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Iodine-catalyzed three-component reaction of quinazoline-2,5-diones with aldehydes and styrenes for the synthesis of allylamine derivatives

Zhang Zhang [a,b,*], Yu-Shan Zhang [a,b], Zheng-Jun Quan [a,b], Yu-Xia Da [a,b], Xi-Cun Wang [a,b,*]

[a] Key Laboratory of Eco-Environment-Related Polymer Materials, Ministry of Education, China, Gansu 730070, PR China
[b] Gansu Key Laboratory of Polymer Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Anning East Road 967#, Lanzhou, Gansu 730070, PR China

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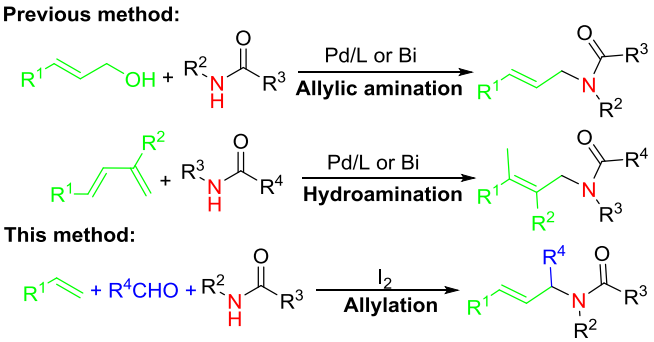
ABSTRACT

Iodine-catalyzed three component reaction of quinazoline-2,5-diones, aldehydes, and styrenes provides allylamine derivatives was described. Both paraformaldehyde and ethyl glyoxalate can be applied in this reaction with simple styrenes with high regioselectivity.

1. Introduction

Allylamines represent an important structural motif frequently found in a wide variety of natural products, pharmaceuticals,[1] bioactive and antimycotic activity products.[2,3] They are one of the most valuable chemical intermediates for a wide range of organic compounds.[4] Among the different types of allylic substitution reactions, the synthesis of allylamines is of special interest. The transition-metal-catalyzed allylic aminations of allylalcohols[5] and their derivatives[6–9] have become a powerful tool for the construction of allylamines. Alternatively, the Lewis acid-promoted reductive amination of cinnamaldehyde giving allylamines has also been reported.[10–12] The sequential hydrozirconation transmetalation imine addition of alkynes establishes an efficient new route for the preparation of synthetically useful allylic amine building blocks.[13] However, such a reaction is a synthetic challenge due to the intrinsic poor nucleophilicity of simple alkenes. Recently, some groups have reported the palladium-catalyzed Heck arylation of allylamine derivatives employing aryl iodide or arenediazonium salts.[14] Huang et al. have developed a novel palladium-catalyzed vinylation reaction that enables the catalytic functionalization of alkenes with aminals.[15] As compared to analogous reactions, the selective N-allylation of electron-deficient *N*-heterocycles and amides with olefins has limitedly been investigated. In this respect, notable progress was made respectively by Beller and Shibasaki groups via the allylic substitution of allylic alcohols with amides to afford allylic amines (Scheme 1).[16] More recently, Beller et al. described a general and regioselective 1,4-addition of electron deficient amides into 1,3-dienes catalyzed by [{Pd(π-cinnamyl)Cl}$_2$] in



Scheme 1. Synthesis of allylamine derivatives.

* Corresponding authors. Tel./fax: +86 931 7972626; e-mail addresses: zhangz@nwnu.edu.cn (Z. Zhang), wangxicun@nwnu.edu.cn (X.-C. Wang).

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0040-4020/

the presence of 1,3-bis(diphenylphosphino)propane to deliver allylamines.[17]

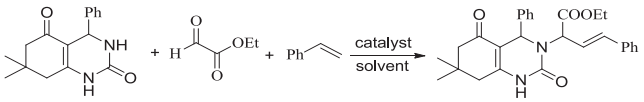
We have recently reported the synthesis of allylamine derivatives via I_2-catalyzed one-pot multi-component reaction of 3,4-dihydropyrimidinones (or amides), paraformaldehyde, and styrenes.[18] This direct method from unactivated styrenes does not need any additives and proceeds with high regioselectivity, which forms water as the sole by-product.

Herein, we became interested in the formation of more challenging allylic amines. Glycinate are fascinating precursors for the synthesis of multifunctionalized heterocycles.[19] Therefore, we present the iodine-catalyzed direct N-allylation of quinazoline-2,5-dione with aldehydes (including ethyl glyoxalate, and paraformaldehyde) and non-activated alkenes (Scheme 1).

2. Results and discussion

Initially, the model reaction of octahydroquinazoline-2,5-dione (**1a**), ethyl glyoxalate (**2a**, 50 wt% solution in toluene), and styrene (**3a**) was used to optimize the reaction conditions (Table 1). Only trace amount of product **4a** was obtained when sulfuric acid-modified polyethylene glycol (PEG-OSO_3H) or trimethylsilyl chloride (TMSCl) was utilized as catalyst (entries 1 and 2). The application of trifluoroacetic acid (TFA) resulted in no conversion (entry 3). When trifluoromethanesulfonic acid (TfOH), the desired product **4a** was isolated in 17% yield (entry 4). Also, some typical Lewis acids such as $ZnCl_2$, $FeCl_3$ were tested in this reaction, and only $FeCl_3$ promoted the reaction in 32% yield of **4a** (entries 5 and 6). Notably, good result was obtained using 0.2 equiv of molecular iodine as the catalyst in 1,4-dioxane at 110 °C for 24 h, and the desired product **4a** was isolated in 60% yield (entry 7). Good reaction yield and activity were also observed using I_2 or $FeCl_3$ combing with TfOH (entries 8 and 9), which provided the desired product **4a** 48% and 58% yield, respectively. Then, the effects of solvent and temperature in this reaction were also investigated. Among the solvents examined, dioxane, which was used in an earlier study gave good result, in contrast to the unsatisfactory result obtained with DMF and DMSO as solvent (entries 12 and 13). Other nonpolar solvents, such as xylene and toluene (entries 10 and 11) only gave a low yield even at higher temperature. When the catalyst loading of I_2 was increased to 40 mol%, a considerably higher yield was observed (entry 14). Reducing the I_2 loading to 30 mol% leaded to a low yield of 57% (entry 15), and increasing the I_2 loading to 50 mol%, the yield have no obvious change (entry 16). It is worth mentioning that the reaction proceeds with highly selective, delivering exclusively the linear *E* isomer of the allylic amine product **4a** in all cases.

