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ORIGINAL PAPER

Synthesis of novel quinazolines via nucleophilic cycloaddition of 2-amino-*N*′-arylbenzimidamides with dimethyl acetylenedicarboxylate and 2-(dicyanomethylene)indan-1,3-dione

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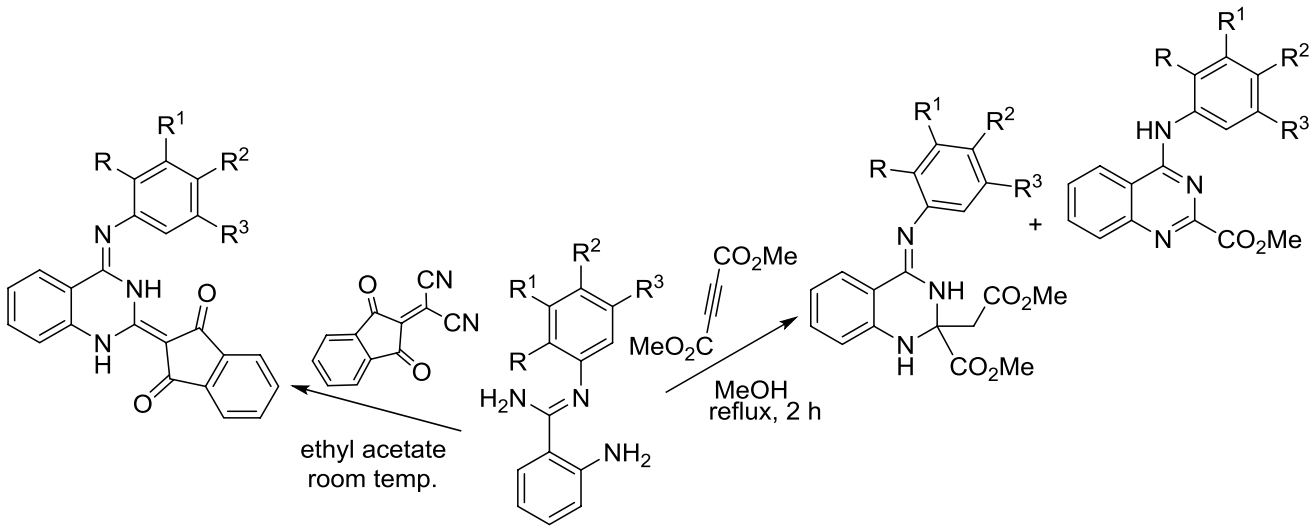
Abstract
Synthesis of novel tetrahydroquinazoline-2-carboxylate and arylaminoquinazoline-2-carboxylate in good yields has been established via the nucleophilic cycloaddition of 2-amino-*N*′-arylbenzimidamides on dimethyl acetylenedicarboxylate. Moreover, studying the reaction of 2-amino-*N*′-arylbenzimidamides with 2-(dicyanomethylene)indan-1,3-dione to give 3,4-dihydroquinazolin derivatives. The results obtained from IR, ^{1}H NMR, and ^{13}C NMR data as well as the mass spectra are in agreement with the assigned structures. A plausible mechanism for the formation of the products is presented.

Graphic abstract



Keywords 2-Amino-*N*′-arylbenzimidamides · Dimethyl acetylenedicarboxylate · 2-(Dicyanomethylene)indan-1,3-dione · Quinazolines

Introduction

Dimethyl acetylenedicarboxylate (DMAD) and 2-(dicyanomethylene)indan-1,3-dione (CNIND) have supposed an important role in modern organic synthesis, not only because it is used as a dienophile in cycloaddition reactions, but also because of their use in combinatorial and multi-component chemistry as well as in heterocyclic synthesis [1–3]. There

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has been considerable interest in the development of reliable and simple preparative methods for the production of quinazolines [4]. Substituted quinazolines have been synthesized by a number of methods involving several substrates such as 2-amino-*N*′-arylbenzamidines [3–7] and 2-aminobenzylamine [8]. Researchers have already determined many therapeutic activities of quinazoline derivatives, including anti-cancer [9], anti-inflammation [10], antibacterial [11], analgesia [12], anti-virus [13], anti-cytotoxin [14], anti-spasm [15], anti-tuberculosis [16], anti-oxidation [17], anti-malarial [18], anti-hypertension [19], anti-psychotic [20], anti-obesity [21], anti-diabetes [22]. Medicinal chemists synthesized a variety of quinazoline compounds with different biological activities by installing various active groups to the quinazoline moiety using developing synthetic methods.

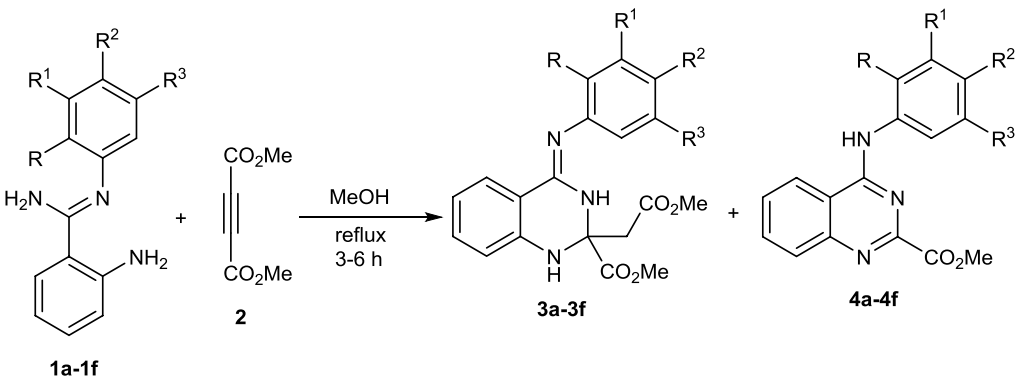
Results and discussion

Quinazoline derivatives conquer an important place in the realm of hetercocyclic organic compounds due to their widespread application. For this reason, their synthesis has received considerable attention. Herein, we have used of nucleophilic cycloaddition reaction of 2-amino-*N*′-arylbenzimidamides **1a**–**1f** with dimethyl acetylenedicarboxylate (DMAD, **2**) to develop a new and suitable methodology for the synthesis of quinazoline derivatives (Scheme 1). The starting materials **1a**–**1f** were prepared in excellent yields by heating 2-aminobenzonitrile with substituted anilines in the presence of aluminium chloride as a catalyst according to the reported procedures [4].

