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Thermo-promoted Reactions of Anthranils with Carboxylic Acids, Amines, Phenols and Malononitrile under Catalyst-free Conditions

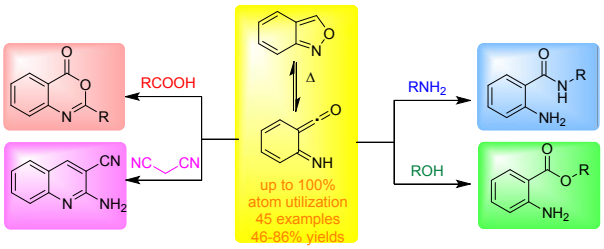
Jing Jiang,[†,‡,§] Xin Cai,[†,§] Yanwei Hu,[†,§] Xuejun Liu,[¢] Xiaodong Chen,[¢] Shun-Yi Wang,[*,ξ] Yinan Zhang,[*,‡] and Shilei Zhang,[*,†]

[†]Jiangsu Key Laboratory of Neuropsychiatric Diseases and College of Pharmaceutical Sciences, Soochow University, 199 Ren'ai Road, Suzhou, Jiangsu, 215123, China

[‡]Jiangsu Key Laboratory for functional substances of Chinese of Medicine, College of Pharmacy, Nanjing University of Chinese Medicine, Nanjing, 210023, China

[ξ]Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science & Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China

[¢]Shanghai Fosun Shino Tech Pharmaceutical Co., Ltd. Building 7, No.1999 ZhangHeng Road, Shanghai, 201203, China



ABSTRACT. A convenient and atom-economical procedure for the thermo-promoted reactions of anthranil with different substrates was developed. The catalyst-free process affords various useful building blocks with good to moderate yields. This chemistry enables several step- and cost-effective approaches for biologically interesting molecules and provides an efficient platform for the investigation of untapped reactions at high temperature.

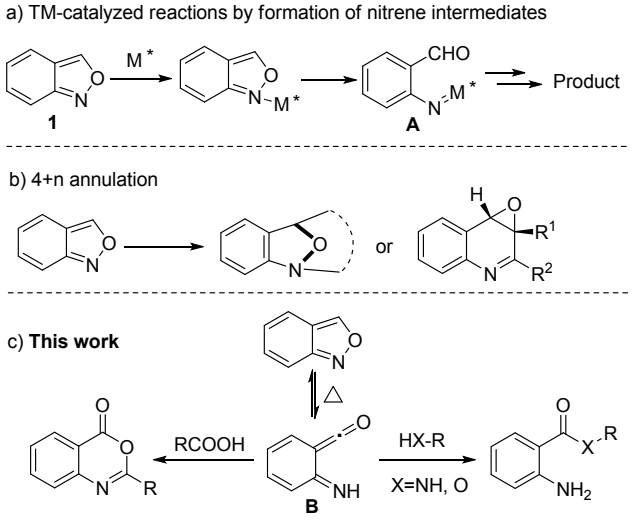
1. INTRODUCTION

Heating is perhaps the most widely used method in conducting organic reactions. In some cases, high temperature is necessary to promote reactions to occur, such as the well-known Ullmann reaction,[1] Chugaev elimination,[2] and Cope rearrangement.[3] The thermo-promoted reactions proceeding without the application of any catalysts, or/and additives are more economical due to lower material costs, fewer contaminants, and easier purification of desired products. However, high temperature is notorious for causing decomposition for many organic compounds, resulting in complicated reaction mixtures and low reaction yields. On this account, high-temperature reactions with satisfactory yields are difficult to achieve and thus are rarely documented.

Anthranil, a simple 2,1-benzisoxazole heterocycle, has recently been recognized as a bifunctional reagent for a broad range of organic transformations due to its unique electronic properties.[4-9] Several transition metals, such as Au,[4] Co,[5] Rh[6] and Cu,[7] can cleave the labile N-O bond of anthranil to form ortho-formyl nitrene intermediate **A** (Scheme 1a), which can be further converted into various products, especially the useful nitrogen-containing heterocycles. For example, Hashmi[4] reported the gold-catalyzed synthesis of 7-acylindoles and quinolines from alkynes and propargyl silyl ethers, respectively, with anthranils. Li's,[5, 6a-c] Jiao's,[6d-e] Kim's[6f-g] and other groups[6h-i, 7a] also reported a series of significant aminations using anthranils as N-sources through transition-metal catalyzed C-H activations. Very recently, our group[7b] described the Cu/Ag-catalyzed synthesis of 2-aryl-3-sulfonyl substituted quinolines from sulfonylhydrazone and anthranils in which the nitrene species acted as a key intermediate as well. Meanwhile, studies from the research groups of Luo,[8a] Liu,[8b] Tang[8c] and Tiwari[8d-e] demonstrated that anthranil was a good reaction partner for '4+n' annulations (Scheme 1b). These reactions obviously underwent different mechanisms from that of the nitrene mode since activation of the benzisoxazole moiety was not involved here.

In this context, we envisioned that the N-O bond of anthranil might be stimulated by high temperature instead of the use of transition metals, producing highly reactive ketene species **B**,[9g] which could be further trapped by various commonly used nucleophiles (Scheme 1c). In this way, an efficient platform for screening of new reactions was created, enabling the rapid discovery of diverse pharmaceutically interesting compounds in a cheap and convenient fashion. Herein, we report our procedures for the discovery and optimization of a series of condensation reactions of anthranil with carboxylic acids, amines, phenols and malononitrile with moderate to good yields under heating-only reaction conditions.

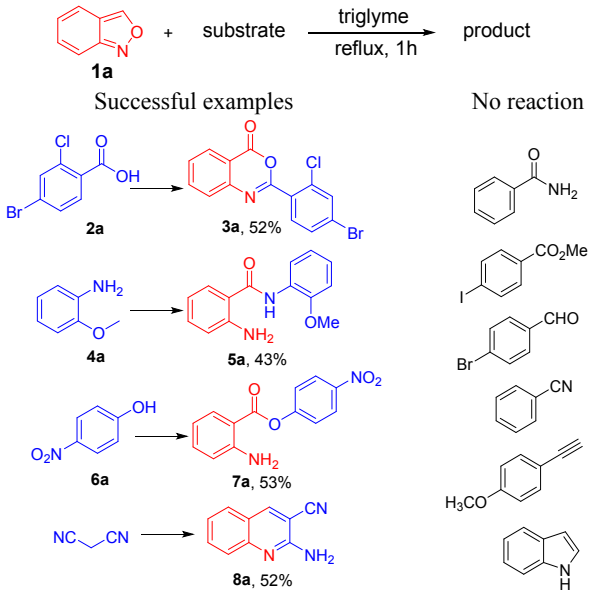
Scheme 1. The reactions of anthranil



2. RESULTS AND DISCUSSION

Based on the above assumptions, we commenced our investigations by heating anthranil in combination with various compounds bearing different functional groups (Table 1). Triglyme (triethylene glycol dimethyl ether) was selected as the solvent because of the appropriate boiling point (216 °C) and miscibility with water, which facilitates the final work-up through simple extraction.