Table 1
Optimization of the three-component reaction conditions[a]

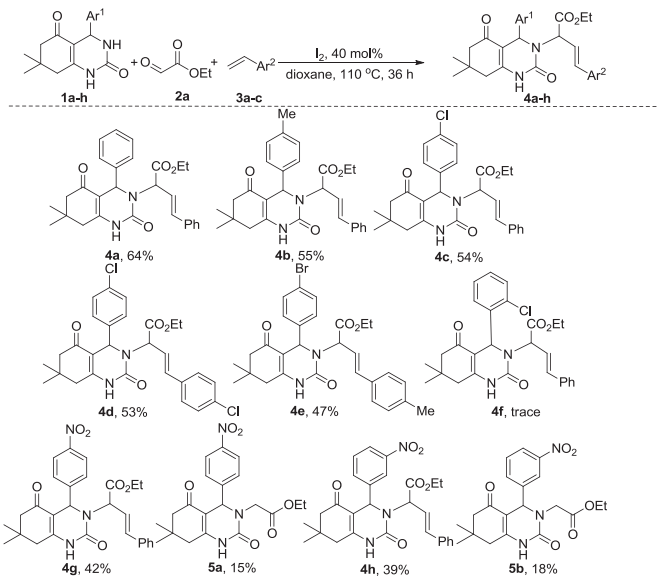


1a 2a 3a 4a

Entry	Catalysis (mol/%)	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	PEG-OSO_3H (20)	Dioxane	110	24	Trace
2	TMSCl (20)	Dioxane	110	24	Trace
3	TFA (20)	Dioxane	110	24	nd[c]
4	TfOH (20)	Dioxane	110	24	17
5	$ZnCl_2$ (20)	Dioxane	110	24	Trace
6	$FeCl_3$ (20)	Dioxane	110	24	32
7	I_2 (20)	Dioxane	110	24	60
8	$FeCl_3$ (20)/TfOH (2)	Dioxane	110	24	48
9	I_2 (20)/TfOH (2)	Dioxane	110	24	58
10	I_2 (20)	Xylene	120	24	35
11	I_2 (20)	Toluene	110	24	42
12	I_2 (20)	DMF	150	24	nd[c]
13	I_2 (20)	DMSO	150	24	Trace
14	I_2 (40)	Dioxane	110	36	64
15	I_2 (30)	Dioxane	110	36	57
16	I_2 (50)	Dioxane	110	36	65

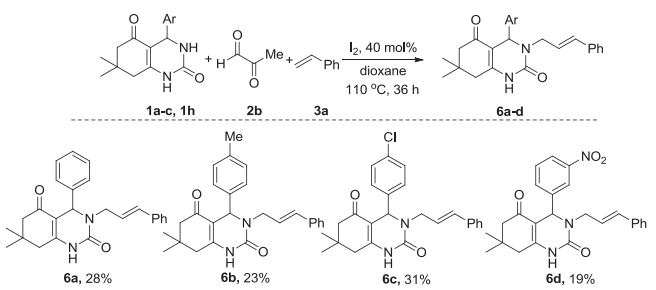
[a] Reaction conditions: quinazoline-2,5-dione (**1a**, 0.5 mmol), ethyl glyoxylate (**2a**, 1.5 mmol), styrene (**3a**, 0.75 mmol), catalyst, solvent (3 mL), 110 °C.
[b] Isolated yield of **4a** after purification by flash chromatography.
[c] Not detected in the reaction mixture.

With the optimized conditions in hand, a wide variety of substituted quinazoline-2,5-diones (**1**), **2a**, and styrenes (**3**) were submitted to investigate its substrate scope and generality (Scheme 2). A series of allylamine derivatives **4a**–**h** were obtained with moderate yield and high regioselectivity. No significant difference in yield was observed with electron-donating or electron-withdrawing substituents on the phenyl group of substrates **1**. However, steric effects has a negative effect on the reaction. When introducing steric hindrance ortho to the aromatic ring, trace desired product **4f** with a mixture was detected. The reaction of 4-NO_2 or 3-NO_2 substituted quinazoline-2,5-diones **1g**–**h** with **2a** and **3a** resulted in the formation of **4g**–**h** in 39–42% yield, respectively, whereas a minor amount of by-products as **5a** and **5b** were also isolated. Notably, in all reactions in which we observed lower yields of **4**, starting materials were recovered. In some experiments, we also observed the formation of trace amount of by-products.



Scheme 2. Three-component reaction of quinazoline-2,5-diones, ethyl glyoxylate, and styrenes.

Next, we tried to extend the scope of the methodology to the use of methylglyoxal instead of ethyl glyoxylate in the three-component reaction (Scheme 3). To our surprise, the reaction only provide product (**6a**) with recovered **1a**. Similarly, 4-Me, 4-Cl or 3-NO_2 substituted quinazoline-2,5-diones reacted well to deliver the corresponding products **6c**–**d**.[20] The mechanism studies on the deacylation are underway.



Scheme 3. Reaction between quinazoline-2,5-dione, methylglyoxal, and styrene.

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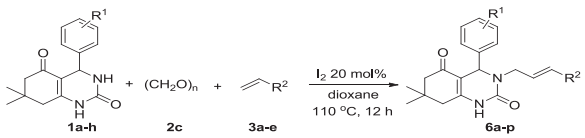
To further expand the scope of substrates, we examined paraformaldehyde (**2c**) as the aldehyde partner in the three-component reaction (Table 2). When decreasing the catalyst of I_2 loading to 20 mol% in dioxane at 110 °C within 12 h, the three-component reaction proceeded to deliver the allylamine derivatives **6a**–**p** in good yields. We found that quinazoline-2,5-diones bearing electron-withdrawing groups (4-NO_2, 4-Cl, 4-F, and 4-Br) provided higher yields than those containing electron-donating groups (4-Me) on the phenyl ring. Styrenes bearing electron-withdrawing groups provided higher yields than those containing electron-donating groups (entries 1-15). Steric effects due to the installation of *ortho*-substituents (2-Cl) were negligible (entry 16). When the styrene was replaced with 2-vinylnaphthalene, the reaction also resulted in the formation of allylamine derivatives **6q**–**6r** in 60–64% yield (entries 17 and 18). However, some limitations were noted in case of alkyl olefin (1-octene) or heteroaromatic olefin (4-vinyl pyridine or 2-vinyl pyridine); they were unreactive in this reaction.