We examine the reactivity of compounds **1a**–**1f** towards DMAD by heating methanol solutions of them in a molar ratios (1:1) under reflux conditions for 3–6 h. The reaction mixture was subjected to preparative layer chromatography (PLC). Separation of the residue afforded two zones from which 1,2,3,4-tetrahydroquinazoline-2-carboxylate **3a**–**3f** and arylamino-quinazoline-2-carboxylate **4a**–**4f** have been isolated. The structure of compounds was deduced by IR, ^{1}H NMR, ^{13}C NMR, and mass spectra as well as elemental analyses. The first product is assigned as (*Z*)-methyl 2-(2-methoxy-2-oxoethyl)-4-(*p*-tolylimino)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (**3a**). The IR spectrum of **3a** showed two broad absorption bands for NH groups at $\bar{\nu}=3444$ and 3258 cm^{-1}. Moreover there are three different absorptions in IR spectrum at $\bar{\nu}=1745$, 1719, and 1640 cm^{-1} characteristic for the two carbonyl and C=N groups, respectively. The ^{1}H NMR spectrum of **3a** showed, in addition to the aromatic protons, three sharp singlets resonated at $\delta=2.34$, 3.79, and 3.97 ppm related to the protons of the three different methyl groups. However, the two methylene protons resonated in the ^{1}H NMR spectrum as a sharp singlet at 3.63 ppm. While the two different NH protons resonated as two different broad signals at 8.16 and 8.28 ppm. Moreover, the ^{13}C NMR spectrum clearly showed the presence of quaternary carbon atom which resonated at $\delta=76.43$ ppm. Furthermore, ^{13}C NMR spectrum revealed the presence of the methyl and the two methoxy groups as resonating peaks at 21.10, 51.81, and 53.38 ppm, respectively. As a result of the existence of a stereogenic center (quinazoline-C-2) in the compounds **3a**–**3f**, racemic mixtures were obtained. Thus duplication for most signals in ^{1}H and ^{13}C NMR spectra could be noticed. Attempts to separate the isomers by chromatography were not successful. The mass spectrometry of the products **3a**–**3f** showed the following fragments common to all products [M^{+}–Me] and [M^{+}–CO_2Me]. Elemental analyses confirm the structure of the products **3a**–**3f**.

The second product of the same reaction is assigned as methyl 4-(*p*-tolylamino)quinazoline-2-carboxylate (**4a**). The IR spectrum of **4a** showed two strong absorption bands at $\bar{\nu}=3441$ and 1730 cm^{-1}, indicating the presence of (NH) and (CO) groups. While the C=N group absorbed in the IR

Scheme 1



a, R = R^1 = R^3 = H, R^2 = CH_3; **b**, R^1 = R^3 = H, R = R^2 = CH_3; **c**, R = R^3 = CH_3, R^1 = R^2 = H;
d, R = R^3 = H, R^1 = R^2 = Cl; **e**, R = R^3, R^1 = H, R^2 = Cl; **f**, R = R^1 = R^3 = R^2 = H

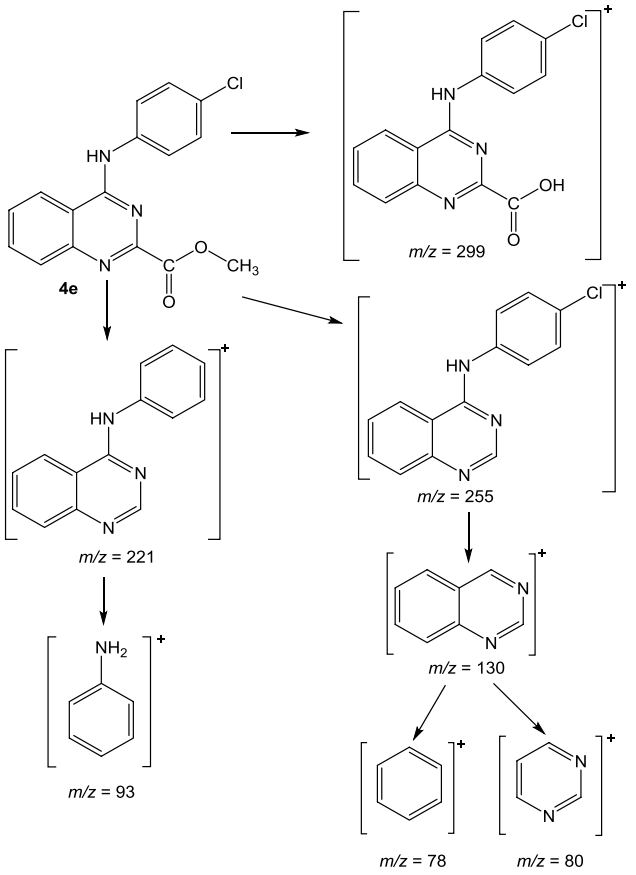
spectrum at 1623 cm^{-1}. However, the ^1H NMR spectrum of **4a** showed the disappearance of data duplication for protons due to disappearance of chirality center as the result of losing methyl acetate. Thus ^1H NMR spectrum of **4a** revealed one broad resonance at $\delta = 9.99$ ppm for exchangeable proton (NH). Moreover, there are two sharp singlets at 2.32 and 3.89 ppm characteristic for both aromatic and carbomethoxy methyl protons, respectively. In addition to two multiples in the range of 7.21–8.66 ppm related to the aromatic protons. The ^{13}C NMR spectrum of **4a** announced two distinct resonances resonated at $\delta = 20.96$ and 53.01 ppm assignable for the two different CH_3, respectively. While the C=N and CO carbon atoms resonated at 153.03 and 165.25 ppm, respectively. The fragmentation pattern of mass spectrum of **4a** is in full agreement with structure where it gave the molecular ion peak at $m/z = 293$ which is in accordance with the molecular weight of it. In addition to two fragmentations at $m/z = 278$ and 236 which are related to both (M^+–CH_3) and (M^+–$COOCH_3$), respectively. The electron-withdrawing affinity of substituents in compounds **4d**, **4e** appeared clearly in the deshielding effect on the NH protons where they resonated at $\delta = 10.55$, 10.15, and 10.01 ppm. Other common features noted in the fragmentation pattern of **4e** are $m/z = 15$, 59, and 134, as shown in Scheme 2.

