KF/Al_2O_3 promoted aza-Michael addition of 4-aryl-7,7-dimethyloctahydroquinazolinones to α, β-ethylenic compounds

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The aza-Michael addition reaction of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones to *α,β*-ethylenic compounds in the presence of KF/Al_2O_3 furnishes *N*3-substituted quinazolinone derivatives. Those groups (NO_2, MeO) with larger steric hindrance at the *o*-position of the phenyl ring of quinazolinone have an apparent affect on the chemical selectivity thus giving the *N1*-subsituted products.

Keywords: quinazolinone derivatives, potassium fluoride, Michael addition

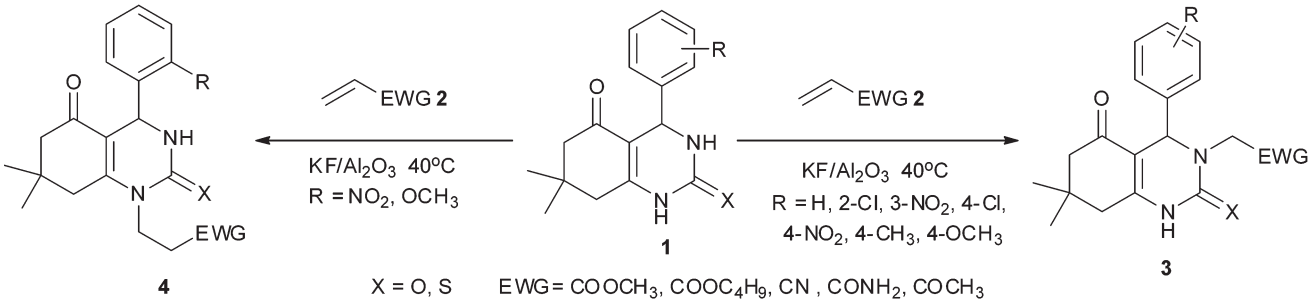
3,4-Dihydropyrimidinone (DHPM) was first reported 118 years ago by Biginelli.[1] It has gained great therapeutic significance as a calcium-channel modulator in the treatment of cardiovascular diseases, such as hypertension, cardiac arrythmias or angina.[2] In recent years, interest has been focused on Biginelli-like reactions in which open chain β-dicarbonyl compounds have been extended to cyclic β-diketones, β-ketolactones, β-diamides, or cyclic β-diesters, benzocyclic ketones, and α-keto acids under a variety of conditions, and the heterocycles thus obtained exhibit a wide range of biological activities, such as antiviral, antitumour, antihypertensive, and neuropeptide Y(NPY) antagonism.[3–7] Among the synthetic products *via* Biginelli reaction, octahydroquinazolin-5-one derivatives are interesting compounds because of their wide range of biological activities. Octahydroquinazolinones have exhibited potent antibacterial activity[8,9] and calcium antagonist activity.[10–12] It has been reported that N-methyl substituted octahydroquinazolinones were more active derivatives than those without a substituted group at the N-atom.[13] However, few methods are available for the preparation of the N-substituted octahydroquinazolinones.[13] To the best of our knowledge no precedent for the Michael reaction of quinazoline-2,5-diones for *N*-substituted derivatives has been reported.

Recently, we reported the Michael reaction of 3,4-dihydropyrimidinones with α, β-ethylenic compounds to give the N3-substituted DHPMs regioselectively using KF/Al_2O_3 or PEG-400/K_2CO_3 as a mild and efficient reagent.[14,15] When trying to apply PEG-400/K_2CO_3 to *N*-quinazoline-2,5-diones (**1**) the reaction failed to give the desired product and only the starting materials were obtained. Using KF/Al_2O_3 as catalyst, N1 substituted products were isolated instead of the expected N3-products when the aryl group of the quinazoline-2-one-5-ones carried an *o*-substituent such as NO_2, and MeO. Here, we report the Michael reaction of quinazoline-2, 5-diones with α, β-ethylenic compounds to give the N-substituted derivatives using KF/Al_2O_3 as the catalyst (Scheme 1).

Results and discussion

Initially, octahydroquinazoline-2,5-diones were prepared according to the corresponding literature procedures via the Biginelli reaction between a cyclohexa-1,3-dione, benzaldehyde and urea.[4,16] Then, we selected 4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione **1a** and methyl acrylate **2a** as the model substrates to optimise reaction conditions including catalysts, bases, solvents, and reaction temperatures. The best yield of **3a** (86%) was obtained by reaction in DMF at 40 °C overnight using equivalent amounts of **1a**, methyl acrylate **2a**, and 10 mmol% of KF/Al_2O_3. No reaction was observed in the presence of Et_3N or absence of any catalyst (Table 2, entries 6 and 7). In general, the use of polar solvents such as DMSO, DMF and MeCN resulted in better results than those with less polar solvents (THF and DCM) (Table 1).

Under the optimal conditions, a combination of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones **1** and α, β-ethylenic compounds **2** was investigated. As shown in Table 2, a smooth reaction occurred to provide the desired Michael additional products **3** in good to high yields (69–92%). All products showed that the aza-Michael addition occurred exclusively at the N3 position of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones. The regioselectivity of the reaction is consistent with other results of alkylation reactions.[17] The single crystal X-ray crystallography of product **3d** also confirmed the structures of the obtained products **3a–v** (Fig. 1).



Scheme 1 Synthesis of N-substituted octahydroquinazoline-2-one/thione-5-ones **3** and **4**.

