Synthesis of furyl-, furylvinyl-, thienyl-, pyrrolinylquinazolines and isoindolo[2,1-*a*]quinazolines

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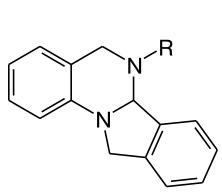
A method for the synthesis of hydrogenated furyl-, furylvinyl-, thienyl-, and pyrrolinyl-substituted quinazolin-4-ones was developed. A possibility of the reaction of 2-furylquinazolines with maleic anhydride was demonstrated. A number of quinazolines obtained were subjected to a primary bioscreening on inhibition of acetylcholinesterase.

Key words: anthranilamide, 2-furylquinazolin-4-ones, isoindolo[2,1-*a*]quinazolines, intramolecular [2+4] cycloaddition, Diels—Alder reaction, inhibition of acetylcholinesterase.

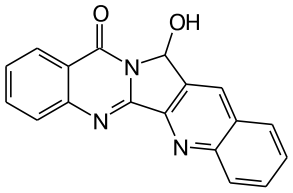
Fused 3a,6-epoxyisoindolone are of interest as available starting compounds for the construction of polycyclic structures *via* the epoxy bridge cleavage upon treatment with both electrophilic and nucleophilic agents.[1—7]

During the last years, we have been developing a general strategy for the synthesis of epoxyisoindoles fused with a heterocyclic ring based on the [2+4] cycloaddition reaction of α-furyl-substituted azaheterocycles with anhydrides and halides of α,β-unsaturated acids. Earlier, we have suggested a preparative synthesis of epoxyisoindoles fused with the piperidine, quinoline, isoquinoline, oxazine, thiazine, oxazole, and thiazole fragments.[2,3,6—12] In the present work, we report a method for the synthesis of 2-heteroarylquinazolin-4-ones, a possible precursors of isoindoloquinazolines.

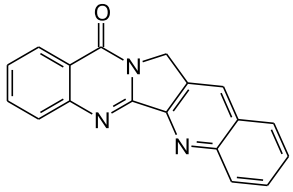
The carbon skeletons of azaisoindolo[1,2-*b*]quinazoline and indolo[2,1-*b*]quinazoline constitute a framework of alkaloids *Luotonin A*, *Luotonin B*, *and Tryptanthrine*.[13—24] Isoindolo[2,1-*a*]quinazolines structurally similar to alkaloids exhibit a wide range of biological activity: inhibit the TNF-α protein, possess sedative, analgesic, and hypotensive activity.[25—28] In the framework of a general approach to the synthesis of fused epoxyisoindoles,[2,3,6—12] the preparation of heterocycles indicated above required a convenient method for the synthesis of 2-furyl-substituted quinazolines to be developed.



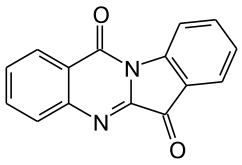
Isoindolo[2,1-*a*]quinazoline



Luotonin **A**



Luotonin **B**



Tryptanthrine

The condensation of anthranilic acid amides with aldehydes described in the works[29—33] is the most convenient approach to 2-substituted quinazolines. However, furyl-, thienyl-, and pyrrolylcarboxaldehydes and furyl ketones were not virtually used in these transformations. One

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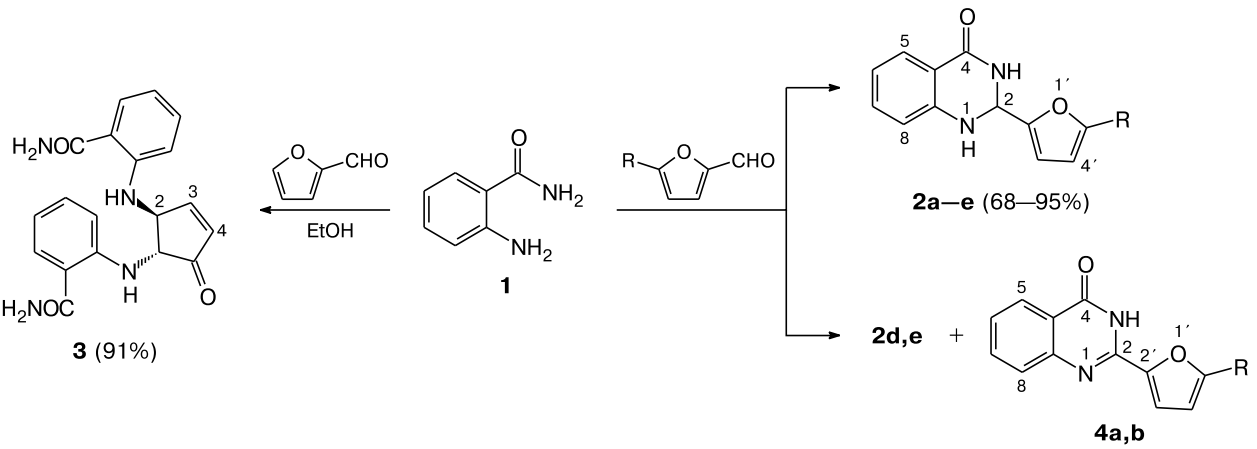
Scheme 1



R = H (**2a**), Me (**2b**), NO_2 (**2c**), Br (**2d**, **4a**), I (**2e**, **4b**)

of the goals of the present work is the studies of these carbonyl compounds in the synthesis of 2-hetarylquinazolines and optimization of this process.

The condensation of anthranilamide **1** with 5-methyl-, 5-nitro-, 5-bromo-, and 5-iodofurancarboxaldehydes in EtOH at room temperature gave 2-furylquinazolin-4-ones **2** in high yields (Scheme 1).

The reaction of anthranilamide **1** with furfural in EtOH led to [(5-oxocyclopent-3-en-1,2-diyl)di(imino)]dibenzamide **3** in 91% yield instead of the target quinazoline **2a** (see Scheme 1). Apparently, after the initial formation of azomethine, a nucleophilic attack by the nitrogen atom of the second anthranilamide molecule at α-position of the furan ring with subsequent recyclization takes place.

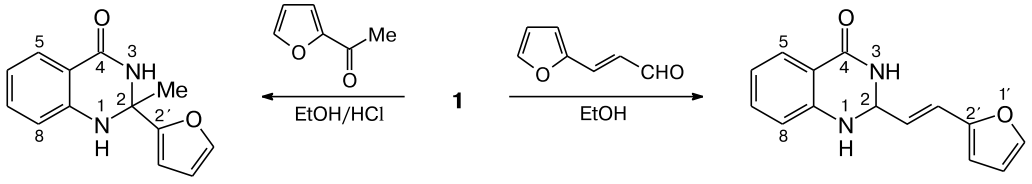
The structure of compound **3** was confirmed by analogy with the works[34—37] and based on 2D COSY, TOCSY, NOESY, HSQC, and HMBC NMR spectra on ^{1}H, ^{13}C, and ^{15}N nuclei. The spatial *trans*-arrangement of substituents in cyclopentenone **3** was determined using the 2D NOESY NMR spectra, which exhibit characteristic strong cross-peaks between the spatially close protons (C(1)NHAr—H(2); C(2)NHAr—H(1); C(2)NHAr—H(3)). The NOE cross-peaks between H(1) and H(2) atoms turned out to be weak because of their *trans*-position ($^{3}J_{1,2}$ = 3.2 Hz).

The use in this reaction of CH_2Cl_2 instead of EtOH made it possible to obtain quinazolin-4-one (**2a**) in 71% yield. In contrast to the data reported in the literature,[29—33] compound **2a** was formed without assistance of a catalyst at room temperature. The condensation of compound **1** with 5-halo-substituted furancarboxaldehydes was accompanied by a gradual oxidation of the tetrahydropyrimidine fragment, that led to the formation of the mixtures of **2d** with **4a** and **2e** with **4b** in about an equal ratios. Under argon, the yields of quinazolines **2d**,**e** were 83 and 93%, respectively.

The condensation of anthranilamide **1** with 2-acetylfuran in the presence of concentrated HCl gave 2-(2-furyl)-2-methylquinazolin-4-one **5** (Scheme 2). All the physicochemical characteristics of the latter are similar to those described earlier[32] (no NMR or mass spectral data were reported in the published work). Furylacrolein reacted with anthranilamide **1** to give 2-furylvinyl substituted quinazolinone **6** with *trans*-arrangement of substituents at the double bond, that follows from the spin-spin coupling constant value of the CH=CH protons (J = 15.8 Hz).

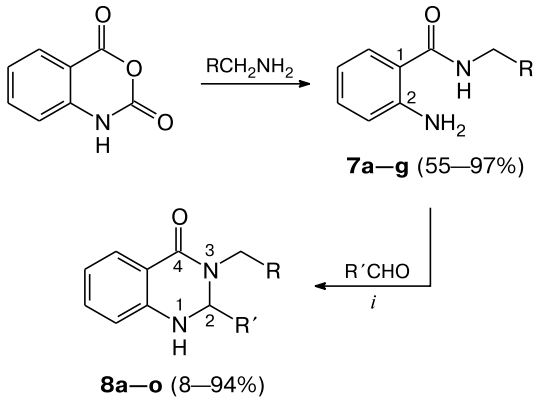
Secondary anthranilamides **7a**—**g** were used for the synthesis of quinazolines substituted at N(3) nitrogen atom, which, in turn, were synthesized based on isatoic anhydride and primary amines according to the described

Scheme 2



procedure.[38] Anthranilamides **7a—g** were treated with furfural, 5-methyl- and 5-phenylfurfural, furylacrolein, thienyl-, benzothienyl-, pyrrol-, and *N*-tosylpyrrol-2-carboxaldehydes at room temperature in the presence of an acid catalyst to be converted to 3-substituted 2-furyl-, 2-thienyl- and 2-pyrrolyl substituted quinazolines **8a—o** (Scheme 3).

