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# A CONVENIENT SYNTHESIS OF 1,2,4-TRIAZINO[2,3-*b*]-INDAZOL-3-AMINE DERIVATIVES VIA TANDEM ABNORMAL STAUDINGER/AZA-WITTIG/ISOMERIZATION REACTION

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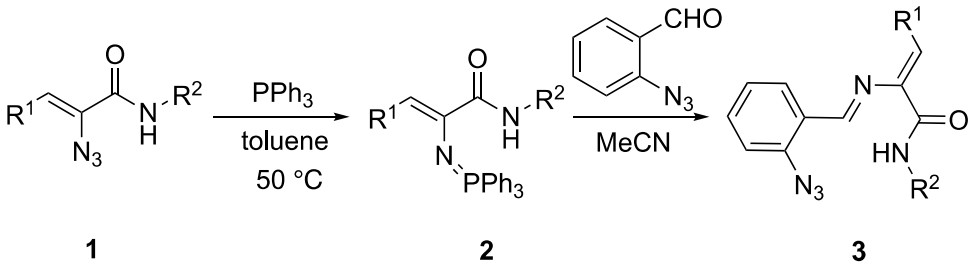
**Abstract** – A Convenient synthesis route of 1,2,4-triazino[2,3-*b*]indazol-3-amine analogs by iminophosphoranes with in situ generated from acrylamide containing azide and imino groups and tributylphosphine is herein described. This annulation reaction proceeds through a tandem abnormal Staudinger reaction, intramolecular aza-Wittig reaction and isomerization reaction. This operating procedure has the advantages of simple, cheap and easily available starting materials, mild reaction conditions, no catalyst required, simple operation, and good yield (78-86%). The structures of the synthesized compounds were confirmed by IR, NMR, HRMS and X-ray diffraction.

Fused heterocycles, a class of important heterocyclic compounds, exhibit synergistic activities and diverse biological activities. Many combinations of fused heterocyclic structures can be designed to develop new chemical entities with versatile physical, chemical, and biological properties.[1] Indazole skeleton possessed a wide range of pharmacological activities, such as antitumor,[2] antimicrobial,[3] antiarrhythmic,[4] antifungal,[5] antihypertensive,[6] antibacterial,[7] and anti-HIV activities.[8] 1,2,4-Triazine scaffold also showed marvelous biological activities including antiviral,[9] anticancer,[10] anti-inflammatory,[11] antimicrobial,[12] antimalarial,[13] antibacterial,[14] anticonvulsant,[15] antifungal,[16] and anti-HIV[17] activities. The fused triazine-indazole may also have pharmacological activity.

In our previous work,[18] we synthesized the first 1,2,4-triazino[2,3-*b*]indazole derivatives by Staudinger and aza-Wittig reaction. The Staudinger and aza-Wittig reaction[19] were carried out under neutral conditions, with mild conditions and simple operation, and had become one of the important methods for constructing nitrogen-containing heterocycles. We have developed a series of methods for the synthesis of nitrogen-containing heterocycles by tandem Staudinger/aza-Wittig reaction such as oxazole,[20]

1,4-benzodiazepines,[21] and bis-1,2,4-oxadiazole[22] in our previous works. Herein, we again report an convenient tandem abnormal Staudinger/aza-Wittig/isomerization reaction as a new route to 1,2,4-triazino[2,3-*b*]indazol-3-amines bearing a variety of functional groups.

The initial reactions were carried out using α-azidocinnamamide **1a** as the substrates and $PPh_3$ as a reductant to afford vinyliminophosphorane **2a** at 65 °C in high yield according to the literature report.[23] The vinyliminophosphorane **2a** was then converted into acrylamide **3a** by treatment with 2-azidobenzaldehyde and the reaction proceeded smoothly with 89% yield (Scheme **1**). The vinyliminophosphoranes **2** were directly separated from the solvent toluene and can proceed to the next reaction without further purification. The preparation methodology of acrylamides **3** features a classic and reliable aza-Wittig reaction, which has the characteristics of cheap raw materials, no catalyst required, high yield, and simple operation.