Table 1. Exploration of reactions of anthranil with various substrates at high temperature[a,b]

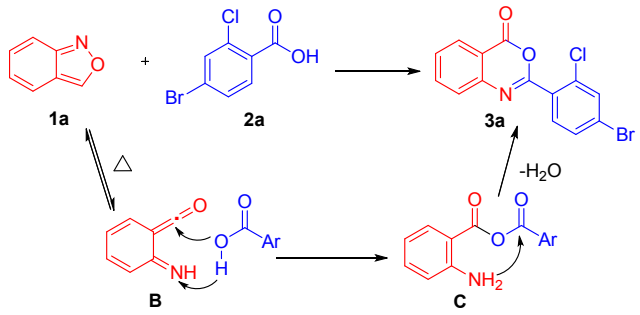


[a]Reaction conditions: unless stated otherwise, a solution of anthranil **1a** (1.0 mmol) and substrate (1.2 mmol) in triglyme (2 mL) was stirred under reflux for 1 h. [b]Isolated yield.

To our delight, several substrates were identified to react with anthranil at refluxing temperature (Table 1). When benzoic acid **2a** was used as the nucleophile, the benzoxazinone heterocycle **3a** was generated after 1 h. In this reaction, the direct employment of easily available carboxylic acids relative to traditional toxic and non-stable acyl chlorides[10], anhydrides[11] or other methods[12] represents the simplest and most economical approach to this pharmaceutically important scaffold.[13] The other carbonyl-group-containing reagents, such as benzamide, benzoate ester and benzaldehyde, were also evaluated, but all failed to yield any product. As common nucleophiles, aniline **4a** and phenol **6a** were verified as good reaction partners with anthranil, affording the corresponding ortho-aminobenzoyl products **5a** and **7a** respectively. It should be noted that the current method is a single-step conversion compared to the classic multi-step procedure.[14] Next, in the screening of other substrates, only malononitrile provided a positive result by the formation of quinoline **8a**.[9g] For these four successful reactions, it is particularly noteworthy that as high as 100% of the starting atom materials were incorporated into the final products (**5a** and **7a**), or only water was produced as the by-product (**3a**), or the extrusion of one oxygen atom took place (**8a**).[9g] The proposed reaction mechanism is shown in Table 2 by employing benzoic acid **2a** as a representative substrate. The ketene **B** generated in situ from

1a reacted with benzoic acid to afford intermediate **C**, which was then transformed into product **3a** through intramolecular condensation of amine group and anhydride moiety.

Table 2. Optimization of the reaction conditions of anthranil and benzoic acid[a]



Entry	Solvent	2a (equiv.)	t (h)	Temp (°C)[b]	Yield (%)[c]
1	triglyme	1.2	1	216	52
2	DMI	1.2	1	225	28
3	TEG	1.2	1	230	15
4	DOA	1.2	1	230	32
5	diglyme	1.2	3	160	NR[d]
6	DMF	1.2	3	153	NR[d]
7	DMSO	1.2	3	189	NR[d]
8	triglyme	1.0	1	216	38
9	triglyme	1.5	1	216	65
10	triglyme	2.0	1	216	57
11	triglyme	1.5	2	200	56
12	triglyme	1.5	3	180	24
13	triglyme	1.5	5	160	NR[d]
14	triglyme	1.5	0.5	216	52
15	triglyme	1.5	1.5	216	63

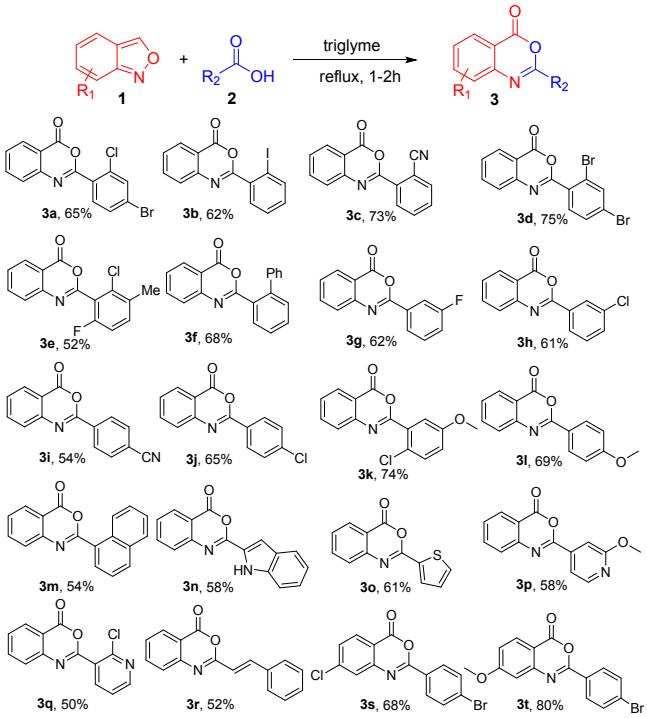
[a]Reaction conditions: unless stated otherwise, a solution of anthranil **1a** (1.0 mmol) and benzoic acid **2a** (1.0-2.0 mmol) in solvent (2 mL) was stirred under specified temperature conditions. [b]For entries 1-7, if the boiling point of the solvent was higher than 230 °C, the reaction was carried out at 230 °C; otherwise, the reaction was refluxed. [c]Isolated yield. [d]No reaction.

