d, *J*=8.0 Hz, 1H), 7.44–7.29 (m, 7H), 7.06 (t, *J*=7.5 Hz, 1H), 6.91 (s, 1H), 6.63 (s, 1H), 6.54 (d, *J*=9.0 Hz, 2H), 6.42 (d, *J*=9.0 Hz, 2H), 3.90 (s, 3H), 3.65 (s, 3H), 3.57 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.3, 163.7, 159.7, 158.1, 155.7, 141.9, 135.2, 130.6, 130.0, 129.7, 129.5, 129.4, 129.3, 129.1, 128.8, 126.2, 124.2, 120.0, 115.4, 113.6, 106.7, 75.8, 55.5, 53.3, 52.5; IR (KBr): 3058, 2951, 2840, 1746, 1704, 1667, 1557, 1509, 1442, 1249, 1168, 1097, 1026, 921, 845, 795, 761, 734, 698 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{29}H_{24}N_2O_6$: 496.1634, found: 496.1645.

*4.3.29. 10-Benzyl-1-(4-methoxy-phenyl)-4-oxo-1,4-dihydro-pyrimido[1,2-a]in- dole-2,3-dicarboxylic acid dimethyl ester (**6a**).* Yellow solid (17 mg, 14%); mp: 79–80 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.90 (d, *J*=8.5 Hz, 1H), 7.36–7.26 (m, 3H), 7.19–7.17 (m, 2H), 7.11–7.09 (m, 3H), 6.75–6.70 (m, 4H), 3.95 (s, 3H), 3.81 (s, 3H), 3.55 (s, 3H), 3.35 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.4, 162.0, 161.2, 156.8, 151.6, 139.8, 131.8, 130.9, 130.6, 130.4, 129.0, 128.2, 127.8, 126.1, 124.6, 123.6, 118.1, 117.1, 114.5, 99.9, 97.0, 55.9, 53.3, 52.9, 28.6; IR (KBr): 3025, 2951, 2840, 1746, 1704, 1614, 1547, 1510, 1462, 1443, 1253, 1168, 1064, 1027, 955, 910, 848, 793, 731, 696 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{29}H_{24}N_2O_6$: 496.1634, found: 496.1633.

*4.3.30. 10-(4-Methoxy-benzylidene)-1-(4-methoxy-phenyl)-4-oxo-1,4,10,10a-tetrahydro-pyrimido[1,2-a]indole-2,3-dicarboxylic acid dimethyl ester (**5b**).* Yellow solid (92 mg, 70%); mp: 103–105 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.11 (d, *J*=7.5 Hz, 1H), 7.39–7.33 (m, 3H), 7.28–7.25 (m, 1H), 7.05–6.96 (m, 3H), 6.85 (s, 1H), 6.61 (d, *J*=8.5 Hz, 2H), 6.53 (s, 1H), 6.45 (d, *J*=9.0 Hz, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.65 (s, 3H), 3.59 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.3, 163.9, 160.1, 159.7, 158.1, 155.4, 141.5, 131.0, 130.0, 129.8, 127.9, 126.8, 126.0, 124.2, 119.6, 115.3, 114.6, 113.7, 107.4, 76.0, 55.6, 55.5, 53.3, 52.5; IR (KBr): 3055, 2951, 2838, 1743, 1694, 1662, 1605, 1511, 1437, 1248, 1179, 1119, 1028, 921, 831, 787, 753, 722, 696 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{30}H_{26}N_2O_7$: 526.1740, found: 526.1747.

*4.3.31. 10-(4-Methoxy-benzylidene)-4-oxo-1-phenyl-1,4,10,10a-tetrahydropyrimido[1,2-a]indole-2,3-dicarboxylic acid dimethyl ester (**5c**).* Yellow solid (81 mg, 65%); mp: 101–102 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.11 (d, *J*=8.0 Hz, 1H), 7.34–7.28 (m, 3H), 7.27–7.26 (m, 1H), 7.13–7.10 (m, 1H), 7.05–6.95 (m, 5H), 6.82 (s, 1H), 6.69 (d, *J*=7.5 Hz, 2H), 6.56 (s, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.56 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.2, 163.8, 160.1, 157.9, 154.9, 141.3, 137.3, 130.9, 130.0, 129.9, 129.0, 128.6, 128.5, 127.8, 126.7, 126.0, 124.3, 119.6, 115.3, 114.6, 107.9, 76.0, 55.6, 53.3, 52.5; IR (KBr): 3062, 2950, 2830, 1740, 1700, 1685, 1604, 1512, 1466, 1437, 1250, 1178, 1096, 1032, 917, 804, 755, 697 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{29}H_{24}N_2O_6$: 496.1634, found: 496.1639.