Table 2
Three-component reaction of quinazoline-2,5-diones, paraformaldehyde, and styrenes[a]



Entry	R^1	R^2	Product	Yield[b] (%)
1	H	C_6H_5	**6a**	70
2	4-CH_3	C_6H_5	**6b**	52
3	4-Cl	C_6H_5	**6c**	61
4	3-NO_2	C_6H_5	**6d**	62
5	H	4-ClC_6H_5	**6e**	53
6	H	4-BrC_6H_5	**6f**	56
7	H	4-$CH_3C_6H_5$	**6g**	41
8	4-CH_3	4-$CH_3C_6H_5$	**6h**	39
9	4-CH_3	4-ClC_6H_5	**6i**	51
10	4-F	C_6H_5	**6j**	64
11	4-Br	C_6H_5	**6k**	63
12	4-NO_2	C_6H_5	**6l**	60
13	4-NO_2	4-$CH_3C_6H_5$	**6m**	42
14	4-NO_2	4-ClC_6H_5	**6n**	53
15	3-NO_2	4-BrC_6H_5	**6o**	61
16	2-Cl	C_6H_5	**6p**	65
17	H	$C_{12}H_{10}$	**6q**	64
18	4-Cl	$C_{12}H_{10}$	**6r**	60

[a] Reaction conditions: quinazoline-2,5-dione (0.5 mmol), paraformaldehyde (3.0 mmol), styrene (0.75 mmol), I_2 (20% mmol), dioxane (3 mL), 110 °C, 12 h.
[b] Isolated yield of 4a after purification by flash chromatography.

3. Conclusions

In summary, we have documented the I_2-catalyzed three-component reaction of octahydroquinazoline-2,5-diones with ethyl glyoxylate or paraformaldehyde and styrenes. The reaction proceeds with high regioselectivity to deliver allylic amine derivatives and shows good tolerance towards wide substrate scope, as demonstrated by the application of paraformaldehyde, and ethyl glyoxylate.

4. Experimental section

4.1. General procedure

4.1.1. Preparation of 4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione. The reaction of benzaldehyde (10 mmol) with urea (12 mmol), and 5,5-dimethylcyclohexane-1,3-dione (10 mmol) in the presence of H_2SO_4 (10% mmol) as catalyst in ethanol (15 mL) at 80 °C for 8 h produced 4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7, 8-octahydroquinazoline-2,5-dione. After the reaction was completed (monitored by TLC), pure product was obtained from the crude product by filtration and recrystallization to afford.[21]

4.2. General procedure for three-component reactions

The mixture of quinazoline-2,5-dione (**1a**, 0.5 mmol, 135.0 mg), ethyl glyoxylate (**2a**, 3.0 equiv, 1.5 mmol, 306 mg), styrene (**3a**, 1.5 equiv, 0.75 mmol, 78.0 mg), I_2 (0.2 equiv, 0.1 mmol, 25.4 mg) and 1,4-dioxane (3 mL) was stirred at 110 °C. After the starting material **1a** had been consumed (monitored by TLC), 15 mL water were added and the mixture was extracted with EtOAc (3×15 mL). The extract was washed with 10% $Na_2S_2O_3$ solution (w/w), dried over anhydrous Na_2SO_4 and evaporation. The product was purified by flash chromatography on silica gel using ethyl acetate/petroleum ether as eluent to provide the corresponding allylamine.

*4.2.1. (E)-Ethyl-2-(7,7-dimethyl-2,5-dioxo-4-phenyl-1,2,5,6,7,8-hexahydroquinazolin-3(4H)-yl)-4-phenyl-3-butenoate (**4a**).* White solid, mp 95–96 °C; yield: 64% (ethyl acetate/petroleum ether: 1/2.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.75 (br, 1H, NH), 7.40 (d, J=8.0 Hz, 2H, ArH), 7.30–7.22 (m, 8H, ArH), 6.48 (d, J=16.0 Hz, 1H, CH), 6.24–6.18 (q, 1H, CH), 5.56 (s, 1H, CH), 4.80 (d, J=8.0 Hz, 1H, CH), 4.16–4.11 (q, 2H, CH_2), 2.41–2.11 (m, 4H, $2CH_2$), 2.20 (t, J=8.0 Hz,3H, CH_3), 1.08 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.4, 169.2, 153.1, 149.5, 141.5, 135.8, 135.7, 128.5, 128.4, 128.2, 127.8, 127.4, 126.7, 121.7, 110.1, 61.7, 61.3, 58.0, 50.3, 39.8, 32.8, 29.2, 27.1, 14.1; HRMS $[M+H]^+$ calcd for $C_{28}H_{30}N_2O_4$ 459.2278, found 459.2287.

*4.2.2. (E)-Ethyl-2-(7,7-dimethyl-2,5-dioxo-4-(p-tolyl)-1,2,5,6,7,8-hexahydroquinazolin-3(4H)-yl)-4-phenyl-3-butenoate (**4b**).* White solid, mp 196–197 °C; yield: 55% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.36 (br, 1H, NH), 7.24–7.17 (m, 7H, ArH), 7.02 (d, J=8.0 Hz, 2H, ArH), 6.42 (d, J=16.0 Hz, 1H, CH), 6.20–6.13 (q, 1H, CH), 5.45 (s, 1H, CH), 4.70 (d, J=8.0 Hz, 1H, CH), 4.10–4.04 (q, 2H, CH_2), 2.34–2.03 (m, 7H, CH_3, $2CH_2$), 1.14 (t, J=8.0 Hz, 3H, CH_3), 1.01 (s, 3H, CH_3), 0.85 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.4, 169.2, 153.1, 149.3, 138.5, 137.4, 135.9, 135.4, 129.0, 128.4, 128.2, 127.4, 126.7, 121.8, 110.1, 61.6, 61.3, 57.9, 50.3, 39.7, 32.7, 29.2, 27.2, 21.1, 14.1; HRMS $[M+H]^+$ calcd for $C_{29}H_{32}N_2O_4$ 473.2435, found 473.2444.