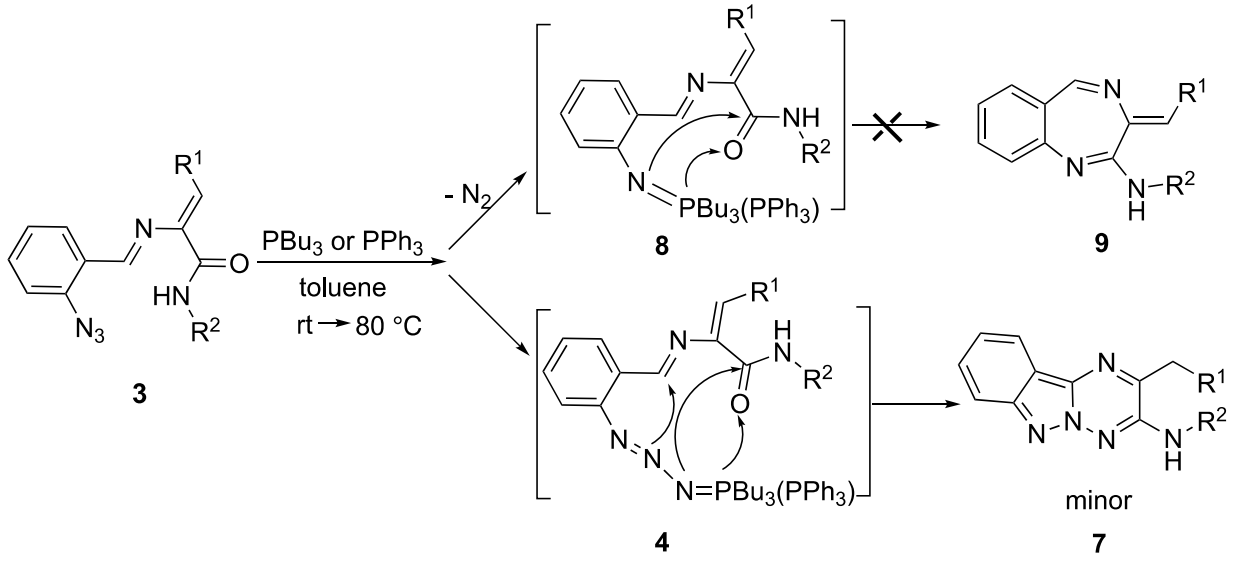

**Scheme 1.** Synthesis of acrylamide derivatives **3**

**Table 1.** Preparation of acrylamide derivatives **3**

| Comp. | $R^1$ | $R^2$ | Reaction Time | Yield(%) |
|---|---|---|---|---|
| **3a** | Ph | Me | 7 h | 89 |
| **3b** | Ph | $CH_2Me$ | 7 h | 82 |
| **3c** | Ph | $CH_2CH_2Me$ | 7 h | 80 |
| **3d** | 4-$MeC_6H_4$ | Me | 5 h | 84 |
| **3e** | 2-$BrC_6H_4$ | Me | 5 h | 80 |
| **3f** | 4-$FC_6H_4$ | Me | 5 h | 88 |
| **3g** | 4-$ClC_6H_4$ | Me | 5 h | 91 |

Firstly, acrylamide **3a** was treated with $PPh_3$ at room temperature in $CH_2Cl_2$, but the reaction system is complex with no main products, subsequently we tried to use $PMePh_2$, the reaction system is still complex. We also attempted to control the reaction using temperature, but the complexity of the system did not fundamentally improve from room temperature to 80 °C. Interestingly, when $Bu_3P$ was used for the reactions, we found that the reaction did not yield the expected 1,4 benzodiazepine compound **9**, but a