The formation of the products **3a**–**3f** and **4a**–**4f** reaction can be rationalized by nucleophilic addition of the lone pair of electrons of the aromatic amino group of compounds **1a**–**1f** on the sp-hybridized C≡C of the reactant **2** to give the intermediates **5a**–**5f** which suffered from 1,3-H^+ shift yielding dimethyl maleate derivatives **6a**–**6f**. The latter compound undergoes intramolecular nucleophilic addition by attacking the aliphatic amino group (amidines-NH_2) by its lone pair of electrons on the π* of the C=C to form the tetrahedral intermediates **7a**–**7f**. After 1,3-H^+ shift has been occurred the chiral quinazoline derivatives **3a**–**3f** were formed. The latter products lost methyl acetate under the reaction conditions to give the achiral aromatic quinazoline derivatives **4a**–**4f** (Scheme 3).

In continuing research of the new quinazoline scaffolds, we report here the reaction of 2-amino-*N*′-arylbenzimidamides **1a**–**1d** with CNIND. Solutions of **1a**–**1d** (1 mmol) in dry ethyl acetate were added into a solution of **8** (1 mmol) in dry ethyl acetate (Scheme 4).

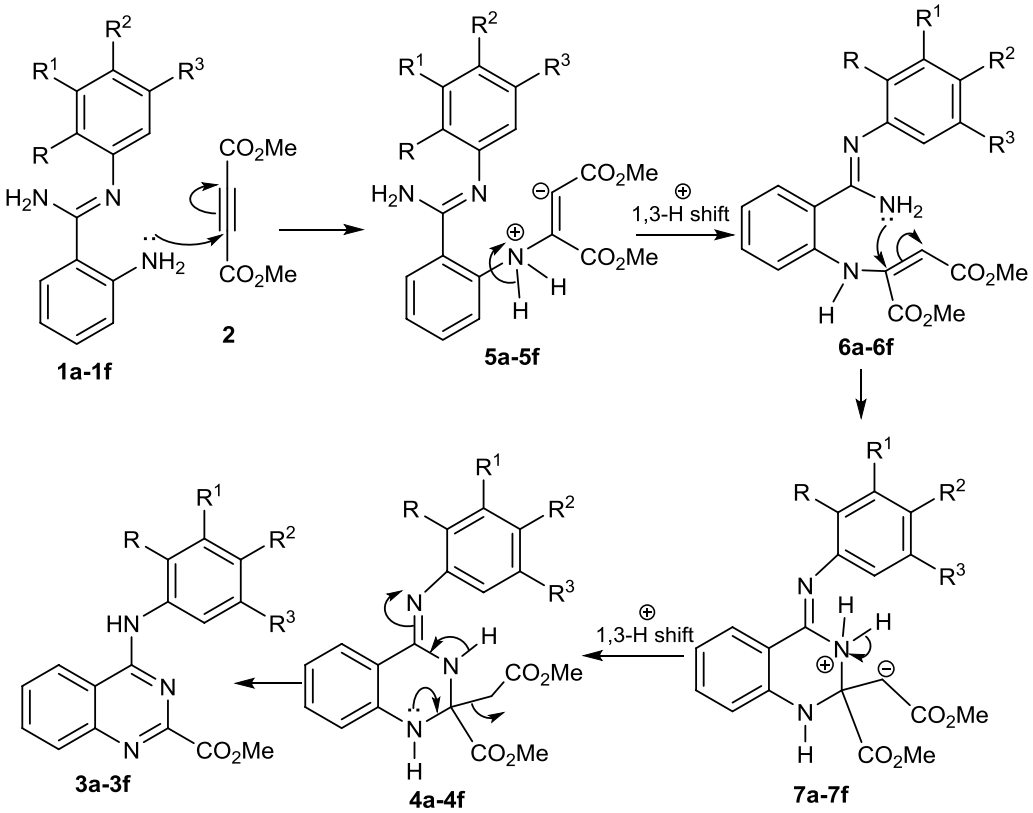
The reaction proceeded to give (*Z*)-2-[4-(arylimino)-3,4-dihydro-quinazolin-2(1*H*)-ylidene]-1*H*-indene-1,3(2*H*)-dione **9a**–**9d** in 50–60% yields. Products **9a**–**9d** were formed by participation of two amino groups of **1a**–**1d** in the reaction, in which two equivalents of HCN were eliminated. The stability of the products could be rationalized due to the intramolecular hydrogen bonds which are further substantiated from the down field shift of the two –NH groups. The structure of the products was

