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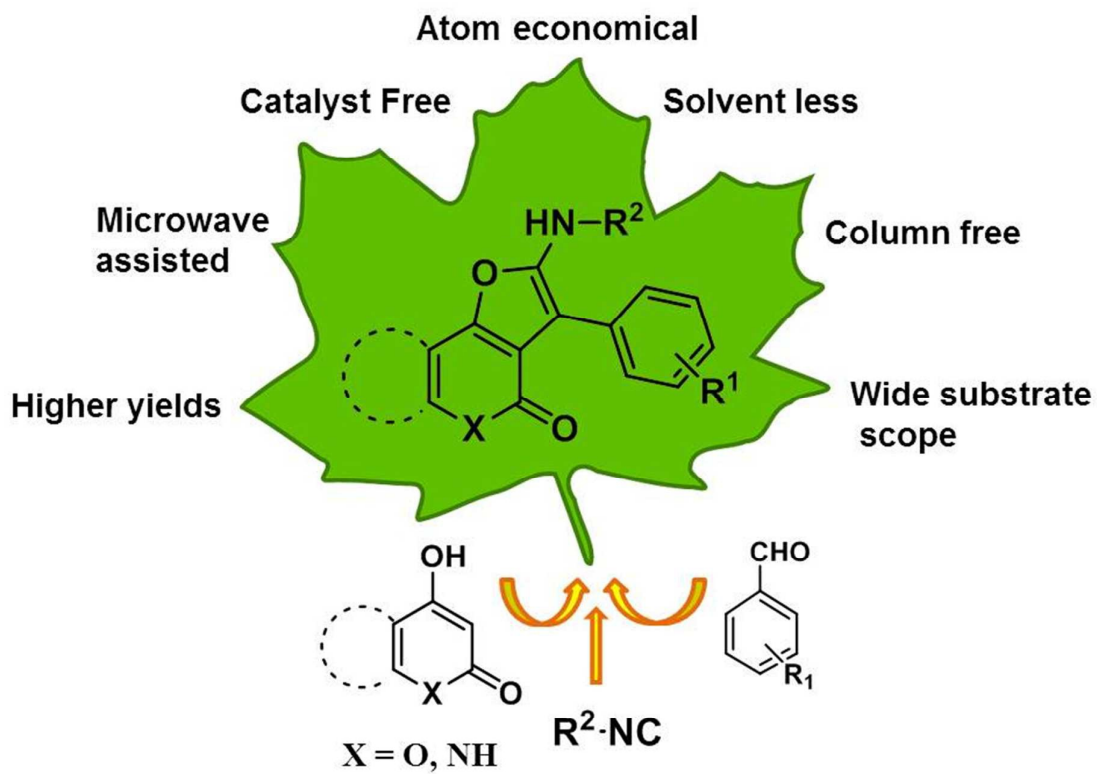
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TOC entry



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## ARTICLE TYPE

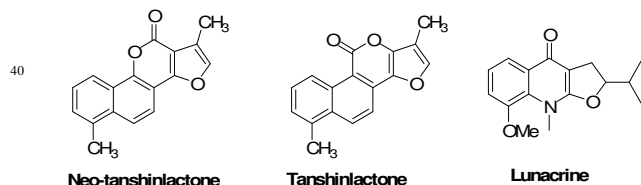
**A green, catalyst-free, solvent-free, high yielding one step synthesis of functionalized benzo[*f*]furo[3,2-*c*]chromen-4-(5*H*)-ones and furo[3,2-*c*]quinolin-4-(5*H*)-ones**

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A green, three-component reaction of 1-hydroxy-3*H*-benzo[*f*]chromen-3-ones and 4-hydroxyquinolin-2(1*H*)-ones, aromatic aldehyde, and isonitrile was developed, for the first time, which resulted in a variety of substituted functionalized benzo[*f*]furo[3,2-*c*]chromen-4-(5*H*)-ones and furo[3,2-*c*]quinolin-4-(5*H*)-ones in excellent yields. The merits of the present protocol include use of microwave irradiation, catalyst-free, solvent free, atom-efficient, no work up or column purification. The present method is milder yet advanced than the previous reports for the synthesis of related structures, furo-chromen-4-ones, furopyrimidines, furopyranones *etc.* The synthesized compounds have been virtually screened against a series of therapeutic targets and have shown promising binding with some of them.

**INTRODUCTION.** In the contemporary world of organic synthesis, the merits of a protocol is gauged by not the intricate complications involved in its bringing but is rather measured by inexpensive starting materials, speed, atom efficiency, energy requirements and compatibility to automation.<sup>1</sup> Reactions assisted by microwave irradiations, use of environment-friendly reagents and catalysts, aqueous based or solvent-less protocols, atom economical processes have collectively contributed to propound the above school of modern synthesis.<sup>2</sup> In the same way, Isocyanide based multi-component synthesis has revolutionized the art of molecular design in terms of simplicity in approach, yet complexity, diversity and uniqueness in the products.<sup>3</sup> IMCRs such as Ugi, Passerini, Groebke-Blackburn-Bienymé and related ones are the masterpiece of simplicity, atom economy, synthetic efficiency and are highly compatible with the goals of green chemistry.<sup>4</sup>

The construction of benzo[*f*]furo[3,2-*c*]chromen-4-(5*H*)-ones and furo[3,2-*c*]quinolin-4-(5*H*)-ones is important from a thematic standpoint in organic synthesis. In general, there is limited literature on these atypical scaffolds in comparison to functionalized benzofuranones which are known to possess wide ranging activities such as antibacterial, antifungal, anti-trypanosomal, antioxidant and insecticidal.<sup>5</sup> Some natural furo-benzochromenones (Fig. 1) such as anticancerous tansinones; tanshinlactone and neo-tanshinlactone were isolated from *Salvia multiorrhiza*.<sup>6</sup>



**Fig. 1** Structures of some naturally occurring bioactive furo-benzochromenones and furo-quinolone

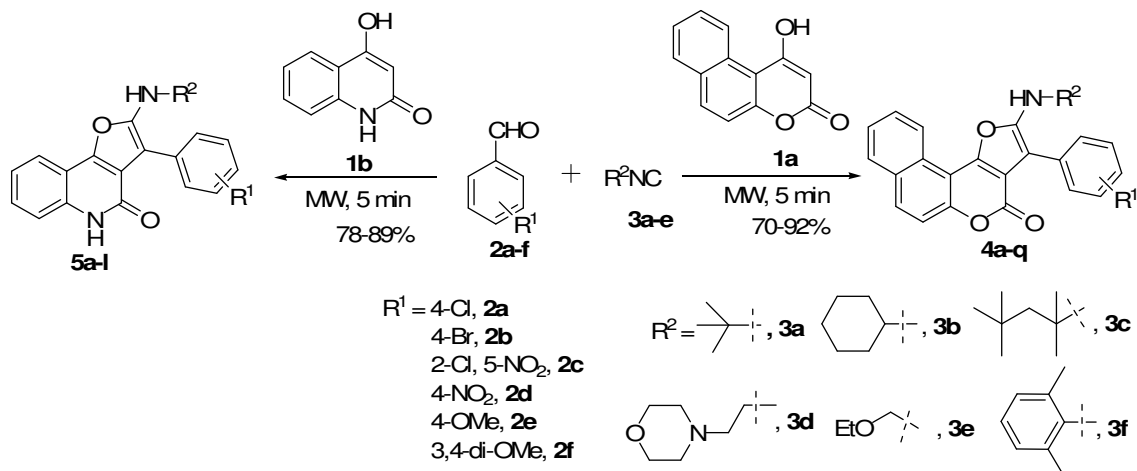
This class of compounds exhibited wide array of biological activities *viz.* antitumor, antibacterial, antiallergic, antioxidant and antiplatelet aggregation.<sup>7</sup> Likewise, several furoquinolones

such as lunacrine originated from plant sources, have been ascribed to various pharmacological activities including phytotoxic activity against bacteria and other pathogens.<sup>8</sup>

In literature, there are several reports for the synthesis of furocoumarins and furopyrimidines and the most common method for their preparation remains [4+1] cycloaddition reaction between coumarins/pyridines with aryl aldehydes and isonitriles under various conditions.<sup>9</sup> Nair *et al.* (2006) synthesized furocoumarins and furoquinolones in a one-pot synthesis, but the reaction took long hours (17 h) under reflux conditions in benzene.<sup>10</sup> Later on, similar reaction was attempted using dimethyl formamide as a solvent under microwave irradiation, but the products were purified on preparative TLC.<sup>11</sup> In general, most of these methods are marred by one or the other drawback such as long reaction times, toxic catalysts and reagents, use of carcinogenic solvent, limited substrate scope, low to moderate yields, tedious work-up and purification.<sup>10-12</sup> Lately, there have been a couple of environmentally benign protocols reported for the synthesis of furocoumarins and furopyridones albeit in the presence of an acid catalyst.<sup>12</sup> However, to the best of our knowledge, benzo[*f*]furo[3,2-*c*]chromen-4-(5*H*)-ones and furo[3,2-*c*]quinolin-4-(5*H*)-ones have never been involved in the reported methods and natural extension of the above reported methods on these scaffolds is not trivial.

