RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2014, **4**, 19422

$InCl_3$-mediated eco-friendly three-component domino reaction for synthesis of highly functionalized triazolylspiroxindolinopyrans and triazolylpyrans under solvent-free conditions†

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Received 21st February 2014
Accepted 4th April 2014

DOI: 10.1039/c4ra01524j

www.rsc.org/advances

A one pot domino protocol has been developed for the efficient synthesis of novel triazolylspiroxindolinopyrans and triazolylpyran derivatives. The synthesis was achieved by reacting phenacyltriazole, isatin/aromatic aldehyde and active methylene compounds in the presence of $InCl_3$ under solvent-free conditions at 100 °C. This novel strategy affording biologically relevant heterocyclic compounds presumably involves Knoevenagel condensation/Michael addition/6-exo-dig-cyclisation sequences.

Introduction

Synthetic organic chemistry lies at the heart of modern drug discovery and developments in that field. It consists of making or breaking carbon–carbon (C–C) and carbon–heteroatom (C–X) bonds for construction of biologically significant heterocyclic compounds. This synthetic methodology resulting in simple to complex structural diversity with the minimum number of steps and reasonable yields in both academic and industrial settings is highly desirable. Multicomponent reactions (MCR)[1] have emerged as a powerful tool for delivering highly functionalized small and complex molecules mimicking important natural products that are promising candidates as probes in chemical biology to investigate biological phenomena and for drug development. Owing to ecological concerns, organic chemists pay much attention to synthetic pathways for greener approaches to reduce the drastic prerequisites for reaction. Due to the harmful effects of organic solvents on the environment and humans, solvent-free reactions have become a powerful tool in organic synthesis for delivering a huge number of biologically important heterocyclics in greener approaches. Furthermore, solvent-free reactions offer several advantages such as faster reaction rate, reduced reaction time, lower energy consumption, easy separation, and products with high yields and purity.[2]

The spiro-oxindole ring system has acquired a special place in the heterocyclic field since it is a frequently encountered structural motif in many natural alkaloids[3,4] (Fig. 1). For example, spirotryprostatin A[5] is one of the natural alkaloids isolated from *Aspergillus fumigatus*, and has been identified as a novel inhibitor of microtubule assembly, and pteropodine and isopteropodine have been shown to modulate the function of muscarinic serotonin receptors.[6] Similarly, many of the spiro-oxindole frameworks deliver important pharmacological activity such as vasodilatory, hypoglycaemic, anti-inflammatory, analgesic and antipyretic activities.[7] Owing to the unique pharmacological properties of the spiro-oxindole framework, the development of synthetic methods enabling facile access to this heterocyclic is still desirable.

Multi-functionalized 4*H*-pyrans are an important class of compounds present in several natural or synthetic products with important biological or pharmacological activities such as anticoagulant, anticancer, antioxidant, spasmolytic, diuretic, and anti-anaphylactic activities.[8] In particular, large numbers of

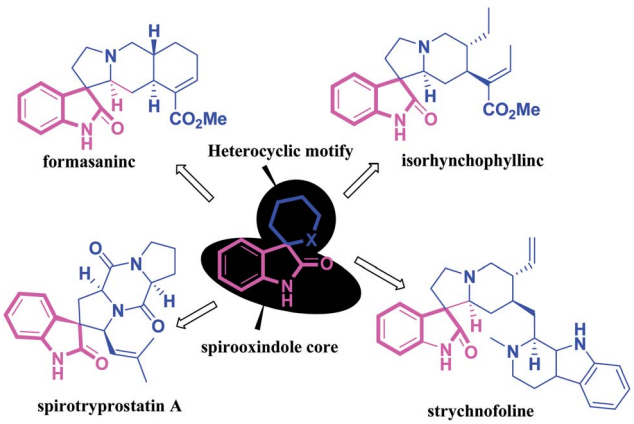

Fig. 1 Typical natural products containing spiro-oxindole scaffolds.

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† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR spectra of all compounds. CCDC 953661 for **5x**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ra01524j

2-amino-4*H*-pyran derivatives are used as photoactive materials, cosmetics, and pigments.[9]

Usually, oxindole derivatives containing spirocarbon and heterocyclics at the C3 position enhance their biological activity.[10] Isatin and its derivatives play an important role in the synthesis of oxindoles and are widely used as precursors for many natural products.[11] This encouraged us to focus on Target Oriented Synthesis (TOS) to design novel heterocyclic compounds with new synthetic methodology for the efficient synthesis of triazolylspiroxindolinopyrans.

Click chemistry[12] is a modular approach that uses only the most practical and reliable chemical transformations. In particular, Huisgen [3 + 2] cycloaddition[13] has emerged as a 'near perfect' (very fast, selective, high-yield, and wide scope) carbon–nitrogen bond forming reaction in the synthesis of N-substituted 1,2,3-triazoles. This process, which occurs between organic azides and alkynes, is significantly accelerated by Cu(I) catalysis[14] and it offers easy access to the 1,4-disubstituted isomer. The triazole products are more than just passive linkers; they readily associate with biological targets, through hydrogen bonding and dipole interactions. Their applications are increasingly found in all aspects of drug discovery, ranging from lead finding through combinatorial chemistry and target-template *in situ* chemistry, to proteomics and DNA research, using bioconjugation reactions.[15] Based on these pharmacological applications, we incorporated a spiro-oxindole core in a triazole motif to obtain a hybrid molecule of triazolylspirooxindolopyran with greater biological impact and enhanced biological activity.

Results and discussion

This novel strategy to introduce a synthon which has a biologically important heterocyclic core triazole with an active methyl group has great potential for the development of triazolylspiroxindolinopyrans in an effective manner. 1-Phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethanone is one such versatile intermediate, with an active methylene ketone motif (Fig. 2). Due to the electron withdrawing nature of carbonyl and triazole groups, the central $-CH_2$ group acts as an active methylene group and hence is a good Michael donor. In the presence of catalyst, the more acidic active methylene hydrogen undergoes keto–enol tautomerism to give alcohol, a precursor of the oxygen heterocyclics. Based on these key features, herein we demonstrate the use of the special reactivity of phenacyltriazole for convenient combinatorial synthesis of triazolylspiroxindolinopyrans. In recent times, the utility of indium(III) Lewis acids[16] in organic synthesis has received much attention because of their biocompatibility, such as lower toxicity, stability in air and water, and recyclability. To the best of our knowledge, there have been no reports on the synthesis of triazole derivatives, including spiropyranyl moieties using phenacyltriazoles as a new synthon. As part of our effort to develop heterocyclic compounds with biological potential by new synthetic methods,[17,18] and to apply $InCl_3$ in organic synthesis,[19] we report for the first time the facile and efficient synthesis of triazolylspiroxindolinopyrans by a one-pot three-component coupling of 1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl) ethanone, substituted isatin and active methylenes under solvent-free conditions at 100 °C in the presence of $InCl_3$ (Scheme 1).

The reactions were accomplished within 1–2 h and the pure solid products were sequestered in good yields by simple addition of ethanol to the reaction mixture. The synthetic route is more facile, convenient and permits easy placement of pyran with triazole heterocyclics in the spiro-oxindole core to deliver a new hybrid of the heterocyclic ring system.

The precursor phenacyltriazoles were synthesized in good yield (75–85%) within 2 h by the reaction of substituted phenacyl bromide and sodium azide with phenylacetylene in the presence of CuI in acetone (Table 1) and used for synthesis of novel triazolylspiroxindolinopyrans.

For the initial investigation, phenacyltriazole, isatin and malononitrile were selected as a trial substrate to optimize the reaction conditions. Initially, the above three-component reaction was carried out at room temperature in EtOH followed by reflux without any catalyst to establish the real effectiveness of the catalyst. There was no product formation even after 24 h. Next, we tried to optimize the reaction conditions with different catalysts, different amounts of catalyst and different solvents. When the reaction was carried out in Et_3N and ethanol combination, only 50% product conversion was observed. In order to enhance the yield, looking for other effective methodology was highly desirable. The solvent-free condition is a powerful technique to deliver large amounts of heterocyclics in an eco-compatible manner. We used this technique and obtained good yields in the minimum reaction period.

