

Facile and Efficient Synthesis of Indol-3-yl Substituted Pyran Derivatives *via* One-Pot Multicomponent Reactions under Ultrasonic Irradiation

Tao Chen, Xiao-Ping Xu, and Shun-Jun Ji*

Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123

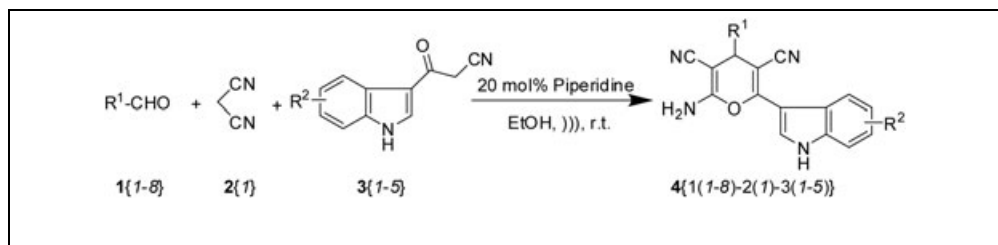
People's Republic of China

*E-mail: chemjsj@suda.edu.cn

Received February 24, 2011

DOI 10.1002/jhet.983

Published online 00 Month 2013 in Wiley Online Library (wileyonlinelibrary.com).



A series of polysubstituted indol-3-yl substituted pyran derivatives have been synthesized *via* one-pot multicomponent reactions of aldehydes, malononitrile with 3-cyanoacetyl indoles under ultrasonic irradiation. This method has the advantages of high yield, easy operation, short-reaction time, mild-reaction condition, and catalyst recyclability.

J. Heterocyclic Chem., **00**, 00 (2013).

INTRODUCTION

Indoles substituted with heterocyclic rings at the 3-position are featured in a wide variety of pharmacologically and biologically active compounds especially with anticancer, antitumor, hypoglycemic, anti-inflammatory, analgesic, and antipyretic activities [1] (Fig. 1). For instance, nortopsentins A–C exhibit *in vitro* cytotoxicity against P388 cells [2]; meridianins A–E show cytotoxicity toward murine tumor cell lines and have potent inhibition against several protein kinases [3]. Thus, synthetic methods and the structure decoration of indole derivatives have received an increasing attention in recent years.

Polysubstituted 4*H*-pyran derivatives occupy a special place in organic and medicinal chemistry because these compounds show various biological properties, such as anticoagulant, anticancer, antioxidant, spasmolytic, diuretic, and antianaphylactic activities. A great many of 2-amino-4*H*-pyran derivatives are employed as photoactive materials, cosmetics, and pigments [4–11]. With all these fascinating applications, much research has been devoted to the development of directed synthetic routes to suitable 4*H*-pyran units, as well as effective functionalized strategies [12–15].

Multicomponent reactions (MCRs) are powerful tools in preparing libraries to screen for biologically active compounds and potent drug candidates. A wide range of advantages offered by MCRs, such as high degree of atom

economy, convergence, ease of execution, and access to complex molecules has been recognized in the past decade [16]. Also, ultrasound irradiation has been considered as a clean and useful protocol in organic synthesis during the last three decades. Compared with traditional methods, the procedure is more convenient. Moreover, a large number of organic reactions can be carried out in higher yield, shorter reaction time, or milder conditions under ultrasonic irradiation [17].

Because of the potent and diverse biological activities of indoles and 4*H*-pyrans, guided by the observation that the presence of two or more different heterocyclic moieties in a single molecule often enhances the biocidal profile remarkably and out of our interest in the multicomponent synthesis and in continuation of our work on the synthesis of indole derivatives [18]. Herein, we report the synthesis of various indol-3-yl substituted pyran derivatives *via* a facile, efficient, one-pot, atom-economical, and three-component reaction under ultrasonic irradiation in much shorter time compared with the reported literatures [19].

RESULTS AND DISCUSSION

In our initial study, the reaction of 4-bromobenzaldehyde **1** (**1**) (0.5 mmol), malononitrile **2** (**1**) (0.5 mmol), and 3-(5-bromo-1*H*-indol-3-yl)-3-oxopropanenitrile **3** (**1**)

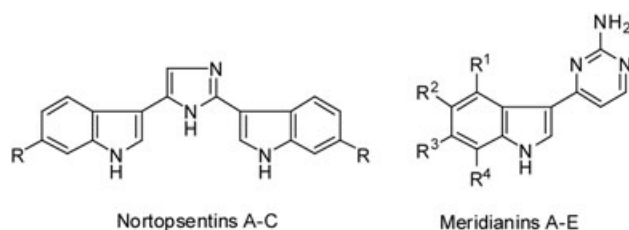


Figure 1. Representatives of important indol-3-yl substituted heterocycles.

(0.5 mmol) was chosen as a model reaction (Scheme 1) to establish the feasibility of the strategy and optimize the reaction conditions. The results are summarized in Table 1.

The reaction was first carried out in ethanol in the absence of any catalyst at room temperature. However, after 3 h, product 4{1, 1, 1} was not obtained, even if the reaction was catalyzed by *p*-TsOH, Bi(NO₃)₃ or FeCl₃ (Table 1, entries 1–4). Ceric ammonium nitrate could catalyze this reaction to lead to the desired product, but, in trace amount (Table 1 entry 5). To our delight, 35% of the target compound 4{1, 1, 1} was obtained when NaOH was used as catalyst (Table 1, entry 6). Encouraged by this success, as seen in Table 1, entries 7–11, a variety of bases, such as Et₃N, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,4-diazabicyclo[2.2.2]octane, piperidine, and K₂CO₃ were screened in model reaction, and the yield was up to 90% when the reaction was catalyzed by piperidine in EtOH (Table 1, entry 10). Afterward, various solvents were examined for this reaction. When the reaction solvent was changed from acetonitrile to N,N-Dimethylformamide (DMF) or Dimethyl sulfoxide (DMSO), the compound 4{1, 1, 1} was produced in moderate yields (Table 1, entries 12–14). When H₂O was used as the reaction solvent, the desired product was obtained in a much lower yield (Table 1, entry 15). Finally, it was found that EtOH was the most suitable solvent for this reaction. In recent years, microwaves [18(i),(j)] and ultrasonic irradiation [18(a),(c),(e)] were always adopted to synthesize many indole-containing compounds in our group, because under these circumstances, the reactions were often greatly accelerated. So the ultrasonic irradiation was applied to improve the rate for the model reaction. It was found that the reaction time was sharply decreased from 60 to 15 min, as is seen from Table 1,

Scheme 1

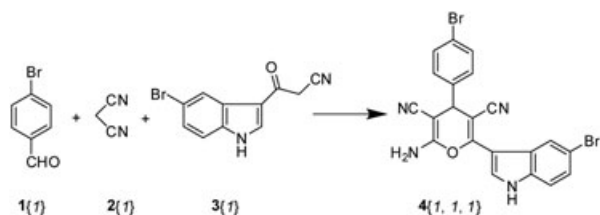


Table 1

Optimization of catalysts and solvents in the synthesis of 4{1, 1, 1}.

Entry ^a	Catalyst (mol %)	Solvent	Time (min)	Yield ^b (%)
1	none	EtOH	180	0
2	<i>p</i> -TsOH (20%)	EtOH	180	0
3	FeCl ₃ (20%)	EtOH	180	0
4	Bi(NO ₃) ₃ (20%)	EtOH	180	0
5	CAN ^c (20%)	EtOH	180	Trace
6	NaOH (20%)	EtOH	60	35
7	Et ₃ N (20%)	EtOH	60	80
8	DBU ^d (20%)	EtOH	60	53
9	DABCO ^e (20%)	EtOH	60	60
10	Piperidine (20%)	EtOH	60	90
11	K ₂ CO ₃ (20%)	EtOH	60	37
12	Piperidine (20%)	CH ₃ CN	60	78
13	Piperidine (20%)	DMF	60	62
14	Piperidine (20%)	DMSO	60	70
15	Piperidine (20%)	H ₂ O	60	18
16 ^f	Piperidine (20%)	EtOH	15	91
17 ^f	Piperidine (15%)	EtOH	15	77
18 ^f	Piperidine (10%)	EtOH	15	61
19 ^f	Piperidine (5%)	EtOH	15	49

^aAll reactions were carried out at room temperature.

^bIsolated yield.

^cCAN = ceric ammonium nitrate.

^dDBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

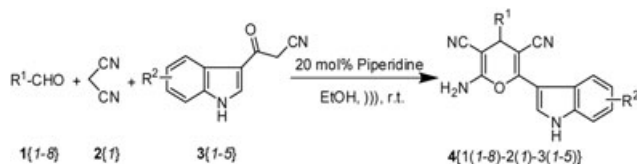
^eDABCO = 1,4-diazabicyclo[2.2.2]octane.

^fThe reaction was carried out under ultrasonic irradiation.

entry 16. We also evaluated the amount of piperidine required for this reaction. The results from Table 1 (entries 16–19) show that 20 mol % piperidine is necessary to complete the reaction in excellent yield 91% under ultrasonic irradiation within 15 min at room temperature. Under ultrasonic irradiation in EtOH, the reaction yield would obviously decrease along with cutting down the loading of the catalyst.

With this result in hand, we went on to study the scope of the methodology (Scheme 2). Using the optimized reaction conditions, a variety of structurally diverse aryl aldehydes 1{1–8} and 3-(1*H*-indol-3-yl)-3-oxopropanenitriles 3{1–5} were investigated (Fig. 4). The results can be represented as in Table 2. As shown in Table 2, when aromatic aldehydes with electron-withdrawing groups (such as nitro and halide groups) 1{1–5} reacted with malononitrile 2{1} and 3-(1*H*-indol-3-yl)-3-oxopropanenitriles both with electron-withdrawing and electron-donating groups 3{1–5}, the corresponding products were obtained smoothly; when alde-

Scheme 2



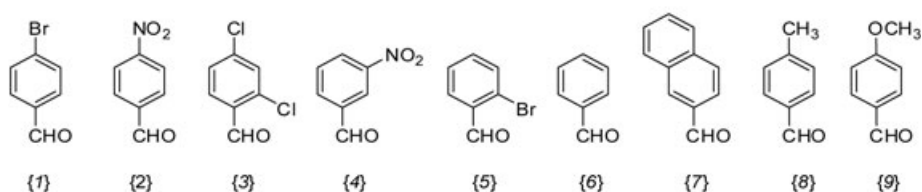
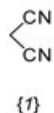
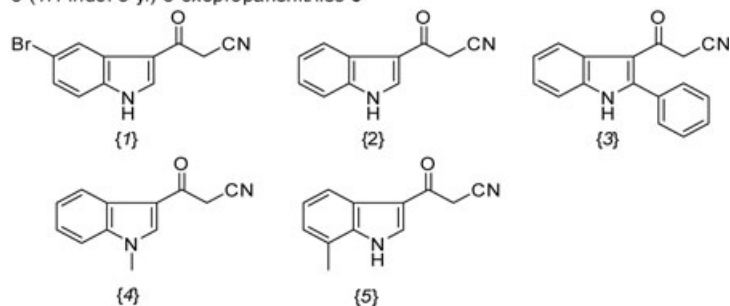
aryl aldehydes **1**malononitrile **2**3-(1*H*-indol-3-yl)-3-oxopropanenitriles **3**

Figure 2. Diversity of reagents.

hydes changed to benzaldehyde and 2-naphthaldehyde, the reaction time was prolonged to 60–90 min, and the yield was reduced to 74–79%, while the reaction temperature

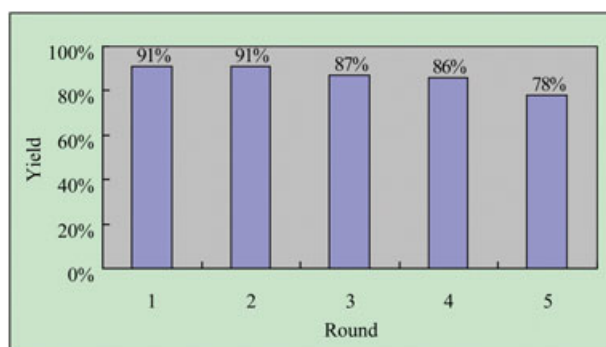
was increased to 50°C. The yields of the expected products were very poor as the aldehydes with electron-donating group **1**{8–9} were used as substrates.