In this context, we present the first synthesis of benzo[*f*]furo[3,2-*c*]chromen-4-(5*H*)-ones and furo[3,2-*c*]quinolin-4-(5*H*)-ones in minutes without any catalyst and solvent under microwave irradiation. Moreover, the products crystallized out in high yields in the reaction vial by mere addition of water:ethanol (4:1) or water:isopropanol (4:1) and further workup or column chromatography is not required.

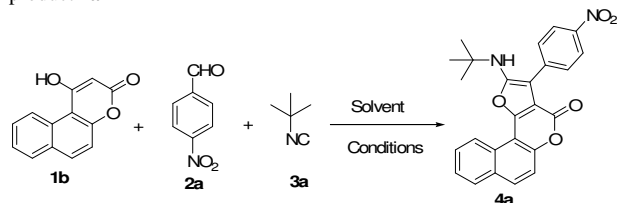
**RESULTS AND DISCUSSION.** In our continuous pursuit to explore isonitrile based multi-component reactions,<sup>13</sup> we sought to explore *enroute* towards construction of annulated furanoid scaffolds from relatively less explored CH-acids *e.g.* 1-hydroxy-3*H* benzo[*f*]chromen-3-ones and 4-hydroxyquinolin-2(1*H*)-ones as natural extension of our work (Scheme 1).



**Scheme 1** Microwave assisted one-pot protocol for the synthesis of annulated furans.

In a prototypical reaction, 1-hydroxy-3*H*-benzo[*f*]chromen-3-ones **1a**, was reacted with 4-nitrobenzaldehyde **2a** and *tert*-butyl isonitrile **3a** without any solvent under microwave irradiation for 10 min which to our delight, provided 95% yield of the product **4a** (Table 1, entry 1).

**Table 1.** Optimization of the reaction conditions for the synthesis of product **4a**<sup>a</sup>



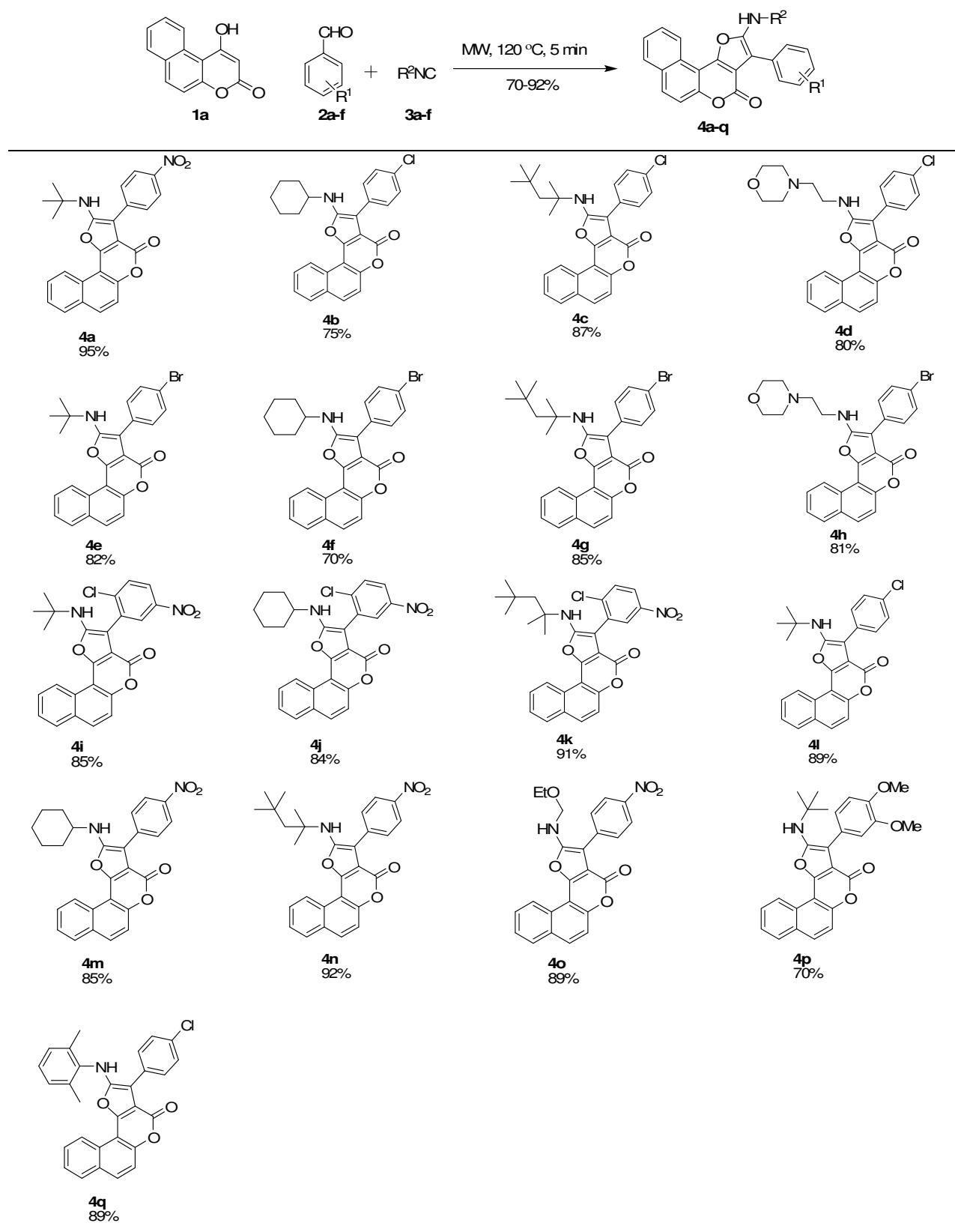
| Entry | Solvent | Catalyst <sup>b</sup> | Conditions      | Temp. (°C) | Time (min) | Yield (%) <sup>d</sup> |
|-------|---------|-----------------------|-----------------|------------|------------|------------------------|
| 1     | neat    | -                     | MW <sup>c</sup> | 120        | 10         | 95                     |
| 2     | neat    | -                     | MW <sup>c</sup> | 120        | 2          | 50 <sup>e</sup>        |
| 3     | neat    | -                     | MW <sup>c</sup> | 120        | 5          | 95                     |
| 4     | neat    | -                     | MW <sup>c</sup> | 120        | 20         | 91                     |
| 5     | neat    | -                     | MW <sup>c</sup> | 50         | 5          | 47                     |
| 6     | neat    | -                     | MW <sup>c</sup> | 50         | 20         | 62                     |
| 7     | neat    | -                     | grinding        | rt         | 30         | 21                     |
| 8     | ACN     | -                     | MW <sup>c</sup> | 120        | 10         | 86                     |
| 9     | MeOH    | -                     | MW <sup>c</sup> | 120        | 10         | 87                     |
| 10    | IPA     | -                     | MW <sup>c</sup> | 120        | 10         | 87                     |
| 11    | IPA     | <i>p</i> TSA          | MW <sup>c</sup> | 120        | 10         | 92                     |
| 12    | IPA     | HClO <sub>4</sub>     | MW <sup>c</sup> | 120        | 10         | 90                     |
| 13    | IPA     | CH <sub>3</sub> COOH  | MW <sup>c</sup> | 120        | 10         | 89                     |
| 14    | IPA     | FeCl <sub>3</sub>     | MW <sup>c</sup> | 120        | 10         | 91                     |

<sup>a</sup>General condition: 1-hydroxy-3*H*-benzo[*f*]chromen-3-ones **1a** (1 mmol), 4-nitrobenzaldehyde **2a** (1mmol), *tert*-butylisonitrile **3a** (1.2 mmol); <sup>b</sup>Catalyst loading (10%), <sup>c</sup>Anton Paar Monowave 300 reactor. Irradiation Power: 850 W; Ramp time: 1 min. 70 °C; <sup>d</sup>Isolated yield, <sup>e</sup>Starting material recovered.

Despite excellent results, we explored various other conditions for the above reaction in order to target optimum protocol for the above transformation. To see the effect of microwave irradiation, the reaction mixture was irradiated for variable times (Table 1, entries 2-4) and different temperature (Table 1, entries 5-6). It was found that reducing microwave irradiation to 5 minutes remained equally effective; however reducing it further for 2 minutes brought down the yield of **4a** and a lot of starting material remained unreacted (Table 1, entry 4). Likewise, lowering the temperature of the reaction did not yield fruitful results (Table 1, entries 5-6). In another reaction, substrates were ground for 30 min at room temperature; however, it resulted in meagre yield of the product (Table 1, entry 7).