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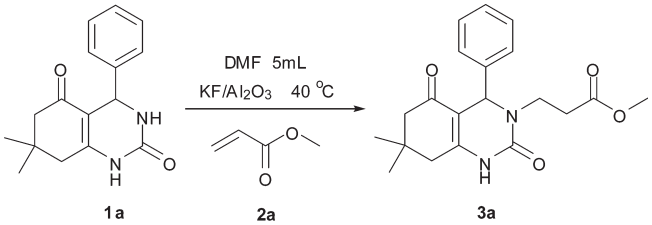
Table 1 Optimisation of Michael reaction conditions



Entry	1	2	3	4	5	6	7	8	9	10	11	12
Base	K_2CO_3	Na_2CO_3	NaOH	KOH	KF/Al_2O_3	Et_3N	No	KF/Al_2O_3	KF/Al_2O_3	KF/Al_2O_3	KF/Al_2O_3	K_2CO_3
Solvent	DMF	DMF	DMF	DMF	DMF	DMF	DMF	DMSO	MeCN	CH_2Cl_2	THF	PEG-400
Time/h	48	48	24	24	12	48	48	12	12	24	24	24
Yield/%	<10	<10	<10	<10	86	0	0	78	53	32	63	0

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), solvents (3 mL), catalysts (10 mmol %), at 40°C temperature for overnight.
[b] Isolated yields.
[c] No detected compound by TLC and ^{1}H NMR.

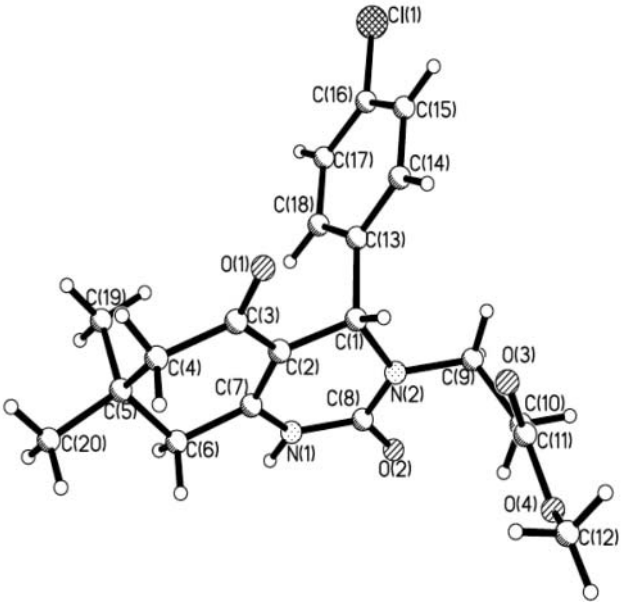


Fig. 1 X-ray crystallography of product **3d**.

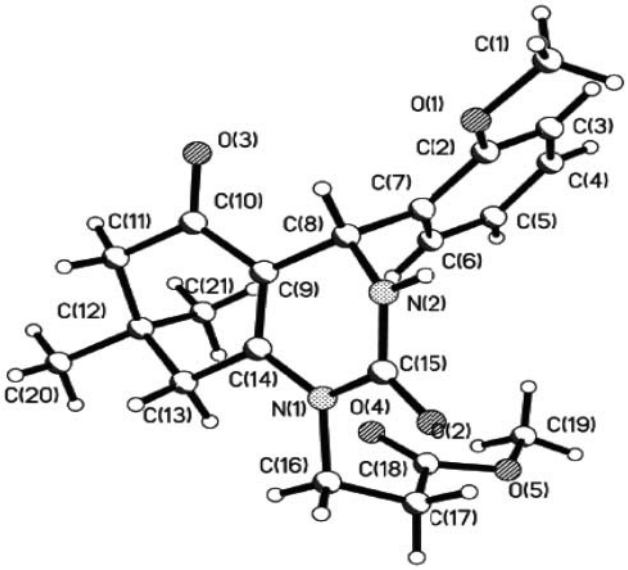


Fig. 2 X-ray crystallography of product **4a**.

However, groups with larger steric hindrance at the *o*-position of the phenyl ring of compound **1** have an apparent affect on the chemical selectivity of the products. For instance, the NO_2 and MeO group at the *o*-position of the phenyl ring only gave the N1-subsituted products **4a–d** (Table 2). The structure of **4a** was also confirmed by X-ray crystallography (Fig. 2). (Crystallographic data for the structure analysis have been deposited at the Cambridge Crystallographic Data Centre as supplementary publications, CCDC No. 807623 for **3d** and No. 817452 for **4a**. Copies of this information can be obtained, free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (44) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk). With a group having a small steric hindrance, such as Cl, no obvious effect was found and the N3-products **3g**, **3r** (Table 2, entries 7 and 19) were obtained. Thus, we postulate that the selectivity at N1 and N3 depended on the hindrance, the position of the substituted groups on the aryl group of the octahydroquinazoline-2-ones **1** and the difference in the electron density at the N1 and N3 positions. Commonly, the nitrogen atom at N3 has higher electron density than that of N1. So the Michael reaction potentially gives the N3 substituted product. However, when a larger steric group is substituted at the *o*-position of the aryl ring of compound **1**, the reaction gives the N1 products selectively.

The ^{1}H NMR spectrum of product DHPMs **3a–v** exhibited a singlet around δ 5.4 as the C_4–H, which confirmed the N3-position of the acyloxymethyl group. Meanwhile, the C_4–H came as a doublet around δ 5 for compounds **4a–d**. According to a previous study, when the methyl or *N*-allyl groups were in the N1 position, two cross peaks between the hydrogen atoms of the N-methyl or NCH_2 groups of the allyl groups and C-2 and -6 were observed.[18]

In conclusion, we have documented that *N*-substituted 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones can be obtained through the aza-Michael addition of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones to α, β-ethylenic compounds in the presence of KF/Al_2O_3 as a catalyst.