Next we optimized the catalytic loading and temperature of reaction. To our delight, the catalytic amount of 20 mol% and

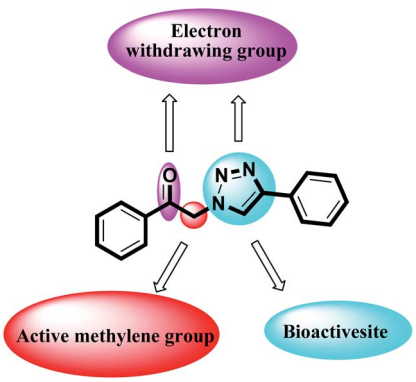
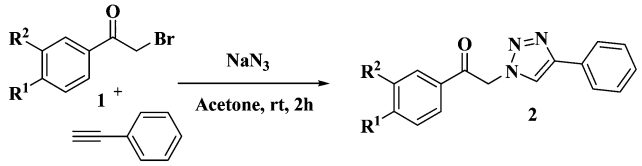


Fig. 2 The special reactive profile of phenacyltriazole.

Scheme 1 Synthesis of triazolylspiroxindolinopyrans 5.

Table 1 Synthesis of phenacyltriazoles 2



Entry	R1	R2	Product	Yield[a]
1	H	H	**2a**	79
2	Cl	H	**2b**	83
3	Br	H	**2c**	85
4	C_4H_4		**2d**	75

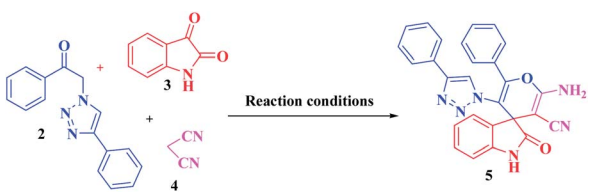
[a] Isolated yield.

100 °C were found to be the optimum reaction conditions. Increasing or decreasing the amount of catalyst as well as temperature resulted in a significant reduction in yield, even with increased reaction times (Table 2).

With these straightforward reaction conditions, to delineate this approach, the scope and generality of this protocol was next examined by employing various phenacyltriazoles, different isatins and active methylenes. Notably, a variety of substituted isatins (including aromatic and N-substitution) and acenaphthoquinone were well tolerated and the products were obtained in high yields (Table 3).

After successfully completing the synthesis of the spiro-motif from isatin/acenaphthoquinone, malononitriles and phenacyltriazoles, we next applied the same methodology with aromatic aldehydes to determine generality of this protocol. We obtained highly substituted triazolylpyrans in good yields (Scheme 2 and Table 4).

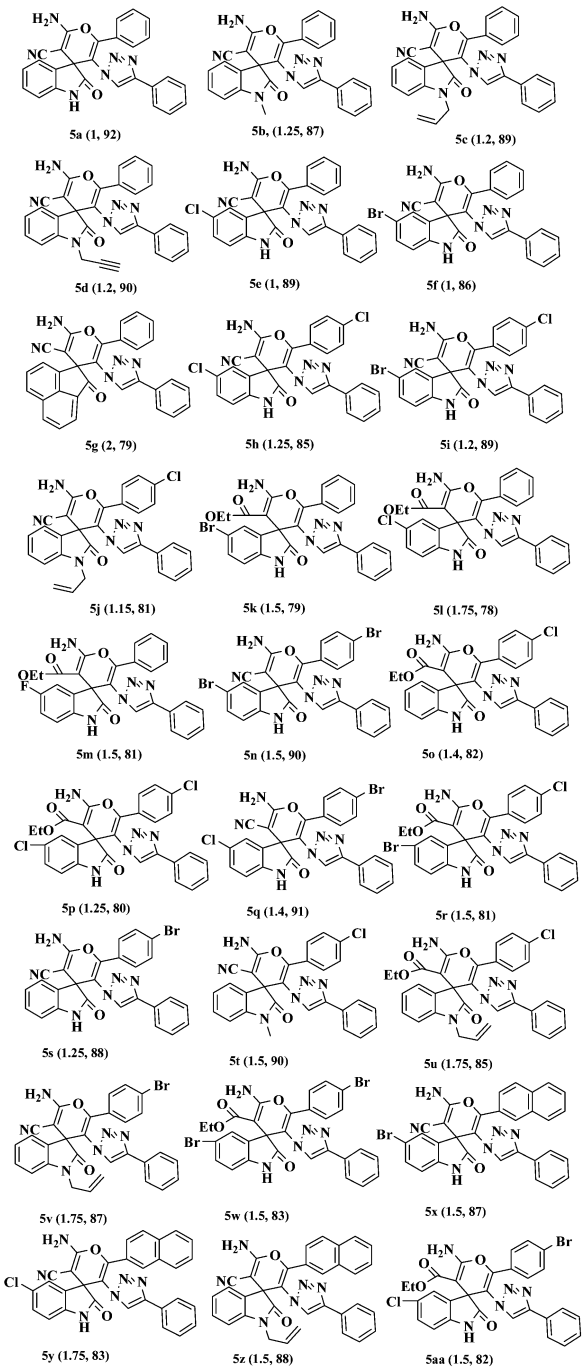
Table 2 Optimization of reaction conditions[a] for the synthesis of triazolylspiroxindolinopyran 5a



Entry	Reaction condition	Time (h)	Yield[b] (%)
1	No catalyst, EtOH, rt	24	—[c]
2	No catalyst, EtOH, reflux	8	—[c]
3	Piperidine (0.1 eq.), EtOH, rt	24	—[c]
4	Piperidine (0.1 eq.), EtOH, reflux	10	43
5	TEA (1.0 eq.), EtOH, reflux	6	45
6	DABCO (1.0 eq.), EtOH, reflux	7	47
7	L-Proline (1.0 eq.), EtOH, reflux	8	28
8	*p*-TSA (1.0 eq.), EtOH, reflux	6	42
9	CAN (1.0 eq.), EtOH, reflux	8	—[c]
10	$InCl_3$ (0.10 eq.), EtOH, reflux	6	55
11	$InCl_3$ (0.20 eq.), EtOH, reflux	6	58
12	$InCl_3$ (0.1 eq.), solvent-free, 80 °C	4	74
13	$InCl_3$ (0.20 eq.), solvent-free, 100 °C	2	92
14	$InCl_3$ (0.20 eq.), solvent-free, 120 °C	6	90
15	$Cu(TfO)_3$ (0.20 eq.), solvent-free, 100 °C	8	68
16	$FeCl_3$ (0.20 eq.), solvent-free, 100 °C	12	48
17	I_2 (0.20 eq.), solvent-free, 100 °C	2	31