The effect of different solvents like acetonitrile, methanol and isopropanol (Table 1, entries 8-10) as well as different acid catalysts like CH<sub>3</sub>COOH, HClO<sub>4</sub> and FeCl<sub>3</sub> (Table 1, entries 12-14), resulted in the lowering the yield of the product **4a**. So, we led to inference that microwave irradiation at 120 °C for 5 minutes resulted in the best yields of the products. Hence, under the optimized reaction conditions, we reacted 1-hydroxy-3*H*-benzo[*f*]chromen-3-ones **1a** (1 mmol), arylaldehydes **2a-f** (1mmol), isocyanides **3a-f** (1.2 mmol) under microwave irradiation at 120°C for 5 minutes furnished excellent yields of the products.

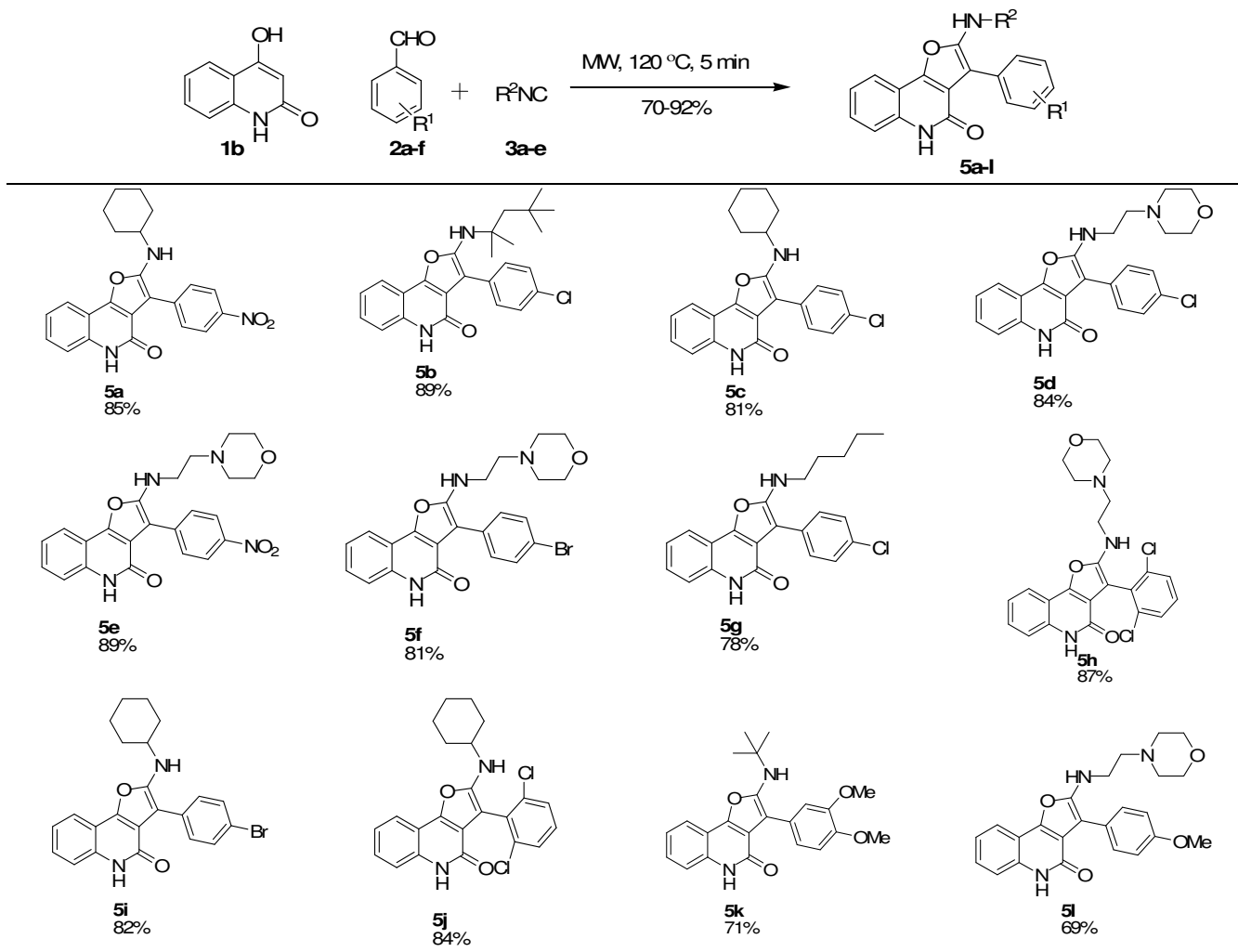
After having optimization conditions in hand, substrate scope and versatility with respect to aldehyde and isocyanides were also examined (Table 2). The method seemed to be well tolerant to various substituted aryl-aldehydes. Especially, the yields were better in case of electron deficient arylaldehydes in comparison to electron rich arylaldehydes (Table 2). The lower yield in electron rich arylaldehyde was expected as the initial enone formed would be less electrophilic and hence less prone to isocyanide attack.

**Table 2.** Scope of the reaction for the synthesis of benzo[*f*]furo[3,2-*c*]chromen-4-(5*H*)-ones

After having obtained success with 1-hydroxy-3*H*-benzo[*f*]chromen-3-ones, we extended the method on 4-

hydroxyquinolin-2(1*H*)-ones and pleasingly it worked equally well on this scaffold as evident from Table 3. The reaction

**Table 3.** Scope of the reaction for the synthesis of furo[3,2-*c*]quinolin-4-(5*H*)-ones



10 tolerated various aryl-aldehydes as well as isocyanides and the general reactivity trend remained similar in both the series. The mechanism of this reaction presumably involves formation of  $\alpha$ ,  $\beta$ -enones from 1-hydroxy-3*H*-benzo[*f*]chromen-3-one **1a**, or 4-  
15 hydroxyquinolin-2(1*H*)-ones **1b** and aldehyde **2a-f** by Knoevenagel condensation (Scheme 2), which would subsequently react with the isocyanide **3a-f** through concerted  
[4+1] cycloaddition followed by cyclisation resulting in the formation of *N*-substituted iminolactone, which employing [1,3]-  
20 proton shift would yield the desired product **4a-q** or **5a-l** (Scheme 2). The probability of the above mechanistic route has already been confirmed using DFT models.<sup>14</sup>

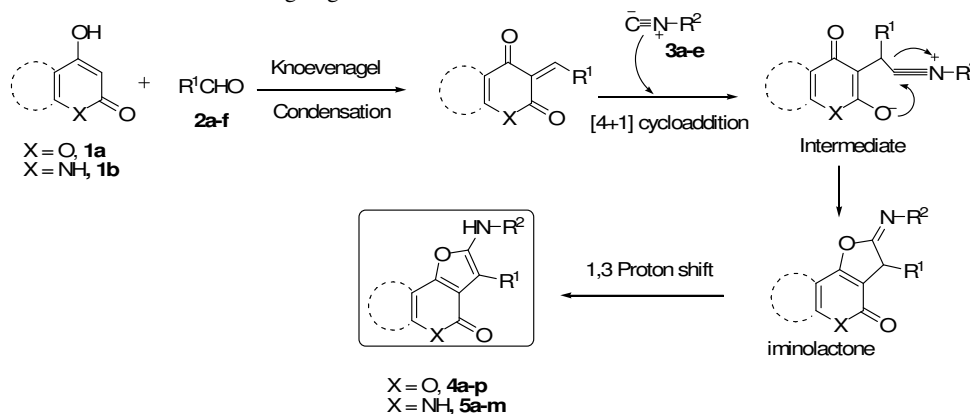
25 Finally, we decided to explore potent applications of these products in chemotherapeutic domain, we performed an “*in-silico* target fishing experiment” using ChemMapper server<sup>15</sup> to find prospective drug targets for these two scaffolds.<sup>16</sup> The results of this experiment indicated that benzo[*f*]furo[3,2-*c*]chromen-4-

30 (*5H*)-ones scaffold can be a hit for Cyclin-Dependent Kinase 2 (CDK2) and Estrogen Receptor beta (ESR2) involved in cancer chemotherapeutics. Likewise, furo[3,2-*c*]quinolin-4-(*5H*)-ones may target Biotin Carboxylase (BC) and Hematopoietic  
35 prostaglandin D synthase involved in antibacterials and inflammation.<sup>17</sup> Detail description is given in the supporting information.