With these preliminary encouraging results in hand, we then turn our attention to optimizing the reaction conditions by taking benzoic acid **2a** as an example. Four representative solvents with high boiling points were screened (Table 2, Entries 1-4, DMI: 1,3-Dimethyl-2-imidazolidinone; TEG: tetraethylene glycol; DOA: dimethyl adipate), and triglyme showed the best yield (Table 2, Entry 1). Anthranil cannot be activated with lower boiling point solvents, such as diglyme (Table 2, Entry 5, 160 °C) and DMF (Table 2, Entry 6, 153 °C). The temperature to trigger the reaction in triglyme was approximately 180 °C (Table 2, Entries 11-13), but DMSO (Table 2, Entry 7) could not initiate the reaction, even at boiling point (189 °C). The trend of reactivity in different solvents could be attributed to the solvent effects where the less polar solvents favor to generate less charged product **3a** compared to the acidic reactants, which also explained the retardation of reactivity in DMSO. A further survey of the loading amount (Table 2, Entries 8-10) and reaction time (Table 2, Entries 14-15) identified the optimal conditions: refluxing anthranil with 1.5 equivalent of benzoic acid in triglyme for 1 h (Table 2, Entry 9). In the optimal condition, full conversion of the reactant **1a** was observed accompanied with 65% isolation yield of product **3a** as well as a small portion of polar and dark lumps sticked on the

column chromatography. No clear by-product was isolated or identified from the NMR and LC-MS profiles of crude products except **3a**.

Having established the optimal reaction conditions, we then examined the generality of this condensation reaction with a wide range of substrates. It was found that the formation of benzoxazinone was unaffected by the electronic nature of the substituents on aromatic rings. Regardless of electron-withdrawing (**3a-j**， **3s**) or electron-donating (**3k**, **3l**, **3t**) groups, the process proceeded efficiently to afford the products in moderate to good yields (50-80%). Furthermore, naphthyl, heteroaromatic and alkenyl carboxylic acids were also compatible with this transformation (**3m-r**). Unfortunately, aliphatic carboxylic acid could not deliver the desired product with anthranil. The structures of **3** were confirmed by comparing the ^{1}H and ^{13}C NMR spectra of **3j**, **3l** and **3o** with those of the literature.[12b,15]

Table 3. Scope of the reactions of anthranils with carboxylic acids[a]



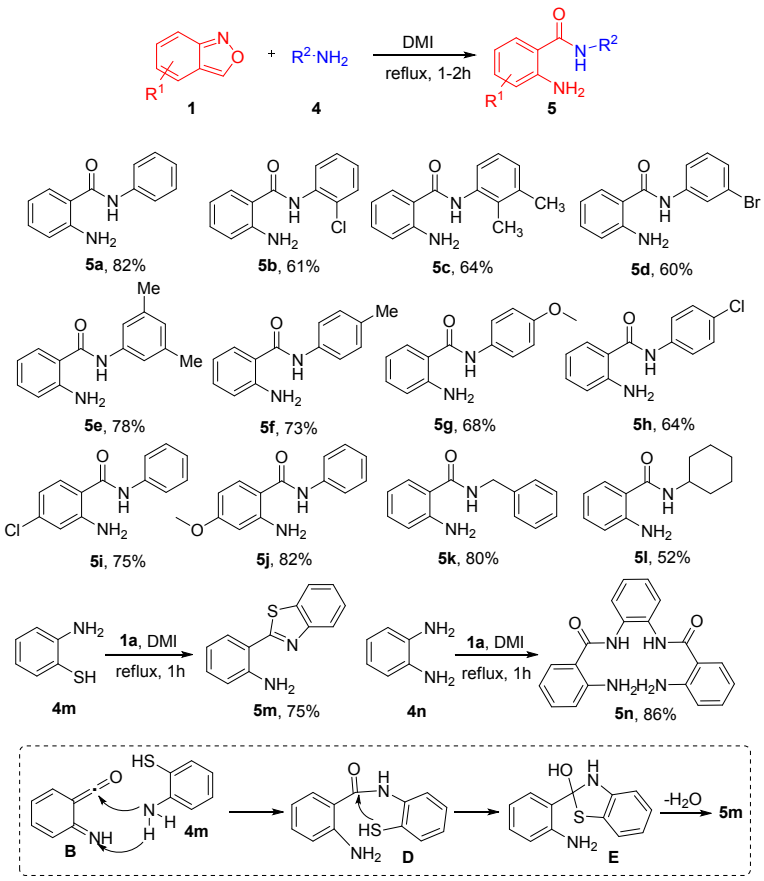
[a]Reaction conditions: see experimental section.

Next, a variety of anilines were examined in the reaction with anthranils (Table 4).[16] It was found that anilines bearing electron-donating and weak electron-withdrawing groups exhibited better reactivity than the ones with strong electron-withdrawing substituents (-NO_2, -CN, -$CONH_2$). For example, the substrates with para-methoxy and para-chloro substituents provided 73% and 64% yields of the desired products (**5g** and **5h**), while 4-nitroaniline gave no product at all, probably due to the reduced nucleophilicity of electron-deficient aniline. This fact could explain why the reaction stopped at product **5**, though the newly formed aniline in **5** could potentially react further with another molecule of anthranil. In addition, the reaction also worked well with alphatic amines to afford the desired products

smoothly due to their good nucleophilicity (**5k** and **5l**). Interestingly, ortho-functionalized anilines such as 2-aminobenzenethiol (**4m**) gave benzothiazole **5m**, and 1,2-phenylenediamine (**4n**) gave bisamide **5n** in high yields. The mechanism for the generation of **5m** is suggested in Table 4. First, the amino group of **4m** attacked the ketene moiety of **B** to generate amide **D**, and then the intramolecular attack of carbonyl group by thiol produced intermediate **E**, which was followed by dehydration to give benzothiazole **5m**.

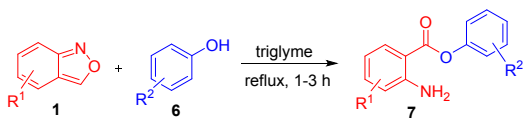
In a similar manner to anilines, phenols reacted with anthranils to deliver esters **7** (Table 5).[16] In contrast to anilines, only phenols bearing electron-withdrawing groups could engage in the process, while no reactions occurred with phenols containing electron-donating substituents.