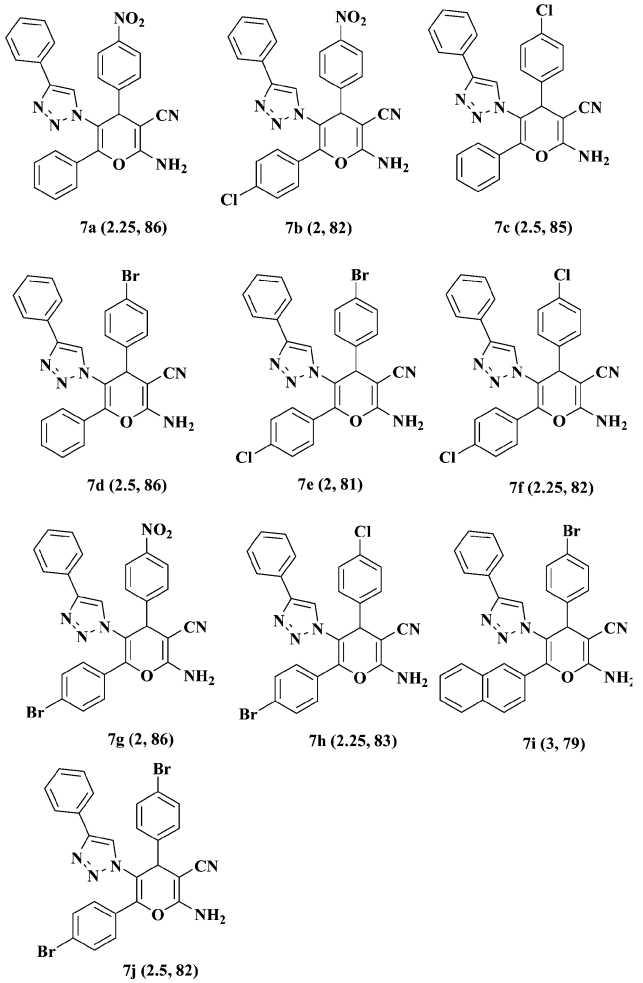
[a] Reactions were carried out using **2** (1.0 mmol), **3** (1.0 mmol), and **4** (1.0 mmol). [b] Isolated yield. [c] No reaction.

Table 3 Synthesis of triazolylspiroxindolinopyrans 5[a]



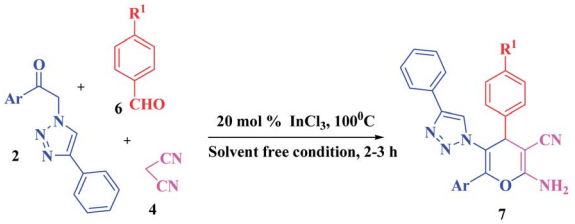
[a] Product 5 (time in h, yield %).

Table 4 Synthesis of triazolylpyrans 7[a]

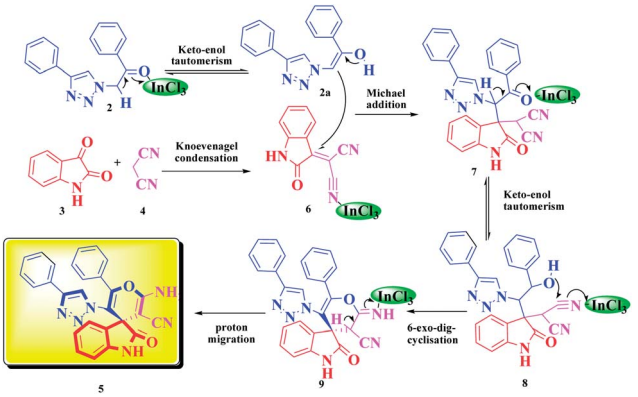


[a] Product 7 (time in h, yield %).

Based on the above results, a plausible mechanism is proposed for the formation of triazolylspiroxindolinopyrans **5** (Scheme 3). Initially, isatin **3** reacts with malononitrile **4** to give an isatylidene malononitrile adduct **6** which acts as a Michael acceptor, and phenacyltriazole **2** may exist as a keto–enol tautomer with the influence of $InCl_3$ which acts as a Michael donor **2a**. The intermediate **2a** undergoes Michael type addition to **6** to provide open chain intermediate **7**. This intermediate may exist as a keto–enol tautomer **8**. This **8** undergoes 6-*exo*-dig-cyclisation to provide **9**. Finally, **9** undergoes proton migration to yield triazolylspiroxindolinopyran **5** in good yield.



Scheme 2 Synthesis of triazolylpyrans.



Scheme 3 Plausible mechanisms for the formation of triazolylspiroxindolinopyrans **5**.

Our efforts to isolate intermediates, other than **6**, by intercepting the reaction at various times before completion of the reaction failed, as only mixtures of intermediate **6**, reactant **2** and the final product **5** were found in varying amounts in the reaction mixture. This shows that, under these reaction conditions, once intermediate **6** is formed, the subsequent Michael addition between **2** and **6** followed by 6-*exo*-dig-cyclisation to give the final product **5** occurs relatively rapidly.

The main advantages of this domino protocol are the simple workup, and that the product is obtained in high purity simply by trituration with ethanol, which makes this methodology facile, practical, and rapid to perform. The purity of the product was sufficient for spectroscopic analysis without any further purification. The structures of all of the newly synthesized compounds **5** and **7** were well characterized from their satisfactory spectra (IR, ^1H, ^{13}C NMR, and mass) data. The mass spectra of the synthesised compounds displayed molecular ion peaks at the appropriate *m*/*z* values. Further, the structure was explicitly established by single crystal X-ray diffraction analysis of compound **5x** (Fig. 3).[20]

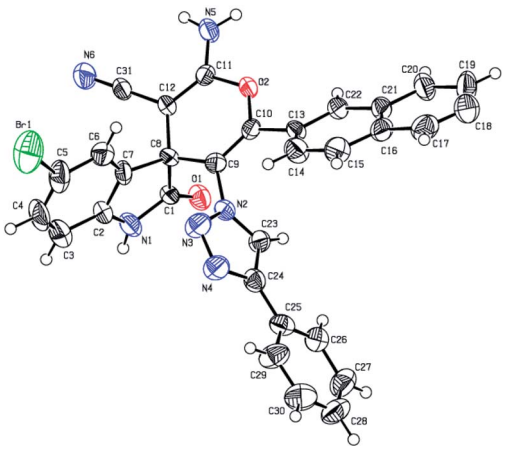


Fig. 3 ORTEP diagram of compound **5x**.

Conclusion

The present work describes for the first time a domino three-component protocol to assemble a series of hitherto unreported triazolylspiroxindolinopyrans and triazolylpyrans from the sequential reaction of phenacyltriazoles, isatin/aromatic aldehyde and active methylene compound in the presence of $InCl_3$ as green catalyst under solvent-free conditions. The notable features of this methodology are that the three biologically important core moieties are brought into a single molecule utilizing green catalyst solvent-free reaction conditions with the formation of only water as by-product and avoiding tedious separation techniques such as column chromatography and recrystallization from ethanol. Hence, a green transformation.

Experimental

General information

Commercially available starting materials were used as received without further purification. Infrared (IR) spectra were recorded in KBr, and wavenumbers (ν) are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on a Bruker (400 MHz). Chemical shifts (δ) are given in parts per million (ppm) with reference to TMS. DMSO-d_6 and $CDCl_3$ were used as solvents. J values are given in Hz. Standard Bruker software was used throughout. Mass spectra were recorded using electrospray ionization (ESI) mass spectrometry; $[M]^+$ $[M^+ + 1]$, $[M^+ + 2]$ mass peaks were observed. The melting points are uncorrected.

General procedure for synthesis of triazolylspiroxindolinopyrans 5

A dried, 10 mL round-bottomed flask was charged with phenacyltriazole (1.0 mmol), isatin (1.0 mmol), and active methylene compound (1.0 mmol), and 20 mol% of $InCl_3$ was added to the reaction mixture and heated in an oil bath at 100 °C for the stipulated period. After completion of the reaction (monitored by TLC), ethanol (2 mL) was added to the reaction mixture. The products appeared as solids, by trituration with ethanol, and were filtered and washed with another 2 mL of EtOH to remove other impurities. Finally, the products **5** were dried and were pure enough for the spectral investigations.