## Conclusions

In summary, neat, atom and step economical, environmentally  
40 benign one pot multi-component synthetic route for the functionalized annulated furans in good yields has been devised under microwave irradiation. The yields of the reactions are excellent and purification of the products is not needed. The present methodology can be used for the design of libraries and  
45 diversity oriented synthesis (DOS) and has potential for automation. Finally, the products of this synthesis are *virtually* propounded as potent therapeutic hits against some therapeutic

targets and further work in this direction is on-going.



**Scheme 2** Proposed mechanism for one-pot three component condensation

### Experimental Part

NMR spectra were recorded on a Bruker Avance<sup>®</sup> 400 and Jeol Resonance ECX-400II. Chemical shifts are reported in parts per million and are referenced to TMS. Spectra were processed using Bruker Topspin<sup>®</sup> 3.0.b.8 and MestReNova software. Mass spectrometry (HRMS) was performed using a Bruker daltronics microTOF-QII<sup>®</sup> spectrometer using ESI ionization, with less than 5 ppm error for all HRMS analyses. Analytical Thin layer chromatography (TLC) was performed on a silica gel plate (Merck<sup>®</sup> 60F<sub>254</sub>). IR spectra were done on Perkin Elmer FT-IR spectrometer (Spectrun Two). Melting points were performed with Ambassador<sup>®</sup> and Digital Melting point apparatus (Nutronics), Popular India. All solvent were distilled prior to use and all chemicals were purchased from sigma-Aldrich<sup>®</sup> and used without further purification.

**Microwave Irradiation Experiment.** All microwave experiments were carried out in a dedicated Anton Paar Monowave 300 reactor<sup>®</sup>, operating at a frequency of 2.455 GHz with continuous irradiation power of 0 to 300 W. The reactions were performed in a G10 Borosilicate glass vial sealed with Teflon septum and placed in a microwave cavity. Initially, microwave of required power was used and temperature was being ramped from room temperature to a desired temperature. Once this temperature was attained, the process vial was held at this temperature for required time. The reactions were continuously stirred. Temperature was measured by an IR sensor. After the experiments a cooling jet cooled the reaction vessel to ambient temperature.

**General procedure for the microwave-assisted three component reaction.** Benzo[*f*]naphthochromen-3-ones **1a** or 4-hydroxyquinolin-2(1*H*)-ones **1b** (1.0 mmol), aryl-aldehyde **2a-f** (1.0 mmol) and isonitrile **3a-f** (1.2 mmol) was mixed well in a G10 process vial capped with Teflon septum. After a pre-stirring of 1 or 2 minutes, the vial was subjected to microwave irradiation with the initial ramp time of 1 minute at 70 °C. The temperature was then raised to 120 °C with the holding time of 5 minutes. After completion of the reaction, the ethanol:water (1:4) or isopropanol:water (1:4) was added into it and the precipitated solids were filtered. All the products were characterized through their <sup>1</sup>H, <sup>13</sup>C NMR, IR and HRMS. <sup>13</sup>C NMR for compound **4p**,

**5d**, **5f**, **5g**, **5k** & **5l** could not be recorded even at higher scans due to their lower solubility in the deuterated solvents.

**2-(*tert*-Butylamino)-3-(4'-nitrophenyl)-4*H*-benzo[*f*]furo[3,2-*c*]chromen-4-one (4a).** Reddish orange solid (95%), Mp decomp. 275-276 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3381, 2977, 2345, 1704, 1603, 1508, 1202. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.38 (s, 9H), 6.36 (s, 1H), 7.56-7.65 (m, 2H), 7.69-7.79 (m, 1H), 7.83 (dt, 2H, *J* = 8.8 & 2.5 Hz), 8.05 (d, 2H, *J* = 9.2 Hz), 8.23 (dt, 2H, *J* = 8.9 & 2.4 Hz), 8.89 (d, 1H, *J* = 8.4 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 30.0, 53.4, 99.6, 106.1, 109.9, 117.1, 123.0, 124.1, 125.8, 126.2, 128.4, 129.1, 130.1, 130.6, 130.7, 138.1, 145.4, 150.5, 151.5, 155.9, 156.7. HRMS (ESI) *m/z* calcd. for C<sub>25</sub>H<sub>20</sub>N<sub>2</sub>O<sub>5</sub> [M]<sup>+</sup>: 428.1366, found: 428.1361.

**2-(Cyclohexylamino)-3-(4'-chlorophenyl)-4*H*-benzo[*f*]furo[3,2-*c*]chromen-4-one (4b).** Pale yellow solid (75%), Mp 190-192 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3299, 2930, 2865, 1707, 1606, 1561, 1505. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.12- 1.22 (m, 1H), 1.26-1.46 (m, 4H), 1.58-1.67 (m, 1H), 1.72-1.81 (m, 2H), 1.92-2.04 (m, 2H), 3.41- 3.53 (m, 1H), 6.78 (d, 1H, *J* = 7.6 Hz), 7.40-7.49 (m, 2H), 7.50-7.61 (m, 4H), 7.64-7.70 (m, 1H), 7.92 (d, 1H, *J* = 9.0 Hz), 7.98 (d, 1H, *J* = 7.9 Hz), 8.70 (d, 1H, *J* = 8.4 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 24.8, 25.2, 33.1, 53.0, 92.3, 106.2, 111.0, 116.7, 124.3, 125.6, 125.8, 127.7, 127.9, 128.7, 129.2, 129.4, 130.0, 130.5, 131.4, 149.3, 149.4, 155.2, 156.7. HRMS (ESI) *m/z* calcd. for C<sub>27</sub>H<sub>22</sub>ClNO<sub>3</sub> [M-H]<sup>+</sup>: 442.1204, found: 442.1201.

**3-(4'-Chlorophenyl)-2-((2',4',4''-trimethylpentan-2-yl)amino)-4*H*-benzo[*f*]furo[3,2-*c*]chromen-4-one (4c).** Yellow solid (87%), Mp 170-172 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 1709, 1613, 1562, 1494, 1439, 1209. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.03(s, 9H), 1.39 (s, 6H), 1.85 (s, 2H), 5.87 (s, 1H), 7.48 (d, 2H, *J* = 8.5 Hz), 7.57-7.68 (m, 4H), 7.74 (t, 1H, *J* = 7.6 Hz), 8.08 (t, 2H, *J* = 9.3 Hz), 8.99 (d, 1H, *J* = 8.4 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 30.0, 31.3, 31.4, 53.7, 56.7, 100.9, 106.3, 110.2, 117.1, 124.1, 125.8, 126.1, 127.8, 128.0, 129.1, 129.4, 130.1, 130.2, 131.2, 131.7, 150.3, 151.0, 154.9, 156.7. HRMS (ESI) *m/z* calcd. for C<sub>29</sub>H<sub>28</sub>ClNO<sub>3</sub> [M-H]<sup>+</sup>: 472.1673, found: 472.1670.

**3-(4'-Chlorophenyl)-2-((2-morpholinoethyl)amino)-4*H*-benzo[*f*]furo[3,2-*c*]chromen-4-one (4d).** Yellow solid (80%), Mp 198-200 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3392, 2961, 2839, 1725, 1612, 1563, 1508. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 2.49 (t, 4H, *J* = 4.2 Hz), 2.67 (t, 2H, *J* = 6.0 Hz), 3.57 (q, 2H, *J* = 5.6 Hz), 3.66 (t,

4H,  $J = 4.3$  Hz), 5.38 (t, 1H,  $J = 5.2$  Hz), 7.41 (d, 2H,  $J = 8.5$  Hz), 7.47-7.57 (m, 4H), 7.67 (t, 1H,  $J = 7.5$  Hz), 7.80 (d, 1H,  $J = 9.0$  Hz), 7.88 (d, 1H,  $J = 8.8$  Hz), 8.85 (d, 1H,  $J = 8.5$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}} = 40.9, 53.3, 57.0, 67.1, 95.6, 107.2,$

5 111.3, 117.3, 125.1, 126.0, 126.6, 128.0, 128.8, 128.9, 129.1, 129.9, 130.5, 130.6, 150.6, 151.5, 155.6, 157.9. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{27}\text{H}_{23}\text{ClN}_2\text{O}_4$   $[\text{M}-\text{H}]^+$ : 473.1262, found: 473.1259.  
**2-(tert-Butylamino)-3-(4'-bromophenyl)-4H-benzof[f]furo[3,2-c]chromen-4-one (4e).** Yellow solid (82%), Mp decomp. 280-  
 10 281 °C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3378, 2978, 1724, 1617, 1562,$  1499, 1212.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 1.36$  (s, 9H), 5.87 (s, 1H), 7.57 (dt, 2H,  $J = 8.6$  & 1.9 Hz), 7.60-7.68 (m, 4H), 7.76-7.82 (m, 1H), 8.05-8.12 (m, 2H), 8.95 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 30.0, 53.4, 102.8, 106.2,$