Experimental

All reagents were obtained commercially and used without further purification. Melting points were determined by an XT-4 electrothermal micromelting point apparatus which is uncorrected. IR spectra were recorded using KBr pellets on Nicolet AVATAR 36 FT-IR spectrophotometer. NMR spectra were recorded at 400 (^{1}H) and 100 (^{13}C) MHz, respectively, on a Varian Mercury plus-400 instrument using $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal standard. Mass spectra were recorded on a ZAB-HS spectrometer. Elemental analyses

Table 2 Synthesis of N-substituted 1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-one **3** and **4**

Entry	Compd	R	EWG	X	Yield/%	Entry	Compd.	R	EWG	X	Yield/%
1	**3a**	H	$COOCH_3$	O	86	12	**3l**	H	$COOCH_3$	S	88
2	**3b**	4-OCH_3	$COOCH_3$	O	89	13	**3m**	4-OCH_3	$COOCH_3$	S	92
3	**3c**	4-CH_3	$COOCH_3$	O	89	14	**3n**	4-CH_3	$COOCH_3$	S	90
4	**3d**	4-Cl	$COOCH_3$	O	85	15	**3o**	4-Cl	$COOCH_3$	S	88
5	**3e**	4-NO_2	$COOCH_3$	O	85	16	**3p**	4-NO_2	$COOCH_3$	S	84
6	**3f**	3-NO_2	$COOCH_3$	O	80	17	**3q**	3-NO_2	$COOCH_3$	S	84
7	**3g**	2-Cl	$COOCH_3$	O	68	18	**3r**	2-Cl	$COOCH_3$	S	65
8	**3h**	H	$COOC_4H_9$	O	84	19	**3s**	H	$COOC_4H_9$	S	76
9	**3i**	H	CN	O	86	20	**3t**	H	CN	S	88
10	**3j**	H	$CONH_2$	O	69	21	**3u**	H	$CONH_2$	S	74
11	**3k**	H	$COCH_3$	O	89	22	**3v**	H	$COCH_3$	S	82
12	**4a**	OCH_3	$COOCH_3$	O	79	23	**4c**	OCH_3	$COOCH_3$	S	77
13	**4b**	NO_2	$COOCH_3$	O	77	24	**4d**	NO_2	$COOCH_3$	S	72

[a] The reaction was conducted with 3,4-dihydropyrimidones (1 mmol), α, β-ethylenic compounds (1.2 mmol), and DMF (5 mL) in the presence of KF/Al_2O_3 (10 mol%) at 40°C for overnight.
[b] Isolated yields.

were performed on a Carlo-Erba 1106 Elemental Analysis instrument.

Preparation of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones; general procedure

The reaction of benzaldehyde (10 mmol) 1 with urea/thiourea (12 mmol) and 5,5-dimethylcyclohexane-1,3-dione (10 mmol) in the presence of H_2SO_4 (10% mmol) as catalyst in ethanol (10 mL) at 80 °C for 8 hours produced 4-aryl-7,7-dimethyl- 1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-ones. After the reaction was completed (monitored by TLC), pure product was obtained from the crude product by filtration and recrystallisation to afford:

4-Phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**1a**): White solid; m.p. 308–310 °C (EtOH) IR (KBr): 3321, 3260, 3098, 1709, 1670 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 9.46 (br, 1H, NH), 7.76 (br, 1H, NH), 7.33–7.20 (m, 5H, C_6H_5), 5.14 (d, *J* = 2.8 Hz, CH), 2.51–2.00 (m, 4H, $2CH_2$), 1.05 (s, 3H, CH_3), 0.89 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ = 192.8, 152.4, 151.9, 144.6, 128.3, 127.1, 126.2, 107.4, 52.0, 51.9, 49.8, 32.3, 28.7, 26.8. MS (FAB): *m/z* = 270 (M^+ +H). Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.31; H, 6.78 N, 10.30%.

4-Phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**1g**): White solid; m.p. 302–304 °C (EtOH) IR (KBr): 3343, 3214, 3033, 1698, 1363 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 10.58 (br, 1H, NH), 9.68 (br, 1H, NH), 7.36–7.21 (m, 5H, C_6H_5), 5.18 (d, *J* = 2.8 Hz, CH), 2.50–2.04 (m, 4H, $2CH_2$) 1.05 (s, 3H, CH_3), 0.89(s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ = 193.6, 174.6, 148.7, 143.3, 128.5, 127.5, 126.4, 108.1, 52.2, 52.1, 49.8, 32.2, 28.8, 26.7. MS (FAB): *m/z* = 286 (M^+ +H). Anal. Calcd for $C_{16}H_{18}N_2OS$: C, 67.10; H, 6.33; N, 9.78. Found: C, 67.28; H, 6.42 N, 9.76%.

Synthesis of compounds **3a–v**, **4a–d***; general procedure*

To a suspension of quinazolinone **1** (1.0 mmol) and α, β-ethylenic compound 2 (1.0 mmol) in DMF (5 mL), KF/Al_2O_3 (10 mol %, 0.16 g) was added in one portion. The mixture was stirred at 40 °C for 12 h and poured onto ice-water. The resulting product was purified by recrystallisation from ethanol.