Apart from the mild conditions of the process and its good results, the simplicity of product isolation and the possibility to recover and recycle the piperidine as catalyst offer a significant advantage. Because piperidine is soluble in the reaction medium (ethanol) and the desired products are less soluble in ethanol, the products can be directly separated by filtering after the reaction is completed. The filtrate containing piperidine can directly be recovered and recycled. Studies using **1**{1}, **2**{1}, and **3**{1} as model substrates showed that the recovered reaction solution could be successively recycled in subsequent reactions without any noticeable decrease of yields for four runs (Fig. 3).

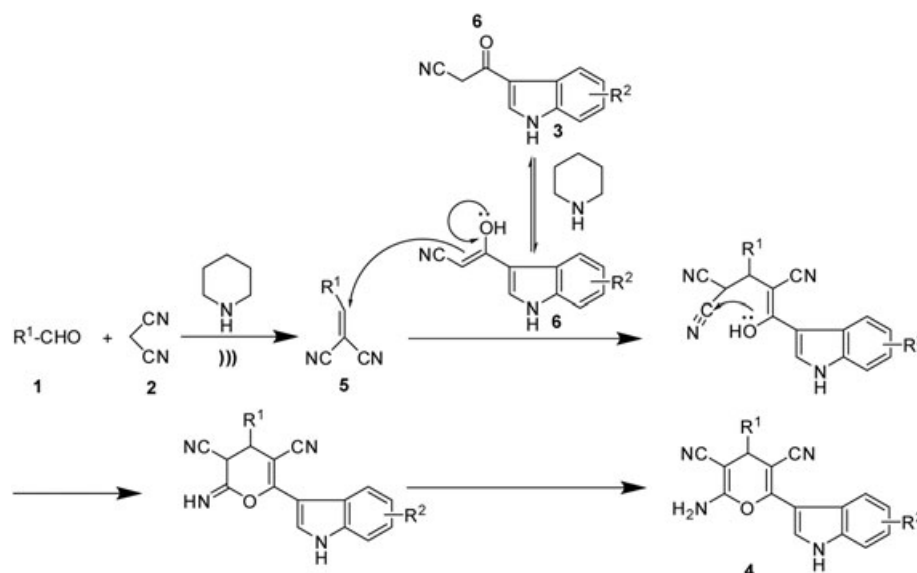
Table 2

Synthesis of indol-3-yl substituted pyran derivatives **4**.

Entry	Time (min)	Yield ^a (%)
4{1, 1, 1}	15	91
4{1, 1, 2}	10	90
4{1, 1, 3}	8	89
4{1, 1, 4}	6	92
4{1, 1, 5}	6	94
4{2, 1, 1}	13	85
4{2, 1, 2}	11	86
4{2, 1, 3}	9	85
4{2, 1, 4}	5	89
4{2, 1, 5}	5	91
4{3, 1, 1}	17	85
4{3, 1, 2}	12	87
4{3, 1, 3}	12	85
4{3, 1, 4}	8	89
4{3, 1, 5}	9	92
4{4, 1, 3}	13	82
4{4, 1, 4}	10	85
4{5, 1, 1}	18	83
4{5, 1, 3}	15	81
4{5, 1, 4}	10	84
4{5, 1, 5}	10	87
4{6, 1, 1} ^b	90	74
4{6, 1, 4} ^b	60	79
4{7, 1, 4} ^b	60	76
4{8, 1, 4} ^b	90	Trace
4{9, 1, 4} ^b	90	Trace

^aIsolated yield.^bThe reaction was carried out at 50°C.Figure 3. Catalyst recycle. Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.

Scheme 3. Supposed reaction mechanism.



Given a number of commercially available aromatic aldehydes and 3-(1*H*-indol-3-yl)-3-oxopropanenitriles, the present method should be applicable to synthesis of libraries with high diversity. We expect this method to find extensive application in the field of combinatorial chemistry, diversity-oriented synthesis, and drug discovery.

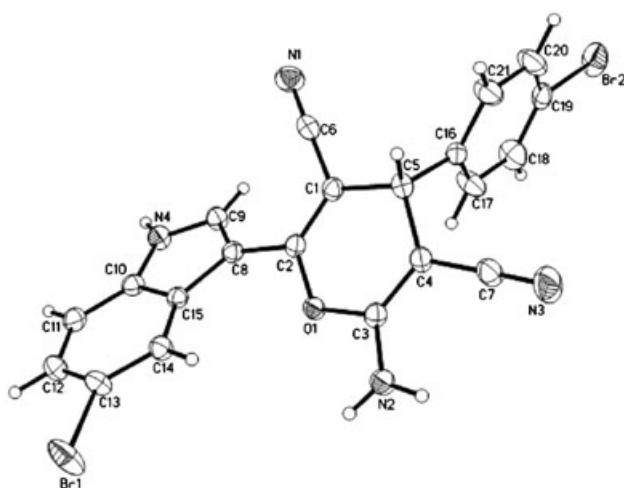
According to the experimental observation, compound **5** was formed from Knoevenagel condensation of aromatic aldehydes and malononitrile, which was faster than Knoevenagel condensation of aromatic aldehydes and 3-(1*H*-indol-3-yl)-3-oxopropanenitriles in the earlier optimized condition. Although the detailed mechanism of the above reaction remains to be fully clarified, compound **4** could

be produced from the intermediate **5** via Michael addition with the tautomer of 3-cyanoacetyl indole **6** followed by intramolecular cyclization (Scheme 3). In this work, the products were characterized by melting point, IR, NMR, and combustion analysis. Furthermore, the structure of **4** {*1*, *1*, *1*} was established by X-ray crystallographic analysis. Its structure is shown in Figure 4, and its crystallographic data are shown in Table 3.

Table 3

Crystallographic data of compound **4**{*1*, *1*, *1*}.

Empirical formula	C ₂₁ H ₁₂ N ₄ Br ₂ O
Formula weight	496.15
Temperature	223(2) K
Wavelength	0.71075 Å
Crystal system	triclinic
Space group	<i>P</i> -1
Unit-cell dimensions	<i>a</i> = 9.4650(3) Å; α = 64.471(8)° <i>b</i> = 11.3668(3) Å; β = 69.884(9)° <i>c</i> = 12.8881(4) Å; γ = 69.542(9)°
Volume	1141.25(6) Å ³
Z	2
Density (calculated) Mg/m ³	1.657
Absorption coefficient mm ⁻¹	3.584
<i>F</i> (000)	568
Crystal size	0.45 × 0.30 × 0.15 mm ³
Theta range for data collection	3.17–27.48°
Limiting indices	–11 ≤ <i>h</i> ≤ 12, –14 ≤ <i>k</i> ≤ 10, –16 ≤ <i>l</i> ≤ 16
Reflections collected	10490/5133 [<i>R</i> (int) = 0.0291]
Data/restraints/parameters	5133/0/304
Goodness-of-fit on <i>F</i> ²	1.010
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ = 0.0373, <i>wR</i> ₂ = 0.0791
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0580, <i>wR</i> ₂ = 0.0854
Largest diff. peak and hole	0.382 and –0.616 e.Å ⁻³

Figure 4. Compound **4**{*1*, *1*, *1*} crystal structure.

CONCLUSION

In summary, we have demonstrated a simple, atom-economical, and efficient approach for the synthesis of indol-3-yl substituted pyran derivatives *via* one-pot, three-component reactions using readily available starting materials. This method incorporates both indole and pyran moieties into a single molecule. In view of the presence of either functionality, these compounds may suppose to demonstrate improvement in biological activities. Prominent among the advantages of this new method are novelty, high yields, easy operation, mild reaction condition, and catalyst recyclability. Further reactivity studies and synthetic applications of this methodology are in progress in our laboratory.

EXPERIMENTAL

Melting points were uncorrected. IR spectra were recorded on a Varian F-1000 spectrometer in KBr with absorptions in cm^{-1} . ^1H -NMR spectra were determined on a Varian-300 or 400 MHz spectrometer in $\text{DMSO}-d_6$ solution. J values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard Tetramethylsilane (TMS). Combustion analysis was performed with Carlo-Erba EA1110CHNO-S elemental analyzer. X-ray crystallographic analysis was performed with a Rigaku Mercury CCD/AFC diffractometer.

General procedure for the synthesis of **4** is represented as follows. A mixture of benzaldehyde **1** (0.5 mmol), malononitrile **2** (0.5 mmol), and 3-(1*H*-indol-3-yl)-3-oxopropanenitrile **3** (0.5 mmol) in 3 mL EtOH was placed in a round bottom flask. The reaction was carried out at room temperature under ultrasonic irradiation for some minutes (the progress was monitored by TLC). Ultrasonication was performed in a KQ-250E ultrasonic cleaner with a frequency of 40 KHz and a normal power of 250 W. After the completion, the reaction mixture was filtered. Then the precipitate was washed with water (5 mL) and ethanol (2 mL) to afford the pure **4**.

2-Amino-6-(5-bromo-1*H*-indol-3-yl)-4-(4-bromophenyl)-4*H*-pyran-3,5-dicarbonitrile (4{1, 1, 1}). Solid; M.p. 243–245°C. IR (potassium bromide): ν 3462.9, 3357.9, 3224.2, 3079.1, 3027.6, 2935.9, 2201.4, 1659.7, 1608.4, 1517.4, 1400.8, 1360.7, 1147.3, 811.2 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 12.15 (s, 1H, NH), 8.16 (d, 1H, $J = 3.2$ Hz, ArH), 8.02 (d, 1H, $J = 1.6$ Hz, ArH), 7.63 (d, 2H, $J = 8.4$ Hz, ArH), 7.48 (d, 1H, $J = 8.4$ Hz, ArH), 7.43 (s, 2H, NH_2), 7.33–7.37 (m, 3H, ArH), 4.49 (s, 1H, CH). ^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$) (δ , ppm): 158.7, 155.2, 142.3, 134.8, 131.8, 130.7, 130.1, 126.1, 125.5, 123.3, 121.0, 119.2, 118.6, 114.3, 113.9, 105.0, 84.6, 55.3. Anal. calcd for $\text{C}_{21}\text{H}_{12}\text{Br}_2\text{N}_4\text{O}$: C, 50.84; H, 2.44; N, 11.29. Found: C, 50.94; H, 2.61; N, 11.38.