15 109.9, 117.1, 119.9, 124.1, 125.9, 126.1, 128.3, 129.0, 129.7, 130.1, 130.5, 130.7, 132.0, 150.6, 151.6, 154.8, 156.7. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{25}\text{H}_{20}\text{BrNO}_3$   $[\text{M}]^+$ : 461.0621, found: 461.0619.  
**2-(Cyclohexylamino)-3-(4'-bromophenyl)-4H-benzof[f]furo**  
**[3,2-c]chromen-4-one (4f).** Brown solid (70%), Mp 175-177 °C; IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3378, 2980, 1723, 1563, 1496, 1212.$   $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 1.09$ -1.24 (m, 1H), 1.27-1.48 (m, 4H), 1.57-1.68 (m, 1H), 1.71-1.84 (m, 1H), 1.90-2.07 (m, 1H), 3.44-3.56 (m, 1H), 6.81 (d, 1H,  $J = 7.6$  Hz), 7.48 (dt, 2H,  $J =$   
 25 8.5 & 2.4 Hz), 7.53-7.62 (m, 4H), 7.70 (t, 1H,  $J = 7.7$  Hz), 7.95 (d, 1H,  $J = 9.0$  Hz), 8.00 (d, 1H,  $J = 8.0$  Hz), 8.75 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 24.8, 25.2, 33.1, 53.0,$  92.3, 106.2, 110.9, 116.8, 119.1, 124.3, 125.6, 125.9, 128.0, 128.8, 129.3, 129.8, 130.0, 130.7, 131.8, 149.4, 149.5, 155.2, 156.7.  
 30 HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{27}\text{H}_{22}\text{BrNO}_3$   $[\text{M}-\text{H}]^+$ : 486.0699, found: 486.0691.

**3-(4'-Bromophenyl)-2-((2'',4'',4''-trimethylpentan-2-yl)amino)-4H-benzof[f]furo[3,2-c]chromen-4-one (4g).** Light yellow solid (85%); Mp 168-170 °C; IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3379,$   
 35 2963, 2900, 1728, 1612, 1558, 1496, 1216.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 1.04$  (s, 9H), 1.40 (s, 6H), 1.86 (s, 2H), 5.90 (s, 1H), 7.54 (dt, 2H,  $J = 8.4$  & 2.4 Hz), 7.62 (dt, 2H,  $J = 9.0$  & 2.3 Hz), 7.73-7.79 (m, 2H), 7.73-7.79 (m, 1H), 8.10 (t, 2H,  $J = 9.2$  Hz), 9.01 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  
 40  $\delta_{\text{C}} = 30.1, 31.3, 31.5, 53.7, 56.7, 100.7, 106.3, 110.2, 117.1,$  119.7, 124.1, 125.8, 126.1, 128.0, 129.1, 129.8, 130.1, 130.2, 130.7, 132.0, 150.3, 151.0, 154.9, 156.7. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{29}\text{H}_{28}\text{BrNO}_3$   $[\text{M}-\text{H}]^+$ : 516.1168, found: 516.1167.

**3-(4'-Bromophenyl)-2-((2-morpholinoethyl)amino)-4H-benzof[f]furo[3,2-c]chromen-4-one (4h).** Yellow orange solid (81%), Mp 210-211 °C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3379, 2965, 2841, 1731,$   
 45 1611, 1567, 1502, 1429.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}} = 2.35$ -2.55 (br m, 4H), 2.67 (t, 2H,  $J = 5.8$  Hz), 3.45 (q, 2H,  $J = 5.5$  Hz), 3.62-3.78 (br m, 4H), 5.38 (t, 1H,  $J = 2.2$  Hz), 7.41-7.66 (m, 6H),  
 50 7.68 (t, 1H,  $J = 7.1$  Hz), 7.82 (d, 1H,  $J = 8.9$  Hz), 7.89 (d, 1H,  $J = 8.0$  Hz), 8.87 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 31.2, 53.9, 58.6, 66.7, 92.5, 106.9, 111.6, 117.5, 119.6,$  125.2, 126.2, 126.7, 128.7, 129.4, 130.0, 130.2, 130.7, 131.4, 132.2, 150.0, 150.1, 156.7, 157.4. HRMS (ESI)  $m/z$  calcd. for  
 55  $\text{C}_{27}\text{H}_{23}\text{BrN}_2\text{O}_2$   $[\text{M}]^+$ : 518.0835, found: 518.0834.

**2-(tert-Butylamino)-3-(2'-chloro-5'-nitrophenyl)-4H-benzof[f]furo[3,2-c]chromen-4-one (4i).** Orange solid (85%), Mp decomp. 280-281 °C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3361, 3097, 2973,$

1734, 1621, 1521, 1344.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} =$   
 60 1.43 (s, 9H), 6.30 (s, 1H), 7.63-7.70 (m, 2H), 7.78-7.84 (m, 1H), 7.87 (d, 1H,  $J = 8.8$  Hz), 8.10 (t, 2H,  $J = 9.1$  Hz), 8.26 (dd, 1H,  $J = 8.8$  & 2.8 Hz), 8.31 (d, 1H,  $J = 2.8$  Hz), 8.94 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 30.1, 53.3, 95.6,$  106.4, 111.5, 117.1, 123.8, 124.1, 125.8, 126.2, 127.9, 128.3,  
 65 129.1, 130.1, 130.2, 130.5, 131.3, 141.9, 145.9, 150.2, 150.5, 155.8, 156.5. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{25}\text{H}_{19}\text{ClN}_2\text{O}_5$   $[\text{M}]^+$ : 462.0977, found: 462.0972.

**2-(Cyclohexylamino)-3-(2'-chloro-5'-nitrophenyl)-4H-benzof[f]furo[3,2-c]chromen-4-one (4j).** Brown solid (84%), Mp 215-  
 70 220 °C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3403, 2932, 2852, 1723, 1628,$  1527, 1345.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 1.08$ -1.43 (m, 5H), 1.59 (br s, 1H), 1.75 (br s, 2H), 1.97 (br s, 2H), 3.40-3.53 (m, 1H), 7.14 (s, 1H), 7.64 (br s, 2H), 7.73-7.93 (m, 2H), 7.95-8.15 (m, 2H), 8.16-8.43 (m, 2H), 8.86 (br s, 1H).  $^{13}\text{C}$  NMR (100  
 75 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 24.6, 25.1, 33.1, 33.2, 52.8, 87.4, 99.4,$  106.4, 116.9, 123.5, 124.4, 125.6, 126.1, 128.0, 128.1, 128.9, 129.4, 130.1, 130.4, 131.4, 141.9, 145.7, 149.5, 155.6, 156.6. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{27}\text{H}_{21}\text{ClN}_2\text{O}_5$   $[\text{M}-\text{H}]^+$ : 488.1133, found: 488.1129.

**3-(2'-Chloro-5'-nitrophenyl)-2-((2'',4'',4''-trimethylpentan-2-yl)amino)-4H-benzof[f]furo[3,2-c]chromen-4-one (4k).** Light yellow solid (91%), Mp 194-196 °C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} =$   
 80 3357, 2964, 2901, 1728, 1615, 1532, 1344, 1214.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 0.98$  (s, 9H), 1.44 (d, 6H,  $J = 11.0$  Hz),  
 85 1.86 (q, 2H,  $J = 7.5$  Hz), 6.25 (s, 1H), 7.59-7.68 (m, 2H), 7.72-7.79 (m, 1H), 7.87 (d, 1H,  $J = 8.8$  Hz), 8.04 (d, 1H,  $J = 9.0$  Hz), 8.08 (d, 1H,  $J = 7.9$  Hz), 8.26 (td, 2H,  $J = 9.0$  & 2.8 Hz), 8.94 (d, 1H,  $J = 8.5$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 30.1,$  30.3, 31.2, 31.4, 53.2, 56.6, 94.4, 106.4, 111.7, 117.1, 123.7,  
 90 124.0, 125.6, 126.1, 127.9, 128.0, 129.0, 129.9, 130.1, 130.5, 131.5, 142.0, 145.9, 150.1, 155.7, 156.5. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{29}\text{H}_{27}\text{ClN}_2\text{O}_3$   $[\text{M}-\text{H}]^+$ : 518.1603, found: 518.1609.