3-(2-Methoxycarbonyl-ethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3a**): White solid; m.p. 183–184 °C (EtOH) IR (KBr): 3290, 3089, 1734, 1681, 1644 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.32 (br,1H, NH), 7.40–7.24 (m, 5H, C_6H_5), 5.44 (s, 1H, CH), 3.89–3.82 (m, 1H, CH_2), 3.66 (s, 3H, OCH_3), 3.28–3.21 (m, 1H, CH_2), 2.72–2.65 (m, 1H, CH_2), 2.50–2.42 (m, 1H, CH_2), 2.37–2.16 (m, 4H, $2CH_2$) , 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.6, 171.8, 153.3, 150.1, 141.4, 128.7, 128.0, 126.9, 109.4, 58.4, 51.8, 50.3, 42.2, 39.7, 32.8, 32.4, 29.2, 27.1. MS (FAB): *m/z* = 356 (M^+ +H). Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.62; H, 6.73; N, 7.92%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-methoxylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3b**): White solid; m.p. 226–227 °C (EtOH) IR (KBr): 3432, 3046, 1666, 1626, 1607 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.38 (br, 1H, NH), 6.96 (d, 2H, *J* = 8.0 Hz, C_6H_4), 6.53 (d, 2H, *J* = 8.0 Hz, C_6H_4), 5.93 (s, 1H, CH), 3.89–3.82 (m, 1H, CH_2), 3.75 (s, 3H, OCH_3), 3.72–3.69 (m, 1H, CH_2), 3.66 (s, 3H, OCH_3), 2.72–2.65 (m, 1H, CH_2), 2.56–2.44 (m, 1H, CH_2), 2.38–2.19 (m, 4H, $2CH_2$), 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.4, 171.9, 153.8, 150.2, 141.2, 137.2, 128.2, 115.1, 109.5, 59.2, 56.3, 52.1, 50.2, 47.3, 39.5, 33.0, 31.7, 29.5, 27.1. MS (FAB): *m/z* =386 (M^+ +H). Anal. Calcd for $C_{20}H_{26}N_2O_5$: C, 65.27; H, 6.78; N, 7.25. Found: C, 65.46; H, 6.83; N, 7.31%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-methylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3c**): White solid; m.p. 188–189 °C (EtOH) IR (KBr): 3306, 3050, 1735, 1681, 1639 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.26 (br, 1H, NH), 6.87 (d, 2H, *J* = 8.0 Hz, C_6H_4), 6.44 (d, 2H, *J* = 8.0 Hz, C_6H_4), 5.87 (s, 1H, CH), 3.86–3.79 (m, 1H, CH_2), 3.72 (s, 3H, OCH_3), 3.70–3.66 (m, 1H, CH_2), 2.71–2.64 (m, 1H, CH_2), 2.53–2.41 (m, 1H, CH_2), 2.37 (m, 3H, CH_3), 2.36–2.18 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3) , 0.96 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 195.2, 173.6, 152.9, 151.2, 141.2, 139.5, 129.4, 127.8, 110.2, 58.4, 53.5, 50.8, 48.4, 39.6, 33.7, 32.9, 28.7, 27.4, 22.0. MS (FAB): *m/z* =370 (M^+ +H). Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 68.30; H, 7.15; N, 7.50%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-chlorophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3d**): White solid; m.p. 181–182 °C (EtOH) IR (KBr): 3308, 3048, 1733, 1684, 1638 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.30 (br, ^1H, NH), 7.33 (d, 2H, *J* = 8.0. Hz, C_6H_4), 7.29 (d, 2H, *J* = 8.0 Hz, C_6H_4), 5.60 (s, 1H, CH), 3.85–3.82 (m, 1H, CH_2), 3.66 (s, 3H, OCH_3), 3.29–3.21 (m, 1H, CH_2), 2.72–2.65 (m, 1H, CH_2), 2.50–2.46 (m, 1H, CH_2), 2.44–2.12 (m, 4H, $2CH_2$), 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 194.2, 173.6, 154.8, 152.3, 140.2, 134.7, 129.6, 128.7, 109.4, 59.3, 51.7, 52.6, 44.6, 40.7, 31.5, 33.2, 29.5, 27.2. MS (FAB): *m/z* = 390, 392 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_2ClO_4$: C, 61.46; H, 5.93; N, 7.17. Found: C, 61.27; H, 5.99; N, 7.11%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-nitrophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3e**): White solid; m.p. 232–233 °C (EtOH) IR (KBr): 3356, 3046, 1748, 1663, 1617 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.52 (br, 1H, NH), 8.22 (d, 2H, *J* = 8.0 Hz, C_6H_4), 7.61 (d, 2H, *J* = 8.0 Hz, C_6H_4), 5.56 (s, 1H, CH), 3.92–3.86 (m, 1H, CH_2), 3.72 (s, 3H, OCH_3), 3.33–3.30 (m, 1H, CH_2), 2.76–2.72 (m, 1H, CH_2), 2.56–2.48 (m, 1H, CH_2), 2.40–2.15 (m, 4H, $2CH_2$) , 1.10 (s, 3H, CH_3) , 0.95 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 196.3, 172.9, 152.4, 148.6, 147.9, 144.3, 128.6, 127.2, 107.2, 62.4, 52.6, 51.3, 43.5, 40.9, 33.4, 32.7, 29.2, 27.4. MS (FAB): *m/z* =401 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_3O_6$: C, 59.84; H, 5.78; N, 10.47. Found: C, 59.69; H, 5.83; N, 10.42%.

3-(2-Methoxycarbonyl-ethyl)-4-(3-nitrophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3f**): White solid; m.p. 214–215 °C (EtOH) IR (KBr): 3348, 3048, 1737, 1656, 1619 cm^{-1}. ^1H NMR ($CDCl_2$): δ = 9.46 (br, 1H, NH), 8.22–8.13 (m, 2H, C_6H_4), 7.79 (d, *J* = 3.2, Hz, 1H, C_6H_4), 7.18–7.14 (q, *J* = 16.0, 1H, C_6H_4), 5.79 (s, 1H, CH), 4.54–4.49 (m, 1H, CH_2), 3.70 (s, 3H, OCH_3), 3.68–3.57 (m, 1H, CH_2), 3.15–2.98 (m, 1H, CH_2), 2.77–2.64 (m, 1H, CH_2), 2.52–2.31 (m, 4H, $2CH_2$) , 1.11 (s, 3H, CH_3) , 0.92 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.4, 175.3, 172.0, 149.1, 147.5, 141.8, 138.2, 129.6 124.2, 122.3, 109.6, 59.0, 52.4, 51.1, 49.2, 39.7, 33.6, 32.2, 29.5, 27.4. MS (FAB): *m/z* =401 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_3O_6$: C, 59.84; H, 5.78; N, 10.47. Found: C, 59.95; H, 5.70; N, 10.53%.