Scheme 3



i. MeCN, 25 °C, TsOH.

R = 2-furyl (**7a**, **8a**), Ph (**7b**, **8b**,**h**,**j—o**), Me (**7c**, **8c**), vinyl (**7d**, **8d**,**i**), Bn (**7e**, **8e**), 3,4-$(MeO)_2C_6H_3CH_2$ (**7f**, **8f**), 2-thienyl (**7g**, **8g**)

R′ = 2-furyl (**8a—g**), 5-Me-2-furyl (**8h**,**i**), 5-Ph-2-furyl (**8j**), (*E*)-2-(2-furyl)vinyl (**8k**), 2-thienyl (**8l**), 2-benzo[*b*]thienyl (**8m**), 2-pyrrolinyl (**8n**), *N*-Ts-2-pyrrolinyl (**8o**)

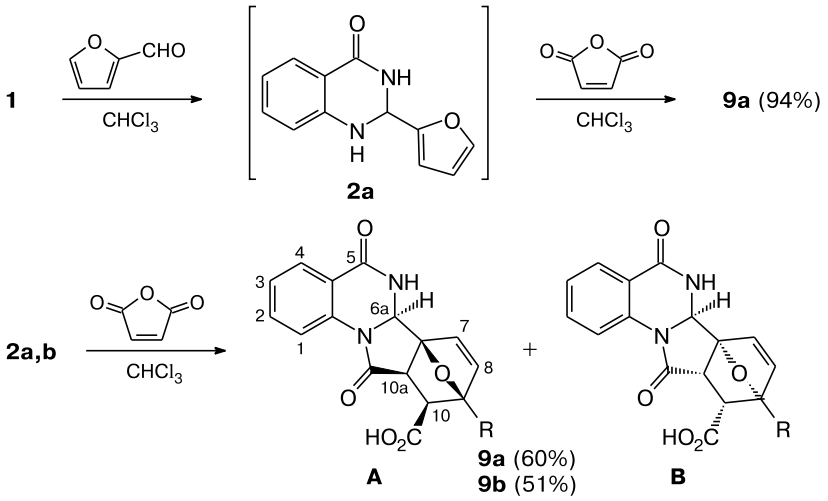
The reaction of amide **7b** with furfural has been chosen as a model for the selection of optimal conditions. The most efficient catalyst was TsOH in MeCN: the yield of quinazoline **8b** under these conditions was as high as 79%. In the presence of other catalysts (AcOH or concentrated HCl in MeCN or EtOH), the yield of the target **8b** was not higher than 30%.

Taking synthesis of quinazoline **8b** as an example, we also showed a possibility of a *one-pot* approach (see Experimental), in this case the yield of the target product did not considerably change as compared to the two-step version. The physicochemical characteristics of compounds **8a—c** are completely the same as those data reported in the work.[39] The ^{1}H NMR spectrum of 3-substituted quinazolines **8d—o**, apart from the characteristic signals for the NH and H(2) protons in the region of δ_H 4.42—4.71 and δ_H 4.99—5.98, respectively, also exhibit signals for the chemically nonequivalent protons of the CH_2 group as an AB-system with the spin-spin coupling constant $^2J_{A,B}$ = 15.1—15.8 Hz (except **8e**,**f**). In the ^{13}C NMR spectra, the most characteristic is the chemical shift for C(2) carbon atom in the region of δ_C 64.4—67.2.

Some of the synthesized quinazolines were subjected to a preliminary bioscreening *in vitro* for the inhibition of acetylcholinesterase (AChE).[40] It was found that the inhibiting activity of quinazolines **2—6**, **8** and cyclopentanone **3** ranged from low to moderate (%): 33 (**2a**), 14 (**2b**), 24 (**2d**), 7 (**2e**), 22 (**3**), 18 (**4b**), 9 (**5**), 33 (**6**), 15 (**8b**), 34 (**8d**), 12 (**8e**), 18 (**8f**), 14 (**8g**), 30 (**8h**), 12 (**8j**), 22 (**8k**), 5 (**8l**), 18 (**8m**), 19 (**8o**).

Furyl-substituted quinazolines **2a,b** with maleic anhydride in $CHCl_3$ at 20 °C undergo an *exo*-[2+4] cycloaddition to form a mixture of isomers of epoxyisoindolo[2,1-*a*]-quinazoline-10-carboxylic acid **9a,b** differing in the arrangement of the epoxy bridge and H(6a) proton (the ratio of isomers is given in Experimental). The *one-pot* version of this reaction without isolation of 2-furylquinazoline **2a** gave a higher yield of epoxyisoindoloquinazolinecarboxylic acid **9a** (94%), with the ratio of isomers in the mixture remaining the same (Scheme 4). Carrying out the reaction in refluxing $CHCl_3$ or 1,2-dichloroethane almost have no

Scheme 4



R = H (**9a**), Me (**9b**)

effect on the ratio of isomers **A**/**B** (55 : 45). The stereochemistry of the isomeric adducts **9a**,**b** was established based on the data in the work.[39] In the ^{1}H NMR spectra of these adducts, the signal for H(1) proton in *trans*-isomers **A** is ~0.2 ppm more downfield shifted as compared to the corresponding proton in *cis*-isomers **B**.

In conclusion, we synthesized the libraries of 2-heteroaryl-substituted quinazolines, carried out their bioscreening with regard to the inhibition of acetylcholinesterase, and showed a principal possibility of the transformation of 2-furylquinazolines to epoxyisoindoloquinazolines.

Experimental

IR spectra were recorded on a Infralyum FT-801 Fourier-transform spectrometer in KBr pellets. ^{1}H NMR spectra were recorded on Bruker AMX-400 (400 MHz) or JEOL JNM-ECA600 (600 MHz) spectrometers for ~3% solutions in $CDCl_3$ or DMSO-d_6, using residual signals of the solvent as a reference (δ 7.26 for $CHCl_3$ and 2.49 for DMSO-d_6). ^{13}C NMR spectra were recorded on Bruker Avance 600 (150 MHz) or Bruker AMX-400 (100 MHz) spectrometers, the central signals of the $CDCl_3$ triplet (d 77.4) or the DMSO-d_6 multiplet (δ 40.0) were used as a reference. Mass spectra were obtained on a Thermo Trace DSQ mass spectrometer (electron ionization 70 eV, temperature of the source of ions 200 °C, direct injection) or a Thermo DSQ II — Focus GC GC-MS spectrometer (electron ionization 70 eV, temperature of the source of ions 200 °C, carrier gas helium, a RTX-5MS column). Elemental analysis was carried out on a EuroVector EA 3000 CHNS-analyzer. Melting points of the synthesized compounds were determined on SMP 10 and SMP 30 instruments (were not corrected). Bioscreening data were obtained for solutions of quinazolines in DMSO (10^{-5} mol L^{-1})[40] on Tecan Infinite M1000 Pro multifunctional plate analyzer. Sorbfil PTSKh-AF-A-UV 254 plates were used for TLC, visualization was carried out in iodine vapors. Ratios of products in the isomeric mixtures (for **9a**,**b**) were determined based on the ^{1}H NMR spectra from the ratios of integral intensities of the signals for similar protons.

Commercially available reactants from Acros Organics and Alfa Aesar were used without additional purification, solvents were purified by distillation. Synthesis, spectral and physicochemical characteristics, as well as elemental analysis data for compounds **2a**, **5**, and **8a**—**c** were published earlier.[32,39,41,42]

2-(5-R-2-Furyl)-2,3-dihydroquinazolin-4(1*H*)-ones 2b—e and 2-(5-R-2-furyl)quinazolin-4(3*H*)-ones 4a,b (general procedure). ***A.*** A corresponding aldehyde (0.05 mol) was added to a solution of anthranilamide **1** (6.81 g, 0.05 mol) in EtOH (50 mL) under argon (for **2d,e**). The reaction mixture was stirred at room temperature for 72 h (for **2b**), 0.5 h for (**2c**), 48 h (for **2d**), or 5 days (for **2e**). The crystals formed were filtered, washed with Et_2O (20 mL), and purified by recrystallization.

B. 5-Halofurfural (11.4 mmol) was added to a solution of anthranilamide **1** (1.55 g, 11.4 mmol) in EtOH (30 mL). The reaction mixture was stirred for 48 h (TLC monitoring). The crystals formed were filtered off and washed with Et_2O (20 mL). The resulting mixture was subjected to chromatography (Al_2O_3 (4×25 cm), eluent hexane, then EtOAc—hexane 1 : 10, 1 : 5, 1 : 1) to obtain quinazoline **2d** (0.94 g, 28%), quinazoline **4a** (1.26 g, 38%) and quinazoline **2e** (1.71 g, 44%), quinazoline **4b** (1.46 g, 38%), respectively. The mixed probe of the samples obtained by methods ***A*** and ***B*** showed no temperature depression.

