

HETEROCYCLES, Vol. 86, No. 1, 2012, pp. 189 - 201. © 2012 The Japan Institute of Heterocyclic Chemistry
Received, 23rd February, 2012, Accepted, 26th April, 2012, Published online, 8th May, 2012
DOI: 10.3987/COM-12-S(N)1

A DIVERSIFIED APPROACH TO THE SYNTHESIS OF HIGHLY FUNCTIONALIZED NOVEL AZINES AND AZOLES FROM 2*H*-PYRAN-2-ONES

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Abstract – One-pot regioselective synthesis of 2,6-diarylpyrimidines (**4**), 2,6-disubstituted pyridines (**5** and **6**), 5-aryl-3-cyanomethyl-1*H*-pyrazoles (**7**) through base catalyzed ring transformation of suitably functionalized 2*H*-pyran-2-ones by arylamidines, cyanamide, ammonium carbonate, hydrazines respectively has been developed. Our synthetic approach opened a new avenue for the regioselective synthesis of 2,6-diarylpyrimidines and 2,6-disubstituted pyridines and cyanomethylpyrazoles. The procedure is very simple, efficient and economically viable. The protocol provides an efficient methodology for the preparation of new class of medicinally useful and highly functionalized azines and azoles from single precursor 2*H*-pyran-2-ones.

INTRODUCTION

The pyridine and pyrimidine rings are extensively present in the biological system and their role has been greatly realized because of their presence as substructure in enzymes, vitamins, and biopolymers of therapeutic importance, involved in oxidation-reduction processes. The potent biological activity of various vitamins and drugs¹⁻⁴ is primarily contributed due to the presence of pyridine and pyrimidine moieties in their molecular architecture. Besides various therapeutic applications, pyridines have contributed immensely in the preparative organic chemistry. 4-Dimethylaminopyridine (DMAP), a highly demanding

This paper is dedicated to Professor Ei-ichi Negishi on celebration of his 77th birthday.

reagent is used as catalyst in acylation reaction and also in activation of carboxylic acids without racemization of α -chiral center.⁵ The coordinating ability of pyridine and pyrimidine derivatives with various metal ions has made them highly sensitive analytical reagents, sensor systems, luminescent agents and building blocks for supramolecular,⁶ metallo-gridlike architecture^{7,8} and in novel inorganic-organic hybrid molecular wires.⁹ Alkene pendant pyridine polymers are industrially useful as acid scavengers^{3b} and materials for chemical separations. Various functionalized pyrimidines are known to display anticonvulsant,¹⁰ anti-inflammatory,¹¹ antibacterial¹² and antimycotic¹³ activities. The wide-ranging applications of various pyridine and pyrimidine derivatives as drugs, catalysts and agrochemicals¹⁴ have significantly augmented the potential of both the ring systems to develop an expedient synthesis devoid from the shortfalls of the earlier procedures in terms of generality, multistep sequences and complex work-up.

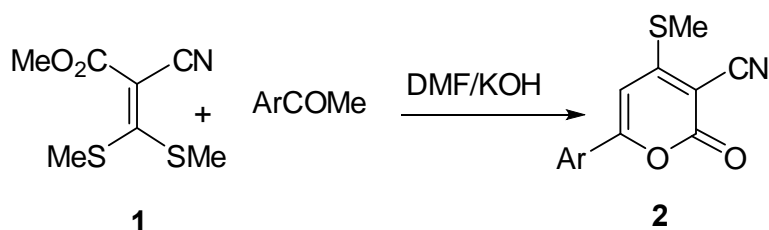
Numerous protocols for the construction of pyridines and pyrimidines with varying substitution patterns around the ring are delineated in the chemical literature. The commonest approach for the synthesis of pyridines¹⁵ is the condensation of 1,5-diketones with ammonia followed by nitric acid oxidation. 2-Acetylfuran has also been used as a 1,5-dicarbonyl equivalent for the construction of congested pyridines and dipyridyls.¹⁶ Katritzky *et al.*¹⁷ have reported the synthesis of nicotinonitriles from the reaction of dienamine and ketone using substituted-1,2,3-benzotriazole as a reagent. 2-Amino-4-arylpyridine-3,5-dinitriles have been prepared¹⁸ by base catalyzed reaction of malononitrile with an aldehyde. One of the most versatile approaches for the construction of unsymmetrical pyridines is through the condensation of 1,3-dicarbonyl compounds and 3-aminoenones or nitriles.¹ 2*H*-Pyran-2-ones have also been used as a diene equivalent for the preparation¹⁹ of congested ethyl nicotines on reaction with aryl nitriles under Diels-Alder conditions. 2-Aminonicotinonitrile²⁰ has also been synthesized through base catalyzed ring transformation of 6-aryl-4-methylsulfanyl-2*H*-pyran-2-ones by cyanamide. The reaction of deoxybenzoin, vinamidium species and ammonia is also one of the good methods for the preparation of trisubstituted pyridines as Cox-2 inhibitors.^{21,22} The synthesis of dihydro- or tetrahydropyridines has been achieved by interactions of 2-azadiene with a suitable dienophile. Using 1,2,4-triazines,^{23,24} a 2-azadiene equivalent, on reaction with suitable alkyne affords highly functionalized pyridines in excellent yields. A synthetic strategy for the construction of piperidine substituted nicotinic acid has been followed²⁵ through the reaction of enamine with alkynone. Thiopyridines such as 2-amino-3,5-dicyano-6-sulfanylpyridines and corresponding 1,4-dihydropyridines have also been prepared²⁶ from the reaction of an aldehyde, malononitrile and a thiol. Cyclotrimerization of a nitrile and two alkynes in the presence of cobalt (I) catalyst²⁷ is an alternative approach for the construction of highly functionalized pyridines. A regioselective synthesis of 6-amino-5-benzoyl-1-substituted-2-(1*H*)-pyridones has also been reported recently from the reaction of a cyclic ketene aminal with propiolic acid ester.^{28,29}

