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Facile approach to diverse range of 1,3-diaza-heterocycles: angular/linear selectivity paradigm and a remarkable intramolecular methyl migration

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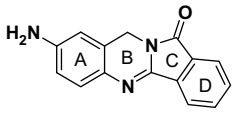
ABSTRACT

Starting from cyclic anhydrides and *tert*-butyl 2-aminobenzylcarbamate, simple and efficient synthesis of diverse range of kinetically controlled angular and thermodynamically controlled linear tricyclic and tetracyclic 1,3-diaza-heterocycles have been described via the intramolecular cyclizations of the corresponding imides/anilic acid esters. The effect of imide stability on the angular/linear product selectivity has also been described. The kinetically controlled angular products were successfully transformed to the corresponding thermodynamically controlled linear products by refluxing in methanol or methanol and acetic acid mixture. An interesting in situ 1,2-intramolecular methyl group migration has also been described.

1. Introduction

A large number of biological activities have been conferred to heterocycles and they play a pivotal role as both pharmaceutical and agrochemical products.[1] Batracylin displays antitumor activity in vivo against murine leukemia P-388 and colon adenocarcinoma 38 cell lines that are resistant to adriamycin, cisplatin, and methotrexate.[2,3]



Batracylin

However, because of the high toxicity of batracylin, it has never been approved for further clinical trials in human beings.[4a] In this context, new approaches to provide a wide variety of analogs of the antitumor agent batracylin have been reported in the literature by using intramolecular aza-Wittig reactions, Mitsunobu coupling reactions and condensation of *o*-aminobenzylamine with *o*-cyanomethylbenzoic acid but with some limitations.[4] In continuation of our studies on the cyclic anhydrides chemistry to design the bioactive natural and unnatural heterocyclic compounds,[5] we reasoned and planned to study the nucleophilic reactions of several cyclic anhydrides with *tert*-butyl 2-aminobenzylcarbamate to provide an avenue to both angular and linear 1,3-diaza-heterocycles in line with their selective formation with respect to the thermodynamic stability. Now, starting from imides/anilic acid esters, we report herein a simple and efficient access to several angular/linear 1,3-diazatricyclic/tetracyclic batracylin analogs along with a very interesting case of intramolecular methyl group migration (Schemes 1 and 2).

2. Results and discussion

The reactions of *tert*-butyl 2-aminobenzylcarbamate (**1**) with succinic anhydride (**2a**), glutaric anhydride (**2b**), maleic anhydride (**2c**), phthalic anhydride (**2f**), and homophthalic anhydride (**2g**) in diethyl ether at room temperature furnished the required anilic acids **3a**, **3b**, **3c**, **3f**, and **3g**, respectively, in very good yields. The reaction of *tert*-butyl 2-aminobenzylcarbamate (**1**) with methylmaleic anhydride (**2d**) was not completely regioselective and as expected, the mixture of two regioisomers [major (attack at unhindered carbonyl): minor (attack at hindered carbonyl)=85:15] in quantitative yield was obtained. One recrystalization of the above mixture from ethyl acetate provided the desired major isomer **3d** in good yield (71%). The reaction of *tert*-butyl 2-aminobenzylcarbamate (**1**) with dimethylmaleic anhydride (**2e**) directly furnished the expected imide **5e** in quantitative yield via the unisolable intermediate anilic acid **3e**. The anilic acids **3a**, **3b**, **3c**, **3d**, and **3g** on treatment with requisite amount of diazomethane in diethyl ether at 0 °C in 30–40 min furnished the corresponding methyl esters **4a**, **4b**, **4c**, **4d**, and **4g** in high yields. The reaction of phthalanilic acid **3f** with diazomethane directly provided the

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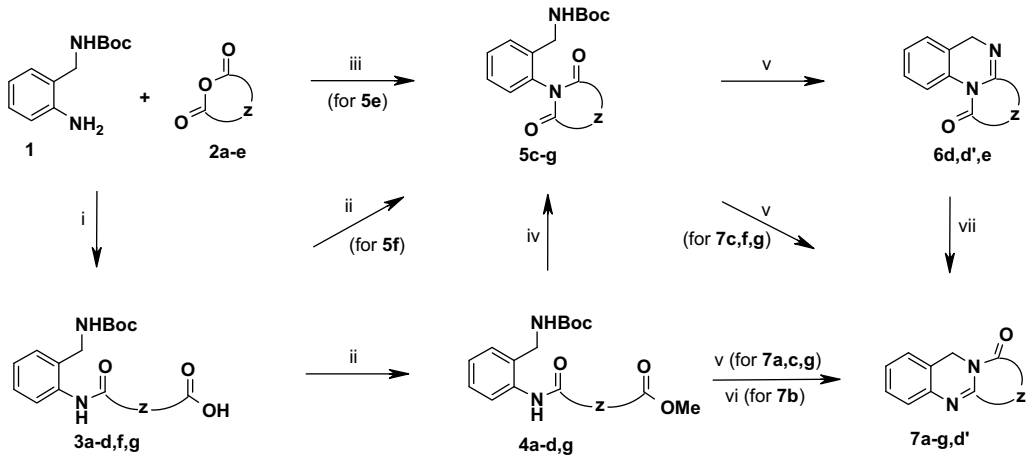
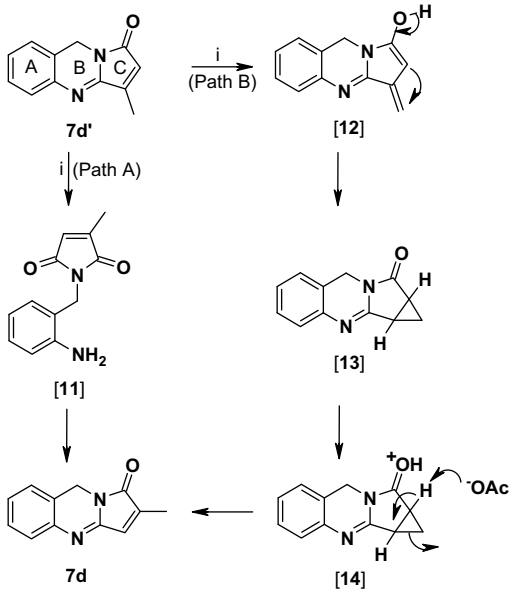