2-Amino-4-(4-bromophenyl)-6-(1*H*-indol-3-yl)-4*H*-pyran-3,5-dicarbonitrile (4{1, 1, 2}). Solid; M.p. 202–204°C. IR (potassium bromide): ν 3457.0, 3306.5, 3256.6, 3209.9, 3055.6, 2200.9, 1615.6, 1586.7, 1522.0, 1488.6, 1430.8, 1410.2, 877.0, 737.6 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 12.00 (s, 1H, NH), 8.14–8.15 (m, 1H, ArH), 7.94–7.96 (m, 1H, ArH), 7.63 (d, 2H, $J = 8.4$ Hz, ArH), 7.51 (d, 1H, $J = 8.0$ Hz, ArH), 7.32–7.36 (m, 4H, NH_2 + ArH), 7.22–7.26 (m, 1H, ArH), 7.15–7.19 (m, 1H, ArH), 4.49 (s, 1H, CH). ^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$) (δ , ppm): 158.8, 156.0, 142.5, 136.0, 131.9, 130.0,

129.5, 124.5, 122.7, 121.6, 121.0, 121.0, 119.2, 118.9, 112.4, 105.4, 83.5, 55.5, 39.2. Anal. calcd for $\text{C}_{21}\text{H}_{13}\text{BrN}_4\text{O}$: C, 60.45; H, 3.14; N, 13.43. Found: C, 60.47; H, 3.28; N, 13.45.

2-Amino-4-(4-bromophenyl)-6-(2-phenyl-1*H*-indol-3-yl)-4*H*-pyran-3,5-dicarbonitrile (4{1, 1, 3}). Solid; M.p. 206–208°C. IR (potassium bromide): ν 3445.1, 3396.3, 3312.5, 3186.5, 2201.6, 1681.4, 1599.8, 1486.1, 1451.0, 1396.5, 1217.5, 1133.6, 1010.9, 927.6, 752.6 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 12.13 (s, 1H, NH), 7.66 (d, 2H, $J = 8.4$ Hz, ArH), 7.58 (d, 2H, $J = 7.2$ Hz, ArH), 7.38–7.54 (m, 5H, ArH), 7.32 (d, $J = 8.4$ Hz, 2H, ArH), 7.22–7.26 (m, 3H, NH_2 + ArH), 7.17 (t, $J = 7.6$ Hz, 1H, ArH), 4.48 (s, 1H, CH). ^{13}C -NMR (75 MHz, $\text{DMSO}-d_6$) (δ , ppm): 159.3, 155.1, 141.6, 139.5, 135.7, 131.9, 130.9, 130.1, 129.0, 128.8, 127.5, 127.0, 122.9, 121.0, 120.9, 119.2, 119.1, 116.6, 112.0, 102.3, 92.3, 54.9. Anal. calcd for $\text{C}_{27}\text{H}_{17}\text{BrN}_4\text{O}$: C, 65.73; H, 3.47; N, 11.36. Found: C, 65.89; H, 3.55; N, 11.36.

2-Amino-4-(4-bromophenyl)-6-(1-methyl-1*H*-indol-3-yl)-4*H*-pyran-3,5-dicarbonitrile (4{1, 1, 4}). Solid; M.p. 236–238°C. IR (potassium bromide): ν 3346.6, 3335.7, 3058.1, 2933.7, 2197.0, 1672.6, 1614.5, 1587.7, 1528.1, 1474.5, 1404.5, 1364.7, 1121.4, 738.1 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 8.15 (s, 1H, ArH), 7.97 (d, 1H, $J = 8.0$ Hz, ArH), 7.63 (d, 2H, $J = 8.4$ Hz, ArH), 7.56 (d, 1H, $J = 8.4$ Hz, ArH), 7.29–7.35 (m, 5H, NH_2 + ArH), 7.19–7.23 (m, 1H, ArH), 4.48 (s, 1H, CH), 3.88 (s, 3H, CH_3). ^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$) (δ , ppm): 158.7, 155.4, 142.5, 136.5, 132.9, 131.8, 129.9, 124.9, 122.8, 121.8, 121.3, 120.9, 119.1, 118.7, 110.6, 104.3, 83.3, 55.4, 39.2, 33.2. Anal. calcd for $\text{C}_{22}\text{H}_{15}\text{BrN}_4\text{O}$: C, 61.27; H, 3.51; N, 12.99. Found: C, 61.45; H, 3.77; N, 13.05.

2-Amino-4-(4-bromophenyl)-6-(7-methyl-1*H*-indol-3-yl)-4*H*-pyran-3,5-dicarbonitrile (4{1, 1, 5}). Solid; M.p. 250–252°C. IR (potassium bromide): ν 3467.3, 3204.5, 3054.5, 2200.8, 1615.2, 1521.9, 1444.3, 1360.7, 1160.9, 1009.4, 737.5 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 12.01 (s, 1H, NH), 8.10 (d, 1H, $J = 3.2$ Hz, ArH), 7.70 (d, 1H, $J = 7.6$ Hz, ArH), 7.63 (d, 2H, $J = 8.0$ Hz, ArH), 7.32–7.35 (m, 4H, NH_2 + ArH), 7.03–7.10 (m, 2H, ArH), 4.48 (s, 1H, CH), 2.50 (s, 1H, CH_3). ^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$) (δ , ppm): 158.8, 156.0, 142.5, 135.5, 131.9, 130.0, 129.1, 124.3, 123.2, 121.5, 121.2, 121.0, 119.2, 118.9, 105.8, 83.6, 55.4, 39.2, 16.8. Anal. calcd for $\text{C}_{22}\text{H}_{15}\text{BrN}_4\text{O}$: C, 61.27; H, 3.51; N, 12.99. Found: C, 61.54; H, 3.73; N, 13.14.

2-Amino-6-(5-bromo-1*H*-indol-3-yl)-4-(4-nitrophenyl)-4*H*-pyran-3,5-dicarbonitrile (4{2, 1, 1}). Solid; M.p. 256–258°C. IR (potassium bromide): ν 3481.0, 3379.7, 3294.3, 3072.6, 2194.9, 1658.9, 1613.9, 1514.6, 1452.7, 1351.2, 1148.0, 804.2, 703.3 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 12.19 (d, 1H, $J = 2.4$ Hz, NH), 8.31 (d, 2H, $J = 8.8$ Hz, ArH), 8.20 (d, 1H, $J = 3.2$ Hz, ArH), 8.06 (d, 1H, $J = 1.6$ Hz, ArH), 7.70 (d, 2H, $J = 8.8$ Hz, ArH), 7.56 (s, 2H, NH_2), 7.49 (d, 1H, $J = 8.4$ Hz, ArH), 7.36–7.39 (m, 1H, ArH), 4.72 (s, 1H, CH). ^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$) (δ , ppm): 158.9, 155.8, 150.2, 147.1, 134.8, 131.0, 129.3, 126.1, 125.6, 124.2, 123.4, 119.1, 118.5, 114.4, 114.1, 105.0, 83.7, 54.7, 39.4. Anal. calcd for $\text{C}_{21}\text{H}_{12}\text{BrN}_5\text{O}_3$: C, 54.56; H, 2.62; N, 15.15. Found: C, 55.54; H, 2.71; N, 15.13.

2-Amino-6-(1*H*-indol-3-yl)-4-(4-nitrophenyl)-4*H*-pyran-3,5-dicarbonitrile (4{2, 1, 2}). Solid; M.p. 238–240°C. IR (potassium bromide): ν 3456.0, 3351.8, 3277.8, 2202.7, 1668.2, 1615.0, 1513.9, 1406.9, 1351.9, 1191.1, 922.3, 740.6 cm^{-1} . ^1H -NMR (400 MHz, $\text{DMSO}-d_6$) (δ , ppm): 12.04 (s, 1H, NH), 8.31

(d, 1H, $J = 8.4$ Hz, ArH), 8.17 (d, 1H, $J = 2.4$ Hz, ArH), 7.98 (d, 2H, $J = 8.0$ Hz, ArH) 7.67 (d, 2H, $J = 8.4$ Hz, ArH), 7.52 (d, 1H, $J = 7.6$ Hz, ArH), 7.46 (s, 2H, NH₂), 7.25 (t, 1H, $J = 7.6$ Hz, ArH), 7.18 (t, 1H, $J = 7.6$ Hz, ArH), 4.72 (s, 1H, CH). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 158.9, 156.4, 150.3, 147.1, 136.0, 129.7, 129.2, 124.5, 124.3, 122.8, 121.7, 121.1, 119.0, 118.7, 112.4, 105.2, 82.6, 54.8, 39.3. Anal. calcd for C₂₁H₁₃N₅O₃: C, 65.79; H, 3.42; N, 18.27. Found: C, 65.63; H, 3.47; N, 18.19.

2-Amino-4-(4-nitrophenyl)-6-(2-phenyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{2, 1, 3}). Solid; M.p. 222–224°C. IR (potassium bromide): ν 3441.3, 3371.8, 3308.7, 3182.3, 2198.4, 1677.9, 1594.7, 1518.1, 1396.7, 1348.5, 1130.8, 746.6, 697.7 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.14 (s, 1H, NH), 8.33 (d, 2H, $J = 8.4$ Hz, ArH), 7.66 (d, 2H, $J = 8.8$ Hz, ArH), 7.55–7.59 (m, 3H, ArH), 7.49 (d, 1H, $J = 8.0$ Hz, ArH), 7.38–7.45 (m, 5H, NH₂ + ArH), 7.23–7.27 (m, 1H, ArH), 7.16–7.20 (m, 1H, ArH), 4.70 (s, 1H, CH). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 159.5, 155.8, 149.4, 147.2, 139.9, 135.8, 130.9, 129.4, 129.0, 128.9, 127.7, 127.0, 124.3, 123.0, 121.0, 119.3, 119.1, 116.5, 112.1, 102.1, 91.4, 54.3. Anal. calcd for C₂₇H₁₇N₅O₃: C, 70.58; H, 3.73; N, 15.24. Found: C, 70.59; H, 3.94; N, 15.29.