*4.3.32. 10-Benzylidene-4-oxo-1-phenyl-1,4,10,10a-tetrahydro-pyrimido[1,2-a]indole-2,3-dicarboxylic acid dimethyl ester (**5d**).* Yellow solid (69 mg, 59%); mp: 198–200 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.14 (d, *J*=8.0 Hz, 1H), 7.42–7.32 (m, 7H), 7.13–7.05 (m, 2H), 6.96–6.93 (m, 2H), 6.89 (s, 1H), 6.69 (s, 1H), 6.63 (d, *J*=7.5 Hz, 2H), 3.91 (s, 3H), 3.55 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.2, 163.7, 158.0, 155.2, 141.8, 137.2, 135.1, 130.6, 129.5, 129.3, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 126.2, 124.3, 120.0, 115.6, 107.3, 75.7, 53.2, 52.5. IR (KBr): 3058, 2950, 2855, 1743, 1700, 1663, 1595, 1526, 1493, 1420, 1233, 1151, 1097, 1021, 925, 804, 760, 731, 695 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{28}H_{22}N_2O_5$: 466.1529, found: 466.1531.

*4.3.33. 10-Benzyl-1-(4-methoxy-phenyl)-4-oxo-1,4-dihydropyrimido-[1,2-a] indole-3-carboxylic acid methyl ester (**7a**).* Yellow solid (56 mg, 51%); mp: 175–177 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.91 (d, *J*=8.0 Hz, 1H), 8.22 (s, 1H), 7.37–7.30 (m, 3H), 7.19 (d, *J*=8.5 Hz, 2H), 7.10–7.09 (m, 3H), 6.81 (d, *J*=9.0 Hz, 2H), 6.73–6.72 (m, 2H), 3.90 (s, 3H), 3.83 (s, 3H), 3.50 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.4, 160.8, 157.1, 150.2, 139.8, 133.0, 132.3, 130.6, 130.3, 128.4, 128.2, 127.8, 126.1, 124.3, 123.3, 118.0, 117.0, 115.1, 99.0, 98.4, 55.9, 52.3, 28.8; DEPT135 $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.4, 160.8, 157.1, 150.2, 133.0, 132.3, 130.6, 130.3, 128.4, 128.2, 127.8, 126.1, 124.3, 123.3, 118.0, 117.0, 115.1, 55.9, 52.3, 28.8; IR (KBr): 3059, 2949, 2838, 1741, 1699, 1617, 1588, 1511, 1459, 1436, 1242, 1190, 1055, 1030, 840, 768, 731, 708 $cm^{-1}$; HRMS(ESI): *m*/*z* [M] calcd for $C_{27}H_{22}N_2O_4$: 438.1580, found: 438.1575.

*4.3.34. 10-(4-Methoxy-benzyl)-1-(4-methoxy-phenyl)-4-oxo-1,4-dihydropyrimido[1,2-a]indole-3-carboxylic acid methyl ester (**7b**).* Yellow solid (53 mg, 45%); mp: 200–201 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.91 (d, *J*=8.0 Hz, 1H), 8.22 (s, 1H), 7.38–7.26 (m, 3H), 7.20 (d, *J*=8.5 Hz, 2H), 6.84 (d, *J*=9.0 Hz, 2H), 6.67–6.62 (m, 4H), 3.92 (s, 3H), 3.85 (s, 3H), 3.73 (s, 3H), 3.43 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.5, 160.8, 158.1, 157.1, 150.2, 133.1, 132.2, 131.9, 130.7, 130.3, 128.8, 128.4, 124.3, 123.3, 118.0, 117.1, 115.1, 113.7, 99.5, 98.5, 55.9, 55.5, 52.4, 27.9; IR (KBr): 3071, 2989, 2950, 2836, 1740, 1700, 1617, 1588, 1510, 1459, 1437, 1293, 1243, 1175, 1115, 1033, 910, 839, 786, 734 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{28}H_{24}N_2O_5$: 468.1685, found: 468.1688.

*4.3.35. 10-(4-Methoxy-benzyl)-4-oxo-1-phenyl-1,4-dihydropyrimido-[1,2-a] indole-3-carboxylic acid methyl ester (**7c**).* Yellow solid (52 mg, 47%); mp: 232–233 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.92 (d, *J*=8.0 Hz, 1H), 8.24 (s, 1H), 7.50 (t, *J*=7.5 Hz, 1H), 7.40–7.35 (m, 4H), 7.33–7.30 (m, 3H), 6.65–6.58 (m, 4H), 3.92 (s, 3H), 3.73 (s, 3H), 3.38 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.4, 158.1, 157.0, 149.8, 140.4, 131.8, 131.6, 130.7, 130.34, 130.29, 130.2, 128.7, 127.1, 124.4, 123.4, 118.1, 117.1, 113.7, 99.6, 98.7, 55.4, 52.4, 28.0; IR (KBr): 3058, 2949, 2843, 1740, 1700, 1617, 1582, 1510, 1494, 1436, 1244, 1115, 1055, 1033, 853, 784, 732, 705 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{27}H_{22}N_2O_4$: 438.1580, found: 438.1582.