Scheme 1. General theme for synthesis of linear and angular 1,3-diaza-heterocycles. Reagents and conditions: (i) Et_2O, 0 °C to rt, 3 h; (ii) CH_2N_2, Et_2O, 0 °C, 30 min; (iii) EtOH, reflux, 1 h; (iv) Et_3N, DCM, rt, 5 h; (v) TFA, DCM, rt, 5 h; (vi) TFA, DCM, rt, 5 h then MeOH, reflux, 5 h; (vii) AcOH, MeOH, reflux, 24/48 h.

more stable ring closed product, the imide **5f** in 97% yield and the conditions to obtain the phthalanilic esters are still elusive. In our hands, the dehydrative cyclizations of **3a**/**b** and the intramolecular cyclizations of **4a**/**b** to obtain the corresponding succinimide/glutarimide **5a**/**b** under the several known standard reaction conditions met with failure and we always ended up with corresponding starting materials. Our studies revealed that the formed imides **5a**/**b** (by TLC) are unstable and they undergo an in situ facile ring opening with the anchimeric assistance of the nitrogen lone pair from the suitably *ortho*-substituted $-CH_2NHBoc$ moiety. The base catalyzed intramolecular cyclizations of esters **4c**, **4d**, and **4g**, respectively, furnished the corresponding imides **5c**, **5d**, and **5g** in very good yields. Having prepared several imides and esters, we planned to systematically study the Boc-deprotection and intramolecular double cyclizations of these advanced starting materials to obtain the corresponding desired angular/linear 1,3-diaza-heterocycles, respectively (Scheme 1 and Table 1).

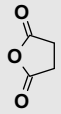
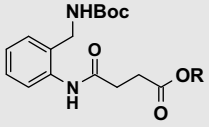
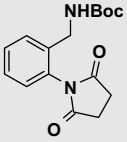
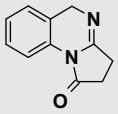
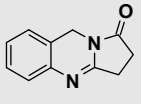
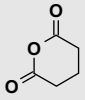
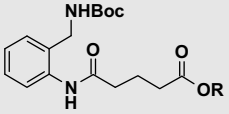
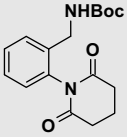
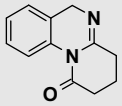
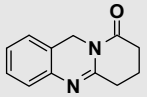
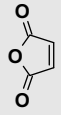
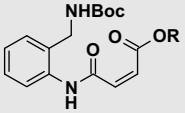
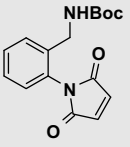
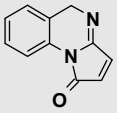
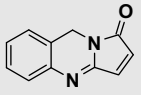
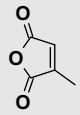
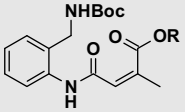
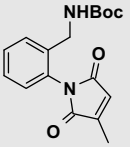
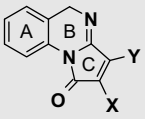
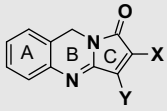
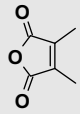
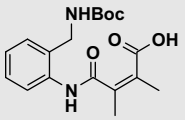
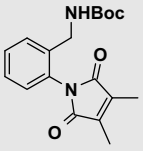
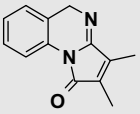
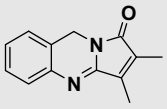
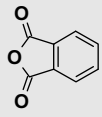
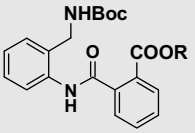
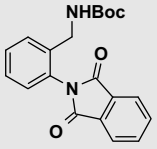
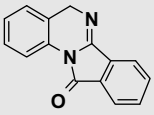
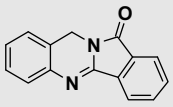
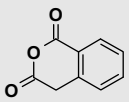
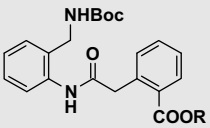
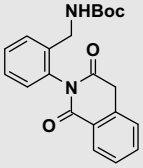
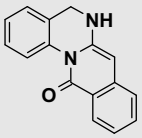
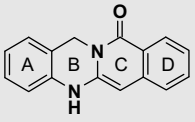


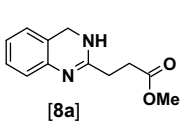
Scheme 2. Proposed mechanisms for the observed 1,2-methyl shift. Reaction condition: (i) AcOH/MeOH, reflux, 15 days (96%).

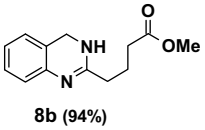
The trifluoroacetic acid induced Boc-deprotection of succinanilic ester **4a** in CH_2Cl_2 at room temperature directly furnished the pyrrolidinoquinazoline **7a** in 91% yield via dehydrative cyclization to form unisolable intermediate **8a** followed by an intramolecular lactamization route. The Boc-deprotection of glutaranilic ester **4b** in CH_2Cl_2 at room temperature furnished the intermediate quinazoline **8b** in quantitative yield via intramolecular monocyclization route, which in refluxing methanol furnished intramolecularly ring closed final product piperidinoquinazoline **7b** in 87% yield. These observations revealed that **4a** passes through an unisolable intermediate **8a** to directly furnish the product **7a**. Itermediate **8a** is less stable relative to **7a** than **8b** is to **7b**. We failed to obtain the corresponding imide intermediates **5a**/**b** and in our hands the intermediate compounds **8a**/**b** furnished only the linear products **7a**/**b**, hence we could not prepare the angular products **6a**/**b**.