2-Amino-6-(1-methyl-1H-indol-3-yl)-4-(4-nitrophenyl)-4H-pyran-3,5-dicarbonitrile (4{2, 1, 4}). Solid; M.p. 232–234°C. IR (potassium bromide): ν 3447.8, 3336.9, 3308.5, 3217.5, 3056.6, 2199.3, 1676.9, 1622.0, 1518.2, 1474.9, 1403.8, 1347.5, 1122.2, 736.2 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 8.30 (d, 2H, $J = 8.4$ Hz, ArH), 8.18 (s, 1H, ArH), 8.00 (d, 1H, $J = 8.0$ Hz, ArH), 7.66 (d, 2H, $J = 8.4$ Hz, ArH), 7.57 (d, 1H, $J = 8.4$ Hz, ArH), 7.46 (s, 2H, NH₂), 7.30–7.33 (m, 1H, ArH), 7.22 (t, 1H, $J = 7.6$ Hz, ArH), 4.71 (s, 1H, CH), 3.88 (s, 3H, CH₃). ¹³C-NMR (100 MHz, DMSO-*d*₆) (δ, ppm): 158.9, 155.9, 150.3, 147.1, 136.5, 133.1, 129.1, 124.9, 124.2, 122.8, 121.9, 121.4, 119.0, 118.6, 110.7, 104.2, 82.4, 54.8, 39.4, 33.3. Anal. calcd for C₂₂H₁₅N₅O₃: C, 66.49; H, 3.80; N, 17.62. Found: C, 66.61; H, 3.85; N, 17.57.

2-Amino-6-(7-methyl-1H-indol-3-yl)-4-(4-nitrophenyl)-4H-pyran-3,5-dicarbonitrile (4{2, 1, 5}). Solid; M.p. 250–252°C. IR (potassium bromide): ν 3440.6, 3299.5, 3208.4, 3056.0, 2203.7, 1681.4, 1621.1, 1595.5, 1518.3, 1406.1, 1350.0, 1164.1, 1011.2, 724.8 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.04 (s, 1H, NH), 8.31 (d, 2H, $J = 8.8$ Hz, ArH), 8.12 (d, 1H, $J = 3.2$ Hz, ArH), 7.78 (d, 1H, $J = 7.6$ Hz, ArH), 7.66 (d, 2H, $J = 8.8$ Hz, ArH), 7.44 (s, 2H, NH₂), 7.04–7.10 (m, 2H, ArH), 4.71 (s, 1H, CH), 2.50 (s, 1H, CH₃). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 158.9, 156.5, 150.3, 147.1, 135.5, 129.3, 129.2, 124.3, 123.3, 121.6, 121.3, 119.2, 119.0, 118.8, 105.7, 82.7, 54.8, 39.4, 16.7. Anal. calcd for C₂₂H₁₅N₅O₃: C, 66.49; H, 3.80; N, 17.62. Found: C, 66.70; H, 3.97; N, 17.85.

2-Amino-6-(5-bromo-1H-indol-3-yl)-4-(2,4-dichlorophenyl)-4H-pyran-3,5-dicarbonitrile (4{3, 1, 1}). Solid; M.p. 298–300°C. IR (KBr): ν 3483.0, 3215.4, 3083.8, 2201.5, 1672.5, 1587.8, 1519.0, 1361.1, 1402.3, 1102.8, 887.0, 825.6 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.17 (d, 2H, $J = 2.0$ Hz, NH), 8.17 (d, 1H, $J = 3.2$ Hz, ArH), 8.03 (d, 1H, $J = 1.6$ Hz, ArH), 7.69 (d, 1H, $J = 1.6$ Hz, ArH), 7.47–7.57 (m, 5H, NH₂ + ArH), 7.35–7.38 (m, 1H, ArH), 4.95 (s, 1H, CH). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 159.1, 155.9, 138.3, 134.8, 133.5, 133.4, 132.6, 130.8, 129.4, 128.4, 126.1, 125.5, 123.3, 118.9, 118.3, 114.4, 114.0, 105.0, 83.0, 53.9, 37.0. Anal. calcd for C₂₁H₁₁BrCl₂N₄O: C, 51.88; H, 2.28; N, 11.52. Found: C, 52.07; H, 2.41; N, 11.53.

2-Amino-4-(2,4-dichlorophenyl)-6-(1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{3, 1, 2}). Solid; M.p. 258–260°C. IR (potassium bromide): ν 3467.1, 3295.9, 3214.7, 2203.6, 1676.0, 1588.7, 1495.1, 1470.1, 1433.8, 1046.1, 740.7, 706.2 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.01 (s, 1H, NH), 8.14 (d, 1H, $J = 3.2$ Hz, ArH), 7.95 (d, 1H, $J = 8.0$ Hz, ArH), 7.69 (s, 1H, ArH), 7.50–7.54 (m, 3H, ArH), 7.41 (s, 2H, NH₂), 7.22–7.26 (m, 1H, ArH), 7.17 (t, 1H, $J = 7.6$ Hz, ArH), 4.94 (s, 1H, CH). ¹³C-NMR (100 MHz, DMSO-*d*₆) (δ, ppm): 159.1, 156.6, 138.5, 136.0, 133.5, 133.3, 132.5, 129.5, 128.4, 124.5, 122.7, 121.6, 121.1, 118.9, 118.6, 112.4, 105.3, 81.9, 54.1, 37.2. Anal. calcd for C₂₁H₁₂Cl₂N₄O: C, 61.93; H, 2.97; N, 13.76. Found: C, 62.18; H, 3.10; N, 13.71.

2-Amino-4-(2,4-dichlorophenyl)-6-(2-phenyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{3, 1, 3}). Solid; M.p. 208–210°C. IR (potassium bromide): ν 3450.5, 3306.9, 3265.3, 3183.8, 2201.5, 1677.7, 1583.4, 1392.4, 1215.2, 1125.0, 748.4 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.15 (s, 1H, NH), 7.40–7.68 (m, 10H, ArH), 7.30 (s, 2H, NH₂), 7.24 (t, 1H, $J = 7.6$ Hz, ArH), 7.17 (t, 1H, $J = 7.6$ Hz, ArH), 4.95 (s, 1H, CH). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 159.6, 155.9, 139.6, 137.8, 135.7, 133.4, 133.3, 132.6, 130.9, 129.5, 129.0, 128.9, 128.4, 127.7, 127.0, 122.9, 120.9, 119.3, 118.9, 116.3, 112.0, 102.1, 90.6, 53.8, 37.2. Anal. calcd for C₂₇H₁₆Cl₂N₄O: C, 67.09; H, 3.34; N, 11.59. Found: C, 67.36; H, 3.50; N, 11.71.

2-Amino-4-(2,4-dichlorophenyl)-6-(1-methyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{3, 1, 4}). Solid; M.p. 262–264°C. IR (potassium bromide): ν 3474.4, 3339.8, 3312.5, 3122.9, 2197.1, 1672.8, 1617.5, 1523.7, 1475.1, 1402.4, 1365.1, 856.6, 735.0 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 8.16 (s, 1H, ArH), 7.97 (d, 1H, $J = 8.0$ Hz, ArH), 7.69 (d, 1H, $J = 1.2$ Hz, ArH), 7.49–7.57 (m, 3H, ArH), 7.41 (s, 2H, NH₂), 7.31 (t, 1H, $J = 7.6$ Hz, ArH), 7.22 (t, 1H, $J = 7.6$ Hz, ArH), 4.93 (s, 1H, CH), 3.88 (s, 3H, CH₃). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 159.0, 156.1, 138.4, 136.5, 133.5, 133.3, 133.0, 132.4, 129.5, 128.3, 124.9, 122.8, 121.8, 121.3, 118.9, 118.5, 110.7, 104.2, 81.7, 54.0, 37.2, 33.2. Anal. calcd for C₂₂H₁₄Cl₂N₄O: C, 62.72; H, 3.35; N, 13.30. Found: C, 62.91; H, 3.60; N, 13.49.

2-Amino-4-(2,4-dichlorophenyl)-6-(7-methyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{3, 1, 5}). Solid; M.p. 266–268°C. IR (potassium bromide): ν 3473.2, 3283.2, 3205.4, 2202.8, 1672.7, 1616.3, 1521.2, 1405.9, 1362.4, 1159.7, 824.7 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.02 (s, 1H, NH), 8.10 (d, 1H, $J = 3.2$ Hz, ArH), 7.77 (d, 1H, $J = 8.4$ Hz, ArH), 7.69 (s, 1H, ArH), 7.50–7.55 (m, 2H, ArH), 7.40 (s, 2H, NH₂), 7.03–7.10 (m, 2H, ArH), 4.94 (s, 1H, CH), 2.50 (s, 3H, CH₃). ¹³C-NMR (75 MHz, DMSO-*d*₆) (δ, ppm): 159.1, 156.6, 138.4, 135.5, 133.5, 133.3, 132.5, 129.5, 129.1, 128.3, 124.3, 123.2, 121.5, 121.2, 119.1, 118.9, 118.5, 105.7, 82.0, 54.0, 37.1, 16.7. Anal. calcd for C₂₂H₁₄Cl₂N₄O: C, 62.72; H, 3.35; N, 13.30. Found: C, 62.83; H, 3.46; N, 13.55.

2-Amino-4-(3-nitrophenyl)-6-(2-phenyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{4, 1, 3}). Solid; M.p. 230–232°C. IR (potassium bromide): ν 3442.5, 3317.5, 2193.0, 1671.8, 1601.0, 1528.2, 1452.5, 1401.1, 1138.8, 741.5 cm⁻¹. ¹H-NMR (400 MHz, DMSO-*d*₆) (δ, ppm): 12.16 (s, 1H, NH), 8.25 (d, 1H, $J = 8.0$ Hz, ArH), 8.21 (s, 1H, ArH), 7.88 (d, 1H, $J = 7.2$ Hz, ArH), 7.80 (t, 1H, $J = 8.0$ Hz, ArH), 7.57 (s, 3H, ArH), 7.50 (d, 1H, $J = 8.0$ Hz, ArH), 7.38–7.40 (m, 5H, NH₂ + ArH), 7.24–7.27 (m, 1H, ArH), 7.16–7.20 (m, 1H, ArH), 4.77 (s, 1H, CH). ¹³C-NMR (100 MHz, DMSO-*d*₆) (δ, ppm): 159.6, 155.7, 148.2, 144.4, 139.8, 135.8, 134.7, 131.0, 130.8, 128.9, 128.8, 127.6, 127.0, 123.0, 122.3, 121.0, 119.2, 119.1, 116.6, 112.1,

102.2, 91.6, 54.5. Anal. calcd for $C_{27}H_{17}N_5O_3$: C, 70.58; H, 3.73; N, 15.24. Found: C, 70.65; H, 3.84; N, 15.33.