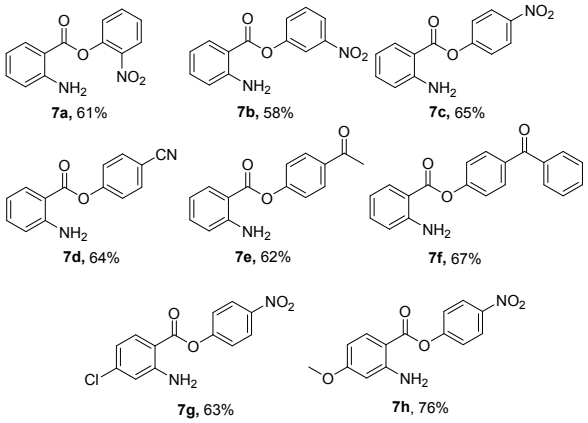
Table 4. Scope of the reactions of anthranils with anilines[a]



[a]Reaction conditions: see experimental section.

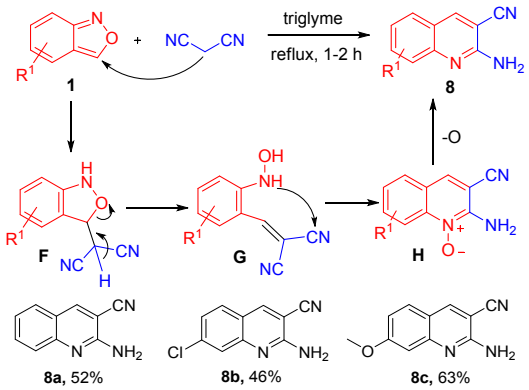
Table 5. Scope of the reactions of anthranils with phenols[a]





[a]Reaction conditions: see experimental section.

Table 6. Scope of the reactions of anthranils with malononitrile[a]



[a]Reaction conditions: see experimental section.

Finally, anthranils bearing different substituents were successfully transformed into quinolines **8** in the reactions with malononitrile (Table 6). Significantly, although the literature method gave quinoline 1-oxide product from the same substrates using piperidine as the catalyst at lower temperature,[9g] our method provided quinoline by extruding one oxygen atom at high temperature. We conjectured that the the formation of **8** is different from **3**, **5** and **7** in which ketene **B** was involved. The reaction should undergo a similar pathway as literature 9g reported, but just lost one oxygen in the final stage in our case (Table 6). We also probed other active methylene compounds such as malonate and 1,3-pentadikeones, but no desired product was obtained.

3. CONCLUSION

In summary, we discovered a novel reaction condition for anthranil to generate a reactive ketene intermediate at high temperature, which allowed for the direct condensation with carboxylic acids, amines, phenols and malononitrile without the use of any catalyst or additive, producing benzoxazinones, amides, esters and quinolines in moderate to good yields. The strategy is featured by its

atom-economy, operational simplicity, and low cost, which is particularly appealing for both academic and industrial laboratories to pursue new synthetic strategies. Further screening of suitable substrates that could react with anthranil as well as other potential architectures is currently underway in our lab.

4. EXPERIMENTAL SECTION

1. General Information. Chemicals, reagents and solvents were purchased from commercial suppliers and used without special instructions. Thin layer chromatography (TLC) was performed on silica gel HSGF254 plates. Column chromatography was performed using either 200-300 Mesh silica gel. Visualization of spots on TLC plate was accomplished with UV light (254 nm). ^{1}HNMR spectra were recorded on a Bruker 400 MHz NMR spectrometer, and ^{13}CNMR spectra were recorded on a Bruker 600 MHz NMR spectrometer. Chemical shifts are reported in ppm and referenced to tetramethylsilane (TMS) or residual solvent peaks as internal standards (for $CDCl_3$, tetramethylsilane 0 ppm for ^{1}H and $CDCl_3$ 77.00 ppm for ^{13}C; for DMSO-d_6, 2.50 ppm for ^{1}H and 39.50 ppm for ^{13}C). High-resolution mass spectra (HRMS) were obtained on a Q Exactive Plus orbitrap mass analyzer (Thermo Fisher Scientific) and are given in m/z.

2. General procedure for reactions of anthranils and benzoic acids (Table 3)
A solution of acid **2** (1.5 mmol) in triglyme (2 mL) was added anthranil **1** (1.0 mmol). The resulting mixture was then stirred under reflux until the reaction was completed monitored by TLC (generally 1-2 h). After cooling, water (10 mL) was added and the mixture was extracted with EtOAc (5 mL ×3). The combined organic layers were washed with water and brine and dried over sodium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography to give desired product **3**.

2-(4-Bromo-2-chlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (3a). White solid (217 mg, 65%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 147-150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.72 (s, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.9, 155.6, 146.2, 136.7, 134.5, 133.8, 132.4, 130.2, 129.1, 129.0, 128.6, 127.4, 126.1, 116.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_8BrClNO_2$ 335.9427, found 335.9422.

2-(2-Iodophenyl)-4H-benzo[d][1,3]oxazin-4-one (3b). Gray solid (216 mg, 62%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.6 (hexanes/EtOAc = 10/1). Mp 120-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.6 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 8.0, 16.8 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.2, 157.7, 141.1, 136.6, 132.2, 130.8, 128.9, 128.6, 127.3, 116.9, 94.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_9INO_2$ 349.9678, found 349.9668. The characterization data is consistant with reported literature.[17]

2-(4-Oxo-4H-benzo[d][1,3]oxazin-2-yl)benzonitrile (3c). Gray solid (181 mg, 73%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 196-197 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 3.6 Hz, 2H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.56-7.52 (m, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.8, 157.9, 149.6, 146.7, 135.5, 135.4, 134.2, 133.3, 129.1, 128.5, 128.4, 128.2, 125.4, 122.9, 122.7. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_9N_2O_2$ 249.0664, found 249.0661.

2-(2,4-Dibromophenyl)-4H-benzo[d][1,3]oxazin-4-one (3d). Yellow solid (285 mg, 75%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 205-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.6 Hz, 1H), 7.92 (s, 1H), 7.87 (t, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 6.8 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.9, 156.2, 146.2, 136.9, 136.7, 132.5, 131.0, 130.8, 129.2, 128.6, 127.4, 126.1, 122.6, 116.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_8Br_2NO_2$ 381.8901, found 381.8894.

2-(2-Chloro-6-fluoro-3-methylphenyl)-4H-benzo[d][1,3]oxazin-4-one (3e). White solid (150 mg, 52%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.5 (hexanes/EtOAc = 10/1). Mp 198-201 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.0 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.38-7.35 (m, 1H), 7.05 (t, *J* = 8.8 Hz, 1H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.1, 158.9 (d, *J* = 250 Hz), 152.9, 146.0, 136.7, 133.6 (d, *J* = 4.5 Hz), 133.3 (d, *J* = 7.5 Hz), 133.0 (d, *J* = 4.5 Hz), 129.4, 128.7, 127.4, 117.2, 114.2 (d, *J* = 19.5 Hz), 19.7. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{10}ClFNO_2$ 290.0384, found 290.0379.