Scheme 2

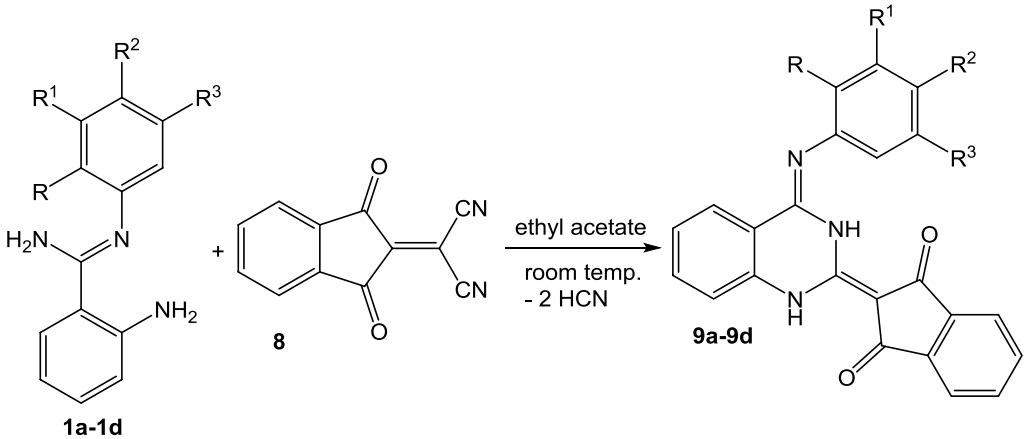


fully consistent with their ^1H NMR, ^{13}C NMR, IR, and mass spectrum. We choose compound **9a** as an example to confirm the structures. ^1H NMR spectrum showed broad exchangeable signals with (D_2O) at $\delta = 10.27$ and 13.22 ppm due to amino groups and singlet signal of methyl group at 2.37 ppm, in addition to aromatic protons. The ^{13}C NMR spectrum showed signals at $\delta = 175.10$ ppm for the two carbonyl groups. Another carbon atom resonated at 98.19 ppm for OC–C–CO and another carbon resonated at 92.15 ppm for HN–C–NH carbon atom. However, the C=N resonated at 157.13 ppm. The molecular formula of **9a** is confirmed as $C_{24}H_{17}N_3O_2$ by mass spectrometry. The proposed mechanism for the formation of products **9a**–**9d** can be rationalized as the results of the nucleophilic attack of the aromatic amino group of **1a**–**1d** to the most electron poor atom "carbon atom that carries the two cyano groups [$C(CN)_2$]" of **8** followed by loosing HCN molecule to give the adducts **11a**–**11d**. These adducts can subsequently be cyclised by nucleophilic attack of the aliphatic amino group to the same carbon atom to give the adduct **12a**–**12d**, this follows by eliminating another molecule of HCN to form the final products **9a**–**9d** (Scheme 5).