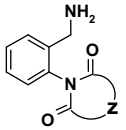
The Boc-deprotection of maleanilic ester **4c** in CH_2Cl_2 at room temperature directly furnished the linear product **7c** via the double intramolecular cyclization pathway. The Boc-deprotection of maleimide **5c** under the similar reaction conditions also furnished only linear product **7c**. We feel that, the formation of angular product **6c** via proposed imide **9**, exclusively provides thermodynamically more stable product **7c** in quantitative yield via opening and closing of the ring 'C'. The corresponding maleanilic acid **3c** on treatment with trifluoroacetic acid underwent decomposition. The Boc-deprotection of maleanilic ester **4d** exclusively furnished the column separable mixture of the ring closed angular products **6d**/**d′** in 85% yield with 13:7 ratio and it could be an effect of the methyl group conferring more stability to the possible imide intermediate **5d**/**9**. The imide **5d** on Boc-deprotection also provided the mixture of ring closed angular products **6d**/**d′** in same yield but at this time with a 1:1 ratio. As expected, in ^1H NMR spectra, the β-vinylic proton signal in **6d** (δ 6.69) was more deshielded than the α-vinylic proton in the corresponding **6d′** (δ 6.33). The column purified product **6d** on refluxing in methanol for 75 h gave corresponding thermodynamically more stable linear product **7d** in high yield via the 'C' ring opening and closing pathway. However, the corresponding unhindered regioisomer **6d′** under the same set of reaction conditions was transformed into **7d′** but only to the extent of 11% in 75 h. As expected, in ^1H NMR spectra, the β-vinylic proton signal in **7d** (δ 6.83) was more deshielded than the α-vinylic proton in the corresponding **7d′** (δ 6.27). The relatively slow conversion of unhindered **6d′** to **7d′** can be attributed to the hyperconjugative

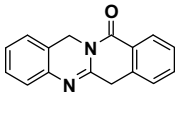
Table 1
Nucleophilic reactions of cyclic anhydrides with *tert*-butyl 2-aminobenzylcarbamate (**1**): synthesis of angular/linear 1,3-diaza-heterocycles from the corresponding esters/imides: **4a** to **7a**, **4b** to **8b** to **7b**, **4c**/**5c** to **7c**, **4d**/**5d** to **6d**/**6d′** to **7d**/**7d′**, **5e** to **6e** to **7e**, **5f** to **7f**, and **4g**/**5g** to **7g** synthetic transformations

Sr. No.	Anhydride	Anilic acid/ester	Imide	Angular product	Linear product
i	 **2a**	 **3a: R = H (92%)** **4a: R = Me (98%)**	 **5a (Unstable)**	 **6a (Not prepared)**	 **7a (91%)**
ii	 **2b**	 **3b: R = H (93%)** **4b: R = Me (95%)**	 **5b (Unstable)**	 **6b (Not prepared)**	 **7b (87%)**
iii	 **2c**	 **3c: R = H (98%)** **4c: R = Me (80%)**	 **5c (75%)**	 **6c (Unisolable)**	 **7c (90%)**
iv	 **2d**	 **3d: R = H (71%)** **4d: R = Me (90%)**	 **5d (90%)**	 **6d: X = Me, Y = H (55%)** **6d': X = H, Y = Me (30%)**	 **7d: X = Me, Y = H (99%)** **7d': X = H, Y = Me (87%)**
v	 **2e**	 **3e (Unisolable)**	 **5e (95%)**	 **6e (94%)**	 **7e (~100%)**
vi	 **2f**	 **3f: R = H (95%)** **4f: R = Me (Unisolable)**	 **5f (97%)**	 **6f (Unisolable)**	 **7f (85%)**
vii	 **2g**	 **3g: R = H (90%)** **4g: R = Me (93%)**	 **5g (87%)**	 **6g (Unisolable)**	 **7g (87%)**


[8a]


8b (94%)


[9] (Z = Imide backbone)


[10]

influence of the β-methyl group in **6d′** on the reactivity of the lactam carbonyl group. The angular product **6d**, on treatment with methanol plus acetic acid at reflux temperature exclusively gave the desired linear product **7d** in 24 h in quantitative yield. The pure **6d′** under the same conditions gave the desired **7d′** with 87% yield in 24 h. We presume that both of the mentioned conversions take place via 'C' ring opening and closing. Surprisingly, during these studies on conversion of pure **6d′** to **7d′** we also noticed the formation of a small amount of compound **7d** (detection by TLC, 7% by ^{1}H NMR). We were very curious about the formation of **7d** in conversion of **6d′** to **7d′** and therefore we refluxed the pure **7d′** in methanol plus acetic acid for 5/10/15 days and obtained the rearranged product **7d** in 52/77/96% yields, respectively, with the change in methyl group position. To explain the observed methyl shift in the conversion of **7d′** to **7d**, two plausible mechanisms are depicted in Scheme 2 (path A/B). The path A with the cleavage of ring 'B' by imine hydrolysis to form the unisolable imide intermediate **11** and an in situ intramolecular ring closing with the other carbonyl group appears simpler and straightforward. We strongly believe that the formation of the free imide intermediate **11** should lead to a mixture of **7d** and **7d′**, as the methyl group on the imide moiety is not expected to control the complete regioselectivity. The slow rate of conversion of **6d′** to **7d′** in refluxing methanol due to the hyperconjugative effect of the methyl group and the exclusive transformation of **6d** to **7d** in refluxing methanol plus acetic acid in 24 h support the mechanistic path B, which does not demand the cleavage of ring 'B'. As depicted in path B, the proton shift from the methyl group to the carbonyl group followed by cyclopropane ring formation is possible. Its cleavage with the abstraction of the more acidic α-proton can also lead to the net methyl shift from the β-carbon to the α-carbon for thermodynamic reasons. In a control experiment, the pure linear product **7d** remained completely unreacted in refluxing methanol plus acetic acid mixture for 72 h and we did not observe any methyl group shuffling. The above observation also supports the mechanistic path B. We feel that the proposed 1,2-methyl shift via the cyclopropane ring formation is important from a mechanistic point of view and appears to be very amenable to isotopic labeling.[6] The Boc-deprotection of the 2,3-dimethyl substituted imide **5e** on intramolecular condensation exclusively formed the angular product **6e** in 94% yield. Interestingly, the reaction of equimolar amounts of *o*-aminobenzylamine and dimethylmaleic anhydride (**2e**) in ethanol at room temperature or in refluxing THF also exclusively furnished only the angular product **6e** in high yield. Herein, the observed selectivity with the presence of two free $-NH_2$ groups (aromatic/aliphatic) is notable. The angular product **6e** in refluxing methanol remained completely unreacted for the span of 5 days. However, the same reaction in the presence of a catalytic amount of acetic acid furnished thermodynamically more stable linear product **7e** with ~100% yield in 48 h via the ring opening and closing mechanism.