2′-Amino-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl) spiro[indoline-3,4′-pyran]-3′-carbonitrile (5a)

White solid; mp 180–182 °C. ^1H NMR (400 MHz, DMSO) δ 10.55 (s, 1H), 8.13 (s, 1H), 7.61–7.52 (m, 3H), 7.25–7.41 (m, 8H), 7.18 (d, J = 7.1 Hz, 2H), 7.12 (t, J = 7.5 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 7.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.94, 160.82, 149.21, 146.28, 142.32, 131.11, 130.14, 130.09, 130.06, 129.77, 129.33, 129.01, 128.60, 127.95, 125.77, 125.48, 124.41, 122.66, 117.89, 112.74, 110.22, 56.35, 53.20. IR (KBr, cm^{-1}): 3352, 3192, 2206, 1712, 1683, 1618, 1602, 1473, 1300, 1226, 1087, 933, 696; ESI-mass m/z: 459 (M^+ + 1). HRMS (ESI) calc. for $C_{27}H_{19}N_6O_2$ $[M^+ + 1]$ 459.15695, found: 459.15738.

2′-Amino-1-methyl-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5b)

White solid; mp 172–174 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.12 (s, 1H), 7.62 (s, 2H), 7.56 (d, J = 7.3 Hz, 2H), 7.45 (d, J = 7.2 Hz, 1H), 7.41–7.12 (m, 9H), 7.03 (t, J = 7.3 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 3.10 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.43, 161.02, 149.24, 146.31, 143.78, 131.18, 130.23, 130.02, 129.70, 129.32, 129.10, 129.04, 128.61, 127.98, 125.49, 125.40, 124.28, 123.33, 117.78, 112.57, 109.22, 55.87, 52.71, 27.08. IR (KBr, cm^{-1}): 3368, 3191, 2199, 1713, 1679, 1645, 1645, 1606, 1469, 1415, 1366, 1154, 1025, 875, 693; ESI-mass m/z: 473 (M^+ + 1). HRMS (ESI) calc. for $C_{28}H_{21}N_6O_2$ $[M^+ + 1]$ 473.17260, found: 473.17294.

1-Allyl-2′-amino-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5c)

White solid; mp 168–170 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.12 (s, 1H), 7.62 (s, 2H), 7.56 (d, J = 7.4 Hz, 2H), 7.49 (d, J = 7.4 Hz, 1H), 7.40–7.24 (m, 7H), 7.20 (t, J = 7.0 Hz, 3H), 7.04 (t, J = 7.5 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 5.80–5.61 (m, 1H), 5.06–5.0 (m, 2H), 4.27 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.20, 160.92, 149.46, 146.41, 142.82, 131.56, 131.18, 130.12, 130.06, 129.70, 129.34, 129.30, 129.03, 128.60, 127.98, 125.62, 125.53, 124.39, 123.37, 117.80, 116.97, 112.43, 109.87, 56.09, 52.85. IR (KBr, cm^{-1}): 3452, 3184, 2193, 1711, 1644, 1605, 1486, 1360, 1284, 1026, 760, 630, 494; ESI-mass m/z: 499 (M^+ + 1). HRMS (ESI) calc. for $C_{30}H_{23}N_6O_2$ $[M^+ + 1]$ 499.18825, found: 499.18945.

2′-Amino-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-(prop-2-ynyl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5d)

White solid; mp 166–168 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.09 (s, 1H), 7.65 (s, 2H), 7.56 (d, J = 7.3 Hz, 2H), 7.49 (d, J = 7.3 Hz, 1H), 7.42–7.30 (m, 5H), 7.26 (t, J = 7.9 Hz, 2H), 7.19 (d, J = 7.4 Hz, 2H), 7.08 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 4.52 (dd, J = 41.9, 17.8 Hz, 2H), 3.11 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.83, 161.04, 149.52, 146.43, 141.93, 131.21, 130.20, 130.07, 129.70, 129.30, 129.08, 129.04, 128.60, 128.00, 125.68, 125.57, 124.13, 123.73, 117.55, 112.23, 109.94, 77.78, 74.90, 55.76, 52.70, 29.82. IR (KBr, cm^{-1}): 3454, 3307, 3191, 2196, 1710, 1640, 1609, 1485, 1467, 1361, 1237, 1090, 958, 875, 695, 536; ESI-mass m/z: 497 (M^+ + 1). HRMS (ESI) calc. for $C_{30}H_{21}N_6O_2$ $[M^+ + 1]$ 497.17260, found: 497.17274, $[M^+ + Na]$ 519.15511.

2′-Amino-5-chloro-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5e)

White solid; mp 176–178 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.22 (s, 1H), 7.65 (s, 2H), 7.60 (d, J = 8.3 Hz, 3H), 7.40–7.27 (m, 6H), 7.24–7.17 (m, 3H), 6.71 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.77, 160.83, 149.55, 146.41, 141.18, 132.25, 131.21, 130.07, 130.00, 129.63, 129.39, 129.01, 128.71, 128.05, 126.72, 126.02, 125.52, 124.47, 117.84, 111.93, 111.71, 55.74, 53.52. IR (KBr, cm^{-1}): 3449, 3350, 2203, 1735, 1694, 1652, 1588, 1478, 1293, 1164, 1029, 966, 818, 692, 558,

462; ESI-mass *m*/*z*: 493 (M^+ + 1). HRMS (ESI) calc. for $C_{27}H_{17}ClN_6NaO_2$ [M^+ + Na] 515.09992, found: 515.10109.

2′-Amino-5-bromo-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5f)

White solid; mp 184–186 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.71 (s, 1H), 8.22 (s, 1H), 7.69 (s, 1H), 7.63–7.59 (m, 4H), 7.38–7.27 (m, 7H), 7.21 (d, J = 7.2 Hz, 2H), 6.65 (d, J = 8.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.60, 160.83, 149.55, 146.40, 141.60, 132.89, 132.63, 131.18, 130.05, 129.66, 129.37, 128.99, 128.74, 128.69, 128.06, 125.54, 124.50, 117.83, 114.35, 112.19, 111.96, 55.79, 53.49. IR (KBr, cm^{-1}): 3399, 3352, 3120, 2197, 1737, 1685, 1635, 1437, 1238, 1162, 1118, 969, 860, 771, 687, 505, 462; ESI-mass *m*/*z*: 537 (M^+ + 1), 538 (M^+ + 2). HRMS (ESI) calc. for $C_{27}H_{17}BrN_6NaO_2$ [M^+ + Na] 559.04941, found: 559.04907.

2′-Amino-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-2*H*-spiro[acenaphthylene-1,4′-pyran]-3′-carbonitrile (5g)

White solid; mp 186–188 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 (d, J = 8.1 Hz, 1H), 8.14 (s, 1H), 8.04 (d, J = 7.0 Hz, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.86–7.75 (m, 2H), 7.74–7.63 (m, 3H), 7.45–7.31 (m, 5H), 7.27 (t, J = 7.4 Hz, 2H), 7.22 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 202.54, 160.82, 148.98, 145.93, 141.89, 138.10, 132.93, 131.20, 130.82, 130.24, 129.79, 129.70, 129.37, 129.33, 129.26, 129.09, 128.59, 127.99, 126.12, 125.34, 124.73, 123.29, 122.73, 118.00, 113.38, 57.23, 57.05. IR (KBr, cm^{-1}): 3377, 3316, 2201, 1720, 1681, 1600, 1644, 1285, 1152, 874, 692, 535; ESI-mass *m*/*z*: 494 (M^+ + 1). HRMS (ESI) calc. for $C_{31}H_{19}N_5NaO_2$ [M^+ + Na] 516.14364, found: 516.14363.

2′-Amino-5-chloro-6′-(4-chlorophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5h)

White solid; mp 200–202 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.24 (s, 1H), 7.66 (s, 2H), 7.62–7.59 (m, 3H), 7.44 (d, J = 8.6 Hz, 2H), 7.37 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.3 Hz, 1H), 7.19 (d, J = 8.5 Hz, 4H), 6.70 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.62, 160.72, 148.48, 146.56, 141.17, 135.94, 132.15, 130.12, 129.94, 129.87, 129.41, 129.23, 128.77, 128.48, 126.72, 126.07, 125.56, 124.36, 117.75, 112.34, 111.73, 55.74, 53.52. IR (KBr, cm^{-1}): 3411, 3382, 3256, 3190, 2200, 1728, 1685, 1646, 1476, 1299, 1155, 1013, 859, 762, 558, 450; ESI-mass *m*/*z*: 527 (M^++1). HRMS (ESI) calc. for $C_{27}H_{17}Cl_2N_6O_2$ [M^+ + 1] 527.07900, found: 527.08002.