Scheme 3



Scheme 4

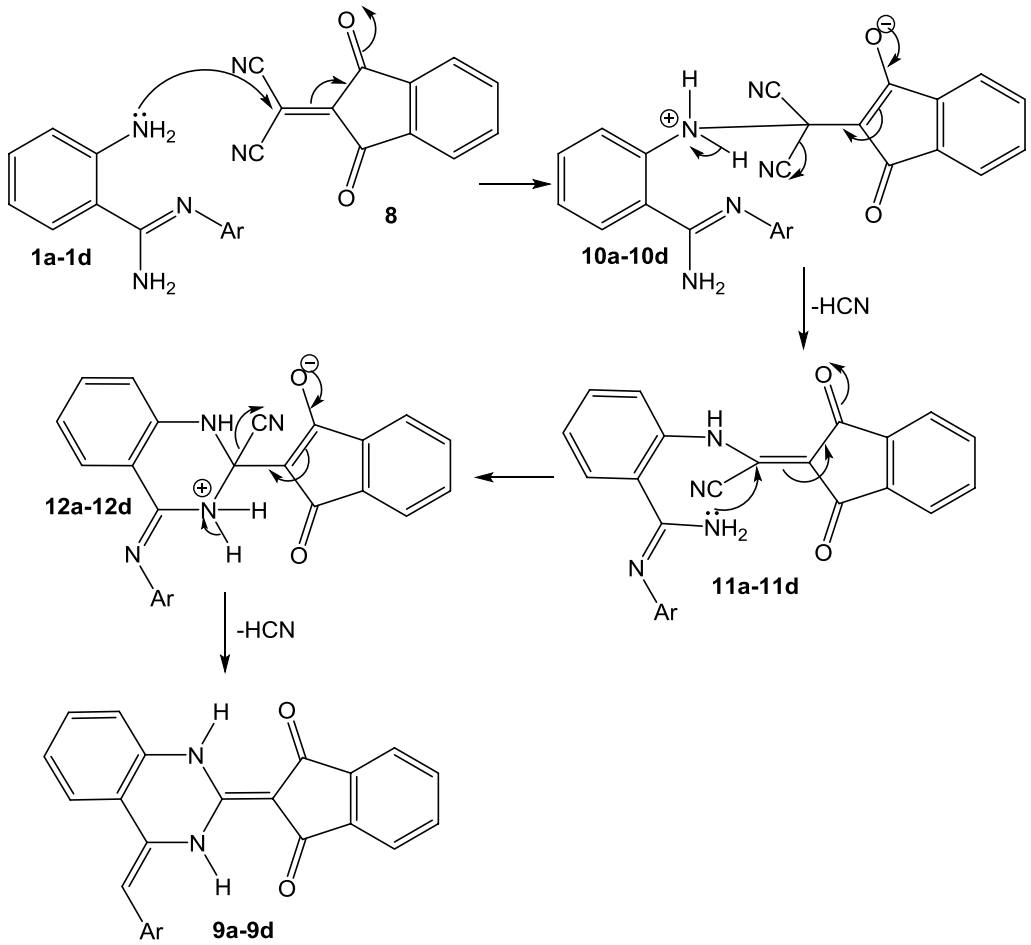


a, R = R^1 = R^3 = H, R^2 = CH_3; **b**, R^1 = R^3 = H, R = R^2 = CH_3; **c**, R = R^3 = CH_3, R^1 = R^2 = H; **d**, R = R^3 = H, R^1 = R^2 = Cl

Conclusion

In summary, the proclivity of 2-amino-*N*′-arylbenzimidamide derivatives **1a**–**1f** towards both dimethyl acetylenedicarboxylate (**2**) and 2-(dicyanomethylene)indan-1,3-dione (CNIND) in boiling methanol and in dry ethyl acetate were investigated. Novel quinazolines were formed and proved by spectral data.

Scheme 5



Experimental

All reagents were purchased from Alfa Aesar or Fluka and were used without further purification. Melting points were measured in capillary tubes using a Büchi 530 melting point apparatus and are uncorrected. IR spectra were measured using a Bruker Tensor 27 instrument. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded in DMSO-d_6 on BrukerAvance II-300 and Avance DRX-400 spectrometers with TMS as the internal standard. Mass spectra measurements (EI, 70 eV) were performed using a Finnigan MAT 8430 spectrometer.

General procedure for synthesis of 3a–3f and 4a–4f

Into a 100 cm^3 round bottom flask containing a solution of **1a**–**1f** (1 mmol) in 30 cm^3 methanol, a solution of **2** (1 mmol) in 10 cm^3 methanol was added. The mixture was heated under reflux conditions for 3–6 h (the reaction was monitored by TLC analyses). The solvent was evaporated under vacuum and the formed solid products were purified by dissolving them in 15 cm^3 dry acetone and then subjected to preparative plate chromatography (silica gel), toluene/acetone (5:1). The obtained products **3a**–**3f** and **4a**–**4f** were recrystallized from ethanol.

(*Z*)-Methyl 2-(2-methoxy-2-oxoethyl)-4-(*p*-tolylimino)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (3a, $C_{20}H_{21}N_3O_4$) Yield: 46%; yellow crystals; m.p.: 200–203 °C (EtOH); ^{1}H NMR(400 MHz, DMSO-d_6): $\delta = 2.34$ (s, 3H, CH_3), 3.63 (s, 2H, CH_2), 3.79 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 6.76–6.80 (t, 1H, $J = 8.0$ Hz, Ar–H), 6.83–6.85 (d, 1H, $J = 8.4$ Hz, Ar–H), 7.17–7.34 (m, 2H, Ar–H), 7.62–7.62 (d, 1H, $J = 7.6$ Hz, Ar–H), 7.76 (s, 1H, Ar–H), 7.88–7.90 (t, 1H, $J = 8.0$ Hz, Ar–H), 8.08–8.10 (t, $J = 8.0$ Hz, 1H, Ar–H), 8.16 (s, 1H, NH), 8.28 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 21.10$ (CH_3), 41.52 (CH_2), 51.81 (CH_3), 53.81 (CH_3), 76.43 (C-2), 115.17, 118.89, 120.51, 126.00, 128.20, 129.58, 131.15, 134.23 (CH–Ar), 135.09, 136.88, 138.05, 145.57 (C–Ar), 163.48 (C=N), 168.43 (C=O), 171.10 (C=O) ppm; IR (KBr): $\bar{\nu} = 3299$ (NH), 1727, 1722 (CO), 1656 (C=N) cm^{-1}; MS: $m/z = 367$ (M$^+$, 30) (100).

(*Z*)-Methyl 4-[(2,4-dimethylphenyl)imino]-2-(2-methoxy-2-oxoethyl)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (3b, $C_{21}H_{23}N_3O_4$) Yield: 48%; yellow crystals; m.p.: 188–191 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.08 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 3.65 (s, 2H, CH_2), 3.81 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 7.11–7.16 (m, 2H, Ar–H), 7.27–7.29 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.34–7.38 (t, 1H, *J* = 8.0 Hz, Ar–H), 7.63–7.65 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.69 (s, 1H, Ar–H), 8.06–8.10 (t, 1H, *J* = 8.0 Hz, Ar–H), 8.15 (s, 1H, NH), 8.28 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 18.25 (CH_3), 21.06 (CH_3), 30.06 (CH_2), 51.92 (CH_3), 53.46 (CH_3), 76.63 (C-2), 115.09, 119.23, 124.70, 127.05, 128.34, 130.75, 131.14 (CH–Ar), 134.13, 136.55, 137.34, 145.85, 148.20 (C–Ar), 162.73 (C=N), 168.25 (C=O), 171.64 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3287 (NH), 1725, 1720 (CO), 1655 (C=N) cm^{-1}; MS: *m/z* = 382 ([M + 1]$^+$, 31), 381 (M$^+$, 28).