The trifluoroacetic acid induced Boc-deprotection of phthalimide **5f** in CH_2Cl_2 at room temperature also formed the linear product **7f** in 85% yield via deprotection, ring closing to **6f** and then the ring opening and ring closing sequence. The Boc-deprotection of homophthalanilic ester **4g** in CH_2Cl_2 at room temperature directly provided the isoquinolinodihydroquinazoline **7g** in 87% yield. Herein, both the intramolecular cyclizations to form the unisolable isoquinolinone intermediate **10** and the prototopic shift to confer the quasi-aromatic character on ring 'C' took place in one pot for thermodynamic reasons. The corresponding imide **5g** on Boc-deprotection also formed only the linear product **7g** in high yield via the unisolable intermediate **6g**.

In all of the studied examples, as expected the linear products had higher melting points than the corresponding angular products. The analytical and spectral data for all the compounds synthesized were in complete agreement with the assigned structures/reported data.[4] The angular and linear products were also clearly distinguished from each other on the basis of ^{1}H NMR data. In all of the angular products **6d**/**6d′**/**6e**, one of the aromatic proton signals was more deshielded (ca. δ 8.38) due to the close proximity with the lactam carbonyl group.

3. Conclusion

In summary, we have systematically studied the nucleophilic reactions of several cyclic anhydrides with *tert*-butyl 2-aminobenzylcarbamate and provided a new practical route to the 1,3-diazatricyclic/tetracyclic heterocycles in high yields. Our present study clearly reveals that in all the cases, the anilic acid esters exclusively provide thermodynamically more stable linear 1,3-diaza-heterocycles, while only the methyl and dimethyl substituted maleimides exclusively provide the corresponding kinetically controlled angular 1,3-diaza-heterocycles. In all of the other imides studied, the formed angular products rearranged to the corresponding more stable linear products. The serendipitously witnessed intramolecular shuffling of the methyl group is also noteworthy and important from the basic chemistry points of view, but the two different mechanistic aspects discussed on observed methyl migration are only the proposals. We feel that our present simple and efficient general approach to these 1,3-diaza-heterocycles will be useful to design the focused libraries of analogs and congeners of such type of new heterocyclic systems for SAR studies.

4. Experimental section

4.1. General

Melting points are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 using TMS as an internal standard on 200 and 400 MHz spectrometers. ^{13}C NMR spectra were recorded on 200, 400, and 500 NMR spectrometers (50, 100, and 125 MHz, respectively). IR spectra were recorded on an FT-IR spectrometer. Elemental analyses were obtained by using Flash EA 1112 series and Elementar Vario EL analyser. Column chromatographic separations were done on silica gel (60–120 mesh). Commercially available anhydrides and trifluoroacetic acid, were used. *tert*-Butyl 2-aminobenzylcarbamate (**1**) was prepared from commercially available *o*-aminobenzylamine using known procedure.[7]

4.2. General procedure for the preparation of anilic acids (3a–d, 3f, 3g)

To a stirred solution of anhydride (2.00 mmol) in diethyl ether (15 mL) at 0 °C was added a solution of *tert*-butyl 2-aminobenzylcarbamate (**1**, 2.00 mmol) in diethyl ether (10 mL) in a dropwise fashion over a period of 10 min and the reaction mixture was further stirred at room temperature for 3 h. The precipitated product was filtered, washed with ether (25 mL) and dried under vacuum to obtain the corresponding anilic acid in quantitative yield.

*4.2.1. 4-(2-((tert-Butoxycarbonylamino)methyl)phenylamino)-5-oxobutanoic acid (**3a**)*

Mp 134–136 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.43 (s, 9H), 2.70–2.90 (m, 4H), 4.25 (d, *J*=6 Hz, 2H), 5.16 (br s, 1H), 7.07 (t, *J*=8 Hz, 1H), 7.14 (t, *J*=8 Hz, 1H), 7.32 (dd, *J*=8 and 2 Hz, 1H), 8.12 (d, *J*=8 Hz, 1H), 9.74 (br s, 1H); ^{13}C NMR (CD_3OD, 50 MHz) δ 28.7, 30.1, 32.0, 41.5, 80.6, 126.1, 126.9, 128.9, 130.4, 134.3, 136.5, 158.9, 173.6, 176.4; IR (Nujol) ν_{max} 3360, 2700–2500, 1711, 1697, 1661 cm^{-1}. R_f (70% EtOAc/petroleum ether) 0.45. Anal. Calcd for $C_{16}H_{22}N_2O_5$: C, 59.62; H, 6.88; N, 8.69. Found: C, 59.55; H, 6.96; N, 8.71.

*4.2.2. 5-(2-((tert-Butoxycarbonylamino)methyl)phenylamino)-5-oxopentanoic acid (**3b**)*

Mp 113–115 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.43 (s, 9H), 2.08 (quint, J=8 Hz, 2H), 2.50 (t, J=8 Hz, 2H), 2.56 (t, J=8 Hz, 2H), 4.25 (d, J=6 Hz, 2H), 5.16 (br s, 1H), 7.05 (t, J=8 Hz, 1H), 7.15 (d, J=6 Hz, 1H), 7.30 (dt, J=8 and 2 Hz, 1H), 8.16 (d, J=8 Hz, 1H), 9.56 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.6, 28.3, 33.2, 36.0, 41.6, 80.7, 122.8, 124.3, 128.8 (two carbons), 130.2, 136.5, 157.3, 171.8, 178.0; IR (Neat) ν_{max} 3329, 2974, 2700–2500, 1713, 1682, 1659 cm^{-1}. R_f (75% EtOAc/Petroleum Ether) 0.52. Anal. Calcd for $C_{17}H_{24}N_2O_5$: C, 60.70; H, 7.19; N, 8.33. Found: C, 60.51; H, 7.04; N, 8.29.

*4.2.3. (Z)-4-(2-((tert-Butoxycarbonylamino)methyl)phenylamino)-4-oxobut-2-enoic acid (**3c**)*

Mp 140–142 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.45 (s, 9H), 4.28 (d, J=8 Hz, 2H), 5.45 (br t, J=8 Hz, 1H), 6.48 (d, J=14 Hz, 1H), 6.72 (d, J=12 Hz, 1H), 7.15–7.29 (m, 2H), 7.34–7.44 (m, 1H), 8.18 (d, J=8 Hz, 1H), 11.19 (br s, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.5, 40.1, 78.6, 125.0, 125.9, 127.5, 128.4, 130.3, 132.9, 133.8, 134.8, 156.5, 164.2, 167.0; IR (Nujol) ν_{max} 3487, 3057, 2700–2500, 1707, 1636 cm^{-1}. R_f (70% EtOAc/petroleum ether) 0.38. Anal. Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74. Found: C, 60.08; H, 6.13; N, 8.65.