2-([1,1'-Biphenyl]-4-yl)-4H-benzo[d][1,3]oxazin-4-one (3f). White solid (203 mg, 68%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 221-223 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 6.4 Hz, 4H), 7.35 (s, 5H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.2, 159.1, 130.2, 128.4, 128.4, 128.3, 128.2, 127.4, 127.3, 116.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{14}NO_2$ 300.1025, found 300.1015. The characterization data is consistant with reported literature.[18]

2-(3-Fluorophenyl)-4H-benzo[d][1,3]oxazin-4-one (3g). White solid (149 mg, 62%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.5 (hexanes/EtOAc = 10/1). Mp 115-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.6 Hz, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 9.6 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.50 (dd, *J* =8.0, 13.6 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.8 (d, *J* = 246 Hz), 159.2, 155.9 (d, *J* = 4.5 Hz), 146.6, 136.7, 132.4 (d, *J* = 9.0 Hz), 130.4 (d, *J* = 7.5 Hz), 128.7, 128.6, 127.3, 123.9 (d, *J* = 3.0 Hz), 119.7 (d, *J* = 21.0 Hz), 117.0, 115.3 (d, *J* = 24.0 Hz). HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_9FNO_2$ 242.0617, found 242.0615. The characterization data is consistant with reported literature.[19]

2-(3-Chlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (3h). White solid (157 mg, 61%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.5 (hexanes/EtOAc = 10/1). Mp 128-130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 7.6 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.57-7.54 (m, 2H), 7.46 (t, *J* = 8.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.1, 155.8, 146.6, 136.7, 134.9, 132.5, 132.0, 130.0, 128.7, 128.6, 128.2, 127.3, 126.3, 117.0. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_9ClNO_2$ 258.0322, found 258.0320. The characterization data is consistant with reported literature.[19]

4-(4-Oxo-4H-benzo[d][1,3]oxazin-2-yl)benzonitrile (3i). Yellow solid (134 mg, 54%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 221-223 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.0 Hz, 1H), 8.28 (d,

J = 7.6 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 158.8, 155.2, 146.3, 136.8, 134.2, 132.7, 132.4, 129.2, 128.8, 128.7, 127.6, 118.0, 117.1, 115.8. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_9N_2O_2$ 249.0664, found 249.0654. The characterization data is consistant with reported literature.[18]

2-(4-Chlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (3j). White solid (167 mg, 65%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.5 (hexanes/EtOAc = 10/1). Mp 191-193°C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.6 Hz, 1H), 7.84 (t, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 159.3, 156.2, 146.7, 139.0, 136.6, 129.6, 129.1, 128.7, 128.6, 128.4, 127.2, 116.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_9ClNO_2$ 258.0322, found 258.0316. The characterization data is consistant with reported literature.[17]

2-(2-Chloro-5-methoxyphenyl)-4H-benzo[d][1,3]oxazin-4-one (3k). White solid (212 mg, 74%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 213-215°C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 6.8 Hz, 1H), 7.86 (d, *J* = 6.4 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 6.4 Hz, 1H), 7.41 (s, 2H), 7.01 (d, *J* = 7.2 Hz, 1H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 159.4, 158.4, 156.6, 146.6, 136.8, 132.1, 130.9, 129.1, 128.8, 127.6, 124.9, 119.0, 117.2, 116.2, 55.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{11}ClNO_3$ 288.0427, found 288.0424.

2-(4-Methoxyphenyl)-4H-benzo[d][1,3]oxazin-4-one (3l). White solid (174 mg, 69%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 157-158 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.8 Hz, 1H), 8.23 (d, *J* = 7.6 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 3.90 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 163.3, 159.8, 157.1, 147.3, 136.5, 130.3, 128.5, 127.7, 126.9, 122.5, 116.7, 114.1, 55.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{12}NO_3$ 254.0817, found 254.0812. The characterization data is consistant with reported literature.[12b]

2-(Naphthalen-1-yl)-4H-benzo[d][1,3]oxazin-4-one (3m). Yellow solid (147 mg, 54%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 118-128 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 9.18 (d, *J* = 8.8 Hz, 1H), 8.36-8.33 (m, 2H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.92-7.89 (m, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.71-7.68 (m, 1H), 7.61 (q, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 159.8, 157.7, 146.8, 136.6, 134.07, 133.2, 130.8, 130.0, 128.8, 128.6, 128.6, 127.9, 127.4, 127.0, 126.4, 125.8, 124.8, 117.0. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{18}H_{12}NO_2$ 274.0868, found 274.0858. The characterization data is consistant with reported literature.[19]

2-(1H-indol-2-yl)-4H-benzo[d][1,3]oxazin-4-one (3n). Yellow solid (152 mg, 58%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 198-200 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 9.16 (br, 1H), 8.23 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 6.8 Hz, 1H), 7.72 (d, *J* = 6.8 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.51-7.44 (m, 3H), 7.36-7.33 (m, 1H), 7.18 (d, *J* = 6.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 158.9, 152.3, 146.8, 137.6, 136.7, 128.9, 127.9, 127.5, 126.6, 125.7, 122.5, 121.0, 116.9, 111.6, 108.6. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{16}H_{11}N_2O_2$ 263.0821, found 263.0818. The characterization data is consistant with reported literature.[20]

2-(Thiophen-2-yl)-4H-benzo[d][1,3]oxazin-4-one (3o). White solid (140 mg, 61%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 128-130 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 2.8 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.65-7.61 (m, 2H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 4.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 159.0, 153.7, 147.1, 136.6, 132.4, 128.7, 128.3, 127.9, 116.7. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{12}H_8NO_2S$ 230.0276, found 230.0274. The characterization data is consistant with reported literature.[19]

2-(2-Methoxypyridin-4-yl)-4H-benzo[d][1,3]oxazin-4-one (3p). White solid (147 mg, 58%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 145-148 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 5.2 Hz, 1H), 8.27 (d, *J* = 7.6 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.72 (dd, *J* = 6.8, 16.8 Hz, 2H), 7.70-7.58 (m, 2H), 4.01 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 165.0, 158.8, 155.1, 147.8, 146.2, 140.4, 136.7, 129.2, 128.7, 127.6, 117.4, 114.4, 109.7, 53.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{11}N_2O_3$ 255.0770, found 255.0760.