(*Z*)-Methyl 4-[(2,5-dimethylphenyl)imino]-2-(2-methoxy-2-oxoethyl)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (3c, $C_{21}H_{23}N_3O_4$) Yield: 48%; yellow crystals; m.p.: 172–174 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.06 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.63 (s, 2H, CH_2), 3.79 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 6.80–6.87 (m, 2H, Ar–H), 7.30–7.42 (m, 2H, Ar–H), 7.53–7.54 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.63–7.65 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.71 (s, 1H, Ar–H), 8.18 (s, 1H, NH), 8.29 (s, 1H, NH) ppm; IR (KBr): $\bar{\nu}$ = 3298 (NH), 1732, 1726 (CO), 1655 (C=N) cm^{-1}; MS: *m/z* = 381 (M$^+$, 28).

(*Z*)-Methyl 4-[(3,4-dichlorophenyl)imino]-2-(2-methoxy-2-oxoethyl)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (3d, $C_{19}H_{17}Cl_2N_3O_4$) Yield: 50%; yellow crystals; m.p.: 118–119 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.61 (s, 2H, CH_2), 3.70 (s, 3H, CH_3), 3.93 (s, 3H, CH_3), 6.67–6.71 (t, 1H, *J* = 7.6 Hz, Ar–H), 6.76–6.78 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.01 (s, 1H, Ar–H), 7.21–7.24 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.45–7.48 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.65–7.72 (m, 2H, Ar–H), 8.37 (s, 1H, NH), 8.92 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 45.64 (CH_2), 51.97 (CH_3), 52.71 (CH_3), 73.81 (C-2), 111.83, 114.74, 117.31, 120.23, 121.46, 122.95, 124.45 (CH–Ar), 130.23, 130.80, 133.10, 141.81, 146.12 (C–Ar), 152.61 (C=N), 170.07 (C=O), 172.27 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3245 (NH), 1732, 1720 (CO), 1658 (C=N) cm^{-1}; MS: *m/z* = 423 ([M + 2]$^+$, 12), 421 (M$^+$, 19).

(*Z*)-Methyl 4-[(4-chlorophenyl)imino]-2-(2-methoxy-2-oxoethyl)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (3e, $C_{19}H_{18}ClN_3O_4$) Yield: 49%; yellow crystals; m.p.: 149–150 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.64 (s, 2H, CH_2), 3.79 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 6.78–6.85 (m, 1H, Ar–H), 7.35–7.37 (m, 1H, Ar–H), 7.45–7.49 (m, 1H, Ar–H), 7.55–7.53 (m, 1H, Ar–H), 7.63–7.65 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.77 (s, 1H, Ar–H), 7.87–7.90 (t, 1H, *J* = 7.6 Hz, Ar–H), 8.07–8.10 (t, 1H, *J* = 7.6 Hz, Ar–H), 8.21 (s, 1H, NH), 8.31 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 41.50 (CH_2), 51.88 (CH_3), 53.50 (CH_3), 76.44 (C-2), 114.86, 119.04, 122.04, 128.27, 129.09, 129.76, 133.33 (CH–Ar), 133.78, 134.45, 136.75, 145.55 (C–Ar), 163.45 (C=N), 168.37 (C=O), 171.01 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3252 (NH), 1745, 1719 (CO), 1640 (C=N) cm^{-1}; MS: *m/z* = 389 ([M + 2]$^+$, 25), 387 (M$^+$, 35).

(*Z*)-Methyl 2-(2-methoxy-2-oxoethyl)-4-(phenylimino)-1,2,3,4-tetrahydroquinazoline-2-carboxylate (3f, $C_{19}H_{19}N_3O_4$) Yield: 47%; yellow crystals; m.p.: 143–144 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.64 (s, 2H, CH_2), 3.80 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 6.68–6.85 (m, 2H, Ar–H), 6.91–6.95 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.09–7.22 (m, 2H, Ar–H), 7.30–7.55 (m, 2H, Ar–H), 7.64–7.66 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.72 (s, 1H, Ar–H), 8.29 (s, 1H, NH), 8.40 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 41.55 (CH_2), 51.84 (CH_3), 53.43 (CH_3), 76.36 (C-2), 114.81, 115.21, 118.94, 120.44, 128.25, 128.60, 129.08, 129.89, 131.53 (CH–Ar), 134.27, 137.81, 145.57 (C–Ar), 163.36 (C=N), 168.39 (C=O), 171.08 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3298 (NH), 1716, 1710 (CO), 1622 (C=N) cm^{-1}; MS: *m/z* = 354 ([M + 1]$^+$, 10), 353 (M$^+$, 15).

Methyl 4-(*p*-tolylamino)quinazoline-2-carboxylate (4a, $C_{17}H_{15}N_3O_2$) Yield: 54%; yellow crystals; m.p.: 188–190 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 7.21–7.23 (d, 1H, *J* = 8.4 Hz, Ar–H), 7.73–7.76 (t, 1H, *J* = 6.8 Hz, Ar–H), 7.86–7.88 (d, 1H, *J* = 8.4 Hz, Ar–H), 7.90–7.98 (m, 4H, Ar–H), 8.64–8.66 (d, 1H, *J* = 8.0 Hz, Ar–H), 9.99 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.96 (CH_3), 53.01 (CH_3), 115.49, 122.69, 123.51, 128.42, 128.97, 129.42 (CH–Ar), 133.63, 134.12, 136.77, 149.69 (C–Ar), 153.03 (C=N), 158.72 (C=N), 165.25 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3310 (NH), 1710 (CO), 1654 (C=N) cm^{-1}; MS: *m/z* = 294 ([M + 1]$^+$, 100), 293 (M$^+$, 30).