small amount of compound **7a** was produced (Scheme **2**). This has aroused our great interest, according to our previous research results,[18] and we believe that this is a controllable reaction. We speculated that it may be due to the addition of phosphorus reagents that other unpredictable reactions occur between NH in the amide and double bonds in the molecule or carbon atoms in the imine. However, when tributylphosphine is added, the steric hindrance of tributylphosphine is smaller than that of triphenylphosphine and diphenylmethylphosphine, and it can also activate azide compounds to some extent, making it easier to form carbon nitrogen double bonds. Therefore, we chose acrylamide **3a** to react with $Bu_3P$ in toluene at 0 °C to produce iminophosphorane **5a**, then, the iminophosphorane **5a** underwent an tandem abnormal Staudinger/aza-Wittig/isomerization reaction at reflux to afford the target molecule **7a** in 86% yield. After above mentioned attempts, the optimized conditions for the synthesis was to carry out the reactions using 1 equiv. of **3a** with 1.1 equiv. of $Bu_3P$ in toluene at 0 °C for 1 h, and then which afforded **7a** at 115 °C for 2 h in 86% isolated yields (Table **2**).



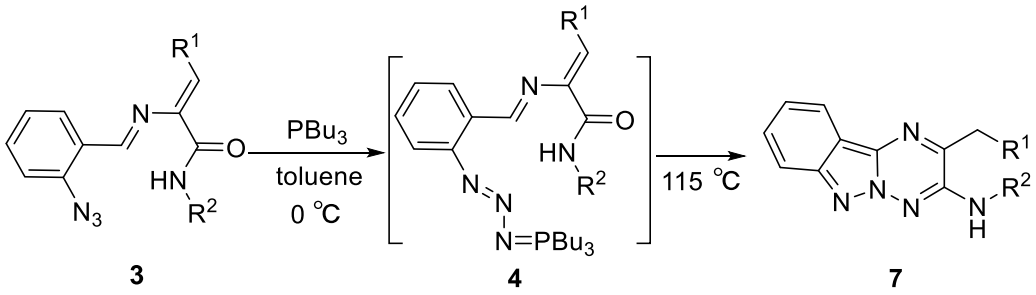

**Scheme 2.** Exploration of reaction conditions

**Table 2.** Optimization of reaction conditions

| Entry | Reagent | Solvent | Temperture(°C) | Yield[a](Comp.**7a**/**9a**)% |
|---|---|---|---|---|
| **1** | $PPh_3$ | $CH_2Cl_2$ | 25 | 0/0 |
| **2** | $PPh_3$ | toluene | 25-80 | minor[b]/0 |
| **3** | $PMePh_2$ | $CH_2Cl_2$ | 25 | 0/0 |
| **4** | $PMePh_2$ | toluene | 25-80 | minor[b]/0 |
| **5** | $Bu_3P$ | $CH_2Cl_2$ | 25 | 11/0 |
| **6** | $Bu_3P$ | toluene | 0 | 86/0 |

[a] isolated yield; [b] determined by TLC.

With the optimized reaction conditions in hand, various acrylamide derivatives **3** were surveyed to react with tributylphosphine, and the results were shown in Table **2**. Generally, when an aryl group was present at the $R^1$ position and an alkyl group at the $R^2$ position, various substituted acrylamide derivatives **3** worked well with tributylphosphine to provide the desired 1,2,4-triazino[2,3-*b*]indazol-3-amines **7** in good to excellent isolated yields (Scheme **3** and Table **3**). But when an aryl group was present at the $R^2$ position, the reaction gave almost no desired products.