2-(5-Methyl-2-furyl)-2,3-dihydroquinazolin-4(1*H*)-one (2b). The yield was 8.4 g (68%). A colorless powder, m.p. 177—178 °C (EtOH—DMF), R_f 0.64 (EtOAc—hexane, 4 : 1). IR, ν/cm^{-1}: 3288 (N—H), 1646 (NC=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.27 (d, 3 H, Me, J = 0.8 Hz); 4.56 (br.s, 1 H, NH); 5.85 (t, 1 H, H(2), J = 1.8 Hz); 5.91 (dq, 1 H, H_{Fur}(4′), J = 0.8 Hz, J = 3.2 Hz); 6.09 (br.s, 1 H, NH); 6.29 (d, 1 H, H_{Fur}(3′), J = 3.2 Hz); 6.68 (dd, 1 H, H(8), J = 0.8 Hz, J = 8.0 Hz); 6.87 (ddd, 1 H, H(6), J = 0.8 Hz, J = 7.5 Hz, J = 8.0 Hz); 7.31 (ddd, 1 H, H(7), J = 1.4 Hz, J = 7.5 Hz, J = 8.0 Hz); 7.90 (dd, 1 H, H(5), J = 1.4 Hz, J = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 13.3 (Me); 60.3 (C(2)); 106.3, 108.1, 114.5, 114.9, 117.1, 127.2, 133.2 (Ar); 147.2, 151.4, 152.2 (C(8a), C_{Fur}(2′), C_{Fur}(5′)); 163.3 (C=O). MS, m/z (I_{rel} (%)): 228 $[M]^+$ (83), 213 (60), 185 (68), 147 (75), 120 (100), 109 (52), 92 (66), 81 (36), 65 (71), 59 (52), 55 (26), 43 (47). Found (%): C, 68.59; H, 5.11; N, 12.56. $C_{13}H_{12}N_2O_2$. Calculated (%): C, 68.41; H, 5.30; N, 12.27.

2-(2-Furyl-5-nitro)-2,3-dihydroquinazolin-4(1*H*)-one (2c). The yield was 12.4 g (95%). A powder, m.p. 168—169 °C (EtOH—DMF), R_f 0.50 (EtOAc—hexane, 4 : 1). IR, ν/cm^{-1}: 3294 (N—H), 1668 (NC=O). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 7.30 (br.d, 1 H, H(8), J = 7.5 Hz); 7.40 (br.t, 1 H, H(6), J = 7.5 Hz); 7.52 (d, 1 H, H_{Fur}(3′), J = 3.7 Hz); 7.56 (dt, 1 H, H(7), J = 1.2 Hz, J = 7.5 Hz); 7.61 (br.s, 1 H, NH); 7.84 (d, 1 H, H_{Fur}(4′), J = 3.7 Hz); 7.88 (dd, 1 H, H(5), J = 1.2 Hz, J = 7.5 Hz); 8.11 (br.s, 1 H, NH); 8.58 (s, 1 H, H(2)). MS, m/z (I_{rel} (%)): 259 $[M]^+$ (18), 242 (100), 213 (33), 185 (31), 168 (20), 147 (54), 140 (50), 130 (58), 119 (33), 105 (76), 92 (34), 79 (26), 65 (27), 51 (41), 43 (36). Found (%): C, 55.55; H, 3.68; N, 16.13. $C_{12}H_9N_3O_4$. Calculated (%): C, 55.60; H, 3.50; N, 16.21.

2-(5-Bromo-2-furyl)-2,3-dihydroquinazolin-4(1*H*)-one (2d). The yield was 12.2 g (83%) by method ***A*** and 0.94 g (28%) by method ***B***. Light yellow plates, m.p. 153—154 °C (EtOAc—EtOH), R_f 0.65 (EtOAc—hexane, 2 : 1). IR, ν/cm^{-1}: 3266 (N—H), 1651 (NC=O). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 5.72 (t, 1 H, H(2), J = 2.8 Hz); 6.26 (d, 1 H, H_{Fur}(3′), J = 3.4 Hz); 6.45 (d, 1 H, H_{Fur}(4′), J = 3.4 Hz); 6.66 (dt, 1 H, H(6), J = 1.4 Hz, J = 8.2 Hz); 6.72 (d, 1 H, H(8), J = 7.6 Hz); 7.22 (ddd, 1 H, H(7), J = 1.4 Hz, J = 7.6 Hz, J = 8.2 Hz); 7.25 (br.s, 1 H, NH); 7.57 (dd, 1 H, H(5), J = 1.4 Hz, J = 8.2 Hz); 8.11 (br.d, 1 H, NH, J = 2.8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 60.1 (C(2)); 110.2, 112.3, 114.6, 114.9, 117.5, 120.9, 127.3, 133.3 (Ar); 146.8, 156.6 (C(8a), C_{Fur}(2′)); 163.1 (C=O). MS, m/z (I_{rel} (%)): 294 $[M]^+$ (for ^{81}Br) (94), 292 (95), 213 (66), 185 (24), 174 (19), 148 (17), 147 (99), 130 (21), 121 (25), 120 (62), 119 (100), 102 (18), 93 (14), 92 (83), 66 (23), 65 (70), 52 (20), 51 (38), 43 (28). Found (%): C, 48.98; H, 3.20; N, 9.71. $C_{12}H_9BrN_2O_2$. Calculated (%): C, 49.17; H, 3.09; N, 9.56.

2-(2-Furyl-5-iodo)-2,3-dihydroquinazolin-4(1*H*)-one (2e). The yield was 15.8 g (93%) by method ***A*** and 1.71 g (44%) by method ***B***. Brick-red fine needles, m.p. 172—173 °C (EtOAc—EtOH), R_f 0.65 (EtOAc—hexane, 1 : 1). IR, ν/cm^{-1}: 3270 (N—H), 1653 (NC=O). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 5.71 (d, 1 H, H(2), J = 3.4 Hz); 6.15 (dd, 1 H, H_{Fur}(3′), J = 0.6 Hz, J = 3.4 Hz); 6.52 (d, 1 H, H_{Fur}(4′), J = 3.4 Hz); 6.63 (dt, 1 H, H(6), J = 0.9 Hz, J = 7.7 Hz); 6.71 (br.d, 1 H, H(8), J = 8.2 Hz); 7.18 (br.s, 1 H, NH); 7.19 (ddd, 1 H, H(7), J = 1.6 Hz, J = 7.7 Hz, J = 8.2 Hz); 7.57 (dd, 1 H, H(5), J = 1.6 Hz, J = 7.7 Hz); 8.36 (d, 1 H, NH,

J = 3.4 Hz). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 60.0 (C(2)); 91.4 (C_{Fur}(5′)); 110.3, 114.5, 114.9, 117.4, 120.4, 127.3, 133.3 (Ar); 146.9, 159.6 (C(8a), C_{Fur}(2′)); 163.1 (C=O). MS, m/z (I_{rel} (%)): 340 $[M]^+$ (50), 213 (100), 194 (19), 183 (15), 156 (15), 147 (30), 130 (33), 120 (75), 77 (19), 64 (29), 59 (25), 43 (43). Found (%): C, 42.45; H, 2.51; N, 8.06. $C_{12}H_9IN_2O_2$. Calculated (%): C, 42.38; H, 2.67; N, 8.24.

2-(5-Bromo-2-furyl)quinazolin-4(3*H*)-one (4a). The yield was 1.26 g (38%) by method ***B***. Yellow thin thread-like crystals, m.p. 259—260 °C (EtOAc—EtOH), R_f 0.81 (EtOAc—hexane, 1 : 1). IR, ν/cm^{-1}: 1658 (NC=O). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 6.81 (d, 1 H, H_{Fur}(3′), J = 3.4 Hz); 7.45 (t, 1 H, H(6), J = 7.6 Hz); 7.62 (d, 1 H, H_{Fur}(4′), J = 3.4 Hz); 7.68 (d, 1 H, H(8), J = 7.6 Hz); 7.76 (t, 1 H, H(7), J = 7.6 Hz); 8.08 (d, 1 H, H(5), J = 7.6 Hz); 8.24 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 292 $[M]^+$ (for ^{81}Br) (100), 290 (99), 211 (25), 183 (21), 156 (29), 145 (16), 102 (16), 90 (39), 43 (35), 39 (18). Found (%): C, 49.50; H, 2.17; N, 9.73. $C_{12}H_7BrN_2O_2$. Calculated (%): C, 49.51; H, 2.42; N, 9.62.

2-(2-Furyl-5-iodo)quinazolin-4(3*H*)-one (4b). The yield was 1.46 g (38%) by method ***B***. Light yellow thin thread-like crystals, m.p. 265—268 °C (EtOAc—EtOH), R_f 0.91 (EtOAc—hexane, 1 : 1). IR, ν/cm^{-1}: 1656 (NC=O). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 6.93 (d, 1 H, H_{Fur}(3′), J = 3.6 Hz); 7.47 (ddd, 1 H, H(6), J = 0.8 Hz, J = 7.6 Hz, J = 7.9 Hz); 7.54 (d, 1 H, H_{Fur}(4′), J = 3.6 Hz); 7.70 (dd, 1 H, H(8), J = 0.8 Hz, J = 8.2 Hz); 7.79 (ddd, 1 H, H(7), J = 1.5 Hz, J = 7.6 Hz, J = 8.2 Hz); 8.11 (dd, 1 H, H(5), J = 1.5 Hz, J = 7.9 Hz); 8.27 (s, 1 H, NH). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 98.1 (C_{Fur}(5′)); 116.8, 121.2, 122.6, 125.9, 126.5, 127.2, 134.6 (Ar); 142.9, 148.4, 150.8 (C(2), C(8a), C_{Fur}(2′)); 161.4 (C=O). MS, m/z (I_{rel} (%)): 338 $[M]^+$ (100), 211 (42), 183 (33), 130 (15), 102 (24), 90 (22), 64 (23), 59 (17), 43 (40). Found (%): C, 42.44; H, 2.20; N, 8.32. $C_{12}H_7IN_2O_2$. Calculated (%): C, 42.63; H, 2.09; N, 8.29.