2′-Amino-5-bromo-6′-(4-chlorophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5i)

White solid; mp 192–194 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.74 (s, 1H), 8.24 (s, 1H), 7.69 (d, J = 15.1 Hz, 3H), 7.61 (d, J = 7.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.35–7.26 (m, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.66 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.50, 160.71, 148.51, 146.55, 141.55, 135.93, 132.94, 132.49, 129.93, 129.88, 129.42, 128.77, 128.48, 125.56, 124.38, 117.76, 114.37, 112.31, 112.23, 100.00, 55.75, 53.46. IR (KBr, cm^{-1}): 3432, 3392, 3308, 3258, 2206, 1744, 1725, 1693, 1494, 1455, 1350, 1196, 958, 856, 699543, 449; ESI-mass *m*/*z*: 571 (M^+ + 1), 573 (M^+ + 2). HRMS (ESI) calc. for $C_{27}H_{17}BrClN_6O_2$ [M^+ + 1] 571.02849, found: 571.01050.

1-Allyl-2′-amino-6′-(4-chlorophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5j)

White solid; mp 194–196 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.15 (s, 1H), 7.65 (s, 2H), 7.58 (d, J = 7.2 Hz, 2H), 7.49 (d, J = 7.4 Hz, 1H), 7.44 (d, J = 8.7 Hz, 2H), 7.35 (t, J = 7.4 Hz, 2H), 7.29 (d, J = 7.3 Hz, 1H), 7.22–7.17 (m, 3H), 7.04 (t, J = 7.5 Hz, 1H), 6.80 (d, J = 7.8 Hz, 1H), 5.78–5.64 (m, 1H), 5.08–4.97 (m, 2H), 4.27 (d, J = 2.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.52, 160.28, 147.86, 146.03, 142.25, 135.39, 130.97, 129.63, 129.42, 129.23, 128.76, 128.68, 128.65, 128.11, 127.97, 125.08, 125.01, 123.70, 122.84, 117.16, 116.41, 112.27, 109.34, 55.53, 52.28, 41.81. IR (KBr, cm^{-1}): 3474, 3315, 3170, 2200, 1954, 1707, 1641, 1606, 1358, 1245, 989, 876, 711, 641, 521, 489; ESI-mass *m*/*z*: 533 (M^+ + 1). HRMS (ESI) calc. for $C_{30}H_{21}ClN_6NaO_2$ [M^+ + 1] 555.13122, found: 555.13270.

Ethyl 2′-amino-5-bromo-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5k)

White solid; mp 220–222 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 8.07 (s, 2H), 8.04 (s, 1H), 7.63 (d, J = 7.2 Hz, 2H), 7.53 (d, J = 1.9 Hz, 1H), 7.40–7.23 (m, 7H), 7.22–7.16 (m, 2H), 6.50 (d, J = 8.2 Hz, 1H), 3.85–3.70 (m, 2H), 0.75 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.49, 166.82, 160.03, 147.84, 145.46, 141.65, 135.94, 131.04, 130.35, 129.67, 129.23, 128.77, 128.30, 128.00, 127.33, 126.85, 124.97, 124.21, 113.49, 113.22, 110.55, 73.74, 58.95, 53.00, 13.06. IR (KBr, cm^{-1}): 3428, 3320, 3120, 1732, 1712, 1615, 1580, 1263, 1164, 1107, 999, 872, 752, 620, 533; ESI-mass *m*/*z*: 584 (M^+ + 2Na).

Ethyl 2′-amino-5-chloro-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5l)

White solid; mp 226–228 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.33 (s, 1H), 8.08 (s, 2H), 8.05 (s, 1H), 7.63 (d, J = 7.4 Hz, 2H), 7.43 (d, J = 1.8 Hz, 1H), 7.33 (ddd, J = 14.4, 10.8, 4.9 Hz, 6H), 7.20 (d, J = 7.3 Hz, 2H), 7.14 (dd, J = 8.2, 2.0 Hz, 1H), 6.55 (d, J = 8.2 Hz, 1H), 3.86–3.69 (m, 2H), 0.75 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.22, 167.41, 160.61, 148.43, 146.04, 141.81, 136.18, 130.94, 130.22, 129.80, 129.35, 128.89, 128.77, 128.59, 127.90, 126.15, 125.54, 124.78, 114.06, 110.60, 74.29, 59.55, 53.62, 13.63. IR (KBr, cm^{-1}): 3404, 3297, 3125, 1729, 1697, 1674, 1616, 1529, 1429, 1366, 1223, 1084, 965, 765, 695, 622, 509; ESI-mass *m*/*z*: 540 (M^+ + 2Na).

Ethyl 2′-amino-5-fluoro-2-oxo-6′-phenyl-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5m)

White solid; mp 216–218 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.21 (s, 1H), 8.07 (s, 2H), 8.00 (s, 1H), 7.63 (d, J = 7.4 Hz, 2H), 7.41–7.24 (m, 7H), 7.19 (d, J = 7.2 Hz, 2H), 6.92 (td, J = 9.5, 2.6 Hz, 1H), 6.52 (dd, J = 8.4, 4.3 Hz, 1H), 3.86–3.68 (m, 2H), 0.74 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.41, 167.48, 162.91, 160.58, 159.84, 157.49, 148.35, 146.00, 139.10, 135.87,

130.91, 130.25, 129.85, 129.33, 128.89, 128.55, 127.88, 125.53, 124.74, 115.20, 114.97, 114.26, 112.56, 112.32, 109.89, 109.81, 74.37, 60.25, 59.48, 53.83, 13.61. IR (KBr, cm^{-1}): 3382, 3210, 1716, 1698, 1483, 1368, 1297, 1219, 1104, 997, 880, 766, 695, 590; ESI-mass *m*/*z*: 524 (M^+ + 2Na).

2′-Amino-5-bromo-6′-(4-bromophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5n)

White solid; mp 194–196 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.72 (s, 1H), 8.24 (s, 1H), 7.70 (s, 1H), 7.65 (s, 2H), 7.59 (dd, J = 12.3, 8.2 Hz, 4H), 7.37 (t, J = 7.5 Hz, 2H), 7.30 (dd, J = 11.5, 5.7 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 6.65 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.39, 159.64, 147.51, 145.49, 140.50, 131.87, 131.42, 131.07, 128.96, 128.88, 128.34, 127.79, 127.71, 124.51, 123.74, 123.31, 116.68, 113.28, 111.25, 111.15, 54.68, 52.40. IR (KBr, cm^{-1}): 3375, 3308, 3186, 2200, 1730, 1605, 1474, 1424, 1297, 1089, 888, 763, 638, 541, 478; ESI-mass *m*/*z*: 615 (M^+), 617 (M^+ + 2).

Ethyl 2′-amino-6′-(4-chlorophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5o)

White solid; mp 202–204 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.03 (s, 2H), 7.83 (s, 1H), 7.60 (d, J = 7.5 Hz, 2H), 7.43–7.26 (m, 6H), 7.17 (d, J = 8.5 Hz, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 6.53 (d, J = 7.6 Hz, 1H), 3.83–3.67 (m, 2H), 0.71 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.91, 172.30, 165.16, 151.72, 150.80, 147.66, 140.33, 138.69, 134.98, 134.37, 134.09, 133.84, 133.69, 133.55, 133.33, 133.02, 130.30, 129.30, 126.95, 120.02, 113.99, 79.49, 64.17, 58.05, 18.33. IR (KBr, cm^{-1}): 3343, 3200, 1710, 1619, 1534, 1365, 1297, 1258, 1183, 1015, 921, 836, 758, 694545; ESI-mass *m*/*z*: 540 (M^+ + 1).