*4.2.3. (E)-Ethyl-2-(4-(4-chlorophenyl)-7,7-dimethyl-2,5-dioxo-1,2,5,6,7,8-hexahydroquinazolin-3(4H)-yl)-4-phenyl-3-butenoate (**4c**).* White solid, mp 197–199 °C; yield: 54% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.78 (br, 1H, NH), 7.36–7.22 (m, 9H, ArH), 6.48 (d, J=16.0 Hz, 1H, CH), 6.22–6.15 (q, 1H, CH), 5.55 (s, 1H, CH), 4.78 (d, J=8.0 Hz, 1H, CH), 4.18–4.13 (q, 1H, CH_2), 2.41–2.11 (m, 4H, $2CH_2$), 1.22 (t, J=8.0 Hz, 1H, CH_3), 1.09 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.3, 169.0, 153.0, 149.6, 140.1, 135.9, 135.7, 133.6, 128.8, 128.6, 128.4, 126.7, 121.4, 109.7, 61.6, 61.4, 57.5, 50.3, 39.8, 32.8, 29.3, 27.1, 14.1; HRMS $[M+H]^+$ calcd for $C_{28}H_{29}ClN_2O_4$ 493.1889, found 493.1898.

*4.2.4. (E)-Ethyl-4-(4-chlorophenyl)-2-(4-(4-chlorophenyl)-7,7-dimethyl-2,5-dioxo-1,2,5,6,7,8-hexahydroquinazolin-3(4H)-yl)-3-butenoate (**4d**).* White solid, mp 203–204 °C; yield: 53% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.17 (br, 1H, NH), 7.27 (d, J=8.0 Hz, 2H, ArH), 7.19 (t, J=8.0 Hz, 4H, ArH), 7.07 (d, J=8.0 Hz, 1H, ArH), 6.36 (d, J=16.0 Hz, 1H, CH), 6.11–6.05 (q, 1H, CH), 5.46 (s, 1H, CH), 4.74 (d, 8.0 Hz, 1H, CH), 4.11–4.06 (q, 2H, CH_2), 2.34–2.04 (m, 4H, $2CH_2$), 1.15 (t, J=8.0 Hz, 1H, CH_3), 1.02 (s, 3H, CH_3), 0.83 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.3, 168.9, 152.9, 149.5, 140.1, 134.5, 134.1, 133.7, 128.8, 128.7, 128.6,

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127.9, 122.2, 109.7, 61.6, 61.4, 57.5, 50.2, 39.8, 32.8, 29.2, 27.1, 14.1; HRMS $[M+H]^+$ calcd for $C_{28}H_{28}Cl_2N_2O_4$ 527.1499, found 527.1510.

*4.2.5. (E)-Ethyl-2-(4-(4-bromophenyl)-7,7-dimethyl-2,5-dioxo-1,2,5,6,7,8,-hexahydroquinazolin-3(4H)-yl)-4-(p-tolyl)-3-buteno-ate (**4e**).* White solid, mp 213–214 °C; yield: 47% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.03 (br, 1H, NH), 7.39 (d, J=8.0 Hz, 2H, ArH), 7.27 (d, J=8.0 Hz, 2H, ArH), 7.11 (s, 5H, ArH), 6.43 (d, J=16.0 Hz, 1H, CH), 6.13–6.07 (q, 1H, CH), 5.54 (s, 1H, CH), 4.79 (d, J=8.0 Hz, 1H), 4.18–4.12 (q, 2H, CH_2), 2.41–2.10 (m, 7H, CH_3, $2CH_2$), 1.22 (t, J=7.0 Hz, 3H, CH_3), 1.08 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.2, 169.1, 152.9, 149.5, 140.6, 138.3, 135.9, 132.8, 131.4, 129.2, 129.1, 126.6, 121.6, 120.2, 109.7, 61.6, 61.4, 57.2, 50.2, 39.8, 32.7, 29.2, 27.0, 21.2, 14.1; HRMS $[M+H]^+$ calcd for $C_{29}H_{31}BrN_2O_4$ 551.1540, found 551.1546.

*4.2.6. (E)-Ethyl-2-(7,7-dimethyl-4-(4-nitrophenyl)-2,5-dioxo-1,2,5,6,7,8-hexahydroquinazolin-3(4H)-yl)-4-phenyl-3-butenoate (**4g**).* White solid, mp 207–209 °C; yield: 42% (ethyl acetate/petroleum ether: 1/2.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.17 (br, 1H, NH), 8.05 (d, J=8.0 Hz, 2H, ArH), 7.53 (d, J=8.0 Hz, 2H, ArH), 7.22–7.11 (m, 5H, ArH), 6.41 (d, J=16.0 Hz, 1H, CH), 6.10–6.04 (q, 1H, CH), 5.66 (s, 1H, CH), 4.82 (d, J=8.0 Hz, 1H, CH), 4.13–4.08 (q, J=16.0, 2H, CH_2), 2.38–2.04 (m, 4H, $2CH_2$), 1.17 (t, J=8.0 Hz, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.80 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.2, 168.9, 152.9, 150.2, 148.7, 147.3, 136.6, 135.3, 128.7, 128.6, 128.2, 126.6, 123.7, 120.9, 109.1, 61.7, 61.6, 57.3, 50.2, 39.9, 32.8, 29.2, 27.0, 14.2; HRMS $[M+H]^+$ calcd for $C_{28}H_{29}N_3O_6$ 504.2129, found 504.2138.

*4.2.7. (E)-Ethyl-2-(7,7-dimethyl-4-(3-nitrophenyl)-2,5-dioxo-1,2,5,6,7,8-hexahydroquinazolin-3(4H)-yl)-4-phenyl-3-butenoate (**4h**).* White solid, mp 174–176 °C; yield: 39% (ethyl acetate/petroleum ether: 1/2.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.63 (br, 1H, NH), 8.28 (s, 1H, ArH), 8.07 (d, J=8.0 Hz, 1H, ArH), 7.79 (d, J=8.0 Hz, 1H, ArH), 7.45 (t, J=8.0 Hz, 1H, ArH), 7.29–7.22 (m, 5H, ArH), 6.50 (d, J=16.0 Hz, 1H, CH), 6.24–6.18 (q, 1H, CH), 5.69 (s, 1H, CH), 4.79 (d, J=8.0 Hz, 1H, CH), 4.18–4.12 (q, J=16.0, 1H, CH_2), 2.45–2.11 (m, 4H, $2CH_2$), 1.20 (t, J=8.0 Hz, 3H, CH_3), 1.10 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.3, 168.8, 152.4, 150.1, 148.3, 143.7, 136.2, 135.4, 133.8, 129.3, 128.5, 126.6, 122.8, 122.4, 121.1, 109.1, 61.6, 61.5, 57.8, 50.1, 39.8, 32.8, 29.1, 27.1, 14.0; HRMS $[M+H]^+$ calcd for $C_{28}H_{29}N_3O_6$ 504.2129, found 504.2137.