*4.2.4. (Z)-4-(2-((tert-Butoxycarbonylamino)methyl)phenylamino)-2-methyl-4-oxobut-2-enoic acid (**3d**)*

Mp 111–113 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.46 (s, 9H), 2.24 (s, 3H), 4.29 (d, J=8 Hz, 2H), 5.37 (br t, J=6 Hz, 1H), 6.76 (s, 1H), 7.02–7.26 (m, 2H), 7.32–7.44 (m, 1H), 8.17 (d, J=8 Hz, 1H), 10.86 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.1, 28.3, 41.5, 81.3, 123.3, 126.2, 127.9, 129.0, 129.9, 130.8, 135.0, 146.4, 158.0, 165.2, 165.9; IR ($CHCl_3$) ν_{max} 3389, 1720, 1715, 1697, 1645 cm^{-1}. R_f (75% EtOAc/petroleum ether) 0.42. Anal. Calcd for $C_{17}H_{22}N_2O_5$: C, 61.07; H, 6.63; N, 8.38. Found: C, 60.92; H, 6.54; N, 8.27.

*4.2.5. 2-(2-((tert-Butoxycarbonylamino)methyl)phenylcarbamoyl)benzoic acid (**3f**)*

Mp 155–157 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 1.35 (s, 9H), 4.21 (d, J=6 Hz, 2H), 7.12–7.40 (m, 4H), 7.45–7.75 (m, 4H), 7.88 (d, J=8 Hz, 1H), 9.94 (br s, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.5, 40.1, 78.4, 125.8 (two carbons), 127.3, 128.2 (two carbons), 129.7, 129.8, 130.3, 132.0, 134.4, 135.7, 139.2, 156.5, 168.0, 168.2; IR (Nujol) ν_{max} 3350, 3288, 2700–2500, 1707, 1690, 1657 cm^{-1}. R_f (80% EtOAc/petroleum ether) 0.51. Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.98; H, 5.87; N, 7.60.

*4.2.6. 2-(2-(2-((tert-Butoxycarbonylamino)methyl)phenylamino)-2-oxoethyl)benzoic acid (**3g**)*

Mp 148–150 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 1.39 (s, 9H), 4.10 (s, 2H), 4.12 (d, J=8 Hz, 2H), 7.05–7.28 (m, 2H), 7.30–7.60 (m, 5H), 7.89 (dd, J=8 and 2 Hz, 1H), 9.61 (br s, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.5, 40.1, 41.9, 78.5, 124.7, 125.0, 127.2, 127.3, 128.3, 130.7, 131.2, 132.1, 132.7, 133.1, 136.0, 137.3, 156.6, 168.9, 169.7; IR (Nujol) ν_{max} 3346, 3300, 1700, 1693, 1670 cm^{-1}. R_f (75% EtOAc/petroleum ether) 0.49. Anal. Calcd for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.55; H, 6.40; N, 7.16.

4.3. General procedure for the preparation of anilic esters (4a–d, 4g)

An ether solution of diazomethane was added dropwise to a suspension of acid (2.00 mmol) in diethyl ether (15 mL) at 0 °C until the acid dissolved with persistence of light yellow color. The reaction mixture was stirred further 30 min at 0 °C. The solvent was removed under reduced pressure and silica gel column chromatographic purification of the resulting residue using ethyl acetate–petroleum ether as an eluent afforded the corresponding pure ester product. The reaction of **3f** with diazomethane directly furnished the corresponding imide **5f** in 97% yield.

*4.3.1. Methyl 4-(2-((tert-butoxycarbonylamino)methyl)phenylamino)-4-oxobutanoate (**4a**)*

Thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.44 (s, 9H), 2.65–3.85 (m, 4H), 3.69 (s, 3H), 4.25 (d, J=8 Hz, 2H), 5.17 (br t, J=6 Hz, 1H), 7.02 (dt, J=8 and 2 Hz, 1H), 7.13 (dd, J=8 and 2 Hz, 1H), 7.28 (dt, J=8 and 2 Hz, 1H), 8.16 (d, J=8 Hz, 1H), 9.51 (br s, 1H); ^{13}C NMR [$CDCl_3$: CCl_4 (4:1), 50 MHz] δ 28.3, 29.1, 31.5, 41.5, 51.6, 80.3, 122.7, 124.1, 128.6, 128.8, 130.2, 136.6, 157.2, 170.4, 173.1; IR ($CHCl_3$) ν_{max} 3447, 3327, 1738, 1688, 1682 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.56. Anal. Calcd for $C_{17}H_{24}N_2O_5$: C, 60.70; H, 7.19; N, 8.33. Found: C, 60.57; H, 7.03; N, 8.24.

*4.3.2. Methyl 5-(2-((tert-butoxycarbonylamino)methyl)phenylamino)-5-oxopentanoate (**4b**)*

Mp 73–75 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.44 (s, 9H), 2.08 (quint, J=8 Hz, 2H), 2.46 (t, J=8 Hz, 2H), 2.52 (t, J=8 Hz, 2H), 3.67 (s, 3H), 4.24 (d, J=8 Hz, 2H), 5.25 (br s, 1H), 7.04 (t, J=8 Hz, 1H), 7.14 (d, J=8 Hz, 1H), 7.29 (t, J=8 Hz, 1H), 8.17 (d, J=8 Hz, 1H), 9.50 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.8, 28.3, 33.3, 36.2, 41.6, 51.5, 80.6, 122.5, 124.0, 128.5, 128.8, 130.3, 136.7, 157.2, 171.4, 173.6; IR ($CHCl_3$) ν_{max} 3323, 3277, 1734, 1686, 1676 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.53. Anal. Calcd for $C_{18}H_{26}N_2O_5$: C, 61.70; H, 7.48; N, 7.99. Found: C, 61.77; H, 7.39; N, 8.04.