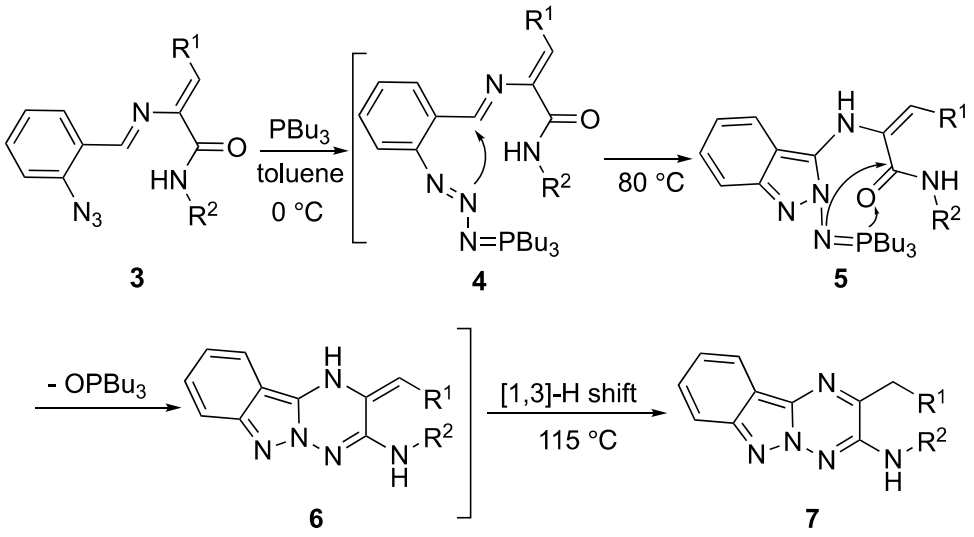



**Scheme 3.** Synthesis of 1,2,4-triazino[2,3-*b*]indazol-3-amine **7**

**Table 3.** Preparation of 1,2,4-triazino[2,3-*b*]indazol-3-amine **7**

| Comp. | $R^1$ | $R^2$ | Reaction Time | Yield(%) |
|---|---|---|---|---|
| **7a** | Ph | Me | 1 h | 86 |
| **7b** | Ph | $CH_2Me$ | 1 h | 84 |
| **7c** | Ph | $CH_2CH_2Me$ | 1 h | 82 |
| **7d** | 4-$MeC_6H_4$ | Me | 2 h | 80 |
| **7e** | 2-$BrC_6H_4$ | Me | 2 h | 78 |
| **7f** | 4-$FC_6H_4$ | Me | 2 h | 81 |
| **7g** | 4-$ClC_6H_4$ | Me | 2 h | 84 |

On the basis of the experimental observations and literature reports,[19,24] a plausible mechanism for the tandem abnormal Staudinger/aza-Wittig/isomerization reaction is proposed in Scheme **4** below. At 0 °C, abnormal Staudinger reaction of acrylamide derivatives **3** with $Bu_3P$ takes place to give the intermediacy of phosphazides **4**, which cyclize to give iminophosphoranes **5**. and subsequent intramolecular aza-Wittig reaction of **5** produce cyclized compounds **6**, finally, in which an isomerization reaction leads to the formation of 1,2,4-triazino[2,3-*b*]indazol-3-amines **7**. It is noteworthy that the reaction proceeds under mild conditions to give various substituted 1,2,4-triazino[2,3-*b*]indazol-3-amines **7** and the overall transformation is run in a simple one-pot procedure from acrylamide derivatives **3**.




**Scheme 4.** Proposed mechanism for the synthesis of **7**

Furthermore, single crystal of **7a** was obtained from the petroleum ether and $CH_2Cl_2$ (18 : 1) solution of **7a** and X-ray structure analysis verified the proposed structures (Figure **1**).