2,2′-[[(1*RS*,2*SR*)-5-Oxocyclopent-3-en-1,2-diyl]di(imino)]-dibenzamide (3). Furfural (4.14 mL, 0.05 mol) was added to a solution of anthranilamide **1** (13.62 g, 0.10 mol) in EtOH (50 mL), and the mixture was stirred at room temperature for 48 h (TLC monitoring). The crystals formed were filtered and washed with Et_2O (20 mL) to obtain cyclopentenone **3** (14.75 g (84%) as a colorless powder. M.p. 182—183 °C (EtOAc—EtOH), R_f 0.45 (EtOAc). The use of anhydrous EtOH as the solvent increased the yield of compound **3** to 91%. IR, ν/cm^{-1}: 1613, 1642, 1666, 1728 (C=O), 3179, 3337, 3395 (N—H). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 4.24 (dd, 1 H, H(1), J = 3.2 Hz, J = 6.5 Hz); 4.75 (br.d, 1 H, H(2), J = 7.8 Hz); 6.45 (dd, 1 H, H(4), J = 1.3 Hz, J = 6.5 Hz); 6.55, 6.59 (both t, 1 H each, $H_{C_6H_4}$(5′), J = 7.8 Hz); 6.68, 6.86 (both d, 1 H each, $H_{C_6H_4}$(3′), J = 7.8 Hz); 7.11, 7.19 (both t, 1 H each, $H_{C_6H_4}$(4′), J = 7.8 Hz); 7.23 (br.s, 2 H, NH_2); 7.60, 7.63 (both dd, 1 H each, $H_{C_6H_4}$(6′), J = 1.3 Hz, J = 7.8 Hz); 7.69 (dd, 1 H, H(3), J = 1.3 Hz, J = 6.5 Hz); 7.86 (br.s, 2 H, NH_2); 8.65 (d, 1 H, NH, J = 6.5 Hz); 8.68 (d, 1 H, NH, J = 7.8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 59.4 (C(2)); 64.9 (C(1)); 112.1, 112.4 ($C_{C_6H_4}$(3′)); 114.8, 114.9 ($C_{C_6H_4}$(1′)); 115.1, 115.2 ($C_{C_6H_4}$(5′)); 129.0, 129.2 ($C_{C_6H_4}$(6′)); 132.2 (C(4)); 132.3, 132.6 ($C_{C_6H_4}$(4′)); 148.4, 149.0 ($C_{C_6H_4}$(2′)); 161.0 (C(3)); 171.4, 171.5 ($CONH_2$); 203.4 (C=O). MS, m/z (I_{rel} (%)): 215 $[M - 135]^+$ (21), 197 (8), 185 (10), 169 (12), 136 (100), 119 (82), 92 (66), 65 (48), 43 (29). Found (%): C, 65.37; H, 5.36; N, 16.10. $C_{19}H_{18}N_4O_3$. Calculated (%): C, 65.13; H, 5.18; N, 15.99.

2-(2-Furyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (5). 2-Acetylfuran (8.1 g, 0.074 mol) and concentrated HCl (1 mL) was added to a solution of anthranilamide **1** (10.0 g, 0.074 mol) in EtOH (100 mL), and the mixture was stirred at room temperature for 48 h (TLC monitoring). The crystals formed were filtered, washed with Et_2O (20 mL), and recrystallized from a mixture of EtOAc—hexane to obtain quinazoline **5** (13.25 g, 73%) as a colorless powder. Physicochemical characteristics and the IR spectroscopy data of quinazoline **5** similar to those described in the work.[32] M.p. 226—228 °C (*cf.* Ref. 32: m.p. 221—225 °C), R_f 0.64 (EtOAc—hexane, 3 : 1). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 1.70 (s, 3 H, Me); 6.11 (br.d, 1 H, H_{Fur}(3′), J = 3.1 Hz); 6.29 (dd, 1 H, H_{Fur}(4′), J = 1.9 Hz, J = 3.1 Hz); 6.63 (t, 1 H, H(6), J = 7.6 Hz); 6.68 (d, 1 H, H(8), J = 8.1 Hz); 7.21 (ddd, 1 H, H(7), J = 1.8 Hz, J = 7.6 Hz, J = 8.1 Hz); 7.31 (br.s, 1 H, NH); 7.53 (br.d, 1 H, H_{Fur}(5′), J = 1.9 Hz); 7.56 (dd, 1 H, H(5), J = 1.8 Hz, J = 7.6 Hz); 8.48 (br.s, 1 H, NH). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 27.2 (Me); 66.5 (C(2)); 105.8, 110.0, 114.0, 114.3, 116.9, 127.1, 133.2 (Ar); 142.2 (C_{Fur}(5′)); 146.8, 157.9 (C(8a), C_{Fur}(2′)); 163.5 (C=O). MS, m/z (I_{rel} (%)): 228 $[M]^+$ (34), 213 (100), 184 (18), 161 (11), 145 (10), 120 (46), 110 (13), 92 (39), 65 (41), 59 (10), 43 (21).

2-[(*E*)-2-(2-Furyl)vinyl]-2,3-dihydroquinazolin-4(1*H*)-one (6). Furylacrolein (0.89 g, 7.0 mmol) was added to a solution of anthranilamide **1** (1.0 g, 7.4 mmol) in EtOH (30 mL), and the mixture was stirred at room temperature for 1 month (TLC monitoring). The crystals formed were filtered and washed with Et_2O (20 mL) to obtain quinazoline **6** (0.77 g, 43%). Beige fine plates, m.p. 168—169 °C (EtOH), R_f 0.56 (EtOAc—hexane, 2 : 1). IR, ν/cm^{-1}: 1638 (NC=O), 3253 (N—H). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 5.23 (br.d, 1 H, H(2), J = 6.2 Hz); 6.09 (dd, 1 H, C(2)C<u>H</u>=CH, J = 6.2 Hz, J = 15.8 Hz); 6.45 (dd, 1 H, H_{Fur}(4′), J = 1.9 Hz, J = 3.4 Hz); 6.47 (d, 1 H, H_{Fur}(3′), J = 3.4 Hz); 6.49 (d, 1 H, C(2)CH=C<u>H</u>, J = 15.8 Hz); 6.64 (br.t, 1 H, H(6), J = 7.6 Hz); 6.70 (d, 1 H, H(8), J = 7.6 Hz); 6.86 (s, 1 H, NH); 7.21 (dt, 1 H, H(7), J = 1.4 Hz, J = 7.6 Hz); 7.57 (dd, 1 H, H(5), J = 1.4 Hz, J = 7.6 Hz); 7.59 (d, 1 H, H_{Fur}(5′), J = 1.7 Hz); 8.13 (s, 1 H, NH). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 65.0 (C(2)); 109.6, 111.7, 114.6, 114.9, 117.2, 119.9, 126.7, 127.3, 133.2 (Ar, C(2)C<u>H</u>=CH, C(2)CH=C<u>H</u>); 143.1 (C_{Fur}(5′)); 147.6, 151.1 (C(8a), C_{Fur}(2′)); 163.4 (C=O). MS, m/z (I_{rel} (%)): 240 $[M]^+$ (50), 211 (22), 197 (14), 184 (17), 160 (20), 147 (36), 130 (17), 120 (100), 92 (50), 81 (23), 65 (36), 59 (29), 52 (17), 51 (25), 43 (55). Found (%): C, 69.87; H, 4.89; N, 11.48. $C_{14}H_{12}N_2O_2$. Calculated (%): C, 69.99; H, 5.03; N, 11.66.