*4.2.8. Ethyl 2-(7,7-dimethyl-4-(4-nitrophenyl)-2,5-dioxo-1,2,5,6, 7,8-hexahydroquinazolin-3 (4H)-yl)acetate (**5a**).* White solid, mp 221–222 °C; yield: 15% (ethyl acetate/petroleum ether: 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.53 (br, 1H, NH), 8.20 (d, J=8.0 Hz, 2H, ArH), 7.59 (d, J=8.0 Hz, 2H, ArH), 5.52 (s, 1H, CH), 4.49 (d, J=16.0 Hz, 1H, CH), 4.21–4.16 (q, 2H, CH_2), 3.51 (d, J=16.0 Hz, 1H, CH), 2.47–2.11 (m, 4H, $2CH_2$), 1.26 (t, J=8.0 Hz, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.4, 168.1, 152.9, 150.5, 147.6, 147.5, 128.2, 123.9, 108.3, 61.5, 59.3, 50.1, 47.0, 39.8, 32.7, 29.2, 27.1, 14.1; HRMS $[M+H]^+$ calcd for $C_{20}H_{23}N_3O_6$ 402.1660, found 402.1665.

*4.2.9. Ethyl 2-(7,7-dimethyl-4-(3-nitrophenyl)-2,5-dioxo-1,2,5,6, 7,8-hexahydroquinazolin-3 (4H)-yl)acetate (**5b**).* White solid, mp 202–203 °C; yield: 18% (ethyl acetate/petroleum ether: 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.40 (br, 1H, NH), 8.24 (s, 1H, ArH), 8.15 (d, J=8.0 Hz, 1H, ArH), 7.78 (d, J=8.0 Hz, 1H, ArH), 7.54 (t, J=8.0 Hz, 1H, ArH), 5.52 (s, 1H, CH), 4.46 (d, J=16.0 Hz, 1H, CH), 4.18–4.17 (q, 2H, CH_2), 3.55 (d, J=16.0 Hz, 1H, CH), 2.48–2.11 (m, 4H, $2CH_2$), 1.25 (t, J=8.0 Hz, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.5, 168.1, 152.7, 150.6, 148.5, 142.8, 133.7, 129.7, 123.2, 122.3, 108.4, 61.5, 59.5, 50.2, 47.0, 39.8, 32.8, 29.2, 27.2, 14.1; HRMS $[M+H]^+$ calcd for $C_{20}H_{23}N_3O_6$ 402.1660, found 402.1666.

*4.2.10. (E)-3-Cinnamyl-7,7-dimethyl-4-phenyl-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6a**).* White solid, mp 176–178 °C; yield: 70% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.32 (br, 1H, NH), 7.41 (t, J=4.0 Hz, 2H, ArH), 7.34–7.23 (m, 8H, ArH), 6.48 (d, J=16.0 Hz, 1H, CH), 6.11–6.05 (m, 1H, CH), 5.46 (s, 1H, CH), 4.67 (dd, J=15.0 Hz, 5.0 Hz, 1H, CH_2), 3.49 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.43–2.10 (m, 4H, $2CH_2$), 1.08 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.1, 150.0, 141.3, 136.4, 133.8, 128.6, 128.5, 127.9, 127.8, 127.2, 126.4, 123.5, 109.3, 57.4, 50.4, 46.9, 39.8, 32.8, 29.2, 27.2; HRMS $[M+H]^+$ calcd for $C_{25}H_{26}N_2O_2$ 387.2067, found 387.2072.

*4.2.11. (E)-3-Cinnamyl-7,7-dimethyl-4-p-tolyl-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6b**).* White solid, mp 204–205 °C; yield: 52% (ethyl acetate/petroleum ether: 1/4); 1H NMR (400 MHz, $CDCl_3$) δ=9.43 (br, 1H, NH), 7.36–7.24 (m, 7H, ArH), 7.14 (d, J=8.0 Hz, 2H, ArH), 6.50 (d, J=16.0 Hz, 1H, CH), 6.13–6.06 (m, 1H, CH), 5.44 (s, 1H, CH), 4.68 (dd, J=14.6 Hz, 4.0 Hz, 1H, CH_2), 3.50 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.45–2.11 (m, 7H, CH_3, $2CH_2$), 1.09 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.7, 153.1, 149.9, 138.3, 137.6, 136.4, 133.7, 129.3, 128.5, 127.8, 127.2, 126.4, 123.5, 109.4, 57.1, 50.4, 46.7, 39.8, 32.8, 29.2, 27.2, 21.1; HRMS $[M+H]^+$ calcd for $C_{26}H_{28}N_2O_2$ 401.2224, found 401.2229.

*4.2.12. (E)-3-Cinnamyl-7,7-dimethyl-4-(4-chlorophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6c**).* White solid, mp 216–218 °C; yield: 61% (ethyl acetate/petroleum ether: 1/3); 1H NMR (400 MHz, $CDCl_3$) δ=9.38 (br, 1H, NH), 7.35–7.23 (m, 9H, ArH), 6.46 (d, J=16.0 Hz, 1H, CH), 6.09–6.03 (m, 1H, CH), 5.45 (s, 1H, CH), 4.66 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.47 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.43–2.01 (m, 4H, $2CH_2$), 1.08 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.5, 153.0, 150.1, 139.8, 136.2, 134.0, 133.7, 128.8, 128.6, 128.5, 127.9, 126.4, 123.2, 109.0, 56.8, 50.3, 47.0, 39.8, 32.8, 29.2, 27.1; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}ClN_2O_2$ 421.1677, found 421.1684.