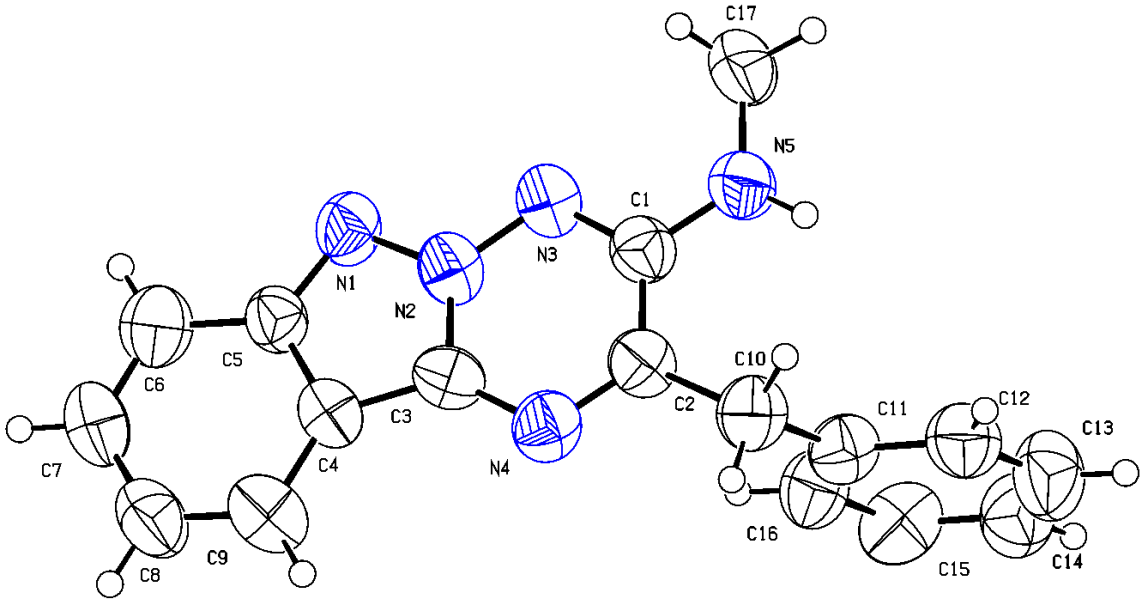



**Figure 1.** X-Ray structure of **7a** CCDC 2281905

In summary, various acrylamides and tributylphosphine can undergo a tandem abnormal Staudinger/aza-Wittig/isomerization reaction under mild conditions, affording 1,2,4-triazino[2,3-*b*]indazol-3-amines in good yields. This strategy provides an efficient and practical method for synthesis of other aromatic fused heterocycle.

## EXPERIMENTAL

All reagents or solvents used in the reaction are chemical pure or analytical pure. Toluene and dichloromethane ($CH_2Cl_2$), and methyl alcohol (MeOH) are used for reaction and dried with anhydrous calcium chloride for 5-7 days. 200-300 mesh silica gel is used for column chromatography. Thin layer chromatography (TLC) is carried out on the silica gel 60F254 plate and observed under 265 nm ultraviolet light.

All melting points were determined using a X-4 model apparatus and were uncorrected. IR were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in $cm^{-1}$. $^1H$ NMR and $^{13}C$ NMR spectra were recorded in $CDCl_3$ on a AVANCE NEO 500M spectrometer and resonances relative to TMS. High resolution mass spectrometry (HRMS) was measured on the Agilent 6224 TOF LC/MS spectrometer, with the bombardment source being E1. Bruker SMART

General procedure for the synthesis of acrylamide derivatives (**3a-3g**)

A solution of vinyl azides **1** (5 mmol) and triphenylphosphine (5 mmol) in 15 mL of dried toluene was stirred at 65 ℃ for 40 min until the vinyliminophosphoranes **2** were formed (monitored by TLC). The vinyliminophosphoranes **2** (5 mmol) and 2-azidobenzaldehyde (5 mmol) in 15 mL of dried MeOH were stirred for 7 h at 50 ℃. When the reaction was finished, the solvent was removed in a rotary evaporator at 37 ℃. And subsequent flash column chromatography (petroleum ether/AcOEt = 3 : 1) gave the desired acrylamide derivatives **3a-3g**.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-N-methyl-3-phenylacrylamide (3a):** yellow flocculent solid (2.47 g, 89%); mp 125.1-125.6 ℃; $^1H$ NMR ($CDCl_3$, 500 MHz) : δ 8.62 (s, N=CH, 1H), 8.20-7.08 (m, Ar-H, 9H), 6.32 (s, =CH, 1H), 2.94 (d, *J* = 5 Hz, $CH_3$, 3H), 1.59 (q, NH, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) : δ 165.4, 161.2, 144.0, 141.1, 134.4, 133.3, 129.8, 128.5, 127.9, 127.6, 126.3, 125.0, 119.5, 118.8, 58.5, 26.5, 18.4; IR(KBr) : 3314, 2129, 1635, 1527, 1295 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{15}N_5O$ $[M+H]^+$: 306.1277; found 306.1356.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-N-ethyl-3-phenylacrylamide (3b):** yellow flocculent solid: (2.32 g, 82%); mp 123.2-123.9 ℃; $^1H$ NMR ($CDCl_3$, 500 MHz) : δ 8.62 (s, N=CH, 1H), 8.19-7.07 (m, Ar-H, 9H), 6.32 (s, =CH, 1H), 3.42 (m, *J* = 25 Hz, $CH_2$, 2H), 1.60 (q, NH, 1H), 1.20 (t, *J* = 15 Hz, $CH_3$, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) : δ 164.6, 161.2, 144.1, 141.1, 134.5, 133.3, 133.3, 129.8, 128.5, 127.9, 127.5, 126.4, 125.0, 119.6, 118.8, 34.7, 30.9, 14.9; IR(KBr) : 3312, 2122, 2080, 1634, 1530, 1278 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{18}H_{17}N_5O$ $[M+H]^+$: 320.1433; found 320.1519.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-3-phenyl-N-propylacrylamide (3c):** yellow flocculent solid: (1.78 g, 80%); mp 117.9-118.4 ℃. $^1H$ NMR ($CDCl_3$, 500 MHz) : δ 8.62 (s, N=CH, 1H), 8.18-7.07 (m, Ar-H, 9H), 6.35 (s, =CH, 1H), 3.33 (q, *J* = 20 Hz, $CH_2$, 2H), 1.62 (q, NH, 1H), 1.58 (m, $CH_2$, 2H), 0.94 (t, *J* = 15 Hz, $CH_3$, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) : δ 164.7, 161.1, 144.2, 141.1, 134.5, 133.3, 129.8,