***N*-Alkyl-2-aminobenzamides 7a—g (general procedure).** A corresponding amine (20.2 mmol) was added to a solution of isatoic anhydride (3.0 g, 18.4 mmol) in anhydrous MeCN (60 mL), and the mixture was stirred for 2 h at room temperature, then 4 h at 50 °C. The solvent was evaporated to obtain amides **7a** (58%), **7b** (86%), **7c** (97%), **7d** (73%), **7e** (80%), **7f** (81%), and **7g** (55%) as colorless crystals. Physicochemical characteristics and spectral data of amides **7a**—**e** are identical to those described in the work.[38]

2-Amino-*N*-[2-(3,4-dimethoxyphenyl)ethyl]benzamide (7f). The yield was 4.47 g (81%). A colorless powder, m.p. 103—104 °C (hexane—EtOAc), R_f 0.56 (EtOAc—hexane, 1 : 1.5). IR, ν/cm^{-1}: 1636, 1517 (NC=O), 3328, 3416 (N—H). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.90 (t, 2 H, $NHCH_2C\underline{H}_2$, J = 6.9 Hz); 3.68 (q, 2 H, $NHC\underline{H}_2CH_2$, J = 6.9 Hz); 3.88, 3.90 (both s, 3 H each, OMe); 6.13 (br.s, 1 H, NH); 6.69 (t, 1 H, H(5), J = 7.3 Hz); 6.78—6.87 (m, 3 H, Ar); 7.21—7.26 (m, 2 H, Ar); 7.29 (d, 1 H, Ar, J = 2.3 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 35.3 ($NCH_2\underline{C}H_2$); 41.0 ($N\underline{C}H_2CH_2$); 55.9, 56.0 (both OMe); 111.6, 112.1, 116.3, 116.7,

117.4, 120.8, 127.1, 131.6, 132.3, 147.8, 148.7, 149.1 (Ar); 169.4 (NC=O). MS, *m/z* (I_{rel} (%)): 300 $[M]^+$ (6), 164 (46), 151 (56), 120 (100), 119 (24), 92 (42), 65 (24). Found (%): C, 68.10; H, 6.82; N, 9.12. $C_{17}H_{20}N_2O_3$. Calculated (%): C, 67.98; H, 6.71; N, 9.33.

2-Amino-*N*-(2-thienylmethyl)benzamide (7g). The yield was 2.35 g (55%). A colorless powder, m.p. 109—110 °C (hexane—EtOAc), R_f 0.55 (EtOAc—hexane, 1 : 1.5). IR, ν/cm^{-1}: 1521, 1580, 1629 (NC=O), 3352, 3473 (N—H). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 4.69 (d, 2 H, NHC$\underline{H}_2$, *J* = 5.5 Hz); 5.41 (s, 2 H, NH_2); 6.33 (s, 1 H, NH); 6.56 (ddd, 1 H, H(5), *J* = 1.4 Hz, *J* = 7.3 Hz, *J* = 8.2 Hz); 6.61 (d, 1 H, H(3), *J* = 8.2 Hz); 6.90 (dd, 1 H, H_{Thien}(4′), *J* = 3.4 Hz, *J* = 5.2 Hz); 6.96 (br.d, 1 H, H_{Thien}(3′), *J* = 3.4 Hz); 7.14 (dt, 1 H, H(4), *J* = 1.4 Hz, *J* = 8.2 Hz); 7.18 (dd, 1 H, H_{Thien}(5′), *J* = 1.4 Hz, *J* = 5.2 Hz); 7.24 (dd, 1 H, H(6), *J* = 1.4 Hz, *J* = 7.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 38.5 (NCH_2); 115.7 (C(1)); 116.7, 117.4, 125.3, 126.1, 127.0, 127.3, 132.6 (C(3), C(4), C(5), C(6) Ar, C_{Thien}(3), C_{Thien}(4), C_{Thien}(5′)); 141.2, 148.9 (C(2) Ar, C_{Thien}(2′)); 169.1 (NCO). MS, *m/z* (I_{rel} (%)): 232 $[M]^+$ (24), 120 (34), 112 (100), 97 (38), 92 (22), 65 (20). Found (%): C, 62.17; H, 5.43; N, 11.87; S, 13.93. $C_{12}H_{12}N_2OS$. Calculated (%): C, 62.04; H, 5.21; N, 12.06; S, 13.80.

Synthesis of 2-(2-furyl)-2,3-dihydroquinazolin-4(1*H*)-ones 8a—o (general procedure). A corresponding aldehyde (2.42 mmol) and TsOH (0.21 g, 1.1 mmol) were added to a solution of 2-aminobenzamide **7a—g** (2.2 mmol) in MeCN (30 mL), and the mixture was stirred at room temperature for 1—4 h (TLC monitoring), poured into water (50 mL), alkalized with an aqueous solution of $NaHCO_3$, and extracted with $CHCl_3$ (3×20 mL). The extract was dried with anhydrous $MgSO_4$. The residue after removal of the solvent was purified by recrystallization from a mixture of EtOAc—hexane. Quinazolines **8a** (63%), **8b** (79%), and **8c** (38%) were obtained earlier, their physicochemical characteristics and spectral data are completely agree with those described in the work.[39]

3-Allyl-2-(2-furyl)-2,3-dihydroquinazolin-4(1*H*)-one (8d). The yield was 0.47 g (85%). Colorless needles, m.p. 119—120 °C, R_f 0.40 (EtOAc—hexane, 1 : 3). IR, ν/cm^{-1}: 1626 (NC=O), 3245 (N—H). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.47 (dd, 1 H, *J* = 7.5 Hz, *J* = 15.6 Hz) and 4.94 (ddd, 1 H, C$\underline{H}_2$CH=CH_2, *J* = 1.8 Hz, *J* = 4.5 Hz, *J* = 15.6 Hz); 4.71 (br.s, 1 H, NH); 5.23 (dd, 1 H, *J* = 1.2 Hz, *J* = 10.0 Hz) and 5.30 (ddd, 1 H, CH_2CH=C$\underline{H}_2$, *J* = 1.2 Hz, *J* = 1.8 Hz, *J* = 17.5 Hz); 5.71 (s, 1 H, H(2)); 5.85 (dddd, 1 H, CH_2C$\underline{H}$=CH_2, *J* = 4.5 Hz, *J* = 7.5 Hz, *J* = 10.0 Hz, *J* = 17.5 Hz); 6.18 (d, 1 H, H_{Fur}(3′), *J* = 3.7 Hz); 6.24 (dd, 1 H, H_{Fur}(4′), *J* = 1.8 Hz, *J* = 3.7 Hz); 6.62 (d, 1 H, H(8), *J* = 8.1 Hz); 6.86 (t, 1 H, H(6), *J* = 7.5 Hz); 7.26 (ddd, 1 H, H(7), *J* = 1.2 Hz, *J* = 7.5 Hz, *J* = 8.1 Hz); 7.31 (br.d, 1 H, H_{Fur}(5′), *J* = 1.8 Hz); 7.94 (dd, 1 H, H(5), *J* = 1.2 Hz, *J* = 7.5 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 46.6 ($\underline{C}H_2$CH=CH_2); 64.4 (C(2)); 108.1, 110.4, 114.9 (Ar); 116.3 (C(4a)); 118.0, 119.3, 128.5, 132.7, 133.6 (Ar, $CH_2\underline{C}$H=CH_2, CH_2CH=$\underline{C}H_2$); 142.9 (C_{Fur}(5′)); 145.5 (C(8a)); 152.4 (C_{Fur}(2′)); 162.9 (C=O). MS, *m/z* (I_{rel} (%)): 254 $[M]^+$ (56), 237 (42), 213 (55), 187 (45), 170 (100), 147 (45), 119 (98), 92 (45), 77 (24), 64 (15), 41 (46). Found (%): C, 71.04; H, 5.54; N, 11.18. $C_{15}H_{14}N_2O_2$. Calculated (%): C, 70.85; H, 5.55; N, 11.02.

2-(2-Furyl)-3-(2-phenylethyl)-2,3-dihydroquinazolin-4(1*H*)-one (8e). The yield was 0.38 g (55%). Colorless spliced needles, m.p. 147—148 °C, R_f 0.51 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1624 (NC=O), 3297 (N—H). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.86—3.01 (m, 2 H, NCH_2C$\underline{H}_2$); 3.09—3.16 (m, 1 H, NC$\underline{H}_2$$CH_2$); 4.27—4.33 (m, 1 H, NC$\underline{H}_2$$CH_2$); 5.45 (s, 1 H, H(2)); 6.16 (br.d, 1 H, H_{Fur}(3′), *J* = 3.4 Hz); 6.22 (dd, 1 H, H_{Fur}(4′), *J* = 1.8 Hz, *J* = 3.2 Hz); 6.60 (d, 1 H, H(8), *J* = 7.8 Hz); 6.86 (t, 1 H, H(7), *J* = 7.8 Hz); 7.21—7.30 (m, 7 H, H(6), H_{Fur}(5′), C_6H_5); 7.93 (dd, 1 H, H(5), *J* = 1.4 Hz, *J* = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 34.8 ($NCH_2\underline{C}H_2$); 47.6 ($N\underline{C}H_2CH_2$); 66.4 (C(2)), 108.4, 110.5, 114.9, 116.9, 119.8, 126.5, 128.5, 128.6, 129.0, 133.4, 139.1 (Ar); 143.0 (C_{Fur}(5′)); 145.1 (C(8a)); 152.3 (C_{Fur}(2′)); 162.9 (C=O). MS, *m/z* (I_{rel} (%)): 318 $[M]^+$ (18), 213 (34), 198 (100), 170 (14), 115 (20), 104 (16), 91 (24), 77 (18), 65 (10), 39 (10). Found (%): C, 75.20; H, 5.54; N, 8.99. $C_{20}H_{18}N_2O_2$. Calculated (%): C, 75.45; H, 5.70; N, 8.80.