2-(2-Chloropyridin-3-yl)-4H-benzo[d][1,3]oxazin-4-one (3q). Yellow solid (129 mg, 50%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 168-170 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 3.2 Hz, 1H), 8.29 (t, *J* = 6.8 Hz, 2H), 7.89 (t, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 4.8, 7.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 158.7, 155.0, 151.6, 149.8, 146.1, 140.1, 136.8, 129.4, 128.7, 127.5, 127.2, 122.2, 117.0. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_8ClN_2O_2$ 259.0274, found 259.0268. The characterization data is consistant with reported literature.[21]

(E)-2-Styryl-4H-benzo[d][1,3]oxazin-4-one (3r). White solid (129 mg, 52%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 144-146 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 16.4 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.62-7.59 (m, 3H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 6.4 Hz, 3H), 6.80 (d, *J* = 16.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 159.3, 157.3, 147.1, 142.0, 136.5, 134.6, 130.3, 129.0, 128.6, 128.2, 128.0, 126.9, 118.8, 116.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{16}H_{12}NO_2$ 250.0868, found 250.0860. The characterization data is consistant with reported literature.[22]

2-(4-Bromophenyl)-7-chloro-4H-benzo[d][1,3]oxazin-4-one (3s). White solid (278 mg, 68%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.5 (hexanes/EtOAc = 10/1). Mp 153-155 °C**.** ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.4 Hz, 3H), 7.68 (d, *J* = 6.0 Hz, 2H), 7.65 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 158.6, 157.7, 148.0, 143.3, 132.3, 130.1, 130.0, 129.2, 127.2, 115.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_8BrClNO_2$ 335.9427, found 335.9419. The characterization data is consistant with reported literature.[23]

2-(4-Bromophenyl)-7-methoxy-4H-benzo[d][1,3]oxazin-4-one (3t). White solid (264 mg, 80%). Flash chromatography eluting with hexanes/ethyl acetate (50:1 → 20:1), R_f = 0.5 (hexanes/EtOAc = 10/1). Mp 156-158 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.8, 12.0 Hz, 3H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 11.2 Hz, 2H), 3.96 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 166.6, 159.1, 157.4, 149.4, 132.2, 130.5, 129.9, 129.5, 127.8, 117.6, 110.0, 109.2, 56.1. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{11}BrNO_3$ 331.9922, found 331.9921.

3. General procedure for reactions of anthranils and anilines (Table 4)

A solution of compound **4** (2.0 mmol) in triglyme (2 mL) was added anthranil **1** (1.0 mmol). The resulting mixture was then stirred under reflux until the reaction was completed monitored by TLC (generally 1-2 h). After cooling, water (10 mL) was added and the mixture was extracted with EtOAc (5 mL ×3). The combined organic layers were washed with water and brine and dried over sodium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography to give desired product **5**.

2-Amino-N-phenylbenzamide (5a). Yellow solid (174 mg, 82%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 115-116 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (br, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.0

Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 6.4 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.75-6.72 (m, 2H), 5.52 (br, 2H). $^{13}C\{^1H\}$ NMR (600 MHz, $CDCl_3$) δ 167.2, 149.4, 134.8, 133.1, 129.1, 127.7, 127.2, 124.6, 123.3, 121.7, 117.7, 116.9, 115.6. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{13}N_2O$ 213.1028, found 213.1020. The characterization data is consistant with reported literature.[24]

2-Amino-N-(2-chlorophenyl)benzamide (5b). Yellow solid (150 mg, 61%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 95-97 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.0 Hz, 1H), 8.35 (br, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.29 (dd, *J* = 8.0, 15.6 Hz, 2H), 7.07 (t, *J* = 7.2 Hz, 1H), 6.74 (t, *J* = 7.2 Hz, 2H), 5.60 (br, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.5, 148.9, 137.8, 132.7, 129.0, 127.1, 124.5, 120.5, 117.5, 116.8, 116.2. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{12}ClN_2O$ 247.0638, found 247.0631. The characterization data is consistant with reported literature.[25]

2-Amino-N-(2,3-dimethylphenyl)benzamide (5c). White solid (154 mg, 64%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 115-116 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (br, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 9.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.73 (t, *J* = 7.2 Hz, 2H), 5.56 (br, 2H), 2.34 (s, 3H), 2.22 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.8, 149.2, 137.6, 135.3, 132.7, 130.3, 127.7, 127.2, 125.9, 122.6, 117.5, 116.7, 115.9, 20.59, 14.0. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{17}N_2O$ 241.1341, found 241.1339. The characterization data is consistant with reported literature.[26]

2-Amino-N-(3-bromophenyl)benzamide (5d). Yellow solid (174 mg, 60%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 155-157 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.79 (br, 1H), 7.45 (t, *J* = 6.4 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.24-7.20 (m, 1H), 6.71 (t, *J* = 7.6 Hz, 2H), 5.50 (br, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.6, 149.3, 139.4, 133.2, 130.4, 127.5, 127.2, 123.5, 122.8, 119.0, 117.8, 117.1, 115.8. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{12}BrN_2O$ 291.0133, found 291.0128. The characterization data is consistant with reported literature.[27]

2-Amino-N-(3,5-dimethylphenyl)benzamide (5e). White solid (187 mg, 78%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 160-162 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (br, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 5.2 Hz, 1H), 7.23 (s, 2H), 6.83 (s, 1H), 6.73 (t, *J* = 8.0 Hz, 2H), 5.52 (br, 2H), 2.36 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.5, 148.9, 138.7, 137.6, 132.6, 127.1, 126.2, 118.3, 117.5, 116.8, 116.4, 21.4. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{17}N_2O$ 241.1341, found 241.1339. The characterization data is consistant with reported literature.[26]

2-Amino-N-(p-tolyl)benzamide (5f). White solid (165 mg, 73%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 148-150 °C. ^1H NMR (165mg, 400 MHz, $CDCl_3$) δ 7.78 (br, 1H), 7.48 (t, *J* = 7.2 Hz, 3H), 7.29 (d, *J* = 6.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.74 (t, *J* = 7.6 Hz, 2H), 5.52 (br, 2H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.5, 148.9, 135.2, 134.2, 132.6, 129.5, 127.1, 120.7, 117.5, 116.8, 116.4, 20.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{15}N_2O$ 227.1184, found 227.1180. The characterization data is consistant with reported literature.[26]