3-(2-Methoxycarbonyl-ethyl)-4-(2-chlorophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3g**): White solid; m.p. 174–175 °C (EtOH) IR (KBr): 3312, 3050, 1739, 1690, 1642 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.50 (br, ^1H, NH), 7.38 (d, *J* = 8.0 Hz, 1H, C_6H_4), 7.31–7.29 (m, 1H, C_6H_4), 7.23–7.19 (m, 2H, C_6H_4), 5.66 (s, 1H, CH), 3.88 (s, 3H, OCH_3),3.80–3.73 (m, 1H, CH_2), 3.42–3.35 (m, 1H, CH_2), 2.68–2.61 (m, 1H, CH_2), 2.44–2.40 (m, 1H, CH_2), 2.36–2.10 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3) , 1.00 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 197.2, 172.6, 152.8, 148.4, 138.6, 133.6, 129.1, 128.6, 128.3, 126.8, 106.5, 59.2, 51.6, 50.6, 42.5, 39.2, 33.1, 32.7, 29.4, 27.2. MS (FAB): *m/z* =390, 392 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_2ClO_4$: C, 61.46; H, 5.93; N, 7.17. Found: C, 61.57; H, 5.98; N, 7.19%.

3-(2-Butyloxycarbonyl-ethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3h**): White solid; m.p. 175–176 °C (EtOH) IR (KBr): 3302, 3026, 1738, 1690, 1669 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.92 (br, 1H, NH), 7.33–7.26 (m, 5H, C_6H_5), 5.62 (s, 1H, CH), 4.47–4.42 (m, 1H, CH_2), 4.07–4.03 (m, 2H, OCH_2), 3.72–3.70 (m, 1H, CH_2), 2.93–2.91 (m, 1H, CH_2), 2.89–2.84 (m, 1H, CH_2), 2.64–2.14 (m, 4H, $2CH_2$) , 1.55–1.48 (m, 2H, CH_2), 1.40–1.30 (m, 2H, CH_2), 1.11 (s, 3H, CH_3), 0.94 (t, *J* = 14.8 Hz, 3H, CH_3) , 0.90 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 192.6, 171.6, 153.8, 146.3, 144.1, 128.8, 128.2, 128.3, 109.8, 63.7, 59.7, 50.6, 48.9, 40.1, 32.9, 31.9, 30.4, 29.5, 27.5, 19.6, 14.9. MS (FAB): *m/z* =398 (M^+ +H). Anal. Calcd for $C_{23}H_{30}N_2O_4$: C, 69.32; H, 7.59; N, 7.03. Found: C, 69.53; H, 7.63; N, 6.97%.

3-(2-Cyanoethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3i**): White solid; m.p. 210–211 °C (EtOH) IR (KBr): 3346, 3046, 2252, 1692, 1683, 1260 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.55 (br, 1H, NH), 7.15–6.88 (m, 5H, C_6H_5), 5.53 (s, 1H, CH), 4.30–4.20 (m, 1H, CH_2),3,93–3.68 (m, 1H, CH_2), 3.09–2.98 (m, 1H, CH_2), 2.86–2.73 (m, 1H, CH_2), 2.50–2.16 (m, 4H, $2CH_2$), 1.10 (s, 3H, CH_3) , 0.91 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 194.2, 154.8, 152.7, 145.3, 133.2, 129.4, 118.0, 115.2, 112.3, 60.9, 50.5, 48.3, 40.2, 33.1, 29.8, 26.9, 15.6. MS (FAB): *m/z* =323 (M^+ +H). Anal. Calcd for $C_{19}H_{21}N_3O_2$: C, 70.57; H, 6.55; N, 12.99. Found: C, 70.35; H, 6.51; N, 12.92%.

3-(2-Aminocarbonyl-ethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3j**): White solid; m.p. 254–255 °C (EtOH) IR (KBr): 3415, 3374, 3206, 3069, 1703, 1675, 1634 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 10.71 (br, 1H, NH), 7.36–7.17 (m, 5H, C_6H_5), 7.08 (br, 1H, NH_2), 6.89 (br, 1H, NH_2), 5.44 (s, 1H, CH), 4.51–4.22 (m, 2H, CH_2), 3.74–3.34 (m, 2H, CH_2), 2.54–1.96 (m, 4H, $2CH_2$) , 1.03 (s, 3H, CH_3), 0.89 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 196.0, 175.0, 162.9, 147.3, 144.2, 128.7, 128.0, 114.4, 108.6, 58.5, 50.0, 47.9, 39.7, 32.5 29.0 26.4, 18.6. MS (FAB): *m/z* =341 (M^+ +H). Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.84; H, 6.79; N, 12.31. Found: C, 66.97; H, 6.72; N, 12.38%.

3-(3-Oxobutyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**3k**): White solid; m.p. 213–214 °C (EtOH) IR (KBr): 3328, 3042, 1736, 1686, 1664 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.34 (br, 1H, NH), 7.42–7.24 (m, 5H, C_6H_5), 5.38 (s, 1H, CH), 3.48–3.39 (m, 2H, CH_2), 2.83–2.74 (m, 2H, CH_2), 2.53–2.12 (m, 4H, $2CH_2$) , 2.14 (s, 3H, CH_3) , 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 202.8, 193.6, 153.5, 150.4, 141.3, 128.5, 127.9, 126.4, 110.1, 57.8, 50.3, 43.0, 39.8, 33.1, 32.8, 29.8, 29.0, 27.1. MS (FAB): *m/z* =340 (M^+ +H). Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.56; H, 7.11; N, 8.23, Found: C, 70.38; H, 7.16; N, 8.19%.