2-Amino-6-(1-methyl-1H-indol-3-yl)-4-(3-nitrophenyl)-4H-pyran-3,5-dicarbonitrile (4{4, 1, 4}). Solid; M.p. 238–240°C. IR (potassium bromide): ν 3439.8, 3346.1, 3123.0, 2933.6, 2194.3, 1671.6, 1621.7, 1588.3, 1530.6, 1408.1, 1349.8, 1307.4, 1155.0, 742.5 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 8.19–8.24 (m, 3H, ArH), 8.00 (d, 1H, J = 8.0 Hz, ArH), 7.88 (d, 1H, J = 7.6 Hz, ArH), 7.77 (t, 1H, J = 8.0 Hz, ArH), 7.57 (d, 1H, J = 8.0 Hz, ArH), 7.48 (m, 2H, NH_2), 7.30–7.34 (m, 1H, ArH), 7.23 (t, 1H, J = 7.6 Hz, ArH), 4.77 (s, 1H, CH), 3.88 (s, 3H, CH_3). ^{13}C -NMR (100 MHz, DMSO- d_6) (δ , ppm): 159., 156.0, 148.2, 145.3, 136.6, 134.6, 133.1, 130.7, 124.9, 122.9, 122.8, 122.2, 122.0, 121.4, 119.1, 118.7, 110.7, 104.3, 82.6, 54.9, 39.2, 33.3. Anal. calcd for $C_{22}H_{15}N_5O_3$: C, 66.49; H, 3.80; N, 17.62. Found: C, 66.55; H, 3.94; N, 17.88.

2-Amino-6-(5-bromo-1H-indol-3-yl)-4-(2-bromophenyl)-4H-pyran-3,5-dicarbonitrile (4{5, 1, 1}). Solid; M.p. 294–296°C. IR (potassium bromide): ν 3449.9, 3202.6, 2192.1, 1665.0, 1625.5, 1518.5, 1465.8, 1359.8, 1157.0, 805.3 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 12.16 (s, 1H, NH), 8.16 (s, 1H, J = 2.8 Hz, ArH), 8.03 (s, 1H, ArH), 7.67 (d, 1H, J = 8.0 Hz, ArH), 7.45–7.49 (m, 5H, NH_2 + ArH), 7.36 (d, 1H, J = 8.8 Hz, ArH), 7.27–7.31 (m, 1H, ArH), 4.92 (s, 1H, CH). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 159.0, 155.7, 140.9, 134.8, 133.3, 131.4, 130.7, 129.9, 128.8, 126.1, 125.5, 123.3, 122.8, 119.0, 118.4, 114.4, 113.9, 105.1, 83.8, 54.6. Anal. calcd for $C_{21}H_{12}Br_2N_4O$: C, 50.84; H, 2.44; N, 11.29. Found: C, 50.88; H, 2.59; N, 11.40.

2-Amino-4-(2-bromophenyl)-6-(2-phenyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{5, 1, 3}). Solid; M.p. 220–222°C. IR (potassium bromide): ν 3447.2, 3378.4, 3314.5, 3184.1, 2201.0, 1672.7, 1394.0, 1126.7, 1023.9, 744.2 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 12.14 (s, 1H, NH), 7.65 (d, 3H, J = 7.6 Hz, ArH), 7.38–7.58 (m, 7H, ArH), 7.22–7.32 (m, 4H, NH_2 + ArH), 7.17 (t, 1H, J = 7.6 Hz, ArH), 4.95 (s, 1H, CH). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 159.5, 155.6, 140.4, 139.5, 135.7, 133.2, 131.2, 130.9, 130.0, 129.0, 128.8, 127.6, 127.0, 122.9, 122.7, 120.8, 119.3, 119.0, 116.4, 112.0, 102.2, 91.3, 54.5. Anal. calcd for $C_{27}H_{17}BrN_4O$: C, 65.73; H, 3.47; N, 11.36. Found: C, 65.93; H, 3.63; N, 11.49.

2-Amino-4-(2-bromophenyl)-6-(1-methyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{5, 1, 4}). Solid; M.p. 250–252°C. IR (potassium bromide): ν 3459.4, 3299.8, 3175.1, 2202.9, 1672.3, 1594.1, 1531.4, 1465.0, 1367.6, 1238.1, 747.1 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 8.15 (s, 1H, ArH), 7.97 (d, 1H, J = 8.0 Hz, ArH), 7.67 (d, 1H, J = 8.0 Hz, ArH), 7.57 (d, 1H, J = 8.0 Hz, ArH), 7.43–7.49 (m, 2H, ArH), 7.27–7.36 (m, 4H, NH_2 + ArH), 7.22 (t, 1H, J = 7.6 Hz, ArH), 4.92 (s, 1H, CH), 3.88 (s, 3H, CH_3). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 158.9, 155.9, 141.0, 136.5, 133.3, 132.9, 131.2, 129.9, 128.7, 124.9, 122.8, 122.7, 121.8, 121.3, 118.9, 118.5, 110.7, 104.3, 82.4, 54.7, 39.7, 33.2. Anal. calcd for $C_{22}H_{15}BrN_4O$: C, 61.27; H, 3.51; N, 12.99. Found: C, 61.45; H, 3.80; N, 13.10.

2-Amino-4-(2-bromophenyl)-6-(7-methyl-1H-indol-3-yl)-4H-pyran-3,5-dicarbonitrile (4{5, 1, 5}). Solid; M.p. 218–220°C. IR (KBr): ν 3473.3, 3260.3, 3054.0, 2881.2, 2195.9, 1667.9, 1621.8, 1522.8, 1442.2, 1396.8, 1156.5, 734.5 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 12.01 (s, 1H, NH), 8.09 (d, 1H, J = 2.8 Hz, ArH), 7.77 (d, 1H, J = 7.6 Hz, ArH), 7.67 (d, 1H, J = 8.0 Hz, ArH), 7.44–7.50 (m, 2H, ArH), 7.27–7.35 (m,

3H, NH_2 + ArH), 7.03–7.09 (m, 2H, ArH), 4.92 (s, 1H, CH), 2.50 (s, 3H, CH_3). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 159.0, 156.4, 141.0, 135.5, 133.3, 131.2, 129.9, 129.0, 128.8, 124.3, 123.2, 122.7, 121.5, 121.2, 119.1, 118.9, 118.6, 105.8, 82.7, 54.7, 39.7, 16.7. Anal. calcd for $C_{22}H_{15}BrN_4O$: C, 61.27; H, 3.51; N, 12.99. Found: C, 61.53; H, 3.79; N, 13.17.

2-Amino-6-(5-bromo-1H-indol-3-yl)-4-phenyl-4H-pyran-3,5-dicarbonitrile (4{6, 1, 1}). Solid; M.p. 238–240°C. IR (potassium bromide): ν 3397.4, 3390.8, 3290.5, 3115.4, 2201.4, 1669.3, 1530.7, 1392.7, 1363.0, 1256.4, 899.1, 799.0 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 12.14 (s, 1H, NH), 8.15 (d, 1H, J = 3.2 Hz, ArH), 8.01 (d, 1H, J = 1.2 Hz, ArH), 7.32–7.49 (m, 9H, NH_2 + ArH), 4.43 (s, 1H, CH). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 158.7, 155.0, 142.9, 134.7, 130.6, 128.9, 127.7, 126.1, 125.5, 123.2, 119.3, 118.7, 114.3, 113.9, 105.1, 85.3, 55.8. Anal. calcd for $C_{21}H_{13}BrN_4O$: C, 60.45; H, 3.14; N, 13.43. Found: C, 60.44; H, 3.19; N, 13.53.

2-Amino-6-(1-methyl-1H-indol-3-yl)-4-phenyl-4H-pyran-3,5-dicarbonitrile (4{6, 1, 4}). Solid; M.p. 242–244°C. IR (potassium bromide): ν 3479.0, 3343.5, 3130.2, 2855.9, 2203.5, 1672.3, 1608.0, 1525.3, 1388.5, 1112.9, 744.2, 708.0 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 8.15 (s, 1H, ArH), 7.97 (d, 1H, J = 8.0 Hz, ArH), 7.56 (d, 1H, J = 8.0 Hz, ArH), 7.41–7.45 (m, 2H, ArH), 7.30–7.35 (m, 6H, NH_2 + ArH), 7.21 (t, 1H, J = 7.6 Hz, ArH), 4.42 (s, 1H, CH), 3.87 (s, 3H, CH_3). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 158.7, 155.3, 143.1, 136.5, 132.8, 128.9, 127.7, 127.6, 124.9, 122.7, 121.8, 121.3, 119.3, 118.9, 110.7, 104.4, 84.0, 55.9, 33.2. Anal. calcd for $C_{22}H_{16}N_4O$: C, 74.98; H, 4.58; N, 15.90. Found: C, 74.99; H, 4.71; N, 16.03.

2-Amino-6-(1-methyl-1H-indol-3-yl)-4-(naphthalen-2-yl)-4H-pyran-3,5-dicarbonitrile (4{7, 1, 4}). Solid; M.p. 244–246°C. IR (potassium bromide): ν 3478.4, 3318.2, 3120.3, 3024.9, 2195.7, 1676.6, 1588.1, 1525.0, 1360.7, 1239.0, 1120.7, 736.9 cm^{-1} . 1H -NMR (400 MHz, DMSO- d_6) (δ , ppm): 8.16 (s, 1H, ArH), 7.93–8.01 (m, 4H, ArH), 7.87 (s, 1H, ArH), 7.48–7.58 (m, 4H, ArH), 7.30–7.36 (m, 3H, NH_2 + ArH), 7.20–7.24 (m, 1H, ArH), 4.62 (s, 1H, CH), 3.87 (s, 3H, CH_3). ^{13}C -NMR (75 MHz, DMSO- d_6) (δ , ppm): 158.7, 155.3, 140.4, 136.5, 132.9, 132.6, 129.0, 127.9, 127.6, 126.6, 126.3, 126.3, 125.5, 124.9, 122.8, 121.8, 121.3, 119.3, 118.9, 110.7, 104.4, 83.8, 55.8, 33.2. Anal. calcd for $C_{26}H_{18}N_4O$: C, 77.59; H, 4.51; N, 13.92. Found: C, 77.32; H, 4.62; N, 13.88.

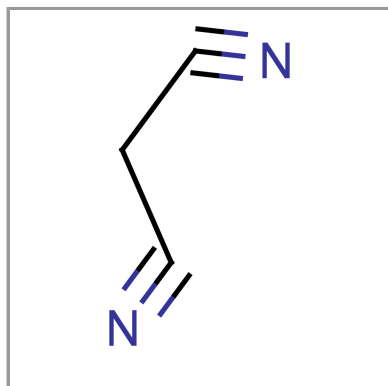
Acknowledgments. The work was partially supported by the National Natural Science Foundation of China (Nos. 20672079, 20910102041, 21042007), Natural Science Foundation of Jiangsu Province (No. BK 2006048), Nature Science Key Basic Research of Jiangsu Province for Higher Education (No. 10KJB150016), the Specialized Research Fund for the Doctoral Program of Higher Education (No. 20060285001), and Key Project in Science and Technology Innovation Cultivation Program of Soochow University.