*4.3.3. (Z)-Methyl 4-(2-((tert-butoxycarbonylamino)methyl)-phenylamino)-4-oxobut-2-enoate (**4c**)*

Mp 93–95 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.42 (s, 9H), 3.82 (s, 3H), 4.28 (d, J=6 Hz, 2H), 5.18 (br t, J=6 Hz, 1H), 6.25 (d, J=12 Hz, 1H), 6.54 (d, J=12 Hz, 1H), 7.09 (dt, J=8 and 2 Hz, 1H), 7.21 (dd, J=8 and 2 Hz, 1H), 7.32 (dt, J=8 and 2 Hz, 1H), 8.17 (d, J=8 Hz, 1H), 10.05 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.3, 41.5, 52.2, 80.5, 123.1, 124.8, 127.8, 128.8, 129.4, 130.2, 133.9, 136.0, 157.1, 162.9, 166.9; IR (Nujol) ν_{max} 3342, 3234, 1732, 1690, 1641 cm^{-1}. R_f (35% EtOAc/petroleum ether) 0.51. Anal. Calcd for $C_{17}H_{22}N_2O_5$: C, 61.07; H, 6.63; N, 8.38. Found: C, 61.23; H, 6.54; N, 8.41.

*4.3.4. (Z)-Methyl 4-(2-((tert-butoxycarbonylamino)methyl)-phenylamino)-2-methyl-4-oxobut-2-enoate (**4d**)*

Mp 105–107 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.45 (s, 9H), 2.10 (s, 3H), 3.86 (s, 3H), 4.27 (d, J=8 Hz, 2H), 5.13 (br t, J=6 Hz, 1H), 6.18 (q, J=2 Hz, 1H), 7.04 (t, J=8 Hz, 1H), 7.14 (dd, J=8 and 2 Hz, 1H), 7.30 (dt, J=8 and 2 Hz, 1H), 8.28 (d, J=8 Hz, 1H), 9.61 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.5, 28.3, 41.6, 52.3, 80.7, 122.5, 124.2 (two carbons), 128.5, 128.9, 130.2, 136.5, 142.6, 157.3, 162.9, 170.5; IR (Nujol) ν_{max} 3369, 3346, 1736, 1678, 1663 cm^{-1}. R_f (40% EtOAc/petroleum ether) 0.58. Anal. Calcd for $C_{18}H_{24}N_2O_5$: C, 62.05; H, 6.94; N, 8.04. Found: C, 62.10; H, 7.00; N, 8.21.

*4.3.5. Methyl 2-(2-(2-((tert-butoxycarbonylamino)methyl)-phenylamino)-2-oxoethyl)benzoate (**4g**)*

Mp 117–119 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.43 (s, 9H), 3.92 (s, 3H), 4.12 (s, 2H), 4.21 (d, J=6 Hz, 2H), 5.15 (br t, J=6 Hz, 1H), 7.06 (dt, J=8 and 2 Hz, 1H), 7.23 (d, J=8 Hz, 2H), 7.27–7.41 (m, 1H), 7.43–7.57 (m, 2H), 7.89–8.03 (m, 2H), 9.26 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.3, 41.4, 42.9, 52.3, 79.9, 123.2, 124.5, 127.2, 128.4, 129.5, 129.6, 130.1, 130.9, 132.2, 132.6, 136.3, 136.8, 156.6, 168.3, 169.8; IR (Nujol) ν_{max} 3341, 3246, 1719, 1674, 1605 cm^{-1}. R_f (50% EtOAc/petroleum ether) 0.59. Anal. Calcd for $C_{22}H_{26}N_2O_5$: C, 66.32; H, 6.58; N, 7.03. Found: C, 66.29; H, 6.56; N, 6.88.

*4.3.6. tert-Butyl 2-(1,3-dioxoisoindolin-2-yl)benzylcarbamate (**5f**)*

Mp 98–100 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.34 (s, 9H), 4.23 (d, J=4 Hz, 2H), 4.95 (br s, 1H), 7.18–7.26 (m, 1H), 7.37–7.48 (m, 2H), 7.49–7.58 (m, 1H), 7.74–7.85 (m, 2H), 7.90–8.01 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.2, 40.9, 79.3, 123.8, 128.6, 129.1, 129.8, 130.0, 130.3, 131.9, 134.3, 137.3, 155.6, 167.6; IR (Nujol) ν_{max} 3327, 1744, 1713, 1684 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.63. Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 67.99; H, 5.64; N, 8.05.

4.4. General procedure for the preparation of imides (5c/d, 5g)

To a stirred solution of ester (1.00 mmol) in dry DCM (10 mL) was added triethylamine (1.00 mmol) at room temperature and the reaction mixture was stirred for 5 h. Then the solvent was removed under reduced pressure and silica gel column chromatographic purification of the resulting residue using ethyl acetate–petroleum ether as an eluent afforded the corresponding pure imide product. The reaction of *tert*-butyl 2-aminobenzylcarbamate (**1**) with dimethylmaleic anhydride (**2e**) in ethanol under reflux for 1 h time provided the corresponding imide **5e** in 95% yield.

*4.4.1. tert-Butyl 2-(2,5-dioxo-2H-pyrrol-1(5H)-yl)benzylcarbamate (**5c**)*

Mp 104–106 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.41 (s, 9H), 4.18 (d, J=6 Hz, 2H), 4.85 (br s, 1H), 6.86 (s, 2H), 7.08–7.18 (m, 1H), 7.34–7.52 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.3, 41.0, 79.5, 128.7, 129.1, 129.6, 129.7, 130.2, 134.4, 137.4, 155.5, 169.8; IR ($CHCl_3$) ν_{max} 3445, 1776, 1715 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.53. Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.57; H, 6.00; N, 9.27. Found: C, 63.42; H, 6.11; N, 9.39.

*4.4.2. tert-Butyl 2-(3-methyl-2,5-dioxo-2H-pyrrol-1(5H)-yl)benzylcarbamate (**5d**)*

Thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.42 (s, 9H), 2.19 (d, J=2 Hz, 3H), 4.19 (d, J=6 Hz, 2H), 4.91 (br t, J=6 Hz, 1H), 6.50 (q, J=2 Hz, 1H), 7.08–7.17 (m, 1H), 7.33–7.53 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.2, 28.3, 40.9, 79.4, 127.6, 128.6, 129.0, 129.6, 129.9, 130.2, 137.3, 146.2, 155.6, 170.0, 170.9; IR (Nujol) ν_{max} 3389, 3368, 1715 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.56. Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.54; H, 6.37; N, 8.85. Found: C, 64.55; H, 6.49; N, 8.72.