3-(2-Methoxycarbonyl-ethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3l**): White solid; m.p. 189–190 °C (EtOH) IR (KBr): 3386, 3034, 1724, 1649, 1246 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.73 (br, 1H, NH), 7.33–7.21 (m, 5H, C_6H_5), 5.62 (s, 1H, CH), 3.74–3.64 (m, 2H, CH_2), 3.66 (s, 3H, OCH_3), 2.72–2.64 (m, 2H, CH_2), 2.47–2.16 (m, 4H, $2CH_2$) , 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.9, 175.3, 171.6, 145.8, 140.5, 128.9, 128.3, 126.7, 110.1, 59.9, 51.9, 50.3, 48.7, 39.2, 32.8, 31.5, 29.3, 27.0. MS (FAB): *m/z* =372 (M^+ +H). Anal. Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52, Found: C, 64.63; H, 6.45; N, 7.57%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-methoxylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3m**): White solid; m.p. 156–156 °C (EtOH) IR (KBr): 3318, 3044, 1739, 1643, 1251 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.28 (br, 1H, NH), 7.26 (d, *J* = 8.0, 2H, C_6H_4), 6.83 (d, *J* = 8.0, 2H, C_6H_4), 5.54 (s, 1H, CH), 4.35–3.69 (m, 2H, CH_2), 3.78 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 2.94–2.78 (m, 1H, CH_2), 2.67–2.55 (m, 1H, CH_2), 2.40–2.14 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3) , 0.91 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 194.2, 175.0, 171.6, 159.5, 145.3, 142.6, 132.7, 128.1, 108.9, 59.5, 55.2, 53.1, 51.9, 48.6, 39.4, 32.9, 31.5, 29.3, 27.1 . MS (FAB): *m/z* =402 (M^+ +H). Anal. Calcd for $C_{21}H_{26}N_3O_4S$: C, 62.66; H, 6.51; N, 6.96, Found: C, 62.79; H, 6.56; N, 6.90%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-methylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3n**): White solid; m.p. 181–182 °C (EtOH) IR (KBr): 3387, 3030, 1685, 1645, 1235 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.50 (br, 1H, NH), 7.19 (d, *J* = 8.0, 2H, C_6H_4), 6.64 (d, *J* = 8.0, 2H, C_6H_4), 5.75 (s, 1H, CH), 3.76–3.67 (m, 1H, CH_2), 3.73 (s, 3H, OCH_3), 3.71–3.68 (m, 1H, CH_2), 2.66–2.59 (m, 1H, CH_2), 2.55–2.50 (m, 1H, CH_2), 2.43 (m, 3H, CH_3), 2.38–2.11 (m, 4H, CH_2), 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.2, 174.8, 159.4, 152.3, 143.1, 137.6, 127.2, 117.5, 111.3, 59.4, 53.6, 51.5, 48.8, 39.4, 32.5, 31.9, 29.1, 27.4, 21,8 . MS (FAB): *m/z* =386 (M^+ +H). Anal. Calcd for $C_{21}H_{26}N_2O_3S$: C, 65.26; H, 6.78; N, 7.25, Found: C, 65.48; H, 6.82; N, 7.31%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-Cl)-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3o**): White solid; m.p. 229–230 °C (EtOH) IR (KBr): 3364, 3044, 1706, 1669, 1224 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.57 (br, 1H, NH), 7.63 (d, *J* = 8.0 Hz, 2H, C_6H_4), 7.36 (d, *J* = 8.0 Hz, 2H, C_6H_4), 5.48 (s, 1H, CH), 3.73–3.77 (m, 1H, CH_2), 3.58 (s, 3H, OCH_3), 3.25–3.18 (m, 1H, CH_2), 2.66–2.63 (m, 1H, CH_2), 2.44–2.41 (m, 1H, CH_2), 2.39–2.10 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3) , 0.95 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 192.8, 172.3, 152.7, 151.1, 139.2, 133.6, 129.4, 128.7, 109.5, 58.8, 52.0, 51.3, 43.2, 40.2, 33.2, 32.8, 29.6, 27.4. MS (FAB): *m/z* = 406, 408 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_2ClO_3S$: C, 59.03; H, 5.70; N, 6.88. Found: C, 58.87; H, 5.65; N, 6.85%.

3-(2-Methoxycarbonyl-ethyl)-4-(4-nitrophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3p**): White solid; m.p. 223–224 °C (EtOH) IR (KBr): 3342, 3036, 1738, 1674, 1224 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.83 (br, 1H, NH), 7.94 (d, *J* = 8.0, 2H, C_6H_4), 7.72 (d, *J* = 8.0, 2H, C_6H_4), 5.53 (s, 1H, CH), 3.84–3.78 (m, 1H, CH_2), 3.84 (s, 3H, OCH_3), 3.50–3.45 (m, 1H, CH_2), 2.70–2.66 (m, 1H, CH_2), 2.53–2.47 (m, 1H, CH_2), 2.41–2.12 (m, 4H, $2CH_2$) , 1.09 (s, 3H, CH_3) , 0.96 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 196.8, 172.3, 154.4, 152.6, 148.2, 136.3, 128.9, 128.2, 109.6, 59.4, 52.2, 51.4, 50.8, 40.1, 32.9, 32.4, 29.7, 27.0. MS (FAB): *m/z* = 417 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_3O_5S$: C, 57.54; H, 5.55; N, 10.07. Found: C, 57.63; H, 5.51; N, 10.14%.