3-[2-(3,4-Dimethoxyphenyl)ethyl]-2-(2-furyl)-2,3-dihydroquinazolin-4(1*H*)-one (8f). The yield was 0.32 g (39%). Colorless fine needles, m.p. 112 °C, R_f 0.57 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1651 (NC=O), 3344 (N—H). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.81—2.96 (m, 2 H, NCH_2C$\underline{H}_2$); 3.02—3.09 (m, 1 H, NC$\underline{H}_2$$CH_2$); 3.80, 3.85 (both s, 3 H each, OMe); 4.28—4.34 (m, 1 H, NC$\underline{H}_2$$CH_2$); 4.59 (br.d, 1 H, NH, *J* = 2.1 Hz); 5.37 (d, 1 H, H(2), *J* = 2.1 Hz); 6.15 (dd, 1 H, H_{Fur}(3′), *J* = 0.9 Hz, *J* = 3.2 Hz); 6.22 (dd, 1 H, H_{Fur}(4′), *J* = 1.8 Hz, *J* = 3.2 Hz); 6.58 (d, 1 H, H(8), *J* = 8.2 Hz); 6.75—6.81 (m, 3 H, C_6H_3); 6.85 (dt, 1 H, H(6), *J* = 0.9 Hz, *J* = 8.2 Hz); 7.24 (dt, 1 H, H(7), *J* = 1.6 Hz, *J* = 8.2 Hz); 7.29 (dd, 1 H, H_{Fur}(5′), *J* = 0.9 Hz, *J* = 1.8 Hz); 7.93 (dd, 1 H, H(5), *J* = 1.6 Hz, *J* = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 34.4 ($NCH_2\underline{C}H_2$); 47.8 ($N\underline{C}H_2CH_2$); 55.9, 56.0 (both OMe); 66.4 (C(2)); 108.3, 110.4, 111.4, 112.4, 114.8, 116.7, 119.7, 120.8, 128.4, 131.8, 133.4 (Ar); 142.9 (C_{Fur}(5′)); 145.2 (C(8a)); 147.7, 148.9 (both $\underline{C}$OMe); 152.4 (C_{Fur}(2′)); 162.9 (C=O). MS, *m/z* (I_{rel} (%)): 378 $[M]^+$ (5), 281 (19), 213 (35), 207 (100), 198 (53), 197 (17), 164 (88), 151 (24), 133 (13), 119 (20), 115 (16), 77 (13), 73 (14), 44 (47). Found (%): C, 70.10; H, 5.77; N, 7.45. $C_{22}H_{22}N_2O_4$. Calculated (%): C, 69.83; H, 5.86; N, 7.40.

2-(2-Furyl)-3-(2-thienylmethyl)-2,3-dihydroquinazolin-4(1*H*)-one (8g). The yield was 0.34 g (50%). Colorless plates, m.p. 139—139.5 °C, R_f 0.49 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1628 (NC=O), 3280 (N—H). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 4.20, 5.21 (both d, 1 H each, NCH_2, *J* =15.8 Hz); 5.79 (br.d, 1 H, H(2), *J* = 2.8 Hz); 6.14 (br.d, 1 H, H_{Fur}(3′), *J* = 3.4 Hz); 6.27 (dd, 1 H, H_{Fur}(4′), *J* = 2.1 Hz, *J* = 3.4 Hz); 6.64 (t, 1 H, H(6), *J* = 7.6 Hz); 6.64 (dd, 1 H, H(8), *J* = 1.4 Hz, *J* = 7.6 Hz); 6.89 (dd, 1 H, H_{Thien}(4′), *J* = 3.4 Hz, *J* = 4.8 Hz); 7.00 (br.d, 1 H, H_{Thien}(3′), *J* = 3.4 Hz); 7.18 (dt, 1 H, H(7), *J* = 1.4 Hz, *J* = 7.6 Hz); 7.32 (br.d, 1 H, NH, *J* = 2.8 Hz); 7.36 (dd, 1 H, H_{Thien}(5′), *J* = 1.4 Hz, *J* = 4.8 Hz); 7.50 (br.d, 1 H, H_{Fur}(5′), *J* = 2.1 Hz); 7.60 (dd, 1 H, H(5) , *J* = 1.4 Hz, *J* = 7.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 42.4 (NCH_2); 64.4 (C(2)); 108.4, 110.4 (C_{Fur}(3′), C_{Fur}(4′)); 114.9, 116.2, 119.6, 125.9, 126.8, 127.2, 128.7, 133.7 (Ar), 139.4 (C_{Thien}(2′)); 143.1 (C_{Fur}(5′)); 145.2, 152.1 (C(8a); C_{Fur}(2′)); 162.8 (C=O). MS, *m/z* (I_{rel} (%)): 310 $[M]^+$ (28), 171 (24), 170 (61), 143 (25), 115 (18), 112 (69), 97 (100), 92 (22). Found (%): C, 65.61; H, 4.43; N, 8.88; S, 10.45. $C_{17}H_{14}N_2O_2S$. Calculated (%): C, 65.79; H, 4.55; N, 9.03; S, 10.33.

3-Benzyl-2-(2-furyl-5-methyl)-2,3-dihydroquinazolin-4(1*H*)-one (8h). The yield was 0.51 g (72%). Colorless fine needles, m.p. 115 °C, R_f 0.6 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1638 (NC=O), 3423 (N—H). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.18

(s, 3 H, Me); 3.91. 5.63 (both d, 1 H each, NCH_2, J = 15.4 Hz); 4.61 (s, 1 H, NH); 5.54 (s, 1 H, H(2)); 5.80 (br.d, 1 H, $H_{Fur}(4')$, J = 3.2 Hz); 6.05 (d, 1 H, $H_{Fur}(3')$, J = 3.2 Hz); 6.59 (d, 1 H, H(8), J = 8.2 Hz); 6.85 (br.t, 1 H, H(6), J = 7.8 Hz); 7.24—7.36 (m, 6 H, Ar), 7.97 (dd, 1 H, H(5), J = 1.4 Hz, J = 7.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 13.6 (Me); 47.4 (NCH_2); 64.6 (C(2)); 106.3, 109.2, 114.8 ($C_{Fur}(3')$, $C_{Fur}(4')$, C(8)); 116.4 (C(4a)); 119.6, 127.6, 128.1, 128.7 (2C), 133.5 (Ar); 137.0 (C(1) Ph); 145.3, 150.0, 152.7 ($C_{Fur}(2')$, $C_{Fur}(5')$, C(8a)); 163.2 (C=O). MS, m/z (I_{rel} (%)): 318 $[M]^+$ (8), 227 (18), 184 (10), 170 (43), 106 (17), 92 (19), 91 (100), 77 (12), 65 (22). Found (%): C, 75.62; H, 5.83; N, 8.96. $C_{20}H_{18}N_2O_2$. Calculated (%): C, 75.45; H, 5.70; N, 8.80.

3-Allyl-2-(2-furyl-5-methyl)-2,3-dihydroquinazolin-4(1*H*)-one (8i). The yield was 0.28 g (47%). Colorless plates, m.p. 84.3—84.6 °C, R_f 0.47 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1634 (NC=O), 3303 (N—H). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 2.16 (s, 3 H, Me), 3.40 (dd, 1 H, J = 6.9 Hz, J = 15.8 Hz) and 4.89 (ddd, 1 H, $C\underline{H}_2CH{=}CH_2$, J = 2.1 Hz, J = 4.1 Hz, J = 15.8 Hz); 4.65 (s, 1 H, NH); 5.17 (d, 1 H, J = 10.3 Hz) and 5.23 (d, 1 H, $CH_2CH{=}C\underline{H}_2$, J = 17.2 Hz); 5.60 (s, 1 H, H(2)); 5.76 (d, 1 H, $H_{Fur}(4')$, J = 2.7 Hz); 5.78—5.83 (m, 1 H, $CH_2C\underline{H}{=}CH_2$); 6.00 (d, 1 H, $H_{Fur}(3')$, J = 2.7 Hz); 6.57 (d, 1 H, H(8), J = 7.6 Hz); 6.80 (ddd, 1 H, H(6), J = 1.4 Hz, J = 7.6 Hz, J = 8.6 Hz); 7.21 (ddd, 1 H, H(7), J = 1.4 Hz, J = 7.6 Hz, J = 8.6 Hz); 7.88 (dd, 1 H, H(5), J = 1.4 Hz, J = 7.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 13.6 (Me); 46.6 ($\underline{C}H_2CH{=}CH_2$); 64.6 (C(2)); 106.3, 109.11 ($C_{Fur}(3')$, $C_{Fur}(4')$); 116.4 (C(4a)); 114.8, 117.8, 119.3, 128.5, 132.9, 133.4 (Ar, $CH_2\underline{C}H{=}CH_2$, $CH_2CH{=}\underline{C}H_2$); 145.5, 150.3 (C(8a), $C_{Fur}(2')$); 152.7 ($C_{Fur}(5')$); 162.9 (C=O). MS, m/z (I_{rel} (%)): 268 $[M]^+$ (45), 267 (23), 227 (56), 225 (34), 187 (56), 184 (28), 170 (100), 147 (84), 119 (44), 92 (32), 41 (36). Found (%): C, 71.43; H, 5.89; N, 10.96. $C_{16}H_{16}N_2O_2$. Calculated (%): C, 71.62; H, 6.01; N, 10.44.