**2-(tert-Butylamino)-3-(4'-chlorophenyl)-4H-benzof[f]furo[3,2-c]chromen-4-one (4l).** Yellow solid (89%), Mp 210-211 °C, IR  
 95 (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 3397, 2942, 2862, 1660, 1597, 1508, 1338.$   $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 1.36$  (s, 9H), 5.85 (s, 1H), 7.50 (dt, 2H,  $J = 8.4$  & 2.9 Hz), 7.60-7.69 (m, 4H), 7.75-7.83 (m, 1H), 8.09 (d, 2H,  $J = 9.2$  Hz), 8.95 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 30.0, 53.4, 103.0, 106.2,$   
 100 110.0, 117.1, 124.1, 126.0, 126.1, 127.8, 128.3, 129.0, 129.3, 130.1, 130.5, 131.3, 131.7, 150.6, 151.6, 154.89, 156.7. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{25}\text{H}_{20}\text{ClNO}_3$   $[\text{M}]^+$ : 417.1126, found: 417.1123.

**2-(Cyclohexylamino)-3-(4'-nitrophenyl)-4H-benzof[f]furo[3,2-c]chromen-4-one (4m).** Brown solid (85%), Mp decomp. 265-  
 105 266 °C, IR (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}} = 2980, 1709, 1606, 1562, 1501,$  1211.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{H}} = 1.12$ -1.26 (m, 1H), 1.29-1.51 (m, 4H), 1.61-1.70 (m, 1H), 1.73-1.88 (m, 2H), 1.95-2.12 (m, 2H), 3.51-3.65 (m, 1H), 7.27 (d, 1H,  $J = 7.4$  Hz), 7.55  
 110 (d, 1H,  $J = 9.0$  Hz), 7.59 (t, 1H,  $J = 7.2$  Hz), 7.69 (t, 1H,  $J = 7.3$  Hz), 7.79 (dt, 2H,  $J = 8.8$  & 2.0 Hz), 7.96 (d, 1H,  $J = 8.0$  Hz), 8.00 (d, 1H,  $J = 4.0$  Hz), 8.24 (d, 2H,  $J = 8.9$  Hz), 8.66 (d, 1H,  $J = 8.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta_{\text{C}} = 24.8, 25.2, 32.9,$  53.1, 91.1, 105.9, 110.4, 116.7, 122.9, 124.1, 125.5, 125.9, 128.0,  
 115 128.8, 129.6, 130.0, 138.2, 144.5, 149.6, 149.8, 156.1, 156.6. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{27}\text{H}_{22}\text{N}_2\text{O}_5$   $[\text{M}]^+$ : 453.1444, found:



453.1440.

**3-(4'-Nitrophenyl)-2-((2'',4'',4'''-trimethylpentan-2-yl) amino)-4H-benzo[*f*]furo[3,2-*c*]chromen-4-one (4n).** Red solid (92%), Mp 192-193 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3397, 2974, 1714, 1616, 1553, 1494. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.04 (s, 9H), 1.49 (s, 6H), 1.95 (s, 2H), 6.48 (s, 1H), 7.64-7.70 (m, 2H), 7.74-7.80 (m, 1H), 7.88 (dt, 1 H, *J* = 8.2 & 1.8 Hz), 8.11 (t, 2H, *J* = 8.8 Hz), 8.27 (dt, 2H, *J* = 8.8 & 2.4 Hz), 9.0 (d, 1H, *J* = 8.4 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 30.1, 31.3, 31.5, 53.3, 56.7, 97.8, 106.2, 110.1, 117.1, 123.0, 124.1, 125.7, 126.2, 128.1, 129.2, 130.1, 130.3, 130.6, 138.2, 145.2, 150.3, 151.0, 155.9, 156.7. HRMS (ESI) *m/z* calcd. for C<sub>29</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub> [M-H]<sup>+</sup>: 483.1914, found: 483.1905.

**2-((Ethoxymethyl)amino)-3-(4'-nitrophenyl)-4H-benzo[*f*]furo[3,2-*c*]chromen-4-one (4o).** Brown solid (89%), Mp 219-220 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3373, 2960, 2855, 2821, 1657, 1603, 1414. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.17 (t, 3H, *J* = 7.1 Hz), 4.13 (q, 2H, *J* = 7.1 Hz), 4.25 (d, 2H, *J* = 6.2 Hz), 7.56-7.61 (m, 2H), 7.64-7.69 (m, 1H), 7.79 (dt, 2H, *J* = 9.0 & 2.5 Hz), 7.92-8.03 (m, 3H), 8.24 (dt, 2H, *J* = 9.0 & 2.5 Hz), 8.61 (d, 1H, *J* = 8.6 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 14.7, 45.1, 61.5, 92.1, 106.5, 111.1, 117.4, 123.7, 124.9, 126.1, 126.7, 128.7, 129.5, 130.5, 130.6, 138.3, 145.4, 150.4, 150.6, 156.6, 157.2, 171.1. HRMS (ESI) *m/z* calcd. for C<sub>24</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub> [M]<sup>+</sup>: 430.1165, found: 430.1161.

**2-(tert-Butylamino)-3-(3',4'-dimethoxyphenyl)-4H-benzo[*f*]furo[3,2-*c*]chromen-4-one (4p).** Yellow solid (70%), IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3372, 2959, 2854, 1654, 1602, 1412. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 1.45 (s, 9H), 3.92 (s, 3H), 3.93 (s, 3H), 4.21 (br s, 1H), 6.96 (d, 1H, *J* = 8.3 Hz), 7.08 (dd, 1H, *J* = 8.2 & 2.0 Hz), 7.14 (d, 1H, *J* = 2.0 Hz), 7.53-7.60 (m, 2H), 7.67-7.73 (m, 1H), 7.86 (d, 1H, *J* = 9.0 Hz), 7.92 (d, 1H, *J* = 7.6 Hz), 9.03 (d, 1H, *J* = 8.8 Hz). HRMS (ESI) *m/z* calcd. for C<sub>27</sub>H<sub>25</sub>NO<sub>5</sub> [M]<sup>+</sup>: 443.1733, found: 443.1721.

**3-(4'-Chlorophenyl)-2,6-(Dimethylphenylamino)-4H-benzo[*f*]furo[3,2-*c*]chromen-4-one (4q).** Yellow-greenish solid (89%), Mp 195-196 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3290, 2360, 1713, 1649, 1619, 1585, 1218, 1091, 813. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 2.19 (s, 6H), 4.01 (s, 1H), 7.01-7.06 (m, 3H), 7.27-7.33 (m, 4H), 7.44 (dt, 2H, *J* = 8.8 & 2.0 Hz), 7.51-7.54 (m, 1H), 7.58-7.61 (m, 2H), 7.64 (d, 1H, *J* = 11.6 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 18.7, 126.3, 126.7, 127.8, 128.6, 128.7, 128.8, 129.0, 130.4, 130.6, 131.1, 131.3, 131.7, 134.4, 136.8, 139.1, 150.6, 150.7, 153.2, 153.5, 157.3, 162.8. HRMS (ESI) *m/z* calcd. for C<sub>29</sub>H<sub>20</sub>ClNO<sub>3</sub> [M]<sup>+</sup>: 465.1126, found: 465.1107.

**2-(Cyclohexylamino)-3-(4'-nitrophenyl)-furo[3,2-*c*]quinolin-4(5H)-one (5a).** Dark red solid (85%), Mp decomp. 200-210 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3397, 2942, 2862, 1660, 1597, 1508, 1338. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.06-1.21 (m, 1H), 1.23-1.48 (m, 4H), 1.49-1.66 (m, 1H), 1.66-1.84 (m, 2H), 1.84-2.06 (m, 2H), 3.54-3.75 (m, 1H), 6.84 (d, 1H, *J* = 7.8 Hz), 7.21-7.27 (m, 1H), 7.31-7.51 (m, 2H), 7.79 (d, 1H, *J* = 7.8 Hz), 7.85 (dt, 2H, *J* = 7.4 & 2.5 Hz), 8.19 (dt, 2H, *J* = 8.9 & 2.5 Hz), 11.67 (s, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 24.8, 25.2, 33.1, 52.6, 93.1, 110.7, 114.8, 115.4, 118.7, 122.1, 122.7, 127.6, 130.1, 135.1, 139.5, 144.1, 147.8, 155.8, 158.5. HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>21</sub>N<sub>3</sub>O<sub>4</sub> [M-H]<sup>+</sup>: 402.1448, found: 402.1442.

**3-(4'-Chlorophenyl)-2-((2'',4'',4'''-trimethylpentan-2-yl)**

**amino)furo[3,2-*c*]quinolin-4(5H)-one (5b).** Dark red solid (89%), Mp decomp. 200-210 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3373, 2865, 2862, 1657, 1609, 1503, 1414. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 0.99 (s, 9H), 1.44 (s, 6H), 1.82 (s, 2H), 6.21 (s, 1H), 7.24-7.35 (m, 1H), 7.38-7.48 (m, 2H), 7.78 (d, 1H, *J* = 7.8 Hz), 7.89 (dt, 2H, *J* = 8.9 & 2.4 Hz), 8.21 (dt, 2H, *J* = 8.9 & 1.8 Hz), 11.69 (s, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 30.3, 31.3, 31.4, 53.0, 56.6, 97.6, 110.7, 114.2, 115.6, 118.7, 122.3, 122.8, 127.9, 130.4, 135.4, 139.5, 144.5, 148.6, 155.7, 158.5. HRMS (ESI) *m/z* calcd. for C<sub>25</sub>H<sub>27</sub>N<sub>3</sub>O<sub>4</sub> [M-H]<sup>+</sup>: 432.1917, found: 432.1911.