*4.2.13. (E)-3-Cinnamyl-7,7-dimethyl-4-(3-nitrophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6d**).* White solid, mp 233–235 °C; yield: 62% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.55 (br, 1H, NH), 8.25 (s, 1H, ArH), 8.12 (t, J=4.0 Hz, 1H, ArH), 7.79 (d, J=8.0 Hz, 1H, ArH), 7.54–7.49 (m, 1H, ArH), 7.32–7.25 (m, 5H, ArH), 6.48 (d, J=12.0 Hz, 1H, CH), 6.10–6.08 (m, 1H, CH), 5.60 (s, 1H, CH), 4.69 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 3.51 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.49–2.11 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.5, 152.7, 150.8, 148.5, 143.5, 136.0, 134.4, 133.6, 129.6, 128.6, 128.0, 126.4, 123.0, 122.8, 122.0, 108.3, 57.1, 50.2, 47.3, 39.8, 32.8, 29.1, 27.2; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}N_3O_4$ 432.1918, found 432.1924.

*4.2.14. (E)-7,7-Dimethyl-4-phenyl-3-(3-(p-chlorophenyl)allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6e**).* White solid, mp 206–208 °C; yield: 53% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.28 (br, 1H, NH), 7.41 (d, J=8.0 Hz, 2H, ArH), 7.35–7.23 (m, 7H, ArH), 6.44 (d, J=16.0 Hz, 1H, CH), 6.09–6.04 (m, 1H, CH), 5.45 (s, 1H, CH), 4.64 (dd, J=15.0 Hz, 5.0 Hz, 1H, CH_2), 3.53 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.45–2.12 (m, 4H, $2CH_2$), 1.10 (s, 3H, CH_3), 0.94 (s, 3H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.0, 149.9, 141.2, 134.9, 133.4, 132.4, 128.7, 128.6, 128.0, 127.6, 127.2, 124.3, 109.4, 57.5, 50.3, 46.9, 39.9, 32.8, 29.2, 27.2; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}ClN_2O_2$ 421.1677, found 421.1683.

*4.2.15. (E)-7,7-Dimethyl-4-phenyl-3-(3-(p-bromophenyl)allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6f**).* White solid, mp

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209–210 °C; yield: 56% (ethyl acetate/petroleum ether: 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.33 (br, 1H, NH), 7.40 (t, J=8.6 Hz, 4H, ArH), 7.34–7.24 (m, 3H, ArH), 7.17 (d, J=8.0 Hz, 2H, ArH), 6.41 (d, J=16.0 Hz, 1H, CH), 6.09–6.02 (m, 1H, CH), 5.44 (s, 1H, CH), 4.62 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.45 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.43–2.11 (m, 4H, $2CH_2$), 1.08 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.0, 150.0, 141.2, 135.3, 132.4, 131.6, 128.6, 128.0, 127.9, 127.1, 124.5, 121.5, 109.3, 57.5, 50.3, 46.9, 39.8, 32.8, 29.2, 27.2; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}BrN_2O_2$ 465.1172, found 465.1180.

*4.2.16. (E)-7,7-Dimethyl-4-phenyl-3-(3-(p-tolyl)allyl)-3,4,7,8-tetr-ahydroquinazoline-2,5(1H,6H)-dione (**6g**).* White solid, mp 216–218 °C; yield: 41% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.72 (br, 1H, NH), 7.41 (d, J=8.0 Hz, 2H, ArH),7.34–7.21 (m, 5H, ArH), 7.11 (d, J=8.0 Hz, 2H, ArH), 6.46 (d, J=16.0 Hz, 1H, CH), 6.07–6.00 (m, 1H, CH), 5.46 (s, 1H, CH), 4.69 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.45 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.44–2.09 (m, 7H, CH_3, $2CH_2$), 1.08 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.2, 150.2, 141.3, 137.6, 133.7, 133.6, 129.2, 128.6, 127.8, 127.2, 126.3, 122.3, 109.2, 57.3, 50.3, 46.8, 39.7, 32.7, 27.1, 21.1; HRMS $[M+H]^+$ calcd for $C_{26}H_{28}N_2O_2$ 401.2224, found 401.2230.

*4.2.17. (E)-7,7-Dimethyl-4-p-tolyl-3-(3-(p-tolyl)allyl)-3,4,7,8-tetr-ahydroquinazoline-2,5(1H,6H)-dione (**6h**).* White solid, mp 222–223 °C; yield: 39% (ethyl acetate/petroleum ether: 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.63 (br, 1H, NH), 7.29 (d, J=8.0 Hz, 2H, ArH), 7.23 (t, J=6.0 Hz, 2H, ArH), 7.11 (t, J=8.0 Hz, 4H, ArH), 6.45 (d, J=16.0 Hz, 1H, CH), 6.06–5.99 (m, 1H, CH), 5.42 (s, 1H, CH), 4.66 (dd, J=15.2 Hz, 4.8 Hz, 1H, CH_2), 3.45 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.43–2.09 (m, 10H, $2CH_3$, $2CH_2$), 1.07 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.2, 153.1, 150.1, 150.0, 138.4, 137.5, 137.5, 133.7, 133.6, 129.2, 129.1, 127.2, 126.3, 122.4, 109.3, 57.1, 50.4, 46.7, 39.7, 32.7, 29.2, 27.2, 21.1, 21.0; HRMS $[M+H]^+$ calcd for $C_{27}H_{30}N_2O_2$ 415.2380, found 415.2386.

*4.2.18. (E)-7,7-Dimethyl-4-p-tolyl-3-(3-(p-chlorophenyl)allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6i**).* White solid, mp 228–230 °C; yield: 51% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.30 (br, 1H, NH), 7.28–7.21 (m, 6H, ArH), 7.12 (d, J=4.0 Hz, 2H, ArH), 6.41 (d, J=16.0 Hz, 1H, CH), 6.07–6.00 (m, 1H, CH), 5.40 (s, 1H, CH), 4.61 (dd, J=15.4 Hz, 4.8 Hz, 1H, CH_2), 3.51 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.42–2.10 (m, 7H, $2CH_2$, CH_3), 1.08 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.0, 150.0, 138.2, 137.7, 134.9, 133.4, 132.2, 129.3, 128.6, 127.6, 127.1, 124.4, 109.4, 57.3, 50.3, 46.7, 39.8, 32.8, 29.2, 27.2, 21.1; HRMS $[M+H]^+$ calcd for $C_{26}H_{27}ClN_2O_2$ 435.1834, found 435.1838.