REFERENCES AND NOTES

- [1] (a) Radwan, M. A. A.; Ragab, E. A.; Sabry, N. M.; Shenawy, S. M. E. *Bioorg Med Chem* 2007, 15, 3832; (b) Yadav, J. S.; Reddy, B. V. S.; Narasimhulu, G.; Reddy, N. S.; Reddy, P. N.; Purnima, K. V.; Naresh, P.; Jagadeesh, B. *Tetrahedron Lett* 2010, 51, 244; (c) Wu, P.; Wan, Y.; Cai, J. *Synlett* 2008, 8, 1193.
- [2] (a) Sakemi, S.; Sun, H. H. *J Org Chem* 1991, 56, 4304; (b) Kawasaki, I.; Yamashita, M.; Ohta, S. *Chem Pharm Bull* 1996, 44, 1831.

- [3] (a) Jiang, B.; Yang, C.-G.; Xiong, W.-N.; Wang, J. *Bioorg Med Chem* 2001, 9, 1149; (b) Gompel, M.; Leost, M.; Joffé, E. B. K.; Puricelli, L.; Franco, L. H.; Palermo, J.; Meijer, L. *Bioorg Med Chem Lett* 2004, 14, 1703.
- [4] Babu, N. S.; Pasha, N.; Rao, K. T. V.; Prasad, P. S. S.; Lingaiah, N. *Tetrahedron Lett* 2008, 49, 2730.
- [5] Kumar, A.; Reddy, V. B.; Sharad, S.; Dube, U.; Kapur, S. *Eur J Med Chem* 2009, 44, 3805.
- [6] Hekmatshoar, R.; Majedi, S.; Bakhtiari, K. *Catal Commun* 2008, 9, 307.
- [7] Balalaie, S.; Ahmadi, M. S.; Morteza, B. *Catal Commun* 2007, 8, 1724.
- [8] Fotouhi, L.; Heravi, M. M.; Fatehi, A.; Bakhtiari, K. *Tetrahedron Lett* 2007, 48, 5379.
- [9] Zhao, S.-L.; Zheng, C.-W.; Zhao, G. *Tetrahedron: Asymmetry* 2009, 20, 1046.
- [10] Pfrengle, F.; Lentz, D.; Reissig, H.-U. *Org Lett* 2009, 11, 5534.
- [11] Rho, H. S.; Baek, H. S.; You, J. W.; Kim, S.; Lee, J. Y.; Kim, D. H.; Chang, I. S. *Bull Korean Chem Soc* 2007, 28, 471.
- [12] (a) Quinterio, M.; Seoane, C.; Soto, J. L. *Tetrahedron* 1977, 18, 1835; (b) Quinterio, M.; Seoane, C.; Soto, J. L. *J. Heterocycl Chem* 1978, 54, 3069; (c) Armesto, D.; Horspool, W. M.; Martin, N.; Ramos, A.; Seoane, C.; Soto, J. L. *J Org Chem* 1989, 15, 57; (d) Martin-Leon, N.; Segura, J. L.; Seoane, C.; Soto, J. L. *J Chem Res Miniprint* 1990, 2434.
- [13] (a) Elmoghayer, M. R. H.; Khalifa, M. A. E.; Ibrahim, M. K. A.; Elnagdi, M. H. *Monatsh Chem* 1982, 113, 53; (b) El-Ahi, A. A. S.; Afeefy, H.; Metwally, M. A. *J Chem Res Miniprint* 1994, 201; (c) Martin-Leon, N.; Segura, J. L.; Seoane, C.; Soto, J. L. *J Chem Res Miniprint* 1990, 2434.
- [14] (a) Heinisch, G.; Holzer, W.; Nawwar, G. A. M. *Monatsh Chem* 1986, 117, 247; (b) Abdel-Latif, F. F.; Mashaly, M. M.; El-Gawish, E. H. *J Chem Res Miniprint* 1995, 1220; (c) Shestopalov, A. M.; Emelianova Yu, M.; Nesterov, V. N. *Russ Chem Bull* 2003, 52, 1164; (d) Devi, I.; Bhuyan, P. J. *Tetrahedron Lett* 2004, 45, 8625; (e) Jin, T.-S.; Wang, A.-Q.; Wang, X.; Zhang, J.-S.; Li, T.-S. *Synlett* 2004, 871; (f) Shi, D.; Mou, J.; Zhuang, Q.; Wang, X. *J Chem Res* 2004, 821; (g) Wang, L.-M.; Shao, J.-H.; Tian, H.; Wang, Y.-H.; Liu, B. *J Fluorine Chem* 2006, 127, 97.
- [15] (a) Wang, X.-S.; Shi, D.-Q.; Tu, S.-J.; Yao, C.-S. *Synth Commun* 2003, 33, 119; (b) Elinson, M. N.; Dorofeev, A. S.; Feducovich, S. K.; Gorbunov, S. V.; Nasybullin, R. F.; Miloserdov, F. M.; Nikishin, G. I. *Eur J Org Chem* 2006, 19, 4335; (c) Li, Y.-L.; Du, B.-X.; Wang, X.-S.; Shi, D.-Q.; Tu, S.-J. *J Heterocycl Chem* 2006, 43, 685; (d) Balalaie, S.; Bararjanian, M.; Mohammad, A.; Movassagh, B. *Synlett* 2006, 263; (e) Balalaie, S.; Bararjanian, M.; Sheikh-Ahmadi, M. *Synth Commun* 2007, 37, 1097; (f) Fotouhi, L.; Heravi, M. M.; Fatehi, A.; Bakhtiari, K. *Tetrahedron Lett* 2007, 48, 537; (g) Abd El-Rahman, N. M.; El-Kateb, A. A.; Mady, M. F. *Synth Commun* 2007, 22, 3961; (h) Litvinov, Y. M.; Mortikov, V. Y.; Shestopalov, A. M. *J Comb Chem* 2008, 10, 741; (i) Shaaabani, A.; Ghadari, R.; Ghasemi, S.; Pedarpour, M.; Rezayan, A. H.; Sarvary, A.; Ng, S. W. *J Comb Chem* 2009, 10, 956; (j) Sabitha, G.; Arundhati, K.; Sudhakar, K.; Sastry, B. S.; Yadav, J. S. *Synth Commun* 2009, 39, 433; (k) Khurana, J. M.; Nand, B.; Saluja, P. *Tetrahedron* 2010, 66, 5637.
- [16] (a) Wender, P. A.; Handy, S. T.; Wright, D. L. *Chem Ind* 1997, 765; (b) Trost, B. M. *Angew Chem Int Ed Engl* 1995, 34, 259; (c) Weber, L.; Ilgen, K.; Almstetter, M. *Synlett* 1999, 366; (d) Bienaymé, H.; Hulme, C.; Odon, G.; Schmitt, P. *Chem Eur J* 2000, 6, 3321; (e) Terrett, N. K. *Combinatorial Chemistry*; Oxford University Press: New York, 1998.
- [17] Mason, T. J., Ed., *Advances in Sonochemistry*; JAI Press: London and Greenwich, CT; Vol.1, 1990.
- [18] (a) Ji, S.-J.; Wang, S.-Y. *Synlett* 2003, 2074; (b) Ji, S.-J.; Wang, S.-Y.; Zhang, Y.; Loh, T.-P. *Tetrahedron* 2004, 60, 2051; (c) Shen, Z.-L.; Ji, S.-J.; Wang, S.-Y.; Zeng, X.-F. *Tetrahedron* 2005, 61, 10552; (d) Gu, D.-G.; Ji, S.-J.; Jiang, Z.-Q.; Zhou, M.-F.; Loh T.-P. *Synlett* 2005, 959; (e) Wang, S.-Y.; Ji, S.-J. *Tetrahedron* 2006, 62, 1527; (f) Sun, C.; Ji, S.-J. *Tetrahedron Lett* 2007, 48, 8987; (g) Wang, S.-Y.; Ji, S.-J. *Synlett* 2007, 2222; (h) Zhu, S.-L.; Ji, S.-J.; Zhang, Y. *Tetrahedron* 2007, 63, 9365; (i) Zhu, S.-L.; Ji, S.-J.; Su, X.-M.; Sun, C.; Liu, Y. *Tetrahedron Lett* 2008, 49, 1777; (j) Zhu, S.-L.; Ji, S.-J.; Zhao, K.; Liu, Y. *Tetrahedron Lett* 2008, 49, 2578; (k) Zhao, K.; Xu, X.-P.; Zhu, S.-L.; Shi, D.-Q.; Zhang, Y.; Ji, S.-J. *Synthesis* 2009, 2697; (l) Zhao, K.; Zhu, S.-L.; Shi, D.-Q.; Zhang, Y.; Xu, X.-P.; Ji, S.-J. *Synthesis* 2010, 1793; (m) Chen, T.; Xu, X.-P.; Ji, S.-J. *J Comb Chem* 2010, 12, 659.
- [19] (a) Behbehani, H.; Ibrahim, H. M.; Makhseed, S. *Heterocycles* 2009, 78, 3081; (b) Lakshmi, N. V.; Thirumurugan, P.; Noorulla, K. M.; Perumal, P. T. *Bioorg Med Chem Lett* 2010, 20, 5054.

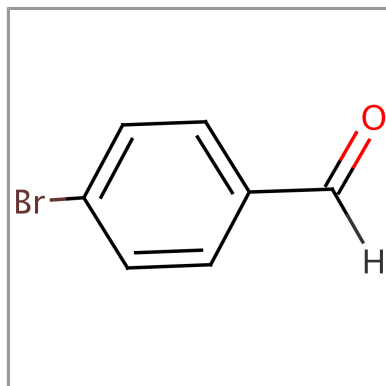
2{1}



[Compound Details](#)

[Structure Search](#)

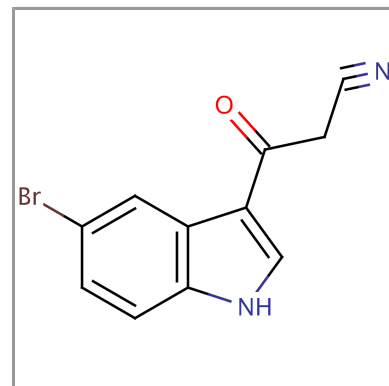
1{1}



[Compound Details](#)

[Structure Search](#)

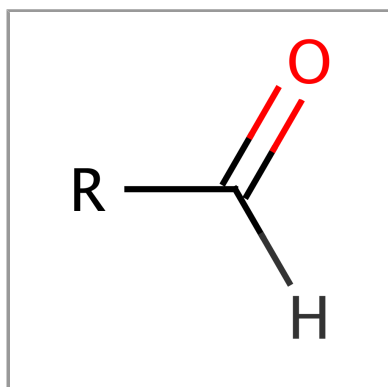
3{1}



[Compound Details](#)

[Structure Search](#)

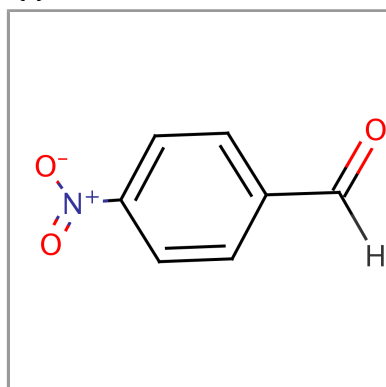
1



[Compound Details](#)