Ethyl 2′-amino-5-chloro-6′-(4-chlorophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5p)

White solid; mp 220–222 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 8.07 (s, 1H), 8.04 (s, 1H), 7.63 (d, J = 7.6 Hz, 2H), 7.46–7.33 (m, 5H), 7.29 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 8.5 Hz, 2H), 7.13 (dd, J = 8.2, 1.7 Hz, 1H), 6.54 (d, J = 8.2 Hz, 1H), 3.84–3.69 (m, 2H), 0.74 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.06, 167.35, 160.50, 147.42, 146.19, 141.82, 140.52, 136.01, 135.68, 130.17, 129.73, 129.37, 129.07, 128.82, 128.67, 128.65, 126.17, 125.59, 124.83, 124.68, 114.49, 110.61, 74.29, 59.55, 53.62, 13.63. IR (KBr, cm^{-1}): 3262, 3188, 3145, 1724, 1702, 1620, 1524, 1475, 1368, 1298, 1166, 898, 762, 560; ESI-mass *m*/*z*: 575 (M^+ + 1), 576 (M^+ + 2).

2′-Amino-6′-(4-bromophenyl)-5-chloro-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5q)

White solid; mp 174–176 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.71 (s, 1H), 7.64 (s, 2H), 7.59 (dd, J = 12.6, 7.9 Hz, 5H), 7.37 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 7.19 (dd, J = 8.3, 1.9 Hz, 1H), 7.12 (d, J = 8.5 Hz, 2H), 6.70 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.61, 160.73, 146.58, 141.19, 132.16, 130.13, 130.04, 129.96, 129.42, 128.87, 128.78, 126.73, 126.08, 125.59, 124.83, 124.36, 56.50, 55.77. IR (KBr, cm^{-1}): 3379, 3318, 3287, 2199, 1728, 1685, 1642, 1599, 1477, 1297, 1157, 1011, 818, 725, 558; ESI-mass *m*/*z*: 570 (M^+), 572 (M^+ + 2).

Ethyl 2′-amino-5-bromo-6′-(4-chlorophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5r)

White solid; mp 238–240 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.33 (s, 1H), 8.08 (s, 2H), 8.05 (s, 1H), 7.64 (d, J = 7.7 Hz, 2H), 7.55 (s, 1H), 7.38 (dd, J = 12.5, 8.1 Hz, 4H), 7.29 (dd, J = 15.1, 7.9 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 6.50 (d, J = 8.2 Hz, 1H), 3.86–3.69 (m, 2H), 0.75 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.38, 166.77, 159.93, 146.84, 145.63, 141.65, 135.80, 135.12, 131.10, 129.60, 129.16, 128.79, 128.49, 128.09, 128.07, 126.93, 125.01, 124.11, 113.89, 113.25, 110.59, 73.72, 58.99, 53.00, 13.06. IR (KBr, cm^{-1}): 3366, 3269, 3188, 1720, 1705, 1620, 1473, 1404, 1298, 1225, 844, 722, 615, 508, 411; ESI-mass *m*/*z*: 617 (M^+), 619 (M^+ + 2).

2′-Amino-6′-(4-bromophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5s)

White solid; mp 200–202 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.58 (s, 1H), 8.16 (s, 1H), 7.58 (t, J = 8.5 Hz, 6H), 7.43–7.32 (m, 3H), 7.28 (t, J = 7.2 Hz, 1H), 7.12 (dd, J = 14.0, 8.0 Hz, 3H), 6.96 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 7.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.25, 160.16, 147.68, 145.89, 141.74, 131.58, 129.56, 129.43, 129.41, 129.34, 128.78, 128.39, 128.11, 125.22, 124.96, 124.17, 123.70, 122.11, 117.25, 112.56, 109.69, 79.06, 55.75, 52.63. IR (KBr, cm^{-1}): 3360, 3321, 3195, 2200, 1721, 1670, 1605, 1421, 1397, 1288, 1156, 1032, 885, 750, 684, 616, 471; ESI-mass *m*/*z*: 537 (M^+ + 1), 538 (M^+ + 2).

2′-Amino-6′-(4-chlorophenyl)-1-methyl-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5t)

White solid; mp 228–230 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (s, 1H), 7.64 (s, 2H), 7.57 (d, J = 7.6 Hz, 2H), 7.43 (d, J = 8.2 Hz, 3H), 7.35 (t, J = 7.5 Hz, 2H), 7.31–7.12 (m, 4H), 7.02 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 3.10 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.24, 159.86, 147.11, 145.42, 142.71, 134.86, 129.22, 128.88, 128.71, 128.27, 128.18, 127.89, 127.61, 127.46, 124.47, 124.35, 123.08, 122.27, 116.63, 111.89, 108.20, 54.79, 51.62, 26.02. IR (KBr, cm^{-1}): 3382, 3311, 3180, 2202, 1697, 1646, 1610, 1491, 1417, 1299, 1128, 836, 689, 543, 488; ESI-mass *m*/*z*: 506 (M^+), 508 (M^+ + 2).

2′-Amino-6′-(4-chlorophenyl)-1-methyl-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5u)

White solid; mp 226–228 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (s, 2H), 7.83 (s, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.39 (dt, J = 18.0, 5.6 Hz, 5H), 7.28 (t, J = 7.2 Hz, 1H), 7.18 (t, J = 7.0 Hz, 3H), 7.06 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 7.7 Hz, 1H), 5.47–5.37 (m, 1H), 4.92 (d, J = 17.2 Hz, 1H), 4.83 (d, J = 10.3 Hz, 1H), 4.24 (dd, J = 16.1, 4.5 Hz, 1H), 3.91 (dd, J = 16.1, 5.8 Hz, 1H), 3.80–3.62 (m, 2H), 0.65 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.24, 167.38, 160.50, 147.26, 146.32, 143.33, 135.69, 133.15,

132.05, 130.18, 129.63, 129.29, 129.11, 129.04, 128.68, 128.58, 125.62, 124.59, 124.41, 123.03, 117.77, 114.85, 108.78, 74.50, 59.31, 52.83, 42.62, 13.96. IR (KBr, cm^{-1}): 3388, 3318, 3180, 2214, 1692, 1656, 1618, 1498, 1425, 1292, 1120, 825, 672, 540, 476; ESI-mass *m*/*z*: 581 (M^+ + 2).

1-Allyl-2′-amino-6′-(4-bromophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5v)

White solid; mp 220–222 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.15 (s, 1H), 7.66 (s, 2H), 7.62–7.53 (m, 4H), 7.48 (d, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.2 Hz, 1H), 7.20 (t, J = 7.7 Hz, 1H), 7.11 (d, J = 8.6 Hz, 2H), 7.04 (t, J = 7.5 Hz, 1H), 6.80 (d, J = 7.8 Hz, 1H), 5.75–5.66 (m, 1H), 5.09–4.96 (m, 2H), 4.27 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.51, 160.26, 147.94, 146.01, 142.22, 131.60, 130.95, 129.63, 129.38, 128.77, 128.59, 128.31, 128.13, 125.07, 124.99, 124.26, 123.70, 122.84, 117.16, 116.38, 112.22, 109.35, 79.05, 55.46, 52.25, 41.79. IR (KBr, cm^{-1}): 3473, 3327, 3140, 2199, 1709, 1606, 1359, 1229, 1198, 1073, 938, 830, 762, 691, 583, 516; ESI-mass *m*/*z*: 576 (M^+), 578 (M^+ + 2).