129.6, 128.5, 127.9, 127.5, 126.4, 125.0, 119.6, 118.8, 41.5, 22.9, 11.4; IR(KBr) : 3368, 2127, 1656, 1620, 1516, 1277 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{19}H_{19}N_5O$ $[M+H]^+$: 334.1590; found 334.1669.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-N-methyl-3-(*p*-tolyl)acrylamide (3d):** yellow flocculent solid: (1.49 g, 84%); mp 124.3-125.4 ℃; $^1$H NMR ($CDCl_3$, 500 MHz) : δ 8.64 (s, N=CH, 1H), 8.21-7.04 (m, Ar-H, 8H), 6.27 (s, =CH, 1H), 2.92 (d, *J* = 5 Hz, $CH_3$, 3H), 2.28 (d, $CH_3$, 3H), 1.58 (q, NH, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 165.5, 161.4, 143.3, 141.0, 137.6, 133.0, 132.1, 129.8, 129.2, 128.6, 127.9, 126.4, 125.0, 119.6, 118.8, 26.5, 26.0, 21.3; IR(KBr) : 3327, 2129, 1633, 1533, 1293 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{18}H_{17}N_5O$ $[M+H]^+$: 320.1433; found 320.1506.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-3-(2-bromophenyl)-N-methylacrylamide (3e):** yellow flocculent solid: (1.67 g, 80%); mp 139.2-139.9 ℃; $^1$H NMR ($CDCl_3$, 500 MHz) : δ 8.69 (s, N=CH, 1H), 8.22-7.13 (m, Ar-H, 8H), 6.35 (s, =CH, 1H), 2.96 (d, *J* = 5 Hz, $CH_3$, 3H), 1.59 (q, NH, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 164.8, 160.9, 145.3, 141.0, 135.1, 133.3, 133.0, 128.6, 127.9, 127.0, 126.2, 125.0, 124.9, 119.0, 118.7, 26.5; IR(KBr) : 3279, 2120, 1639, 1583, 1291 $cm^{-1}$; HRMS (ESI) *m/z:* calcd. for: $C_{17}H_{14}BrN_5O$ $[M+H]^+$: 384.0382; found 384.0459.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-3-(4-fluorophenyl)-N-methylacrylamide (3f):** yellow flocculent solid: (1.56 g, 88%); mp 129.1-129.8 ℃; $^1$H NMR ($CDCl_3$, 500 MHz) : δ 8.61 (s, N=CH, 1H), 8.19-6.92 (m, Ar-H, 8H), 6.25 (s, =CH, 1H), 2.93 (d, *J* = 5 Hz, $CH_3$, 3H), 1.59 (q, NH, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 165.3, 162.9, 161.4, 161.0, 143.8, 141.2, 133.5, 132.6, 132.1, 131.6, 130.5, 128.5, 127.8, 126.2, 125.0, 118.8, 118.4, 115.6, 115.4, 26.5; IR(KBr) : 3310, 2122, 1639, 1595, 1502 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{14}FN_5O$ $[M+H]^+$: 324.1182; found 324.1269.