3-(2-Methoxycarbonyl-ethyl)-4-(3-nitrophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3q**): White solid; m.p. 211–212 °C (EtOH) IR (KBr): 3326, 3015, 1736, 1674, 1210 cm^{-1}. ^1H NMR (CDCl3): δ = 8.35 (s, 1H, NH), 8.19–8.09 (m, 2H, C_6H_4), 7.74–7.66 (d, *J* = 3.2, Hz, 1H, C_6H_4), 7.56–7.52 (q, *J* = 16.0, 1H, C_6H_4), 5.83 (s, 1H, CH), 4.47–4.41 (m, 1H, CH_2), 3.68 (s, 3H, OCH_3), 3.63–3.56 (m, 1H, CH_2), 3.00–2.93 (m, 1H, CH_2), 2.72–2.66 (m, 1H, CH_2), 2.46–2.20 (m, 4H, $2CH_2$) , 1.12 (s, 3H, CH_3) , 0.90 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 196.5, 175.6, 171.6, 148.6, 146.2, 142.6, 138.4, 129.8, 123.4, 121.8, 109.3, 59.3, 52.0, 50.1, 48.8, 39.4, 32.9, 31.5, 29.3, 27.0 . MS (FAB): *m/z* = 417 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_3O_5S$: C, 57.54; H, 5.55; N, 10.07. Found: C, 57.31; H, 5.50; N, 10.12%.

3-(2-Methoxycarbonyl-ethyl)-4-(2-chlorophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3r**): White solid; m.p. 169–170 °C (EtOH) IR (KBr): 3308, 3064, 1728, 1673, 1253 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 10.12 (br, 1H, NH), 7.56 (d, *J* = 8.0 Hz, 1H, C_6H_4), 7.45–7.34 (m, 1H, C_6H_4), 7.30–7.28 (m, 2H, C_6H_4), 5.30 (s, 1H, CH), 3.87–3.77 (m, 1H, CH_2), 3.72 (s, 3H, OCH_3), 3.53–3.44 (m, 1H, CH_2), 2.73–2.68 (m, 1H, CH_2), 2.53–2.47 (m, 1H, CH_2), 2.43–2.13 (m, 4H, $2CH_2$), 1.10 (s, 3H, CH_3) , 0.95 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 198.4, 178.2, 174.1, 159.8, 137.9, 133.2, 129.3, 128.9, 128.3, 126.8, 104.2, 63.7, 52.3, 51.2, 48.0, 40.1, 33.9, 33.2, 29.3, 27.1. MS (FAB): *m/z* = 406, 408 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_2ClO_3S$: C, 59.03; H, 5.70; N, 6.88. Found: C, 59.29; H, 5.75; N, 6.85%.

3-(2-Butyloxycarbonyl-ethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-dione (**3s**): White solid; m.p. 163–164 °C (EtOH) IR (KBr): 3350, 3046, 1727, 1620, 1221 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.15 (br, 1H, NH), 7.33–7.26 (m, 5H, C_6H_5), 5.63 (s, 1H, CH), 4.41–4.26(m, 1H, CH_2), 3.79–3.64 (m, 1H, CH_2), 4.05 (m, 2H, OCH_2), 2.93–2.57 (m, 2H, CH_2), 2.40–2.14 (m, 4H, $2CH_2$), 1.62–1.30 (m, 4H, $2CH_2$) , 1.10 (s, 3H, CH_3) , 0.94 (t, *J* = 14.2 Hz, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 194.4, 175.3, 171.2, 145.5, 140.5, 128.9, 128.3, 126.8, 109.3, 64.8, 59.9, 50.3, 48.8, 39.5,

32.9, 31.8, 30.5, 29.3, 27.0, 19.1, 13.7. MS (FAB): *m/z* = 414 (M^+ +H). Anal. Calcd for $C_{23}H_{30}N_2O_3S$: C, 66.64; H, 7.29; N, 6.76, Found: C, 66.49; H, 7.33; N, 6.71%.

3-(2-Cyanoethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3t**): White solid; m.p. 208–209 °C (EtOH) IR (KBr): 3324, 3048, 2246, 1682, 1620, 1172 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.05 (br, 1H, NH), 6.85–6.42 (m, 5H, C_6H_5), 5.49 (s, 1H, CH), 4.29–3.73 (m, 2H, CH_2), 3.10–2.89 (m, 2H, CH_2), 2.47–2.16 (m, 4H, $2CH_2$), 1.11 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 195.3, 175.6, 159.8, 144.8, 132.2, 128.2, 117.2, 114.5, 110.5, 60.4, 55.3, 48.6, 39.5, 32.9, 29.3, 27.1, 15.3. MS (FAB): *m/z* =339 (M^+ +H). Anal. Calcd for $C_{19}H_{21}N_3OS$: C, 67.23; H, 6.24; N, 12.38, Found: C, 67.46; H, 6.28; N, 12.32%.

3-(2-Aminocarbonyl-ethyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-dione (**3u**): White solid; m.p. 253–254 °C (EtOH) IR (KBr): 3431, 3383, 3221, 3074, 1690, 1682, 1222 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 10.71 (br, 1H, NH), 7.36–7.17 (m, 5H, C_6H_5), 7.12 (s, 1H, NH_2), 6.96 (s, 1H, NH_2), 5.35 (s, 1H, CH), 4.47–4.25 (m, 2H, CH_2), 3.64–3.37 (m, 2H, CH_2), 2.58–2.42 (m, 2H, CH_2), 2.38–1.92 (m, 2H, CH_2) , 1.02 (s, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 194.4, 174.8, 164.2, 145.2, 142.4, 129.1, 127.7, 116.2, 109.2, 57.8, 51.2, 48.3, 40.6, 32.7, 28.6, 25.9, 19.2. MS (FAB): *m/z* =357 (M^+ +H). Anal. Calcd for $C_{19}H_{23}N_3O_2S$: C, 63.84; H, 6.49; N, 11.75, Found: C, 63.65; H, 6.45; N, 11.80%.