Ethyl 2′-amino-5-bromo-6′-(4-bromophenyl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5w)

White solid; mp 242–244 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.33 (s, 1H), 8.08 (s, 2H), 8.05 (s, 1H), 7.64 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 8.7 Hz, 3H), 7.38 (t, J = 7.5 Hz, 2H), 7.29 (dd, J = 15.3, 8.2 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 6.50 (d, J = 8.2 Hz, 1H), 3.86–3.69 (m, 2H), 0.75 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.36, 166.76, 159.91, 146.93, 145.61, 141.63, 135.77, 131.41, 131.10, 129.57, 129.32, 128.80, 128.45, 128.08, 126.92, 125.00, 124.10, 123.97, 113.86, 113.25, 110.58, 73.70, 58.99, 52.99, 13.05. IR (KBr, cm^{-1}): 3379, 3271, 3140, 1723, 1700, 1618, 1526, 1474, 1298, 1222, 1108, 828, 697, 547; ESI-mass *m*/*z*: 664 (M^+ + 2).

2′-Amino-5-bromo-6′-(naphthalen-2-yl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5x)

White solid; mp 240–242 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.75 (s, 1H), 8.25 (s, 1H), 7.95 (s, 1H), 7.85 (dd, J = 16.0, 7.9 Hz, 3H), 7.72 (d, J = 1.2 Hz, 1H), 7.68 (s, 2H), 7.62–7.50 (m, 4H), 7.33 (t, J = 7.1 Hz, 3H), 7.26 (t, J = 7.2 Hz, 1H), 7.10 (d, J = 8.8 Hz, 1H), 6.68 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.66, 160.92, 149.52, 146.50, 141.63, 133.78, 132.94, 132.71, 132.43, 130.00, 129.37, 128.81, 128.74, 128.70, 128.57, 128.36, 128.09, 127.59, 127.03, 125.54, 124.63, 124.36, 117.85, 114.39, 112.26, 55.87, 53.59. IR (KBr, cm^{-1}): 3317, 3185, 2198, 1722, 1676, 1640, 1598, 1474, 14410, 1301, 1201, 1116, 979, 859, 762, 473; ESI-mass *m*/*z*: 588 (M^+ + 2).

2′-Amino-5-chloro-6′-(naphthalen-2-yl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5y)

White solid; mp 218–220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.75 (s, 1H), 8.26 (s, 1H), 7.95 (s, 1H), 7.84 (dd, J = 15.1, 8.1 Hz, 3H), 7.69 (s, 2H), 7.64–7.50 (m, 5H), 7.33 (t, J = 7.4 Hz, 2H), 7.29–7.18 (m, 2H), 7.10 (d, J = 8.6 Hz, 1H), 6.73 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.79, 160.91, 149.50, 146.49, 141.23, 133.78, 132.43, 132.37, 130.11, 129.99, 129.37, 128.82, 128.69, 128.59, 128.56, 128.36, 128.09, 127.60, 127.02, 126.75, 126.04, 125.53, 124.62, 124.34, 117.86, 112.26, 111.76, 55.81, 53.63. IR (KBr, cm^{-1}): 3308, 3184, 2197, 1727, 1679, 1640, 1598, 1477, 1301, 1230, 1199, 981, 820, 692, 560; ESI-mass *m*/*z*: 543 (M^+ + 1), 544 (M^+ + 2).

1-Allyl-2′-amino-6′-(naphthalen-2-yl)-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carbonitrile (5z)

White solid; mp 212–214 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.16 (s, 1H), 7.95 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 8.5 Hz, 2H), 7.68 (s, 2H), 7.60–7.47 (m, 5H), 7.31 (t, J = 7.5 Hz, 2H), 7.27–7.18 (m, 2H), 7.06 (t, J = 7.8 Hz, 2H), 6.81 (d, J = 7.8 Hz, 1H), 5.72 (ddd, J = 15.2, 9.7, 4.6 Hz, 1H), 5.04 (dd, J = 13.9, 6.6 Hz, 2H), 4.29 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.67, 160.43, 148.83, 145.91, 142.28, 133.19, 131.87, 131.00, 128.79, 128.72, 128.24, 128.03, 127.94, 127.78, 127.50, 127.02, 126.47, 125.03, 124.94, 123.96, 123.68, 122.83, 117.26, 116.38, 115.03, 112.13, 109.34, 79.06, 55.53, 52.33. IR (KBr, cm^{-1}): 3475, 3321, 3175, 2197, 1710, 1648, 1487, 1465, 1438, 1407, 1357, 1303, 1196, 888, 759, 515, 477; ESI-mass *m*/*z*: 549 (M^+ + 1).

Ethyl 2′-amino-6′-(4-bromophenyl)-5-chloro-2-oxo-5′-(4-phenyl-1*H*-1,2,3-triazol-1-yl)spiro[indoline-3,4′-pyran]-3′-carboxylate (5aa)

White solid; mp 230–232 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 8.08 (s, 2H), 8.05 (s, 1H), 7.63 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 7.44 (s, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 9.7 Hz, 3H), 6.54 (d, J = 8.2 Hz, 1H), 3.83–3.70 (m, 2H), 0.74 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.47, 166.76, 159.90, 146.91, 145.61, 141.23, 135.42, 131.41, 129.58, 129.31, 128.79, 128.45, 128.24, 128.07, 125.58, 125.00, 124.25, 124.10, 123.97, 113.88, 110.02, 79.06, 58.96, 53.03, 13.05. IR (KBr, cm^{-1}): 3359, 3269, 3142, 1722, 1702, 1619, 1525, 1475, 1385, 1295, 1103, 832, 761, 489; ESI-mass *m*/*z*: 619 (M^+ + 2).

General procedure for synthesis of 7

A dried, 10 mL round-bottomed flask was charged with phenacyltriazole (1.0 mmol), substituted aldehyde (1.0 mmol), and active methylene compound (1.0 mmol), and 20 mol% of $InCl_3$ was added to the reaction mixture and heated in an oil bath at 100 °C for the stipulated time. After completion of the reaction (monitored by TLC), ethanol (2 mL) was added to the reaction mixture. The products appeared as solids, by trituration with ethanol, and were filtered and washed with another 2 mL of EtOH to remove other impurities. Finally, the products 7 were dried and were pure enough for the spectral investigations.

2-Amino-4-(4-nitrophenyl)-6-phenyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7a)

White solid; mp 192–194 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 1H), 8.20 (d, J = 8.7 Hz, 2H), 7.67 (d, J = 7.2 Hz, 2H), 7.58

(d, J = 8.7 Hz, 2H), 7.44–7.27 (m, 8H), 7.25–7.19 (m, 2H), 5.00 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.00, 147.45, 147.22, 146.84, 130.83, 130.23, 130.11, 129.77, 129.40, 128.94, 128.70, 127.99, 125.59, 124.44, 123.55, 119.50, 114.92, 56.24, 43.38. IR (KBr, cm^{-1}): 3473, 3360, 2183, 1688, 1642, 1611, 1521, 1455, 1347, 1263, 1220, 1148, 864, 764, 693, 529, 480; ESI-mass m/z: 463 (M^++1). HRMS (ESI) calc. for $C_{26}H_{18}N_6NaO_3$ [M^+ + Na] 485.13381, found: 485.11270.

2-Amino-6-(4-chlorophenyl)-4-(4-nitrophenyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7b)

White solid; mp 188–190 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (s, 1H), 8.19 (d, J = 8.7 Hz, 2H), 7.69 (d, J = 7.3 Hz, 2H), 7.58 (d, J = 8.7 Hz, 2H), 7.48–7.37 (m, 6H), 7.32 (t, J = 7.3 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H), 5.01 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.85, 148.15, 146.40, 145.90, 145.03, 134.45, 129.15, 128.78, 128.73, 128.33, 128.04, 127.98, 127.66, 124.57, 123.37, 122.33, 118.36, 114.32, 55.15, 42.23. IR (KBr, cm^{-1}): 3461, 3320, 2191, 1684, 1644, 1598, 1518, 1405, 1348, 1263, 1148, 1097, 818, 740, 695, 509, 462; ESI-mass m/z: 498 (M^+ + 2). HRMS (ESI) calc. for $C_{26}H_{16}ClN_6O_3$ [M^+ − 1] 495.09724, found: 495.09705.