*4.4.3. tert-Butyl 2-(3,4-dimethyl-2,5-dioxo-2H-pyrrol-1(5H)-yl)benzylcarbamate (**5e**)*

Thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.42 (s, 9H), 2.06 (s, 6H), 4.16 (d, J=6 Hz, 2H), 4.93 (br t, J=4 Hz, 1H), 7.05–7.15 (m, 1H), 7.31–7.54 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 8.9, 28.3, 40.9, 79.3, 128.5, 128.9 (two carbons), 129.4, 130.2, 137.3, 137.8, 155.7, 171.3; IR ($CHCl_3$) ν_{max} 3443, 1765, 1713 cm^{-1}. R_f (25% EtOAc/petroleum ether) 0.56. Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.55; H, 6.82; N, 8.53.

*4.4.4. tert-Butyl 2-(1,3-dioxo-3,4-dihydroisoquinolin-2(1H)-yl)benzylcarbamate (**5g**)*

Mp 290–292 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.26 (s, 9H), 3.99–4.45 (m, 4H), 4.78 (br t, J=4 Hz, 1H), 7.08–7.18 (m, 1H), 7.35 (d, J=8 Hz, 1H), 7.39–7.52 (m, 4H), 7.64 (dt, J=8 and 2 Hz, 1H), 8.23 (dd, J=8 and 2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.1, 36.9, 41.4, 79.2, 125.2, 127.3, 127.6, 128.9, 129.3, 129.4 (two carbons), 130.4, 134.0, 134.2, 134.7, 136.2, 155.5, 165.2, 170.2; IR (Nujol) ν_{max} 3368, 1701, 1663, 1609 cm^{-1}. R_f (40% EtOAc/petroleum ether) 0.70. Anal. Calcd for $C_{21}H_{22}N_2O_4$: C, 68.84; H, 6.05; N, 7.65. Found: C, 68.68; H, 6.17; N, 7.53.

4.5. General procedure for the preparation of quinazolin-1-one (6d/d′, 6e, 7a–c, 7f, 7g, 8b)

To a stirred solution of imide/ester (2.00 mmol) in dry DCM (15 mL) was added trifluoroacetic acid (10 mmol) and the reaction mixture was stirred at room temperature for 5 h. The reaction mixture was basified slowly with saturated solution of $NaHCO_3$ (10 mL) and extracted with DCM (25 mL×3). The combined organic layer was washed with brine (20 mL) and dried over Na_2SO_4. The concentration of organic layer in vacuo followed by silica gel column chromatographic purification of the resulting residue using ethyl acetate–petroleum ether as an eluent afforded the corresponding pure quinazolinone product. The compound **8b** on refluxing methanol for 5 h time furnished desired ring closed product **7b** in 87% yield.

*4.5.1. 2-Methylpyrrolo[1,2-a]quinazolin-1(5H)-one (**6d**)*

Mp 93–96 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.12 (d, J=2 Hz, 3H), 5.00 (s, 2H), 6.69 (br s, 1H), 7.04–7.18 (m, 2H), 7.27 (dt, J=6 and 2 Hz, 1H), 8.39 (d, J=8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.1, 50.5, 115.3, 120.1, 124.8, 125.6, 127.9, 128.7, 132.3, 142.4, 151.5, 168.5; IR ($CHCl_3$) ν_{max} 1720, 1678, 1640 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.57. Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.48; H, 5.01; N, 14.22.

*4.5.2. 3-Methylpyrrolo[1,2-a]quinazolin-1(5H)-one (**6d′**)*

Mp 155–158 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.21 (d, J=2 Hz, 3H), 5.04 (s, 2H), 6.33 (q, J=2 Hz, 1H), 7.06–7.19 (m, 2H), 7.20–7.33 (m, 1H), 8.37 (d, J=8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.2, 50.6, 115.3, 119.4, 124.8, 125.6, 126.9, 128.0, 132.6, 145.9, 153.2, 167.7; IR ($CHCl_3$) ν_{max} 1722, 1676, 1630 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.59. Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.79; H, 5.03; N, 14.02.

*4.5.3. 2,3-Dimethylpyrrolo[1,2-a]quinazolin-1(5H)-one (**6e**)*

Mp 117–119 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.01 (s, 3H), 2.09 (s, 3H), 4.98 (s, 2H), 7.09 (d, J=4 Hz, 2H), 7.26 (dt, J=8 and 2 Hz, 1H), 8.37 (d, J=8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 8.7, 9.0, 50.3, 115.1, 119.7, 124.4, 125.6, 127.9, 132.5, 135.4, 137.9, 152.7, 168.7; IR (Nujol) ν_{max} 1726, 1715, 1682, 1665 cm^{-1}. R_f (35% EtOAc/petroleum ether) 0.68. Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.77; H, 5.82; N, 13.07.

*4.5.4. 2,3-Dihydropyrrolo[2,1-b]quinazolin-1(9H)-one (**7a**)*

Mp 185–187 °C (lit.[4c] 189–191 °C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.55–2.80 (m, 2H), 2.85–3.00 (m, 2H), 4.80 (s, 2H), 6.95–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.1, 27.4, 41.5, 119.2, 126.0, 126.4 (two carbons), 128.8, 140.1, 157.0, 175.8; IR ($CHCl_3$) ν_{max} 1736, 1665, 1655, 1649 cm^{-1}. R_f (35% EtOAc/petroleum ether) 0.61. Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04. Found: C, 71.11; H, 5.44; N, 15.15.

*4.5.5. 7,8-Dihydro-6H-pyrido[2,1-b]quinazolin-9(11H)-one (**7b**)*

Mp 101–103 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.99 (quint, J=6 Hz, 2H), 2.72 (t, J=6 Hz, 2H), 2.83 (t, J=6 Hz, 2H), 4.90 (s, 2H), 7.00–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 17.7, 31.7, 33.1, 42.2, 122.1, 125.0, 125.7, 126.7, 128.5, 138.7, 152.4, 170.2; IR ($CHCl_3$) ν_{max} 1692, 1682, 1620, 1601 cm^{-1}. R_f (35% EtOAc/petroleum ether) 0.67. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.06; H, 6.00; N, 14.05.