[Structure Search](#)

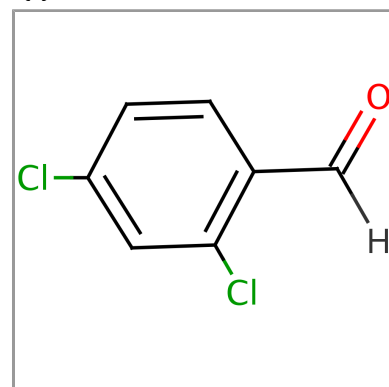
1{2}



[Compound Details](#)

[Structure Search](#)

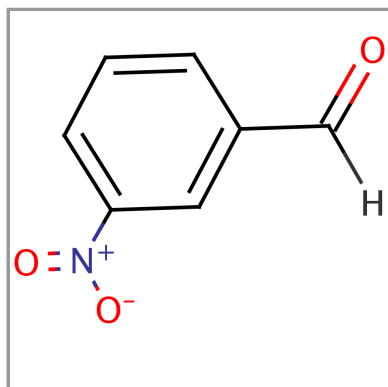
1{3}



[Compound Details](#)

[Structure Search](#)

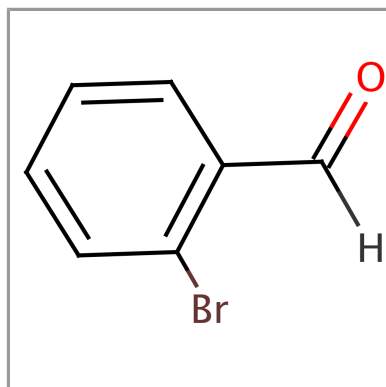
1{4}



[Compound Details](#)

[Structure Search](#)

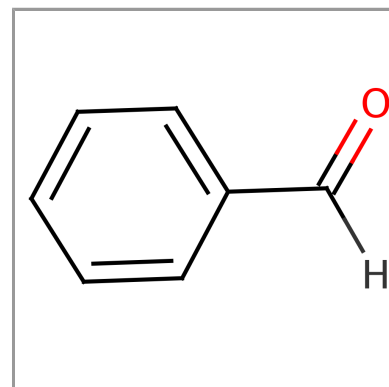
1{5}



[Compound Details](#)

[Structure Search](#)

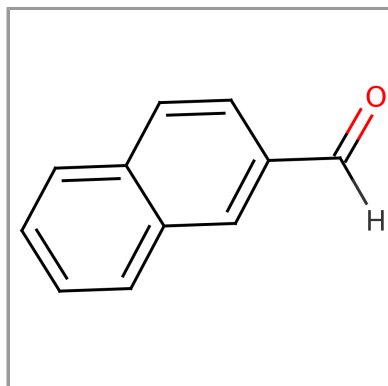
1{6}



[Compound Details](#)

[Structure Search](#)

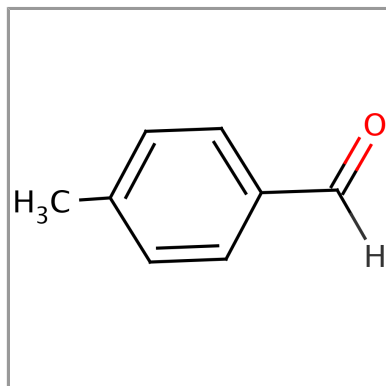
1{7}



[Compound Details](#)

[Structure Search](#)

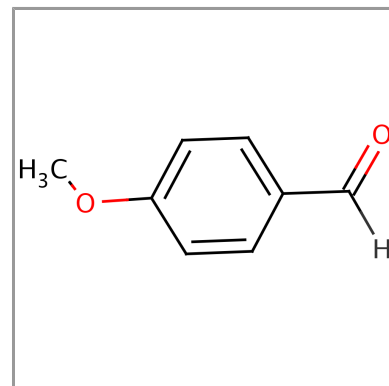
1{8}



[Compound Details](#)

[Structure Search](#)

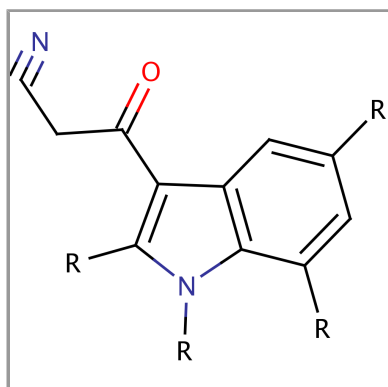
1{9}



[Compound Details](#)

[Structure Search](#)

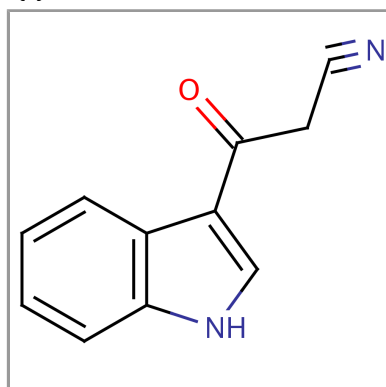
3



[Compound Details](#)

[Structure Search](#)

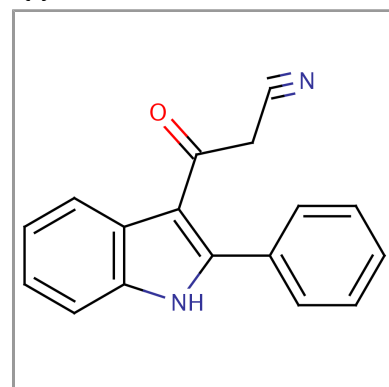
3{2}



[Compound Details](#)

[Structure Search](#)

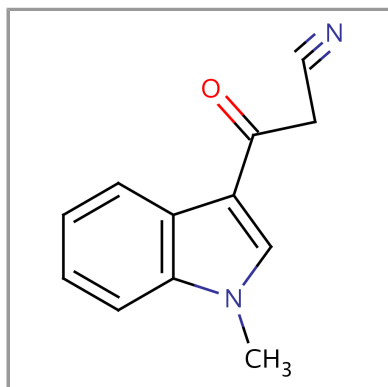
3{3}



[Compound Details](#)

[Structure Search](#)

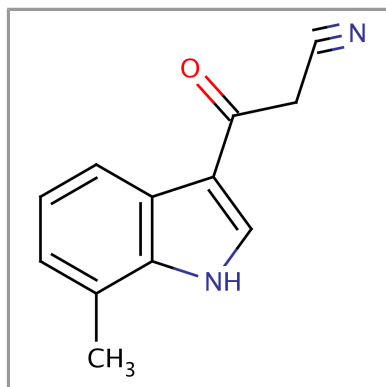
3{4}



[Compound Details](#)

[Structure Search](#)

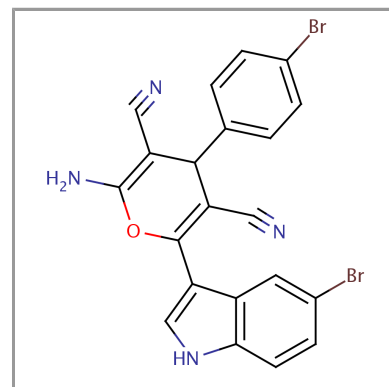
3{5}



[Compound Details](#)

[Structure Search](#)

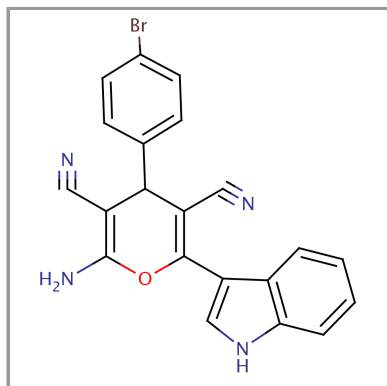
4{1,1,1}



[Compound Details](#)

[Structure Search](#)

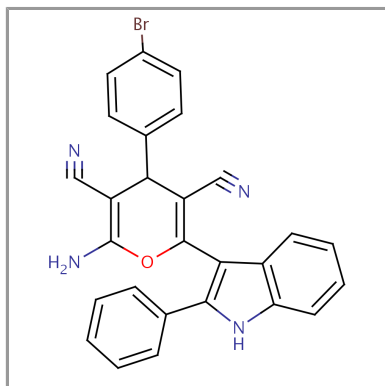
4{1,1,2}



[Compound Details](#)

[Structure Search](#)

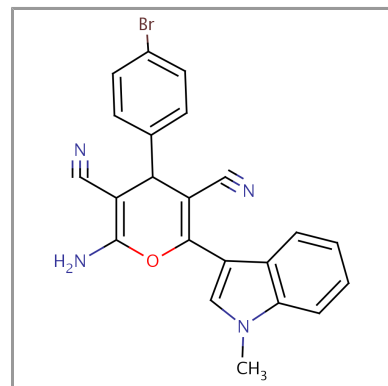
4{1,1,3}



[Compound Details](#)

[Structure Search](#)

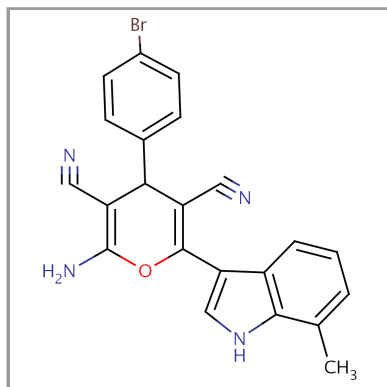
4{1,1,4}



[Compound Details](#)

[Structure Search](#)

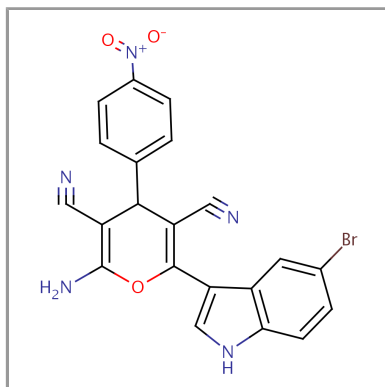
4{1,1,5}



[Compound Details](#)

[Structure Search](#)

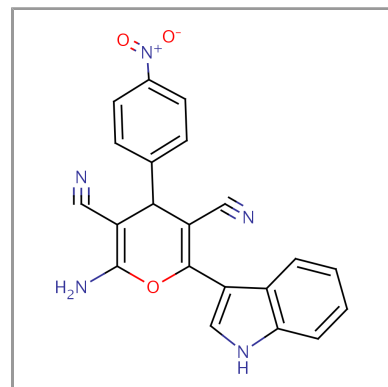
4{2,1,1}



[Compound Details](#)

[Structure Search](#)

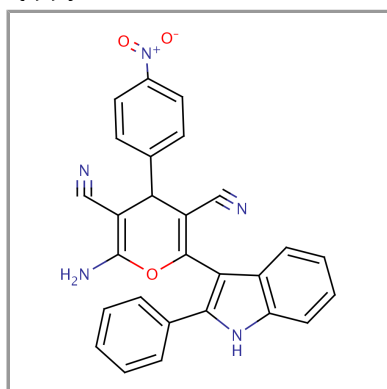
4{2,1,2}



[Compound Details](#)