3-Benzyl-2-(2-furyl-5-phenyl)-2,3-dihydroquinazolin-4(1*H*)-one (8j). The yield was 0.33 g (40%). Brown prisms, m.p. 148—149 °C, R_f 0.71 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1626 (NC=O), 3289 (N—H). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 3.98, 5.70 (both d, 1 H each, NCH_2, J = 15.1 Hz); 4.67 (br.d, 1 H, NH, J = 2.8 Hz); 5.64 (d, 1 H, H(2), J = 2.8 Hz); 6.25 (d, 1 H, $H_{Fur}(4')$, J = 3.4 Hz); 6.48 (d, 1 H, $H_{Fur}(3')$, J = 3.4 Hz); 6.61 (d, 1 H, H(8), J = 8.2 Hz); 6.89 (t, 1 H, H(6), J = 8.2 Hz); 7.23—7.37 (m, 9 H) and 7.49—7.50 (m, 2 H, Ar); 8.02 (dd, 1 H, H(5), J = 1.4 Hz, J = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 47.5 (NCH_2); 64.6 (C(2)); 105.5, 110.2, 114.9, 116.4, 119.7, 123.8, 127.7, 127.8, 128.1, 128.7, 128.7, 128.8, 130.3, 133.6, 136.8, 145.3, 151.6, 154.3 (Ar); 163.2 (C=O). MS, m/z (I_{rel} (%)): 380 $[M]^+$ (41), 290 (20), 289 (100), 246 (16), 237 (19), 170 (52), 147 (35), 144 (56), 91 (52). Found (%): C, 79.00; H, 5.11; N, 7.48. $C_{25}H_{20}N_2O_2$. Calculated (%): C, 78.93; H, 5.30; N, 7.36.

3-Benzyl-2-[(*E*)-2-(2-furyl)vinyl]-2,3-dihydroquinazolin-4(1*H*)-one (8k). The yield was 58 mg (8%). A yellow powder, m.p. 154—155 °C, R_f 0.63 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1645 (NC=O), 3376 (N—H). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 3.86, 5.59 (both d, 1 H each, NCH_2, J = 15.4 Hz); 4.61 (br.s, 1 H, NH); 4.98 (br.d, 1 H, H(2), J = 5.5 Hz); 6.22—6.28 (m, 3 H, $H_{Fur}(3')$, C(2)CH=C$\underline{H}$, C(2)C$\underline{H}$=CH); 6.34 (dd, 1 H, $H_{Fur}(4')$, J = 2.1 Hz, J = 3.4 Hz); 6.60 (d, 1 H, H(8), J = 8.2 Hz); 6.83 (t, 1 H, H(6), J = 7.6 Hz); 7.24—7.34 (m, 7 H, Ar, $H_{Fur}(5')$); 7.96 (dd, 1 H, H(5), J = 1.4 Hz, J = 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 46.7 (NCH_2); 69.8 (C(2)); 109.9, 111.5, 114.8, 115.7, 119.1, 121.1, 123.6, 127.5, 127.9, 128.7, 128.8, 133.6, 136.9 (Ar, C(2)CH=C$\underline{H}$, C(2)C$\underline{H}$=CH); 142.7 ($C_{Fur}(5')$); 145.4, 151.1 (C(8a), $C_{Fur}(2')$); 162.9 (C=O). MS, m/z (I_{rel} (%)): 330 $[M]^+$ (93), 240 (22), 239 (100), 197 (71), 170 (20), 160 (19), 120 (40), 106 (55), 92 (79), 91 (81), 77 (20), 76 (58), 65 (45), 51 (37), 43 (20). Found (%): C, 76.54; H, 5.32; N, 8.57. $C_{21}H_{18}N_2O_2$. Calculated (%): C, 76.34; H, 5.49; N, 8.48.

3-Benzyl-2-(2-thienyl)-2,3-dihydroquinazolin-4(1*H*)-one (8l). The yield was 0.37 g (53%). Colorless fine needles, m.p. 174—176 °C, R_f 0.55 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1625 (NC=O), 3249 (N—H). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.80, 5.65 (both d, 1 H each, NCH_2, J = 15.6 Hz); 4.53 (s, 1 H, NH); 5.82 (d, 1 H, H(2), J = 2.3 Hz); 6.58 (d, 1 H, H(8), J = 8.2 Hz); 6.87—6.93 (m, 3 H, H(6), $H_{Thien}(3')$, $H_{Thien}(4')$); 7.17 (dd, 1 H, $H_{Thien}(5')$, J = 1.4 Hz, J = 5.0 Hz); 7.26—7.35 (m, 6 H, Ar); 8.01—8.02 (dd, 1 H, H(5), J = 0.9 Hz, J = 7.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 47.0 (NCH_2); 66.7 (C(2)); 115.0 (C(8)); 116.2 (C(4a)); 119.9 ($C_{Thien}(3')$); 126.1, 126.3, 126.5, 127.7, 128.1, 128.8, 128.9, 133.8 (Ar, $C_{Thien}(4')$, $C_{Thien}(5')$); 136.81 (C(1) Ph); 143.1 ($C_{Thien}(2')$); 144.9 (C(8a)); 162.7 (C=O). MS, m/z (I_{rel} (%)): 320 $[M]^+$ (14), 237 (18), 229 (82), 215 (18), 186 (36), 119 (16), 106 (38), 92 (20), 91 (100), 65 (18). Found (%): C, 71.35; H, 4.88; N, 8.92; S, 10.29. $C_{19}H_{16}N_2OS$. Calculated (%): C, 71.22; H, 5.03; N, 8.74; S, 10.01.

2-(1-Benzothien-2-yl)-3-benzyl-2,3-dihydroquinazolin-4(1*H*)-one (8m). The yield was 0.46 (57%). Colorless fine needles, m.p. 173—173.3 °C, R_f 0.53 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1633 (NC=O), 3291 (N—H). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 3.78, 5.69 (both d, 1 H each, NCH_2, J = 15.8 Hz); 4.67 (br.s, 1 H, NH); 5.83 (s, 1 H, H(2)); 6.56 (d, 1 H, H(8), J = 8.3 Hz); 6.87 (t, 1 H, H(6), J = 7.6 Hz); 7.08 (s, 1 H, $H_{Thien}(3')$); 7.24—7.30 (m, 2 H) and 7.62—7.65 (m, 8 H, Ar), 8.00 (dd, 1 H, H(5), J = 1.4 Hz, J = 7.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 47.1 (NCH_2); 67.2 (C(2)); 115.2 (C(8)); 116.2 (C(4a)); 119.9 ($C_{Thien}(3')$); 122.6, 123.0, 123.9, 124.7, 125.2, 127.8, 128.2, 128.8, 128.9 133.9, 136.7, 138.6, 139.7, 143.6 (Ar); 144.8 (C(8a)); 162.8 (C=O). MS, m/z (I_{rel} (%)): 370 $[M]^+$ (13), 279 (72), 265 (12), 237 (81), 147 (15), 134 (12), 119 (13), 106 (13), 92 (42), 91 (100), 76 (14), 65 (35), 43 (13). Found (%): C, 74.36; H, 4.79; N, 7.77; S, 8.43. $C_{23}H_{18}N_2OS$. Calculated (%): C, 74.57; H, 4.90; N, 7.56; S, 8.66.

3-Benzyl-2-(1*H*-pyrrol-2-yl)-2,3-dihydroquinazolin-4(1*H*)-one (8n). The yield was 0.10 g (15%). Colorless needles, m.p. 126—127 °C, R_f 0.48 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1609 (NC=O), 3254, 3437 (N—H). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 3.94, 5.22 (both d, 1 H each, NCH_2, J = 15.1 Hz); 4.42 (br.s, 1 H, NH); 5.70 (s, 1 H, H(2)); 6.07 (q, 1 H, $H_{Pyrrol}(4')$, J = 2.8 Hz); 6.11 (m, 1 H, $H_{Pyrrol}(3')$); 6.57 (d, 1 H, H(8), J = 8.2 Hz); 6.63 (m, 1 H, $H_{Pyrrol}(5')$); 6.89 (t, 1 H, H(6), J = 7.6 Hz); 7.17—7.29 (m, 6 H, Ar); 8.00 (dd, 1 H, H(5), J = 1.4 Hz, J = 7.6 Hz); 8.21 (br.s, 1 H, NH). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 50.5 (NCH_2); 77.3 (C(2)); 115.0, 115.6, 117.8, 124.6, 125.4, 127.5, 128.5, 128.9, 129.3, 130.2, 135.3, 137.3 (Ar); 147.5 (C(8a)); 160.1 (C=O). MS, m/z (I_{rel} (%)): 303 $[M]^+$ (41), 236 (15), 212 (77), 197 (20), 170 (17), 169 (93), 156 (15), 120 (46), 115 (25), 106 (41), 93 (18), 92 (62), 91 (100), 78 (21), 69 (21), 68 (82), 64 (15), 59 (14), 58 (41), 52 (21), 51 (29), 44 (18), 43 (74), 41(51). Found (%): C, 75.50; H, 5.33; N, 13.59. $C_{19}H_{17}N_3O$. Calculated (%): C, 75.23; H, 5.65; N, 13.85.