*4.5.6. Pyrrolo[2,1-b]quinazolin-1(9H)-one (**7c**)*

Mp 128–130 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.85 (s, 2H), 6.61 (d, J=6 Hz, 1H), 7.05–7.47 (m, 4H), 7.48 (dd, J=8 and 2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 40.4, 121.9, 127.0, 128.5, 128.8, 128.9, 129.8, 136.3, 140.3, 152.4, 169.5; IR ($CHCl_3$) ν_{max} 1720, 1647, 1641 cm^{-1}. R_f (40% EtOAc/petroleum ether) 0.49. Anal. Calcd for $C_{11}H_8N_2O$: C, 71.73; H, 4.38; N, 15.21. Found: C, 71.82; H, 4.44; N, 15.13.

*4.5.7. Isoindolo[1,2-b]quinazolin-12(10H)-one (**7f**)*

Mp 175–177 °C (lit.[4b] 175–177 °C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.00 (s, 2H), 7.13–7.40 (m, 3H), 7.50 (dd, J=8 and 2 Hz, 1H), 7.61–

7.77 (m, 2H), 7.85–7.96 (m, 1H), 8.01–8.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 40.6, 121.3, 122.2, 123.2, 126.9, 127.7, 128.1, 128.8, 130.4, 132.1, 132.9, 134.4, 140.3, 148.9, 166.9; IR (Nujol) ν_{max} 1726, 1651, 1597 cm^{-1}. R_f (35% EtOAc/petroleum ether) 0.59. Anal. Calcd for $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96. Found: C, 77.08; H, 4.41; N, 12.13.

*4.5.8. 5H-Isoquinolino[3,2-b]quinazolin-11(13H)-one (**7g**)*

Mp 290–292 °C (lit.[4e] 308–310 °C); ^{1}H NMR (DMSO-d_6, 200 MHz) δ 5.07 (s, 2H), 5.86 (s, 1H), 6.88 (d, J=8 Hz, 1H), 6.90 (t, J=8 Hz, 1H), 7.12 (t, J=8 Hz, 1H), 7.20 (t, J=8 Hz, 1H), 7.27 (d, J=8 Hz, 1H), 7.37 (d, J=8 Hz, 1H), 7.50 (dt, J=8 and 2 Hz, 1H), 8.03 (d, J=8 Hz, 1H), 9.72 (br s, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 42.1, 83.3, 113.3, 117.1, 120.0, 121.0, 122.5, 124.3, 126.9, 127.5, 128.8, 132.8, 136.9, 139.0, 140.8, 161.5; IR (Nujol) ν_{max} 1657, 1624, 1607 cm^{-1}. R_f (70% EtOAc/petroleum ether) 0.42. Anal. Calcd for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.43; H, 4.92; N, 11.35.

*4.5.9. Methyl 4-(3,4-dihydroquinazolin-2-yl)butanoate (**8b**)*

Mp 96–98 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.10 (quint, J=8 Hz, 2H), 2.44 (t, J=8 Hz, 2H), 2.76 (t, J=8 Hz, 2H), 3.59 (s, 3H), 4.78 (s, 2H), 6.98 (d, J=8 Hz, 1H), 7.11–7.17 (m, 1H), 7.21 (d, J=4 Hz, 2H), 9.88 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.4, 31.2, 32.7, 42.5, 51.7, 116.8, 117.5, 126.2, 127.0, 129.0, 131.6, 162.5, 172.8; IR (Nujol) ν_{max} 3194, 1735, 1641 cm^{-1}. R_f (80% EtOAc/petroleum ether) 0.43. Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.09; H, 6.82; N, 12.17.

4.6. General procedure for the conversion of angular to linear quinazolin-1-one (7d, 7d′, 7e)

To a stirred solution of angular quinazolin-1-one (1.00 mmol) in methanol (10 mL) was added acetic acid (0.10 mL) and the resulting reaction mixture was refluxed for 24/48 h. Then the reaction mixture was allowed to cool at 25 °C and the solvent was evaporated under reduced pressure. The silica gel column chromatographic purification of the resulting residue using ethyl acetate–petroleum ether as an eluent afforded the corresponding pure quinazolinone product. The transformation of **7d′** to **7d** was completed using the above procedure in 15 days time with 96% yield.

*4.6.1. 2-Methylpyrrolo[2,1-b]quinazolin-1(9H)-one (**7d**)*

Mp 150–152 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.15 (d, J=2 Hz, 3H), 4.82 (s, 2H), 6.83 (q, J=2 Hz, 1H), 7.10–7.50 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.1, 40.4, 121.8, 126.9, 127.9, 128.5, 128.7, 129.8, 140.5, 140.7, 151.9, 170.3; IR (Nujol) ν_{max} 1721, 1650, 1634, 1460 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.57. Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.66; H, 4.83; N, 14.02.

*4.6.2. 3-Methylpyrrolo[2,1-b]quinazolin-1(9H)-one (**7d′**)*

Mp 165–168 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.29 (d, J=2 Hz, 3H), 4.82 (s, 2H), 6.27 (q, J=2 Hz, 1H), 7.13–7.38 (m, 3H), 7.48 (dd, J=8 and 2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 11.4, 40.5, 122.1, 124.7, 126.9, 128.2, 128.7, 128.8, 140.5, 147.8, 153.2, 169.7; IR (Nujol) ν_{max} 1718, 1648, 1634, 1461 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.59. Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.85; H, 5.11; N, 14.04.

*4.6.3. 2,3-Dimethyllpyrrolo[2,1-b]quinazolin-1(9H)-one (**7e**)*

Mp 170–172 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.02 (d, J=2 Hz, 3H), 2.17 (d, J=2 Hz, 3H), 4.79 (s, 2H), 7.11–7.37 (m, 3H), 7.47 (dd, J=8 and 2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 8.7, 9.0, 40.4, 122.1, 126.8, 127.6, 128.4, 128.6, 133.7, 139.5, 140.7, 153.1, 170.7; IR (Nujol) ν_{max} 1712, 1638, 1599, 1459 cm^{-1}. R_f (30% EtOAc/petroleum ether) 0.66. Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.44; H, 5.61; N, 13.35.

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