**(*Z*)-2-(((*E*)-2-Azidobenzylidene)amino)-3-(4-chlorophenyl)-N-methylacrylamide (3g):** yellow flocculent solid: (1.89 g, 91%); mp 133.5.2-134.7 ℃; $^1$H NMR ($CDCl_3$, 500 MHz) : δ 8.59 (s, N=CH, 1H), 8.18-7.01 (m, Ar-H, 8H), 6.27 (s, =CH, 1H), 2.92 (d, *J* = 5 Hz, CH3, 3H), 1.58 (s, NH, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 165.1, 161.3, 144.5, 141.3, 133.5, 132.5, 131.4, 131.0, 129.8, 128.7, 128.4, 128.3, 127.8, 126.1, 125.0, 118.8, 118.2, 26.6, 26.0; IR(KBr) : 3329, 2127, 1639, 1604, 1535, 1487, 1293 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{14}ClN_5O$ $[M+H]^+$: 340.0887; found 340.0964.

General procedure for the synthesis of 1,2,4-triazino[2,3-*b*]indazol-3-amine analogs (**7a-7g)**

A solution of acrylamide derivatives **3** (5 mmol) in toluene (10 mL) was stirred for 10 min under ice water bath conditions, and then tributylphosphine (5.1 mmol) was added to the above solution and the reaction mixture was stirred continuously for 1 h at 0 ℃. When the reaction was completed (monitored by TLC) the intermediate iminophosphorane was obtained. The resulting iminophosphorane can undergo subsequent reactions without further separation, and the reaction mixture was heated at reflux for 1-2 h under an oil bath (115 °C). The solvent was removed by evaporation in vacuo, and the crude residue was purified by column chromatography on a silica gel column, eluting with petroleum ether (60-90)/AcOEt

(3 : 2) and then recrystallized from the appropriate solvent to afford 1,2,4-triazino[2,3-*b*]indazol-3-amine analogs **7a-7g**.

**2-Benzyl-N-methyl-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7a):** yellow solid: (0.39 g, 86%); mp 187.4-187.8 ℃; $^{1}$H NMR ($CDCl_3$, 500 MHz) : δ 8.16-7.26, (m, Ar-H, 9H), 4.64 (q, NH, 1H), 4.28 (s, $CH_2$, 2H), 3.00 (d, *J* = 5 Hz, $CH_3$, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 150.1, 146.3, 140.5, 135.0, 131.1, 129.4, 128.4, 127.8, 127.4, 121.8, 119.0, 116.8, 113.7, 40.8, 30.9, 28.7; IR(KBr) : 3350, 1577, 1489, 1364, 1254, 1187 cm$^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{15}N_5$ $[M+H]^+$: 290.1327; found 290.1412.

**2-Benzyl-N-ethyl-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7b):** yellow solid: (0.27 g, 84%); mp 145.7-146.8 ℃; $^{1}$H NMR ($CDCl_3$, 500 Hz) : δ 8.16-7.26 (m, Ar-H, 9H), 4.51 (q, NH, 1H), 4.28 (s, $CH_2$, 2H), 3.43 (m, *J* = 5 Hz, $CH_2$, 2H), 1.13 (t, *J* = 15 Hz, $CH_3$, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 149.4, 146.3, 140.5, 135.1, 131.0, 129.4, 128.4, 127.8, 127.4, 121.8, 119.0, 116.8, 113.7, 41.0, 36.6, 13.9; IR(KBr) : 3297, 1572, 1493, 1254, 1191 cm$^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{18}H_{17}N_5$ $[M+H]^+$: 304.1484; found 304.1566.