*4.3.36. 10-Benzyl-4-oxo-1-phenyl-1,4-dihydro-pyrimido[1,2-a]indole-3-carboxylic acid methyl ester (**7d**).* Yellow solid (60 mg, 59%); mp: 217–219 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$=8.93 (d, *J*=8.5 Hz, 1H), 8.25 (s, 1H), 7.49 (t, *J*=7.5 Hz, 1H), 7.40–7.28 (m, 7H), 7.10–7.09 (m, 3H), 6.68 (s, 2H), 6.73–6.72 (m, 2H), 3.93 (s, 3H), 3.46 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.5, 157.1, 149.8, 140.4, 139.6, 132.0, 130.7, 130.4, 130.3, 130.2, 128.3, 127.8, 127.2, 126.2, 124.4, 123.5, 118.1, 117.1, 99.1, 98.8, 52.5, 28.9; IR (KBr): 3317, 3059, 2949, 2847, 1740, 1700, 1664, 1617, 1582, 1493, 1461, 1437, 1293, 1244, 1153, 1055, 926, 789, 752, 726, 695 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{26}H_{20}N_2O_3$: 408.1474, found: 408.1479.

*4.3.37. 1-(4-Methoxy-phenyl)-10-(4-nitro-benzyl)-4-oxo-1,4-dihydropyrimido[1,2-a]indole-3-carboxylic acid methyl ester (**7e**).* Yellow solid (42 mg, 35%); mp: 207–209 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=8.94 (d, *J*=8.4 Hz, 1H), 8.23 (s, 1H), 7.98 (d, *J*=8.8 Hz, 2H), 7.40–7.30 (m, 3H), 7.20 (d, *J*=8.8 Hz, 2H), 6.90 (d, *J*=8.8 Hz, 2H), 6.83 (d, *J*=8.8 Hz, 2H), 3.93 (s, 3H), 3.85 (s, 3H), 3.61 (s, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=174.8, 165.3, 161.1, 156.9, 150.2, 147.8, 146.7, 132.8, 130.8, 129.8, 128.6, 128.5, 124.7, 123.7, 123.6, 117.4, 117.3, 115.3, 99.1, 97.1, 56.1, 52.5, 29.0; IR (KBr): 3114, 3062, 2946, 2838, 1743, 1667, 1590, 1511, 1458, 1435, 1343, 1291,

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1241, 1177, 1106, 1027, 838, 784, 745, 735, 715 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{27}H_{21}N_3O_6$: 483.1430, found: 483.1436.

*4.3.38. 10-(4-Nitro-benzyl)-4-oxo-1-phenyl-1,4-dihydropyrimido[1,2-a]indole-3-carboxylic acid methyl ester (**7f**).* Yellow solid (34 mg, 30%); mp: 156–157 °C; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=8.95 (d, *J*=8.4 Hz, 1H), 8.26 (s, 1H), 7.97 (d, *J*=8.8 Hz, 2H), 7.55–7.52 (m, 1H), 7.41–7.29 (m, 7H), 6.85 (d, *J*=8.4 Hz, 2H), 3.94 (s, 3H), 3.56 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$=165.2, 156.8, 149.7, 147.6, 146.7, 140.2, 132.5, 130.8, 130.5, 129.8, 128.6, 127.3, 124.8, 123.8, 123.7, 117.5, 117.3, 99.3, 97.1, 52.6, 29.1; IR (KBr): 3071, 2946, 1739, 1700, 1662, 1620, 1589, 1508, 1454, 1435, 1342, 1288, 1244, 1106, 1054, 933, 855, 785, 746, 691 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{26}H_{19}N_3O_5$: 453.1325, found: 453.1321.

*4.3.39. 1-Phenyl-6-styryl-1,6-dihydro-pyridine-2,3,4,5-tetracarboxylic acid tetramethyl ester (**9**).* Yellow oil (15 mg, 12%); $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=7.45–7.27 (m, 10H), 6.78 (d, *J*=15.6 Hz, 1H), 6.31 (dd, *J*=16.0, 6.0 Hz, 1H), 5.50 (d, *J*=4.2 Hz, 1H), 3.92 (s, 3H), 3.75 (s, 3H), 3.70 (s, 3H), 3.62 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$=167.9, 164.3, 163.8, 148.4, 142.9, 137.6, 136.0, 132.1, 129.5, 128.8, 128.5, 128.4, 127.2, 125.2, 123.0, 109.4, 103.6, 62.0, 53.1, 52.8, 52.6, 52.2; IR (KBr): 2953, 2923, 2851, 1740, 1598, 1493, 1436, 1235, 1121, 1076, 964, 763, 735, 700 $cm^{-1}$; HRMS (ESI): *m*/*z* [M] calcd for $C_{27}H_{25}NO_8$: 491.1580, found: 491.1582.

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