[Structure Search](#)

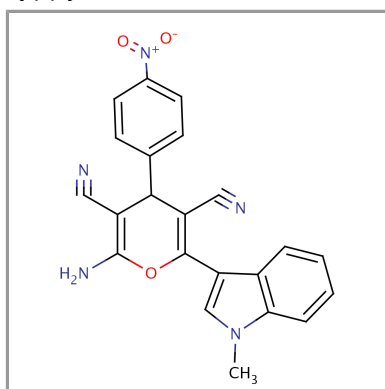
4{2,1,3}



[Compound Details](#)

[Structure Search](#)

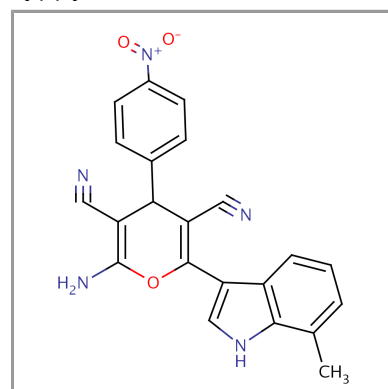
4{2,1,4}



[Compound Details](#)

[Structure Search](#)

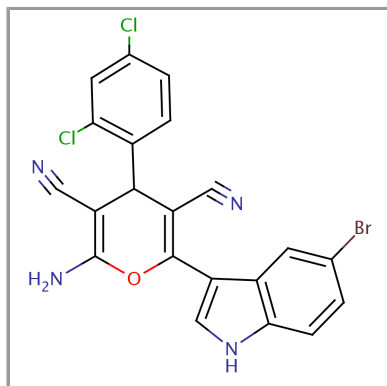
4{2,1,5}



[Compound Details](#)

[Structure Search](#)

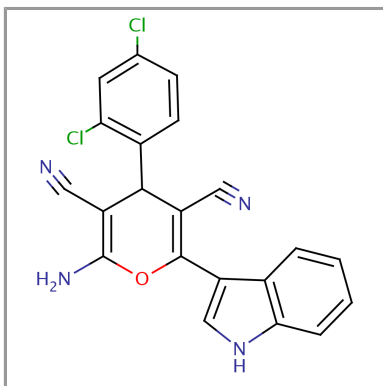
4{3,1,1}



[Compound Details](#)

[Structure Search](#)

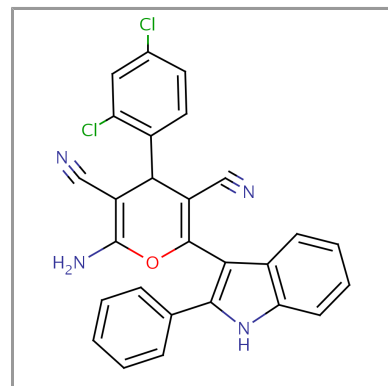
4{3,1,2}



[Compound Details](#)

[Structure Search](#)

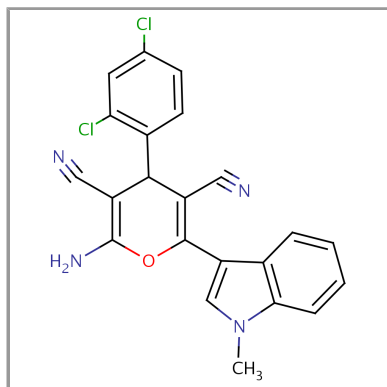
4{3,1,3}



[Compound Details](#)

[Structure Search](#)

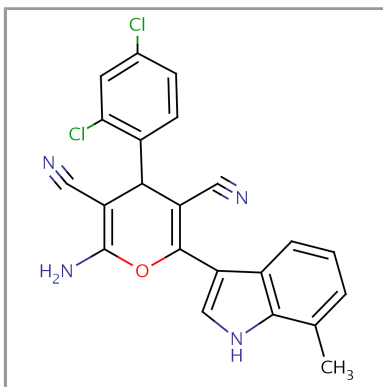
4{3,1,4}



[Compound Details](#)

[Structure Search](#)

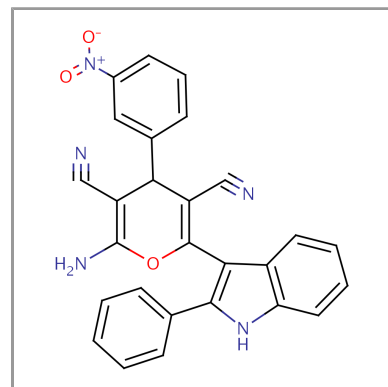
4{3,1,5}



[Compound Details](#)

[Structure Search](#)

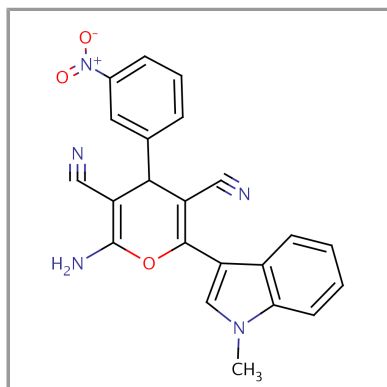
4{4,1,3}



[Compound Details](#)

[Structure Search](#)

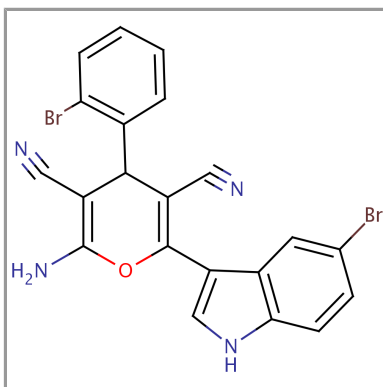
4{4,1,4}



[Compound Details](#)

[Structure Search](#)

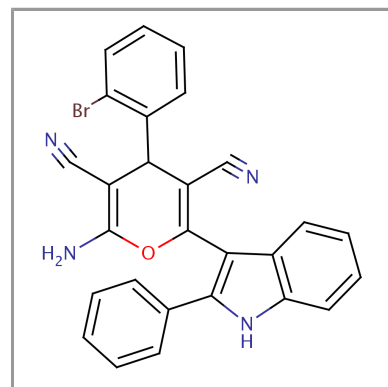
4{5,1,1}



[Compound Details](#)

[Structure Search](#)

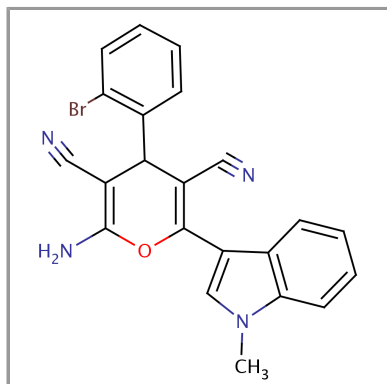
4{5,1,3}



[Compound Details](#)

[Structure Search](#)

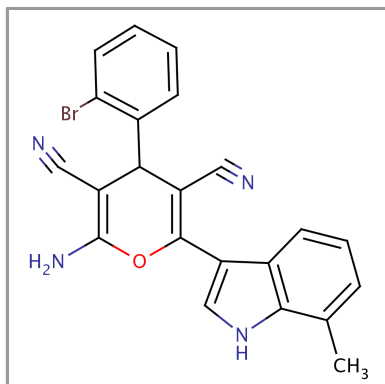
4{5,1,4}



[Compound Details](#)

[Structure Search](#)

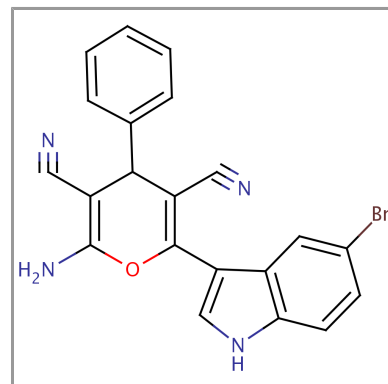
4{5,1,5}



[Compound Details](#)

[Structure Search](#)

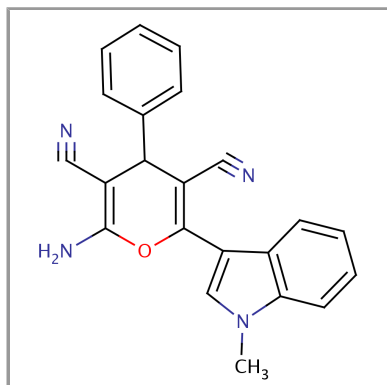
4{6,1,1}



[Compound Details](#)

[Structure Search](#)

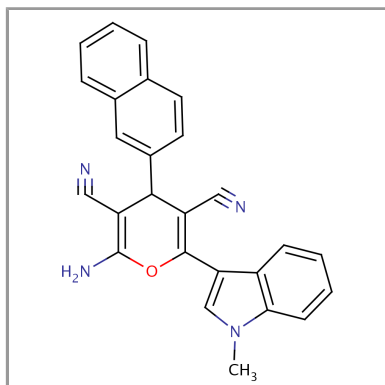
4{6,1,4}



[Compound Details](#)

[Structure Search](#)

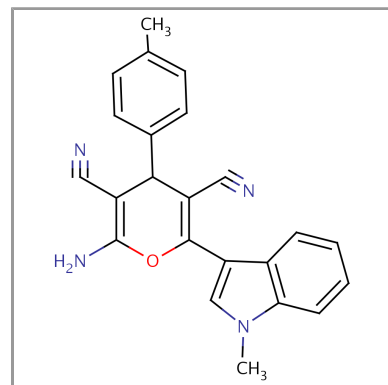
4{7,1,4}



[Compound Details](#)

[Structure Search](#)

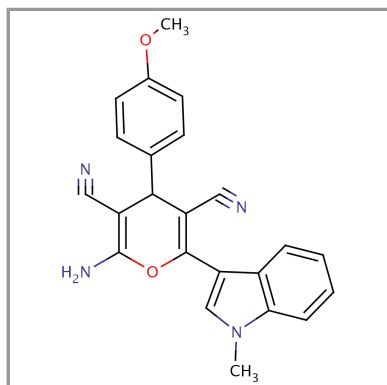
4{8,1,4}



[Compound Details](#)

[Structure Search](#)

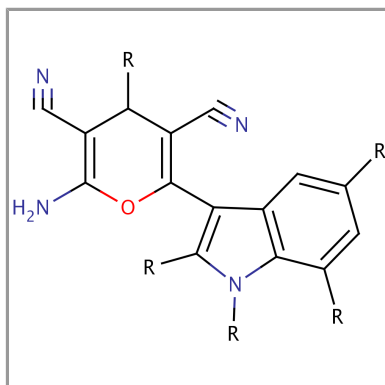
4{9,1,4}



[Compound Details](#)

[Structure Search](#)

4



[Compound Details](#)

[Structure Search](#)