*4.2.19. (E)-3-Cinnamyl-7,7-dimethyl-4-(4-fluorophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6j**).* White solid, mp 215–217 °C; yield: 64% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.44 (br, 1H, NH), 7.40–7.23 (m, 7H, ArH), 7.04–6.98 (q, 2H, ArH), 6.48 (d, J=16.0 Hz, 1H, CH), 6.11–6.05 (m, 1H, CH), 5.45 (s, 1H, CH), 4.69 (dd, J=15.4 Hz, 5.0 Hz, 1H, CH_2), 3.45 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.44–2.10 (m, 4H, $2CH_2$), 1.09 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 163.5, 161.1, 153.0, 150.0, 137.2, 136.3, 133.9, 128.9, 128.8, 128.6, 127.9, 126.4, 123.3, 115.6, 115.4, 109.3, 56.8, 50.3, 46.9, 39.8, 32.8, 29.2, 27.1; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}FN_2O_2$ 405.1973, found 405.1979.

*4.2.20. (E)-3-Cinnamyl-7,7-dimethyl-4-(p-bromophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6k**).* White solid, mp 213–214 °C; yield: 63% (ethyl acetate/petroleum ether: 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.35 (br, 1H, NH), 7.45 (d, J=8.0 Hz, 2H, ArH), 7.32–7.24 (m, 7H, ArH), 6.46 (d, J=16.0 Hz, 1H, CH), 6.09–6.02 (m, 1H, CH), 5.43 (s, 1H, CH), 4.67 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.45 (dd, J=15.2 Hz, 8.0 Hz, 1H, CH_2), 2.44–2.10 (m, 4H, $2CH_2$), 1.09 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.5, 152.9, 150.1, 140.3, 136.2, 134.0, 131.8, 128.9, 128.6, 127.9, 126.4, 123.1, 121.9, 108.9, 56.9, 50.3, 46.9, 39.8, 32.8, 29.2, 27.2; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}BrN_2O_2$ 465.1172, found 465.1179.

*4.2.21. (E)-3-Cinnamyl-7,7-dimethyl-4-(4-nitrophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6l**).* White solid, mp 231–233 °C; yield: 60% (ethyl acetate/petroleum ether: 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.50 (br, 1H, NH), 8.20–8.17 (m, 2H, ArH), 7.61–7.58 (m, 2H, ArH), 7.32–7.25 (m, 5H, ArH), 6.46 (d, J=16.0 Hz, 1H, CH), 6.08–6.02 (m, 1H, CH), 5.60 (s, 1H, CH), 4.70 (dd, J=15.0 Hz, 4.6 Hz, 1H, CH_2), 3.49 (dd, J=15.2 Hz, 8.0 Hz, 1H, CH_2), 2.48–2.11 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.4, 152.9, 150.7, 148.4, 147.5, 136.0, 134.4, 128.6, 128.1, 128.1, 126.4, 124.0, 122.7, 108.3, 57.0, 50.2, 47.5, 39.9, 32.8, 29.2, 27.1; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}N_3O_4$ 432.1918, found 432.1923.

*4.2.22. (E)-7,7-Dimethyl-4-(4-nitrophenyl)-3-(3-(p-tolyl)allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6m**).* White solid, mp 243–245 °C; yield: 42% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.43 (br, 1H, NH), 8.18 (t, J=4.0 Hz, 2H, ArH), 7.59 (t, J=4.0 Hz, 2H, ArH), 7.19 (d, J=8.0 Hz, 2H, ArH), 7.11 (d, J=8.0 Hz, 2H, ArH), 6.42 (d, J=16.0 Hz, 1H, CH), 6.01–5.97 (m, 1H, CH), 5.60 (s, 1H, CH), 4.67 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.47 (dd, J=15.4 Hz, 8.0 Hz, 1H, CH_2), 2.47–2.11 (m, 7H, CH_3, $2CH_2$), 1.10 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.4, 152.9, 150.7, 148.4, 147.5, 138.0, 134.4, 133.2, 129.3, 128.1, 126.3, 123.9, 121.6, 108.3, 56.9, 50.2, 47.5, 39.8, 32.8, 29.2, 27.1, 21.1; HRMS $[M+H]^+$ calcd for $C_{26}H_{27}N_3O_4$ 446.2074, found 446.2081.

*4.2.23. (E)-7,7-Dimethyl-4-(4-nitrophenyl)-3-(3-(p-chlorophenyl)-allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6n**).* White solid, mp 253–255 °C; yield: 53% (ethyl acetate/petroleum ether: 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.21 (br, 1H, NH), 8.19 (d, J=8.0 Hz, 2H, ArH), 7.58 (d, J=8.0 Hz, 2H, ArH), 7.29–7.21 (q, 4H, ArH), 6.41 (d, J=16.0 Hz, 1H, CH), 6.07–6.00 (m, 1H, CH), 5.58 (s, 1H, CH), 4.68 (dd, J=15.2 Hz, 5.2 Hz, 1H, CH_2), 3.47 (dd, J=15.2 Hz, 7.6 Hz, 1H, CH_2), 2.47–2.12 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ=192.5, 152.1, 151.0, 149.3, 146.7, 135.0, 131.9, 131.2, 128.4, 128.1, 127.8, 125.2, 123.7, 106.7, 56.4, 49.5, 46.5, 40.0, 32.2, 28.7, 26.3; HRMS $[M+H]^+$ calcd for $C_{25}H_{24}ClN_3O_4$ 466.1528, found 466.1532.