Methyl 4-[(2,4-dimethylphenyl)amino]quinazoline-2-carboxylate (4b, $C_{18}H_{17}N_3O_2$) Yield: 52%; yellow crystals; m.p.: 156–157 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.17 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 7.06–7.08 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.15 (s, 1H, Ar–H), 7.23–7.25 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.69–7.73 (t, 1H, *J* = 8 Hz, Ar–H), 7.86–7.94 (m, 2H, Ar–H), 8.53–8.55 (d, 1H, *J* = 8.4 Hz, Ar–H), 9.88 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 18.52 (CH_3), 21.06 (CH_3), 52.57 (CH_3), 115.22, 123.59, 127.20, 128.14, 128.80, 131.56, 134.01 (CH–Ar), 134.45, 135.00, 136.12, 149.59 (C–Ar), 153.98 (C=N), 159.90 (C=N), 165.44 (C=O) ppm; IR

(KBr): $\bar{\nu}$ = 3286 (NH), 1714 (CO), 1634 (C=N) cm^{-1}; MS: *m/z* = 308 ($[M+1]^+$, 20), 307 (M^+, 100), 306 ($[M-1]^+$, 8).

Methyl 4-[(2,5-dimethylphenyl)amino]quinazoline-2-carboxylate (4c, $C_{18}H_{17}N_3O_2$) Yield: 48%; yellow crystals; m.p.: 176–178 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.14 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 7.05–7.07 (d, *J* = 7.6 Hz, 1H, Ar–H), 7.19–7.23 (m, 2H, Ar–H), 7.70–7.74 (t, 1H, *J* = 8.0 Hz, Ar–H), 7.87–7.95 (m, 2H, Ar–H), 8.54–8.52 (d, 1H, *J* = 8.4 Hz, Ar–H), 9.91 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 18.24 (CH_3), 20.95 (CH_3), 52.79 (CH_3), 115.19, 123.60, 127.68, 128.12, 128.19, 128.83, 130.83 (CH–Ar), 132.19, 134.03, 135.72, 136.88, 149.62 (C–Ar), 153.92 (C=N), 159.74 (C=N), 165.41 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3332 (NH), 1718 (CO), C=N (1645) cm^{-1}; MS: *m/z* = 308 ($[M+1]^+$, 23), 307 (M^+, 100), 306 ($[M-1]^+$, 8).

Methyl 4-[(3,4-dichlorophenyl)amino]quinazoline-2-carboxylate (4d, $C_{16}H_{11}Cl_2N_3O_2$) Yield: 50%; yellow crystals; m.p.: 162–163 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.96 (s, 3H, CH_3), 6.79–6.89 (m, 2H, Ar–H), 7.35–7.40 (m, 2H, Ar–H), 7.62–7.68 (m, 2H, Ar–H), 7.88 (s, 1H, Ar–H), 10.55 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 53.47 (CH_3), 119.15, 122.24, 125.43, 128.30, 130.16, 131.09, 131.64 (CH–Ar),132.26, 133.80, 134.67, 137.84, 145.54 (C–Ar),164.89 (C=N), 168.46 (C=N), 170.46 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3298 (NH), 1716 (CO), 1644 (CO) cm^{-1}; MS: *m/z* = 349 ($[M+1]^+$, 6), 348 (M^+, 100).

Methyl 4-[(4-chlorophenyl)amino]quinazoline-2-carboxylate (4e, $C_{16}H_{12}ClN_3O_2$) Yield: 51%; yellow crystals; m.p.: 176–177 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.88 (s, 3H, CH_3), 6.71–6.77 (m, 2H, Ar–H), 6.94–7.08 (m, 2H, Ar–H), 7.18–7.29 (m, 2H, Ar–H), 7.76–7.92 (m, 2H, Ar–H), 10.15 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 53.04 (CH_3), 115.54, 123.58, 123.92, 127.96, 128.61, 128.87, 129.17 (CH–Ar), 134.29, 138.54, 149.85 (C–Ar), 152.70 (C=N), 158.56 (C=N), 165.05 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3441 (NH), 1730 (CO), 1623 (C=N) cm^{-1}; MS: *m/z* = 314 ($[M+1]^+$, 38), 313 (M^+, 100), 312 ($[M-1]^+$, 59).

Methyl 4-(phenylamino)quinazoline-2-carboxylate (4f, $C_{16}H_{13}N_3O_2$) Yield: 53%; yellow crystals; m.p.: 104–105 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.90 (s, 3H, CH_3), 7.14–7.18 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.40–7.44 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.74–7.78 (m, 2H, Ar–H), 7.95–7.93 (m, 3H, Ar–H), 8.01–8.03 (d, 1H, *J* = 8.0 Hz, Ar–H), 8.65–8.67 (d, 1H, *J* = 8.0 Hz, Ar–H), 10.01 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 53.00 (CH_3), 115.57, 122.51, 123.60, 124.38, 128.46, 129.00, 129.09 (CH–Ar), 134.17, 139.49, 149.82 (C–Ar), 152.96 (C=N), 158.72 (C=N), 165.19 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3354 (NH), 1720 (CO), 1656 (C=N) cm^{-1}; MS: *m/z* = 279 (M^+, 89), 278 ($[M-1]^+$, 100).

General procedure for synthesis of 9a–9d

To a well stirred solution of 1 mmol of 2-(dicyanomethylene)indan-1,3-dione (CNIND, **8**) dissolved in 20 cm^3 dry ethyl acetate, a solution of 1 mmol of 2-amino-*N*′-arylbenzimidamides **1a**–**1d** in 15 cm^3 dry ethyl acetate was added portion wise at room temperature. The colour of the reaction mixture changed from yellow to red followed by formation of a precipitate. The reaction mixture was stirred at room temperature for 10–12 h. After completion of the reaction (the reaction was followed by TLC), the formed precipitate was collected by filtration, washed and recrystallized from EtOH to afford products **9a**–**9d** in 50–60% yield.