2-Amino-4-(4-chlorophenyl)-6-phenyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7c)

White solid; mp 214–216 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68 (d, J = 7.6 Hz, 2H), 7.44–7.23 (m, 13H), 7.20 (d, J = 7.5 Hz, 2H), 4.81 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.31, 146.17, 146.08, 140.24, 132.11, 130.10, 129.78, 129.74, 129.63, 128.81, 128.59, 128.33, 128.06, 127.39, 125.01, 122.96, 119.11, 115.07, 56.22, 42.58. IR (KBr, cm^{-1}): 3456, 3335, 2193, 1693, 1654, 1599, 1429, 1259, 1142, 1088, 979, 843, 762, 633, 508, 420; ESI-mass m/z: 453 (M^+ + 2). HRMS (ESI) calc. for $C_{26}H_{19}ClN_5O$ [M^+ + 1] 452.12781, found: 452.12866.

2-Amino-4-(4-bromophenyl)-6-phenyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7d)

White solid; mp 212–214 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.69 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.44–7.28 (m, 8H), 7.21 (t, J = 7.2 Hz, 4H), 4.80 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.86, 146.74, 146.65, 141.22, 132.08, 130.68, 130.55, 130.32, 130.28, 129.40, 128.91, 128.65, 127.95, 125.58, 123.52, 121.29, 119.71, 115.53, 56.69, 43.19. IR (KBr, cm^{-1}): 3458, 3335, 2195, 1694, 1656, 1601, 1486, 1260, 1143, 1030, 841, 690, 563; ESI-mass m/z: 495 (M^+), 497 (M^+ + 2). HRMS (ESI) calc. for $C_{26}H_{19}BrN_5O$ [M^+ + 1] 496.07730, found: 496.07687.

2-Amino-4-(4-bromophenyl)-6-(4-chlorophenyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7e)

White solid; mp 220–222 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (s, 1H), 7.70 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.41 (dd, J = 7.8, 5.8 Hz, 4H), 7.36–7.29 (m, 3H), 7.21 (dd, J = 8.3, 6.5 Hz, 4H), 4.81 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.76, 146.89, 145.55, 141.06, 135.37, 132.08, 130.57, 130.26, 129.81, 129.42, 129.20, 129.06, 128.71, 125.62, 123.36, 121.34, 119.64, 115.97, 56.68, 43.10. IR (KBr, cm^{-1}): 3450, 3313, 2204, 1690, 1656, 1600, 1489, 1409, 1263, 1147, 1094, 1073, 933, 837, 760, 690, 507, 406; ESI-mass m/z: 531 (M^+ + 2). HRMS (ESI) calc. for $C_{26}H_{18}BrClN_5O$ [M^+ + 1] 530.03833, found: 530.03851.

2-Amino-4,6-bis(4-chlorophenyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7f)

White solid; mp 216–218 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 (s, 1H), 7.70 (d, J = 7.4 Hz, 2H), 7.45–7.25 (m, 12H), 7.20 (d, J = 8.6 Hz, 2H), 4.82 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.76, 146.88, 145.54, 140.63, 135.37, 132.73, 130.26, 130.23, 129.81, 129.42, 129.21, 129.16, 129.06, 128.71, 125.61, 123.37, 119.64, 116.03, 56.75, 43.03. IR (KBr, cm^{-1}): 3452, 3312, 2203, 1690, 1655, 1599, 1491, 1410, 1263, 1148, 1092, 914, 836, 761, 510, 420; ESI-mass m/z: 485 (M^+).

2-Amino-6-(4-bromophenyl)-4-(4-nitrophenyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7g)

White solid; mp 194-194 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (s, 1H), 8.17 (d, J = 8.0 Hz, 2H), 7.67 (d, J = 7.1 Hz, 2H), 7.61–7.48 (m, 4H), 7.45–7.27 (m, 5H), 7.14 (d, J = 8.0 Hz, 2H), 4.99 (s, 1H). ^{13}C NMR (101 MHz, DMSO) δ 159.84, 149.02, 147.44, 147.02, 146.31, 130.04, 129.98, 129.88, 129.80, 129.46, 129.34, 128.87, 125.62, 124.41, 124.35, 123.35, 119.47, 115.16, 56.19, 43.22. IR (KBr, cm^{-1}): 3379, 3318, 3287, 2199, 1728, 1685, 1642, 1477, 1223, 818, 725, 558; ESI-mass m/z: 542 (M^+ + 2).

2-Amino-6-(4-bromophenyl)-4-(4-chlorophenyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7h)

White solid; mp 214–216 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (s, 1H), 7.68 (d, J = 6.8 Hz, 2H), 7.52 (d, J = 7.7 Hz, 2H), 7.47–7.20 (m, 9H), 7.12 (d, J = 7.6 Hz, 2H), 4.81 (s, 1H). ^{13}C NMR (101 MHz, DMSO) δ 159.68, 146.93, 145.72, 140.43, 132.78, 131.96, 130.22, 130.06, 130.00, 129.51, 129.47, 129.15, 128.83, 125.59, 124.18, 123.30, 119.67, 115.85, 56.77, 42.93. IR (KBr, cm^{-1}): 3366, 3188, 1720, 1705, 1696, 1620, 1473, 1298, 1162, 964, 844, 783, 695, 508, 411; ESI-mass m/z: 529 (M^+).

2-Amino-4-(4-bromophenyl)-6-(naphthalen-2-yl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7i)

White solid; mp 224–226 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 (s, 1H), 7.95 (s, 1H), 7.90–7.77 (m, 3H), 7.66 (d, J = 7.5 Hz, 2H), 7.58–7.48 (m, 4H), 7.27–7.40 (m, 5H), 7.24 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.8 Hz, 1H), 4.85 (s, 1H). ^{13}C NMR (101 MHz, DMSO) δ 158.88, 145.72, 145.49, 138.11, 131.43, 131.03, 129.48, 129.24, 128.31, 127.66, 127.56, 127.34, 127.17, 127.00, 126.96, 126.64, 126.35, 124.51, 123.41, 122.54, 120.22, 118.64, 114.84, 55.65, 42.14. IR (KBr, cm^{-1}): 3449, 3328, 2197, 1689, 1650, 1597, 1407, 1315, 1235, 1191, 1074, 968, 758, 689, 502, 482; ESI-mass m/z: 547 (M^+ + 2).

2-Amino-4,6-bis(4-bromophenyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-4*H*-pyran-3-carbonitrile (7j)

White solid; mp 218–220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (s, 1H), 7.68 (d, J = 7.7 Hz, 2H), 7.50 (dd, J = 14.6, 7.9 Hz,

4H), 7.40 (t, $J = 7.4$ Hz, 2H), 7.32 (t, $J = 7.3$ Hz, 1H), 7.27 (s, 2H), 7.20 (d, $J = 7.9$ Hz, 2H), 7.12 (d, $J = 8.1$ Hz, 2H), 4.79 (s, 1H). ^{13}C NMR (101 MHz, DMSO) δ 159.69, 146.94, 145.75, 140.87, 132.06, 131.96, 130.57, 130.07, 130.00, 129.51, 129.46, 128.83, 125.61, 124.19, 123.30, 121.37, 119.65, 115.79, 56.75, 43.03. IR (KBr, cm^{-1}): 3453, 3335, 2201, 1685, 1659, 1591, 1488, 1413, 1261, 1225, 1077, 830, 761, 690, 581, 465; ESI-mass m/z: 574 (M^+).

Acknowledgements

One of the authors, J. Kamalraja, thanks the Council of Scientific and Industrial Research (CSIR), New Delhi, India for the research fellowship.

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20 Crystallographic data for the compound **5x** in this manuscript have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 953661.†