*4.2.24. (E)-7,7-Dimethyl-4-(3-nitrophenyl)-3-(3-(p-bromophenyl) allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6o**).* White solid, mp 242–244 °C; yield: 61% (ethyl acetate/petroleum ether: 1/3); 1H NMR (400 MHz, $CDCl_3$) δ=9.32 (br, 1H, NH), 8.24 (s, 1H, ArH), 8.12 (d, J=8.0 Hz, 1H, ArH) 7.77 (d, J=8.0 Hz, 1H, ArH) 7.51 (t, J=8.0 Hz, 1H, ArH), 7.43 (d, J=8.0 Hz, 2H, ArH), 7.17 (d, J=8.0 Hz, 2H, ArH), 6.40 (d, J=16.0 Hz, 1H, CH), 6.10–6.03 (m, 1H, CH), 5.58 (s, 1H, CH), 4.65 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 3.52 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.48–2.12 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.5, 152.6, 150.7, 148.6, 143.4, 134.9, 133.5, 133.1, 131.7, 129.7, 127.9, 123.7, 123.1, 122.0, 121.9, 108.3, 57.2, 50.2, 47.3, 39.8, 32.9, 29.2, 27.2; HRMS $[M+H]^+$ calcd for $C_{25}H_{24}BrN_3O_4$ 510.1023, found 510.1029.

*4.2.25. (E)-3-Cinnamyl-7,7-dimethyl-4-(2-chlorophenyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6p**).* White solid, mp 97–99 °C; yield: 65% (ethyl acetate/petroleum ether: 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.57 (br, 1H, NH), 7.47 (t, J=4.0 Hz, 1H, ArH) 7.34–7.16 (m, 8H, ArH), 6.50 (d, J=16.0 Hz, 1H, CH), 6.10–6.03 (m, 1H, CH), 5.89 (s, 1H, CH), 4.47 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.56

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(dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.45–2.08 (m, 4H, $2CH_2$), 1.08 (s, 3H, CH_3), 0.98 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 152.4, 150.7, 138.5, 136.5, 133.6, 133.3, 130.6, 129.9, 129.3, 128.4, 127.7, 127.2, 126.4, 123.3, 107.9, 56.2, 50.3, 46.9, 39.8, 32.7, 29.2, 27.3; HRMS $[M+H]^+$ calcd for $C_{25}H_{25}ClN_2O_2$ 421.1677, found 421.1682.

*4.2.26. (E)-7,7-Dimethyl-3-(3-(2-naphthalenyl)allyl)-4-phenyl-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6q**).* White solid, mp 221–223 °C; yield: 64% (ethyl acetate/petroleum ether: 1/4); ^1H NMR (400 MHz, $CDCl_3$) δ=9.50 (br, 1H, NH), 7.73 (d, J=40.0 Hz, 4H, ArH), 7.53–7.27 (m, 8H, ArH), 6.65 (d, J=16.0 Hz, 1H, CH), 6.23–6.19 (m, 1H, CH), 5.50 (s, 1H, CH), 4.72 (d, J=16.0 Hz, 1H, CH_2), 3.56 (dd, J=16.0 Hz, 8.0 Hz, 1H, CH_2), 2.45–2.09 (m, 4H, $2CH_2$), 1.08 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.1, 150.1, 141.3, 133.9, 133.7, 133.5, 133.0, 128.6, 128.2, 127.9, 127.6, 127.2, 126.4, 126.3, 125.9, 123.9, 123.5, 109.3, 57.5, 50.3, 47.0, 39.8, 32.8, 29.2, 27.1; HRMS $[M+H]^+$ calcd for $C_{29}H_{28}N_2O_2$ 437.2224, found 437.2228.

*4.2.27. (E)-4-(4-Chlorophenyl)-7,7-dimethyl-3-(3-(2-naphthaleny-l) allyl)-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (**6r**).* White solid, mp 249–250 °C; yield: 60% (ethyl acetate/petroleum ether: 1/4); 1H NMR (400 MHz, $CDCl_3$) δ=9.54 (br, 1H, NH), 7.78–7.67 (m, 4H, ArH), 7.52–7.30 (m, 7H, ArH), 6.63 (d, J=16.0 Hz, 1H, CH), 6.22–6.15 (m, 1H, CH), 5.49 (s, 1H, CH), 4.71 (dd, J=16.0 Hz, 4.0 Hz, 1H, CH_2), 3.55 (dd, J=15.2 Hz, 8.0 Hz, 1H, CH_2), 2.45–2.10 (m, 4H, $2CH_2$), 1.08 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=193.6, 153.0, 150.2, 139.9, 134.0, 133.7, 133.7, 133.5, 133.1, 128.8, 128.6, 128.2, 127.9, 127.6, 126.5, 126.3, 126.0, 123.6, 123.4, 109.0, 57.0, 50.3, 47.1, 39.8, 32.8, 29.2, 27.1; HRMS $[M+H]^+$ calcd for $C_{29}H_{27}ClN_2O_2$ 472.1912, found 472.1917.

*4.2.28. (E)-Ethyl 4-(4-chlorophenyl)-3-(1-ethoxy-1-oxo-4-phenyl-3-buten-2-yl)-6-methyl-2-oxo-1,2,3,4,-tetrahydropyrimidine-5-carboxylate (**7a**).* Colorless oil; yield: 41% (acetic acid/petrole-um ether: 1/45); ^1H NMR (400 MHz, $CDCl_3$) δ=8.96 (br, 1H, NH), 7.24–7.14 (m, 9H, ArH), 6.42 (d, J=16.0 Hz, 1H, CH), 6.12–6.06 (q, 1H, CH), 5.42 (s, 1H, CH), 4.76 (d, J=8.0 Hz, 1H, CH), 4.09–4.01 (m, 4H, $2CH_2$), 2.23 (s, 3H, CH_3), 1.16–1.11 (m, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=169.2, 165.3, 153.2, 146.1, 140.8, 135.7, 135.5, 133.6, 129.0, 128.8, 128.5, 128.3, 126.6, 121.9, 102.2, 61.4, 61.1, 60.1, 59.3, 18.4, 14.2, 14.0; HRMS $[M+H]^+$ calcd for $C_{26}H_{27}ClN_2O_5$ 483.1681, found 483.1688.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.10.006.

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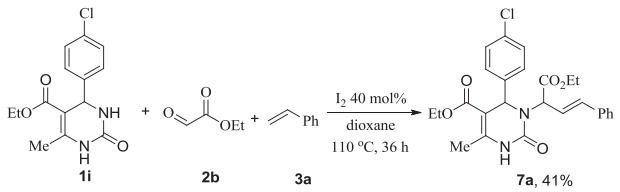
20. In addition, the reaction between 3,4-dihydropyrimidinone (DHPMs, **1i**) with ethyl glyoxylate (**2a**) and styrene (**3a**) under the optimal conditions was tested, and the desired product **7a** was obtained.



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