(*Z*)-2-[4-(*p*-Tolylimino)-3,4-dihydroquinazolin-2(1*H*)-ylidene]-1*H*-indene-1,3(2*H*)-dione (9a, $C_{24}H_{17}N_3O_2$) Yield: 60%; yellow powder; m.p.: > 360 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.37 (s, 3H, CH_3), 7.29–7.31 (d, 2H, *J* = 8.4 Hz, Ar–H), 7.52–7.56 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.59–7.64 (m, 3H, Ar–H), 7.75–7.77 (d, 2H, *J* = 8.4 Hz, Ar–H), 7.85–7.89 (t, 1H, *J* = 7.6 Hz, Ar–H), 8.53–8.55 (d, 2H, *J* = 8.4 Hz, Ar–H), 8.59–8.61 (d, 1H, *J* = 8.4 Hz, Ar–H), 10.27 (s, 1H, NH), 13.22 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.04 ($2CH_3$), 92.15 (HN–C–NH), 98.19 (OC–C–CO), 111.84, 118.67, 120.61, 122.60, 124.39, 125.55, 129.50, 132.99, 134.31, 135.54 (CH–Ar), 136.49, 138.60, 139.50, 154.10 (C–Ar), 157.13 (C=N), 175.10 (2 C=O) ppm; IR (KBr): $\bar{\nu}$ = 3259 (NH), 1685 (CO), 1658 (C=N), 1616 (C=C) cm^{-1}; MS: *m/z* = 379 (M^+, 100).

(*Z*)-2-[4-[(2,4-Dimethylphenyl)imino]-3,4-dihydroquinazolin-2(1*H*)-ylidene]-1*H*-indene-1,3(2*H*)-dione (9b, $C_{25}H_{19}N_3O_2$) Yield: 56%; yellow powder; m.p.: 310–312 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.30 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.11–7.13 (d, 1H, *J* = 8 Hz, Ar–H), 7.19 (s, 1H, Ar–H), 7.50–7.63 (m, 6H, Ar–H), 7.74–7.76 (d, 2H, *J* = 8 Hz, Ar–H), 7.85–7.89 (t, 1H, *J* = 8.0 Hz, Ar–H), 8.44–8.46 (d, 1H, *J* = 8.0 Hz, Ar–H), 10.33 (s, 1H, NH), 13.33 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 18.91 (CH_3), 21.14 (CH_3), 91.98 (HN–C–NH), 98.90 (OC–C–CO), 111.18, 118.51, 120.43, 125.65, 126.89, 127.11, 131.49, 132.83, 134.69 (CH–Ar), 135.62, 139.37, 154.46 (C–Ar), 156.20 (C=N), 174.15 (2 C=O) ppm; IR (KBr): $\bar{\nu}$ = 3235 (NH), 1660 (CO), 1654 (C=N), 1615 (C=C) cm^{-1}; MS: *m/z* = 393 (M^+, 42).

(*Z*)-2-[4-[(2,5-Dimethylphenyl)imino]-3,4-dihydroquinazolin-2(1*H*)-ylidene]-1*H*-indene-1,3(2*H*)-dione (9c, $C_{25}H_{19}N_3O_2$) Yield: 55%; yellow powder; m.p.: > 360 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 2.29$ (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 7.09–7.11 (d, 2H, $J = 8$ Hz, Ar–H), 7.24–7.26 (d, 1H, $J = 8$ Hz, Ar–H), 7.52–7.64 (m, 5H, Ar–H), 7.75–7.77 (d, 2H, $J = 8$ Hz, Ar–H), 7.86–7.90 (t, 1H, $J = 7.6$ Hz, Ar–H), 8.27–8.29 (d, 2H, $J = 8$ Hz, Ar–H), 8.44–8.46 (d, 1H, $J = 8$ Hz, Ar–H), 10.31 (s, 1H, NH), 13.33 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 18.20$ (CH_3), 21.03 (CH_3), 91.90 (HN–C–NH), 98.09 (OC–C–CO), 111.68, 118.70, 120.43, 123.61, 125.50, 126.90, 130.73, 132.80 (CH–Ar), 135.60, 139.43, 154.54 (C–Ar), 157.20 (C=N), 172.19 (2 C=O) ppm; IR (KBr): $\bar{\nu} = 3255$ (NH), 1687 (CO), 1656 (C=N), 1613 (C=C) cm^{-1}; MS: $m/z = 393$ (M^+, 73).

(*Z*)-2-[4-[(3,4-Dichlorophenyl)imino]-3,4-dihydroquinazolin-2(1*H*)-ylidene]-1*H*-indene-1,3(2*H*)-dione (9d, $C_{23}H_{13}Cl_2N_3O_2$) Yield: 52%; yellow powder; m.p.: 358–364 °C (EtOH); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 7.63$–7.99 (m, 9H, Ar–H), 8.57–8.59 (d, 1H, $J = 8.8$ Hz, Ar–H), 8.62–8.66 (t, 1H, $J = 6.4$ Hz, Ar–H), 10.35 (s, 1H, NH), 13.28 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 95.15$ (HN–C–NH), 101.93 (OC–C–CO), 113.12, 118.70, 120.74, 123.95, 130.76, 132.82, 134.35 (CH–Ar), 137.60, 139.55, 155.00 (C–Ar), 162.64 (C=N), 172.90 (2 C=O) ppm; IR (KBr): $\bar{\nu} = 3265$ (NH), 1700 (CO), 1658 (C=N), 1614 (C=C) cm^{-1}; MS: $m/z = 433$ ($[M+1]^+$,10), 434 (M^+, 10).

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