3-Benzyl-2-(1-tosyl-1*H*-pyrrol-2-yl)-2,3-dihydroquinazolin-4(1*H*)-one (8o). The yield was 0.95 g (94%). Colorless needles,

m.p. 196—197 °C, R_f 0.51 (EtOAc—hexane, 1 : 2). IR, ν/cm^{-1}: 1150, 1167 (n_s SO_2), 1355 (n_{as} SO_2), 1643 (NC=O), 3383 (N—H). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 2.35 (s, 3 H, Me); 3.47, 5.22 (both d, 1 H each, NCH_2, J = 15.5 Hz); 5.93 (dd, 1 H, $H_{Pyrrol}(3')$, J = 1.4 Hz, J = 3.4 Hz); 5.98 (d, 1 H, H(2), J = 4.1 Hz); 6.15 (t, 1 H, $H_{Pyrrol}(4')$, J = 3.4 Hz); 6.76 (d, 1 H, NH, J = 4.1 Hz); 6.64—6.68 (m, 2 H), 7.02—7.42 (m, 8 H) and 7.63—7.66 (m, 3 H, Ar); 7.38 (dd, 1 H, $H_{Pyrrol}(5')$, J = 1.4 Hz, J = 3.4 Hz). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 21.1 (Me); 47.0 (NCH_2); 63.1 (C(2)); 112.2, 114.3, 115.1, 115.8, 118.1, 124.8, 124.9, 126.5, 127.2, 127.3, 128.6, 130.3, 132.8, 133.2, 135.3, 137.0, 144.5, 145.7 (Ar); 162.5 (C=O). MS, m/z (I_{rel} (%)): 457 $[M]^+$ (51), 366 (29), 259 (15), 237 (27), 236 (57), 221 (60), 212 (20), 198 (35), 197 (43), 185 (74), 170 (16), 169 (65), 157 (20), 156 (27), 155 (45), 130 (22), 119 (47), 106 (33), 92 (100), 91 (79), 78 (18), 76 (23), 67 (15), 65 (25), 52 (18), 43 (28), 41 (15). Found (%): C, 68.41; H, 4.78; N, 9.40; S, 6.81. $C_{26}H_{23}N_3O_3S$. Calculated (%): C, 68.25; H, 5.07; N, 9.18; S, 7.01.

Synthesis of 3-benzyl-2-(2-furyl)-2,3-dihydroquinazolin-4(*1H*)-one 8b using *one-pot* method. Benzylamine (0.7 mL, 6.4 mmol) was added to a solution of isatoic anhydride (1.0 g, 6.1 mmol) in MeCN (50 mL), and the mixture was stirred for 4 h at 50 °C (TLC monitoring), cooled to room temperature, followed by a sequential addition of TsOH (0.6 g, 3 mmol) and furfural (0.5 mL, 6.1 mmol). The reaction mixture was stirred for 24 h and poured into water (50 mL), after the addition of an aqueous solution of $NaHCO_3$ the mixture was extracted with $CHCl_3$ (3×20 mL). The extract was dried with anhydrous $MgSO_4$. The residue after removal of $CHCl_3$ was purified by recrystallization from a mixture of EtOAc—hexane to obtain **8b** (1.23 g, 66%) as colorless spliced needles with m.p. 175—176 °C. A mixed probe with the authentic sample obtained by the preceding method showed no melting point depression.

6b,9-Epoxyisoindolo[2,1-*a*]quinazoline-10-carboxylic acids (9a,b) (general procedure). ***A.*** A mixture of quinazoline **2a**,**b** (4.4 mmol) and maleic anhydride (0.43 g, 4.6 mmol) in $CHCl_3$ (20 mL) was stirred for 4 h (TLC monitoring). The crystals formed were filtered, washed with diethyl ether (2×20 mL), and dried in air to obtain a mixture of **A**- and **B**-isomers of the Diels—Alder adducts **9a,b** as colorless powders. The yields and the ratios of **A**- and **B**-stereoisomers: 0.88 g (60%) **9a**, 65 : 35 and 0.73 g (51%) **9b**, 30 : 70.

B. Furfural (4.14 mL, 0.05 mol) and anhydrous $MgSO_4$ (12.0 g, 0.1 mol) were added to a solution of 2-aminobenzamide **1** (6.81 g, 0.05 mol) in $CHCl_3$ (100 mL), the mixture was stirred for 2 h (TLC monitoring) and filtered. The residue was washed with $CHCl_3$ (2×20 mL), the combined mother liquor was half concentrated. Maleic anhydride (5.39 g, 0.055 mol) was added to the solution obtained, which was stirred for 30 min. The crystals formed were filtered and washed with ether (2×20 mL) to obtain a mixture of **A**- and **B**-stereoisomers of **9a** (15.3 g, 94%) (65 : 35) as a colorless powder.

(6a*RS*,6b*SR*,9*RS*,10*SR*,10a*RS*)-5,11-Dioxo-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinazoline-10-carboxylic acid (9aA) and (6a*RS*,6b*RS*,9*SR*,10*RS*,10a*SR*)-5,11-dioxo-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo-[2,1-*a*]quinazoline-10-carboxylic acid (9aB). Physicochemical characteristics and elemental analysis data are given for the mixture of stereoisomers. A colorless powder, m.p. 219—221 °C (Pr^iOH—DMF). IR, ν/cm^{-1}: 1675 (NC=O), 1723 (O—C=O), 3183 (N—H).

Isomer **9aA**. ^{1}H NMR (600 MHz, DMSO-d_6), δ: 2.61, 3.17 (both d, 1 H each, H(10), H(10a), J = 9.3 Hz); 5.12 (d, 1 H, H(9), J = 1.7 Hz); 6.05 (s, 1 H, H(6a)); 6.48 (dd, 1 H, H(8), J = 1.7 Hz, J = 5.8 Hz); 6.55 (d, 1 H, H(7), J = 5.8 Hz); 7.23 (dt, 1 H, H(3), J = 1.0 Hz, J = 7.6 Hz); 7.54—7.57 (m, 1 H, H(2)); 7.87 (dd, 1 H, H(4), J = 1.4 Hz, J =7.6 Hz); 8.12 (d, 1 H, H(1), J = 1.0 Hz, J = 8.2 Hz); 8.94 (s, 1 H, NH).

Isomer **9aB**. ^{1}H NMR (600 MHz, DMSO-d_6), δ: 2.63, 3.21 (both d, 1 H each, H(10), H(10a), J = 9.2 Hz); 5.13 (d, 1 H, H(9), J = 1.4 Hz); 5.61 (s, 1 H, H(6a)); 6.53 (dd, 1 H, H(8), J = 1.4 Hz, J = 5.7 Hz); 7.11 (d, 1 H, H(7), J = 5.7 Hz); 7.34 (dd, 1 H, H(3), J = 7.3 Hz, J = 8.0 Hz); 7.56 (d, 1 H, H(4), J = 8.0 Hz); 7.62 (ddd, 1 H, H(2), J = 1.4 Hz, J = 7.3 Hz, J = 8.0 Hz); 7.93 (dd, 1 H, H(1), J = 1.4 Hz, J = 8.0 Hz); 9.22 (s, 1 H, NH).

MS, m/z (I_{rel} (%)): 312 $[M]^+$ (4), 213 (67), 200 (27), 185 (11), 146 (19), 120 (100), 98 (39), 92 (72), 85 (23), 77 (16), 65 (66), 59 (35), 54 (47), 43 (26). Found (%): C, 61.42; H, 4.01; N, 9.09. $C_{16}H_{12}N_2O_5$. Calculated (%): C, 61.54; H, 3.87; N, 8.97.

(6a*RS*,6b*SR*,9*RS*,10*SR*,10a*RS*)-9-Methyl-5,11-dioxo-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]-quinazoline-10-carboxylic acid (9bA) and (6a*RS*,6b*RS*,9*SR*,10*RS*,10a*SR*)-9-methyl-5,11-dioxo-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinazoline-10-carboxylic acid (9bB). Physicochemical characteristics and elemental analysis data are given for the mixture of stereoisomers. A colorless powder, m.p. 180—181 °C (Pr^iOH—DMF). IR, ν/cm^{-1}: 1660, 1678 (NC=O), 1725(O—C=O), 3083, 3179 (N—H).

Isomer **9bA**. ^{1}H NMR (600 MHz, DMSO-d_6), δ: 1.59 (s, 3 H, Me); 2.69, 3.21 (both d, 1 H each, H(10), H(10a), J = 9.2 Hz); 6.01 (s, 1 H, H(6a)); 6.35, 6.63 (both d, 1 H each, H(7), H(8), J = 5.5 Hz); 7.26 (t, 1 H, H(3), J = 7.8 Hz); 7.57—7.60 (m, 1 H, H(2)); 7.91 (dd, 1 H, H(4), J = 1.4 Hz, J = 7.8 Hz); 8.25 (d, 1 H, H(1), J = 8.2 Hz); 8.90 (s, 1 H, NH).

Isomer **9bB**. ^{1}H NMR (600 MHz, DMSO-d_6), δ: 1.57 (s, 3 H, Me); 2.70, 3.26 (both d, 1 H each, H(10), H(10a), J = 8.7 Hz); 5.63 (s, 1 H, H(6a)); 6.40, 7.17 (both d, 1 H each, H(7), H(8), J = 5.5 Hz); 7.38 (t, 1 H, H(3), J = 7.8 Hz); 7.47 (t, 1 H, H(2), J = 7.8 Hz); 7.97 (dd, 1 H, H(4), J = 1.4 Hz, J = 7.8 Hz); 8.11 (d, 1 H, H(1), J = 7.8 Hz); 9.21 (s, 1 H, NH).

MS, m/z (I_{rel} (%)): 326 $[M]^+$ (1), 226 (100), 211 (65), 197 (25), 183 (11), 170 (7), 120 (26), 101 (43), 59 (52). Found (%): C, 62.50; H, 4.17; N, 8.76. $C_{17}H_{14}N_2O_5$. Calculated (%): C, 62.57; H, 4.32; N, 8.59.

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