2-Amino-N-(4-methoxyphenyl)benzamide (5g). White solid (164 mg, 68%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 114-116 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (br, 1H), 7.49 (d, *J* = 8.4 Hz, 3H), 7.29 (d, *J* = 6.8 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.73 (t, *J* = 7.6 Hz, 2H), 5.51 (br, 2H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.5, 156.6, 148.9, 132.6, 130.8, 127.1, 122.6, 117.5, 116.8, 116.4, 114.8, 114.2, 55.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{15}N_2O_2$ 243.1134, found 243.1131. The characterization data is consistant with reported literature.[28]

2-Amino-N-(4-chlorophenyl)benzamide (5h). Gray solid (157 mg, 64%). Flash chromatography eluting with hexanes/ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 142-144 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (br, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.23 (s, 2H), 6.69 (t, *J* = 7.2 Hz, 2H), 5.47 (br, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.4, 149.0, 136.4, 132.9, 129.4, 129.0, 127.1, 121.7, 117.6, 116.9, 115.8. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{12}ClN_2O$ 247.0638, found 247.0630. The characterization data is consistant with the reported literature.[28]

2-Amino-4-chloro-N-phenylbenzamide (5i). White solid (184 mg, 75%). Flash chromatography eluting with hexanes/ ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 138-140 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (br, 1H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 3H), 7.16 (t, *J* = 6.8 Hz, 1H), 6.71 (s, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 5.62 (br, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.0, 150.2, 138.7, 137.7, 129.2, 128.6, 124.9, 120.8, 117.0, 116.9, 114.6. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{12}ClN_2O$ 247.0638, found 247.0631. The characterization data is consistant with reported literature.[27]

2-Amino-4-methoxy-N-phenylbenzamide (5j). White solid (198 mg, 82%). Flash chromatography eluting with hexanes/ ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 152-154 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (br, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 6.28 (d, *J* = 8.8 Hz, 1H), 6.18 (s, 1H), 5.71 (br, 2H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.5, 163.4, 151.5, 138.2, 129.2, 129.0, 124.4, 120.7, 109.3, 104.5, 100.9, 55.4. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{15}N_2O_2$ 243.1134, found 243.1133. The characterization data is consistant with reported literature.[29]

2-Amino-N-benzylbenzamide (5k). White solid (180 mg, 80%). Flash chromatography eluting with hexanes/ ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 10/1). Mp 123-125 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 6H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.63 (t, *J* = 7.6 Hz, 1H), 6.35 (br, 1H), 5.56 (br, 2H), 4.60 (d, *J* = 5.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 169.1, 148.8, 132.4, 128.7, 127.8, 127.5, 127.0, 117.3, 116.6, 115.8, 43.7. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{15}N_2O$ 227.1184, found 227.1177. The characterization data is consistant with reported literature.[29]

2-Amino-N-cyclohexylbenzamide (5l). White solid (113 mg, 52%). Flash chromatography eluting with hexanes/ ethyl acetate (20:1 → 10:1), R_f = 0.2 (hexanes/EtOAc = 10/1). Mp 153-155 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.65 (dd, *J* = 7.6, 14.8 Hz, 2H), 5.89 (br, 1H), 5.47 (br, 2H), 3.92 (td, *J* = 7.2, 14.4 Hz, 1H), 2.01 (d, *J* = 9.6 Hz, 2H), 1.75 (dd, *J* = 3.6, 10.0 Hz, 2H), 1.65 (d, *J* = 12.8 Hz, 1H), 1.42 (dd, *J* = 12.4, 24.8 Hz, 2H), 1.23 (dt, *J* = 8.8, 18.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 168.4, 148.5, 132.0, 127.0, 117.2, 116.7, 116.5, 48.3, 33.2, 25.6, 24.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{19}N_2O$ 219.1497, found 219.1494. The characterization data is consistant with reported literature.[27]

2-(Benzo[d]thiazol-2-yl)aniline (5m). Yellow solid (169 mg, 75%). Flash chromatography eluting with hexanes/ ethyl acetate (50:1 → 20:1), R_f = 0.4 (hexanes/EtOAc = 10/1). Mp 120-122 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 6.78 (dd, *J* = 8.0, 18.4 Hz, 2H), 6.42 (br, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 169.2, 153.7, 146.7, 133.3, 131.6, 130.3, 126.0, 124.8, 122.4, 121.2, 116.9, 116.8, 115.3. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{11}N_2S$ 227.0643, found 227.0636. The characterization data is consistant with reported literature.[30]

N,N'-(1,2-Phenylene)bis(2-aminobenzamide) (5n). White solid (297 mg, 86%). Flash chromatography eluting with hexanes/ ethyl acetate (20:1 → 10:1), R_f = 0.3 (hexanes/EtOAc = 5/1).Mp 217-218 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.58 (br, 4H), 7.20 (dd, *J* = 2.8, 5.6 Hz, 4H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.65 (t, *J* = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (150 MHz,

DMSO-d_6) δ 152.9, 148.6, 130.8, 127.7, 122.3, 116.5, 115.4, 110.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{19}N_4O_2$ 347.1508, found 347.1505. The characterization data is consistant with reported literature.[31]

4. General procedure for reactions of anthranils and phenols (Table 5)

A solution of compound **6** (1.5 mmol) in triglyme (2 mL) was added anthranil **1** (1.0 mmol). The resulting mixture was then stirred under reflux until the reaction was completed monitored by TLC (generally 1-3 h). After cooling, water (10 mL) was added and the mixture was extracted with EtOAc (5 mL ×3). The combined organic layers were washed with water and brine and dried over sodium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography to give desired product **7**.

2-Nitrophenyl 2-aminobenzoate (7a). Yellow solid (157 mg, 61%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.2 (hexanes/EtOAc = 5/1). Mp 114-115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.15 (m, 1H), 8.11-8.09 (m, 1H), 7.74-7.71 (m, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.40-7.37 (m, 2H), 6.77-6.73 (m, 2H), 5.74 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.6, 151.5, 144.3, 142.3, 135.4, 134.5, 131.9, 126.4, 125.7, 125.6, 116.8, 116.6, 108.6. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{11}N_2O_4$ 259.0719, found 259.0709.