**2-(Cyclohexylamino)-3-(4'-chlorophenyl)-furo[3,2-*c*]quinolin-4(5H)-one (5c).** Light yellow solid (81%), Mp decomp. 212-214 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3096, 2896, 1711, 1211, 1003. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.02-1.18 (m, 1H), 1.19-1.42 (m, 4H), 1.53-1.61 (m, 1H), 1.63-1.76 (m, 2H), 1.83-1.99 (m, 2H), 3.41-3.58 (m, 1H), 3.41-3.53 (m, 1H), 6.26 (d, 1H, *J* = 8.0 Hz), 7.22 (td, 1H, *J* = 6.7 & 1.6 Hz), 7.34-7.44 (m, 4H), 7.58 (dt, 2H, *J* = 8.5 & 2.6 Hz), 7.77 (d, 1H, *J* = 7.8 Hz), 11.57 (s, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 24.8, 25.2, 33.2, 52.8, 94.7, 110.9, 115.3, 115.4, 118.6, 121.9, 127.3, 127.5, 130.0, 130.5, 131.6, 135.0, 147.4, 154.7, 158.6. HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>2</sub> [M-H]<sup>+</sup>: 391.1207, found: 391.1201.

**3-(4'-Chlorophenyl)-2-((2-morpholinoethyl)amino)furo[3,2-*c*]quinolin-4(5H)-one (5d).** Light yellow solid (84%), Mp decomp. 263 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3367, 2962, 2864, 2825, 1664, 1592, 1506, 1419. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 2.47 (s, 4H), 2.62 (s, 2H), 3.42-3.52 (m, 2H), 3.66 (s, 4H), 5.26 (s, 1H), 7.21-7.30 (m, 3H), 7.35-7.42 (m, 3H), 7.61 (dt, 2H, *J* = 7.8 & 2.6 Hz), 7.82 (d, 1H, *J* = 7.2 Hz), 10.53 (s, 1H). HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>22</sub>ClN<sub>3</sub>O<sub>3</sub> [M]<sup>+</sup>: 423.1344, found: 423.1341.

**2-((2-Morpholinoethyl)amino)-3-(4'-nitrophenyl)furo[3,2-*c*]quinolin-4(5H)-one (5e).** Orange solid (89%); Mp decomp. 262-263 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3363, 3164, 2959, 2860, 1661, 1603, 1569, 1508. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 2.51 (s, 4H), 2.61-2.71 (m, 2H), 3.52-3.60 (m, 2H), 3.64-3.70 (m, 4H), 5.61 (br s, 1H), 7.21-7.31 (m, 2H), 7.37-7.43 (m, 1H), 7.84 (dt, 3H, *J* = 9.3 & 2.4 Hz), 8.27 (d, 2H, *J* = 8.8 Hz), 9.51 (s, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 49.1, 53.7, 58.6, 66.8, 93.0, 111.2, 115.3, 116.0, 119.3, 122.7, 123.5, 128.2, 130.4, 135.6, 140.1, 144.5, 148.2, 157.3, 159.1. HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>24</sub>N<sub>4</sub>O<sub>5</sub> [M-H]<sup>+</sup>: 433.1506, found: 433.1501.

**3-(4'-Bromophenyl)-2-((2-morpholinoethyl)amino)furo[3,2-*c*]quinolin-4(5H)-one (5f).** Yellow solid (81%), Mp decomp. 258-259 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3369, 2963, 2864, 2821, 1655, 1602, 1498. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 2.47 (s, 4H), 2.61 (s, 2H), 3.42-3.51 (m, 2H), 3.66 (s, 4H), 5.25 (br s, 1H), 7.21-7.30 (m, 3H), 7.35-7.41 (m, 1H), 7.54 (s, 4H), 7.82 (d, 1H, *J* = 7.8 Hz), 10.49 (s, 1H). HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>22</sub>BrN<sub>3</sub>O<sub>3</sub> [M-H]<sup>+</sup>: 466.0760, found: 466.0765.

**3-(4'-Chlorophenyl)-2-(pentylamino)furo[3,2-*c*]quinolin-4(5H)-one (5g).** Yellow solid (78%), Mp 218-220 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3369, 2956, 2863, 2827, 1661, 1606, 1500, 1416. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 0.85-0.95 (m, 3H), 1.30-1.43 (m, 4H), 1.55-1.70 (m, 2H), 3.40 (t, 2H, *J* = 7.8 Hz), 4.40 (br s, 1H), 7.15-7.25 (m, 2H), 7.27-7.35 (m, 2H), 7.41 (dt, 2H, *J* = 8.5 & 1.8 Hz), 7.58 (dt, 2H, *J* = 8.5 & 1.8 Hz), 7.82 (d, 1H, *J* = 7.8 Hz), 11.17 (s, 1H). HRMS (ESI) *m/z* calcd. for C<sub>22</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>2</sub>

[M-H]<sup>+</sup>: 379.1207, found: 379.1207.

**3-(2',6'-Dichlorophenyl)-2-((2-morpholinoethyl)amino)furo[3,2-c]quinolin-4(5H)-one (5h).** Yellow solid (87%), Mp decomp. 271-272 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3433, 2938, 2856, 1661, 1602, 1491, 1350. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 2.41 (s, 4H), 2.54 (t, 2H, *J* = 5.7 Hz), 3.36 (q, 2H, *J* = 5.7 Hz), 3.60 (t, 4H, *J* = 4.4 Hz), 4.77 (t, 1H, *J* = 5.4 Hz), 7.19-7.34 (m, 4H), 7.42-7.47 (m, 2H), 7.81 (dd, 1H, *J* = 7.8 Hz), 11.31 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  = 40.3, 53.2, 57.0, 67.1, 92.0, 112.2, 116.4, 117.2, 119.2, 122.4, 127.5, 127.8, 129.5, 130.0, 135.3, 137.4, 149.2, 155.0, 160.3. HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>21</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub> [M-H]<sup>+</sup>: 456.0876, found 456.0871.

**3-(4'-Bromophenyl)-2-(cyclohexylamino)furo[3,2-c]quinolin-4(5H)-one (5i).** Yellow solid (82%), Mp decomp. 271-272 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3433, 2938, 2856, 1661, 1602, 1491, 1350. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  = 1.11-1.30 (m, 3H), 1.31-1.45 (m, 2H), 1.60-1.70 (m, 1H), 1.70-1.82 (m, 2H), 2.02-2.10 (m, 2H), 3.50-3.66 (m, 1H), 4.20 (br s, 1H), 7.15-7.26 (m, 1H), 7.30-7.35 (m, 2H), 7.50-7.60 (m, 3H), 7.83 (d, 1H, *J* = 7.8 Hz), 11.36 (s, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  = 25.4, 25.8, 33.7, 53.3, 95.0, 111.5, 115.8, 115.9, 119.0, 119.1, 122.5, 127.8, 130.9, 131.4, 132.5, 135.6, 148.0, 155.2, 159.2. HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>21</sub>BrN<sub>2</sub>O<sub>2</sub> [M-H]<sup>+</sup>: 435.0702, found 435.0701.

**2-(Cyclohexylamino)-3-(2',6'-dichlorophenyl)furo[3,2-c]quinolin-4(5H)-one (5j).** White solid (84%), Mp 265-266 °C, IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3433, 2938, 2856, 1661, 1602, 1491, 1350. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 1.10-1.35 (m, 8H), 1.52-1.65 (m, 2H), 1.67-1.77 (m, 1H), 1.97-2.11 (m, 2H), 3.38 - 3.57 (m, 1H), 3.74 (d, 1H, *J* = 8.0 Hz), 7.18-7.34 (m, 4H), 7.45 (d, 2H, *J* = 8.0 Hz), 7.83 (d, 1H, *J* = 7.8 Hz), 10.78 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  = 25.0, 25.4, 25.6, 34.3, 53.7, 92.4, 112.2, 116.2, 117.1, 119.3, 122.4, 127.4, 127.9, 129.5, 130.0, 135.2, 137.4, 149.0, 154.3, 160.0. HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub> [M-H]<sup>+</sup>: 425.0818, found 425.0814.