3-(3-Oxobutyl)-4-phenyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**3v**): White solid; m.p. 221–222 °C (EtOH) IR (KBr): 3340, 3046, 1712, 1620, 1247 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.92 (br, 1H, NH), 7.33–7.15 (m, 5H, C_6H_5), 5.26 (s, 1H, CH), 3.63–3.44 (m, 2H, CH_2), 2.88–2.63 (m, 2H, CH_2), 2.53–2.41 (m, 2H, CH_2), 2.38–2.21 (m, 2H, CH_2) 2.17 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 0.95 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 201.4, 192.3, 163.5, 151.2, 142.4, 128.6, 127.8, 124.2, 111.6, 56.4, 46.2, 40.4, 34.3, 32.9, 30.2, 29.5, 29.1, 27.4. MS (FAB): *m/z* = 356 (M^+ +H). Anal. Calcd for $C_{20}H_{24}N_2O_2S$: C, 67.38; H, 6.79; N, 7.86, Found: C, 67.25; H, 6.83; N, 7.80%.

1-(2-Methoxycarbonyl-ethyl)-4-(2-methoxylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**4a**): M.p. 155–156 °C (EtOH) IR (KBr): 3310, 3046, 1732, 1685, 1639 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.28–7.25 (m, 1H, C_6H_4), 6.86–6.78 (m, 3H, C_6H_4), 5.89 (br, 1H, NH), 5.68 (d, *J* = 2.8 Hz, 1H, CH), 4.00–3.90 (m, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 2.90–2.70 (m, 2H, CH_2), 2.55–2.26 (m, 4H, $2CH_2$), 1.20 (s, 3H, CH_3), 1.07 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.8, 175.4, 158.2, 154.6, 152.7, 128.2, 127.1, 126.4, 121.9, 111.4, 109.7, 57.4, 55.8, 52.1, 49.6, 47.7, 40.9, 38.9, 33.0, 28.9, 27.3. MS (FAB): *m/z* = 386 (M^+ +H). Anal. Calcd for $C_{21}H_{26}N_2O_5$: C, 65.27; H, 6.78; N, 7.25, Found: C, 65.16; H, 6.82; N, 7.29%.

1-(2-Methoxycarbonyl-ethyl)-4-(2-nitrophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (**4b**): White solid; m.p. 177–178 °C (EtOH) IR (KBr): 3312, 3086, 1663, 1625, 1362 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.03–8.00 (q, J = 12.0 Hz, 1H, C_6H_4), 7.59–7.55 (m, 1H, C_6H_4), 7.48–7.47(m, 1H, C_6H_4), 7.35–7.38 (q, *J* = 12.0, 1H, C_6H_4), 6.20 (br, 1H, NH), 5.84 (d, *J* = 2.8 Hz, 1H, CH), 4.11–3.95 (m, 2H, CH_2), 3.78–3.71 (m, 1H, CH_2), 3.70 (s, 3H, OCH_3), 3.69–3.62 (m, 1H, CH_2), 2.66–2.14 (m, 4H, $2CH_2$) , 1.11 (s, 3H, CH_3) , 0.95 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 193.8, 171.9, 154.8, 151.7, 148.4, 136.5, 133.8, 128.9, 128.1, 125.1, 109.1, 51.9, 49.1, 47.7, 39.8, 38.5, 33.6, 32.8, 28.9, 28.5. MS (FAB): *m/z* =401 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_3O_6$: C, 59.84; H, 5.78; N, 10.47, Found: C, 59.63; H, 5.82; N, 10.42%.

1-(2-Methoxycarbonyl-ethyl)-4-(2-methoxylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**4c**): White solid; m.p. 164–165 °C (EtOH) IR (KBr): 3316, 3044, 1732, 1689, 1213 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.23–7.20 (m, 1H, C_6H_4), 6.88–6.79 (m, 3H, C_6H_4), 5.88 (br, 1H, NH), 5.69 (d, *J* = 2.8 Hz,1H, CH), 4.01–3.60 (m, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 2.90–2.72 (m, 2H, CH_2), 2.55–2.26 (m, 4H, $2CH_2$) , 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 194.2, 171.8, 157.0, 153.7, 153.1, 129.1, 128.7, 126.0, 120.3, 110.7, 109.2, 55.3, 51.8, 49.4, 46.9, 39.9, 38.3, 33.8, 32.9, 29.1, 28.4. MS (FAB): *m/z* = 402 (M^+ +H). Anal. Calcd for $C_{21}H_{26}N_2O_4S$: C, 62.66; H, 6.51; N, 6.96. Found: C, 62.37; H, 6.55; N, 6.91%.

1-(2-Methoxycarbonyl-ethyl)-4-(2-nitrylphenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione-5-one (**4d**): White solid; m.p. 172–173 °C (EtOH) IR (KBr): 3310, 3082, 1668, 1631, 1358 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.97–7.94 (q, *J* = 12.0 Hz, 1H, C_6H_4), 7.54–7.50 (m, 1H, C_6H_4), 7.43–7.40(m, 1H, C_6H_4), 7.29–7.26 (q, *J* = 12.0, 1H, C_6H_4), 6.18 (br, 1H, NH), 5.83 (d, *J* = 2.8 Hz,1H, CH), 4.10–3.95 (m, 2H, CH_2), 3.75–3.73 (m, 1H, CH_2), 3.72 (s, 3H, OCH_3), 3.72–3.68 (m, 1H, CH_2), 2.93–2.84 (m, 1H, CH_2), 2.63–2.26 (m, 4H, $2CH_2$) , 1.10 (s, 3H, CH_3) , 0.94 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 198.7, 175.6, 171.4, 158.4, 148.1, 135.3, 131.6, 129.6, 128.6, 127.3, 104.2, 62.7, 52.0, 51.2, 47.8, 39.5, 33.9, 32.6, 27.5, 27.2. MS (FAB): *m/z* = 417 (M^+ +H). Anal. Calcd for $C_{20}H_{23}N_3O_5S$: C, 57.54; H, 5.55; N, 10.07, Found: C, 57.28; H, 5.51; N, 10.03%.

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