**2-Benzyl-N-propyl-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7c):** yellow solid: (0.38 g, 82%); mp 152.5-153.6 ℃; $^{1}$H NMR ($CDCl_3$, 500 MHz) : δ 8.15-7.26 (m, Ar-H, 9H), 4.56 (q, NH, 1H), 4.29 (s, $CH_2$, 2H), 3.36 (q, *J* = 20 Hz, $CH_2$, 2H), 1.51 (m, $CH_2$, 2H), 0.76 (t, *J* = 10 Hz, $CH_3$, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ149.5, 146.3, 140.5, 135.2, 129.5, 128.4, 127.8, 127.4, 121.8, 119.0, 116.8, 113.7, 43.3, 41.2, 21.7, 11.1. IR(KBr) :3343, 1566, 1483, 1247, 1185 cm$^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{19}H_{19}N_5$ $[M+H]^+$: 318.1640; found 318.1720.

**N-Methyl-2-(4-methylbenzyl)-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7d):** yellow solid: (0.25 g, 80%); mp 163.1-163.9 ℃; $^{1}$H NMR ($CDCl_3$, 500 MHz) : δ 8.16-7.16 (m, Ar-H, 8H), 4.63 (q, NH, 1H), 4.24 (s, $CH_2$, 2H), 3.00 (d, *J* = 5 Hz, $CH_3$, 3H), 2.34 (s, $CH_3$, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 150.2, 146.3, 140.8, 137.6, 132.7, 132.1, 131.6, 130.1, 129.4, 128.2, 127.4, 121.8, 119.0, 116.8, 113.7, 40.5, 28.7, 21.1; IR(KBr) : 3272, 1575, 1491, 1408, 1185 cm$^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{18}H_{17}N_5$ $[M+H]^+$: 304.1484; found 304.1566.

**2-(2-Bromobenzyl)-N-methyl-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7e):** yellow solid: (0.38 g, 78%); mp 214.3-215.7 ℃; $^{1}$H NMR ($CDCl_3$, 500 MHz) : δ 8.12-7.17 (m, Ar-H, 8H), 4.94 (q, NH, 1H), 4.37 (s, $CH_2$, 2H), 3.04 (d, *J* = 20 Hz, $CH_3$, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 149.8, 146.3, 139.9, 134.7, 133.2, 130.4, 129.3, 128.2, 127.4, 124.4, 121.9, 119.0, 116.9, 113.7, 39.7, 28.7; IR(KBr) : 3245, 3104, 1566, 1483, 1327, 1185 cm$^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{14}N_5Br$ $[M+H]^+$: 368.0433; found 368.0508.

**2-(4-Fluorobenzyl)-N-methyl-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7f):** yellow solid: (0.36 g, 81%); mp 159.7-160.3 ℃; $^{1}$H NMR ($CDCl_3$, 500 MHz) : δ 8.14-7.03 (m, Ar-H, 8H), 4.65 (q, NH, 1H), 4.23 (s, $CH_2$, 2H), 3.01 (d, *J* = 5 Hz, $CH_3$, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) : δ 163.2, 161.2, 149.9, 146.3, 140.1,

131.0, 130.7, 130.0, 127.5, 121.9, 119.0, 116.9, 116.4, 116.2, 113.7, 39.7, 28.8; IR(KBr) : 3358, 1562, 1510, 1491, 1222, 1183 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{14}N_5F$ $[M+H]^+$: 308.1233; found 308.1314.

**2-(4-Chlorobenzyl)-N-methyl-[1,2,4]triazino[2,3-*b*]indazol-3-amine (7g):** yellow solid: (0.39 g, 84%); mp 183.1-183.9 ℃; $^1H$ NMR ($CDCl_3$, 500 MHz) : δ 8.14-7.20 (m, Ar-H, 8H), 4.57 (q, NH, 1H), 4.24 (s, $CH_2$, 2H), 3.03 (d, *J* = 5 Hz, $CH_3$, 3H) ppm; $^{13}C$ NMR ($CDCl_3$, 125 MHz) : δ 149.9, 146.3, 139.9, 133.5, 132.1, 132.0, 129.8, 129.5, 128.6, 127.5, 121.9, 119.0, 116.9, 113.7, 39.8, 28.7; IR(KBr) : 3335, 1577, 1489, 1412, 1214, 1183 $cm^{-1}$; HRMS (ESI) *m/z*: calcd. for: $C_{17}H_{14}N_5Cl$ $[M+H]^+$: 324.0938; found 324.1013.

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