**2-(tert-Butylamino)-3-(3',4'-dimethoxyphenyl)furo[3,2-c]quinolin-4(5H)-one (5k).** Yellow solid (71%), IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3432, 2935, 2852, 1657, 1487, 1343. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 1.39 (s, 9H), 3.92 (s, 3H), 3.93 (s, 3H), 6.95 (d, 1H, *J* = 8.2 Hz), 7.10 (dd, 1H, *J* = 8.2 & 2.0 Hz), 7.20-7.28 (m, 2H), 7.29-7.40 (m, 2H), 7.85 (d, 1H, *J* = 7.8 Hz), 11.2 (s, 1H). HRMS (ESI) *m/z* calcd. for C<sub>23</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub> [M]<sup>+</sup>: 392.1736, found 392.1729.

**3-(4'-Methoxyphenyl)-2-(2-morpholinoethyl)amino)furo[3,2-c]quinolin-4(5H)-one (5l).** Yellow solid (69%), IR (KBr, cm<sup>-1</sup>):  $\nu_{\max}$  = 3430, 2930, 2852, 1648, 1485, 1341. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  = 2.45 (s, 4H), 2.59 (t, 2H, *J* = 5.6 Hz), 3.44 (q, 2H, *J* = 5.8 Hz), 3.63 (t, 4H, *J* = 4.5 Hz), 5.17 (s, 1H), 6.98 (dt, 2H, *J* = 8.8 & 3.0 Hz), 7.20-7.29 (m, 3H), 7.32-7.38 (m, 1H), 7.56 (dt, 2H, *J* = 8.0 & 3.8 Hz), 7.82 (dd, 1H, *J* = 8.0 & 1.0 Hz), 10.33 (s, 1H). HRMS (ESI) *m/z* calcd. for C<sub>24</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub> [M]<sup>+</sup>: 419.1845, found 419.1839.

#### Supplementary Information:

Supplementary information (Representative <sup>1</sup>H, <sup>13</sup>C NMR and HRMS spectra associated with this work can be found online free of charge.

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#### REFERENCES

- (a) N. Isambert, M. M. S. Duque, J. -C. Plaquevent, Y. Genisson, J. Rodriguez and T. Constantieux, *Chem. Soc. Rev.* 2011, **40**, 1347; (b) S. V. Ryabukhin, D. S. Granat, A. S. Plaskon, A. N. Shivanyuk, A. A. Tolmachev and Y. M. Volovenko, *ACS Comb. Sci.* 2012, **14**, 465; (c) A. Moulin, M. Bibian, A. -L. Blayo, S. E. Habnoui, J. Martinez and J. -A. Fehrentz, *Chem. Rev.* 2010, **110**, 1809.
- (a) X. M. Cheng, *J. Combi. Chem.* 2007, **9**, 906; (b) X. Yang, K. Odelius and M. Hakkarainen, *ACS Sustainable Chem. Eng.* 2014, **2**, 2198; (c) J. Spencer, C. B. Baltus, H. Patel, N. J. Press, S. K. Callear, L. Male and S. J. Coles, *ACS Comb. Sci.* 2011, **13**, 24; (d) V. P. Mehta, A. Sharma and E. Van der Eycken, *Org. Lett.* 2008, **10**, 1147; (e) P. T. Anasta and J. C. Warner, *Green Chemistry: Theory and Practical*, OUP, USA, 2000.
- "Multicomponent Reactions" Ed. J. Zhu and H. Bienayme, Wiley-Interscience: New York, 2005.
- (a) B. Ganem, *Acc. Chem. Res.* 2009, **42**, 463; (b) S. C. Pan and B. List, *Angew. Chem. Int. Ed.* 2008, **47**, 3622; (c) H. Bienayme and K. Bouzid, *Angew. Chem. Int. Ed.* 1998, **37**, 2234; (d) O. Kappe, *Acc. Chem. Res.* 2000, **33**, 879; (e) A. Dömling and I. Ugi, *Angew. Chem. Int. Ed.* 2000, **39**, 3168; (f) R. M. Wilson, J. L. Stockdill, X. Wu, X. Li, P. A. Vadola, P. K. Park, P. Wang and S. J. Danishefsky, *Angew. Chem. Int. Ed.* 2012, **51**, 2834; (g) A. Dömling, *Curr. Opin. Chem. Biol.* 2002, **6**, 306; (h) M. S. Sigman, P. Vachal and E. N. Jacobsen, *Angew. Chem., Int. Ed.* 2000, **39**, 1279.
- (a) P. S. Jacobi, In *Advances in Heterocyclic Natural Product Synthesis* Pearson, W. H., Ed. Jai Press: Connecticut, 1992 Volume 2, ISBN: 1-55938-333-X; (b) N. Tannisever, N. H. Fischer and G. B. Williamson, *Phytochemistry* 1988, **27**, 2523; (c) A. H. Mericli, F. Mericli, J. Jakupovic, F. Bohlmann, X. A. Domiguez and H. S. Vega, *Phytochemistry* 1989, **28**, 1149; (d) P. A. Jacobi and D. G. Walker, *J. Am. Chem. Soc.* 1981, **103**, 4611; (e) T. Koike, N. Takeuchi, T. Ohta and S. Tobinaga, *Chem. Pharm. Bull.* 1999, **47**, 897; (f) M. L. A. Cassará, S. A. Borkosky, M. G. Sierra, A. Bardón and M. I. Ybarra, *Chem. Biodiv.* 2010, **7**, 1745; (e) R. D. H. Murray, *The Natural Coumarins, Occurrence, Chemistry and Biochemistry*; Wiley-Interscience: New York, 1982.
- X. Wang, K. F. Bastow, C. -M. Sun, Y. -L. Lin, H. -J. Yu, M. -J. Don, T. -S. Wu, S. Nakamura and K. -H. Lee, *J. Med. Chem.* 2004, **47**, 5816.
- (a) S. Y. Ryu, C. O. Lee and S. U. Choi, *Planta Med.* 1997, **63**, 339; (b) W. -L. Wu, W. -L. Chang and C. -F. Chen, *Am. J. Chin. Med.* 1991, **19**, 207; (c) E. -H. Cao, X. -Q. Liu, J. -J. Wang and N. -F. Xu, *Free Radic. Biol. Med.* 1996, **20**, 801; (d) M. Onitsuka, M. Fujiu, N. Shinma and H. B. Maruyama, *Chem. Pharm. Bull.* 1983, **31**, 1670; (e) S. Y. Ryu, C. O. Lee and S. U. Choi, *Planta Med.* 1999, **65**, 654.
- (a) M. Rideau, C. Yerchere and P. Hibon, *Phytochemistry* 1979, **18**, 155; (b) J. F. Ayafor, B. L. Sondengam and B. T. Nagadjui, *Planta Med.* 1982, **44**, 139; (c) F. E. Gainer and W. A. Arnett, *J. Pharm. Sci.* 1969, **58**, 1548; (d) E. Y. Chou, K. Hostettmann, I. Kubo, K. Nakanishi and M. Taniguchi, *Heterocycles* 1977, **1**, 969.
- (a) A. Shaabani, M. B. Teimouri and H. R. Bijanzadesh, *Monatsh. Chem.* 2004, **135**, 441. (b) Y. Ito, H. Kato and T. Saegusa, *J. Org. Chem.* 1982, **47**, 741; (c) N. Chatani, M. Oshita, Y. I. Tobisu and S. Murai, *J. Am. Chem. Soc.* 2003, **125**, 7812; (d) M. Oshita, K.

- Yamashita, M. Tobisu and N. Chatani, *J. Am. Chem. Soc.* 2005, **127**, 761; (e) A. Shaabani, E. Soleimani, A. Maleki and J. M. Rad, *Mol. Diversity* 2009, **13**, 269.
- 10 V. Nair, R. S. Menon, A. U. Menon and S. Viji, *Tetrahedron Lett.* 2002, **43**, 2293.
- 11 J. Wu, *Chemistry Lett.*, 2006, **35**, 118.
- 12 (a) M. Bayat, N. Z. Shiraz and S. H. Hosseini, *Helv. Chim. Acta* 2010, **11**, 2189; (b) A. Shaabani, M. B. Teimouri, S. Samadi and K. Soleimani, *Synth. Commun.*, 2005, **35**, 535.
- 10 13 A. Sharma and H. -Y. Li, *Synlett*, 2011, **10**, 1407.
- 14 Y. Wu, K. Xua and D. Xiea, *Tetrahedron*, 2005, **61**, 507.
- 15 J. Gong, C. Cail, X. Liu, X. Ku, H. Jiang, D. Gao and H. Li, *Bioinformatics*, 2013, **29**, 1827.
- 16 S. Kesavan and L. A. Marcaurelle, *Nat. Chem. Bio.* 2013, **9**, 212.
- 15 17 The Uniprot Consortium, *Nucleic Acids Res.* 2014, **42**, D191.