3-Nitrophenyl 2-aminobenzoate (7b). Yellow solid (149 mg, 58%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.2 (hexanes/EtOAc = 5/1). Mp 111-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.6 Hz, 1H), 8.11 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 2H), 5.78 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.9, 151.5, 151.2, 148.8, 135.4, 131.4, 130.0, 128.5, 120.6, 117.8, 116.8, 116.5, 108.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{11}N_2O_4$ 259.0719, found 259.0709. The characterization data is consistant with reported literature.[32]

4-Nitrophenyl 2-aminobenzoate (7c). Yellow solid (167 mg, 65%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.3 (hexanes/EtOAc = 5/1). Mp 114-115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 9.2 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 3H), 6.74 (dd, *J* = 4.8, 8.0 Hz, 2H), 5.79 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.7, 155.8, 151.6, 135.5, 131.5, 125.2, 122.9, 116.9, 116.6, 108.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{11}N_2O_4$ 259.0719, found 259.0709. The characterization data is consistant with reported literature.[33]

4-Cyanophenyl 2-aminobenzoate (7d). Yellow solid (152 mg, 64%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.2 (hexanes/EtOAc = 5/1). Mp 111-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.36 (dd, *J* = 8.0, 17.2 Hz, 3H), 6.73-6.71 (m, 2H), 5.78 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.8, 154.3, 151.6, 135.5, 133.7, 131.5, 123.2, 118.4, 116.9, 116.6, 109.6, 108.6. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{11}N_2O_2$ 239.0821, found 239.0820. The characterization data is consistant with reported literature.[32]

4-Acetylphenyl 2-aminobenzoate (7e). Yellow solid (158 mg, 62%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.3 (hexanes/EtOAc = 5/1). Mp 138-139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (t, *J* = 7.6 Hz, 3H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 7.2 Hz, 2H), 5.78 (br, 2H), 2.62 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 197.0, 166.2, 154.7, 151.5, 135.2, 134.7, 131.6, 130.0, 122.2, 116.9, 116.5, 109.1, 26.7. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{15}H_{14}NO_3$ 256.0974, found 256.0966. The characterization data is consistant with reported literature.[32]

4-Benzoylphenyl 2-aminobenzoate (7f). Yellow solid (212 mg, 67%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.2 (hexanes/EtOAc = 5/1). Mp 157-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.35 (dd, *J* = 8.0, 19.6 Hz, 3H), 6.74 (t, *J* = 7.2 Hz, 2H), 5.80 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 195.7, 166.3, 154.2, 151.5, 137.6, 135.2, 132.5, 131.7, 131.6, 130.0, 128.4, 122.0, 116.9, 116.5, 100.0. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{16}NO_3$ 318.1130, found 318.1121. No characterization data was supplied in the reported literature.[34]

4-Nitrophenyl 2-amino-4-chlorobenzoate (7g). Yellow solid (184 mg, 63%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.2 (hexanes/EtOAc = 5/1). Mp 145-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 2H), 6.74 (s, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 5.86 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.3, 155.7, 152.4, 145.6, 141.9, 133.0, 125.4, 123.0, 117.3, 116.3, 107.3. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{10}ClN_2O_4$ 293.0329, found 293.0323.

4-Nitrophenyl 2-amino-4-methoxybenzoate (7h). Yellow solid (219 mg, 76%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.2 (hexanes/EtOAc = 5/1). Mp 136-138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 6.32 (d, *J* = 8.0 Hz, 1H), 6.15 (s, 1H), 5.85 (br, 2H), 3.84 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.6, 165.4, 156.1, 154.0, 145.3, 133.6, 126.4, 125.3, 123.0, 105.6, 102.3, 99.3, 55.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H13N_2O_5$ 289.0824, found 289.0815.

5. General procedure for reactions of anthranils and malononitrile (Table 6)

A solution of malononitrile (3.0 mmol, 198 mg) in triglyme (2 mL) was added anthranil **1** (1.0 mmol). The resulting mixture was then stirred under reflux until the reaction was completed monitored by TLC (generally 1-2 h). After cooling, water (10 mL) was added and the mixture was extracted with EtOAc (5 mL ×3). The combined organic layers were washed with water and brine and dried over sodium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography to give desired product **8**.

2-Aminoquinoline-3-carbonitrile (8a). Yellow solid (88 mg, 52%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.4 (hexanes/EtOAc = 2/1). Mp 267-269 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 1H), 6.96 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 155.7, 149.1, 145.3, 132.8, 128.5, 125.4, 122.7, 121.0, 116.5, 94.5. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{10}H_8N_3$ 170.0718, found 170.0711. The characterization data is consistant with reported literature.[35]

2-Amino-7-chloroquinoline-3-carbonitrile (8b). Yellow solid (94 mg, 46%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.3 (hexanes/EtOAc = 2/1). Mp 311-313 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.52 (s, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.19 (br, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 156.9, 150.1, 145.8, 137.9, 130.8, 124.5, 123.6, 120.0, 116.6, 95.4. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{10}H_7ClN_3$ 204.0328, found 204.0322. The characterization data is consistant with reported literature.[36]

2-Amino-7-methoxyquinoline-3-carbonitrile (8c). Yellow solid (126 mg, 63%). Flash chromatography eluting with hexanes/ ethyl acetate (10:1 → 5:1), R_f = 0.4 (hexanes/EtOAc = 2/1). Mp 313-305 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.54 (s, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 6.92 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.89 (s, 1H), 6.89 (br, 2H), 3.87 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 163.6, 156.9, 151.8, 144.9, 130.3, 117.4, 116.6, 115.5, 105.2, 91.6, 55.9. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{10}N_3O$ 200.0824, found 200.0819. The

characterization data is consistant with reported literature.[37]

ASSOCIATED CONTENT

AUTHOR INFORMATION

Corresponding Author

*E-mail: shunyi@suda.edu.cn;
yinanzhang@njucm.edu.cn;
zhangshilei@suda.edu.cn.

Author Contributions

§Jing Jiang, Xin Cai and Yanwei Hu contributed equally.

ORCID

Shunyi Wang: 0000-0002-8985-8753
Yinan Zhang: 0000-0002-0362-1473
Shilei Zhang: 0000-0001-8169-0098

Notes

The authors declare no completing financial interest.

Supporting Information Available.

Supporting information: [Optimization of reaction conditions of anthranil with phenols and anilines; the copies of ^{1}H and ^{13}C NMR spectra of products **3-8**]. This material is available free of charge via the Internet at http://pubs.acs.org.

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