The pyrimidine ring, being an electron deficient, resists electrophilic substitution and facilitates nucleophilic addition and substitution reactions.³⁰ A very common approach for the construction of pyrimidine rings is through condensation of 1,3-dicarbonyl compounds with amidines.³¹ However, 2,4,6-triarylpyrimidines are constructed stepwise.³¹ The use of formamide or an ortho ester in combination with ammonia³² as a potential surrogate NCN reagent has been reported in the synthesis of pyrimidines. Tris(formylamino)methanes,³³ 2-amino-2-formylmalonaldehyde³⁴ and 3-methyl-5-nitro-3*H*-pyrimidin-4-one³⁵ have also been used as 1,3-dicarbonyl equivalents in pyrimidine synthesis. Cyclocondensation of amidine with chalcones is one of the most versatile approach for the construction of pyrimidines³⁶ in good yields.

Herein, we report an expedient, and efficient regioselective synthesis of highly congested 2-(2,6-diarylpyrimidin-4-yl)acetonitriles, 2-amino-4-methylsulfanyl-6-arylnicotinonitrile and 4-methylsulfanyl-6-arylpyridin-2-amine in moderate yields through ring transformation of suitably functionalized 2*H*-pyran-2-ones. The methodology is general and flexible to introduce functional groups at appropriate positions by maneuvering the reactants used in the ring transformation reactions.

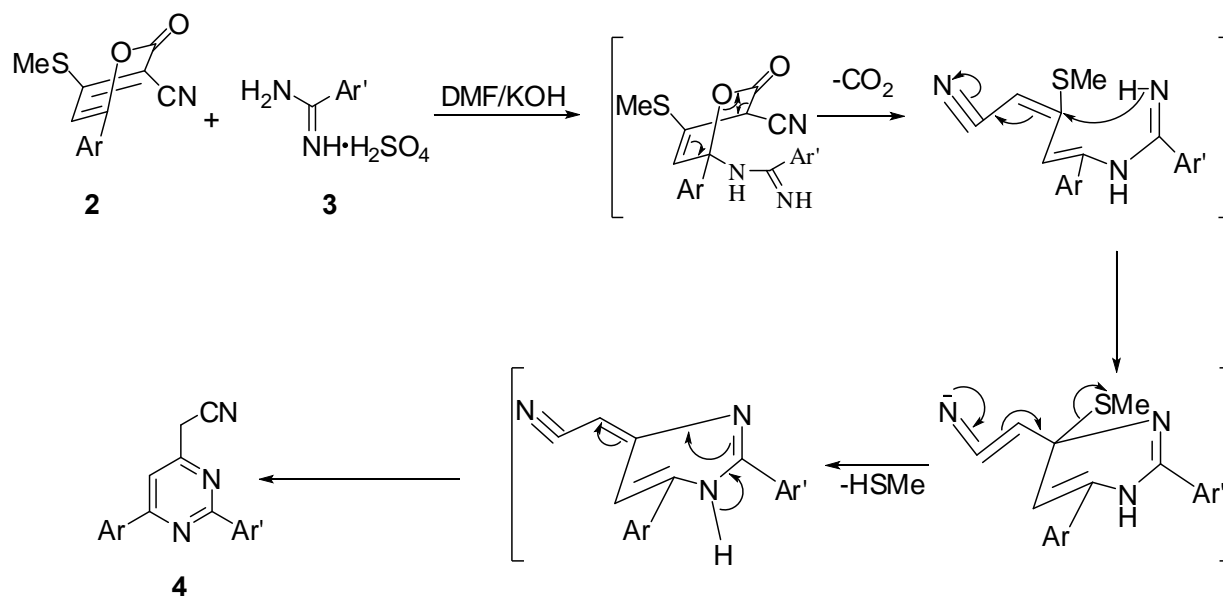
RESULTS AND DISCUSSION

Our synthetic strategy for the construction of highly congested pyrimidines³⁷ is based on the ring transformation of 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**) by arylamidine using powdered KOH as a base in DMF at 30 °C. The 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**) have been conveniently prepared from the reaction of an aryl methyl ketone with methyl 2-cyano-3,3-dimethylthioacrylate (**1**) as described earlier³⁷ (Scheme 1).



Scheme 1

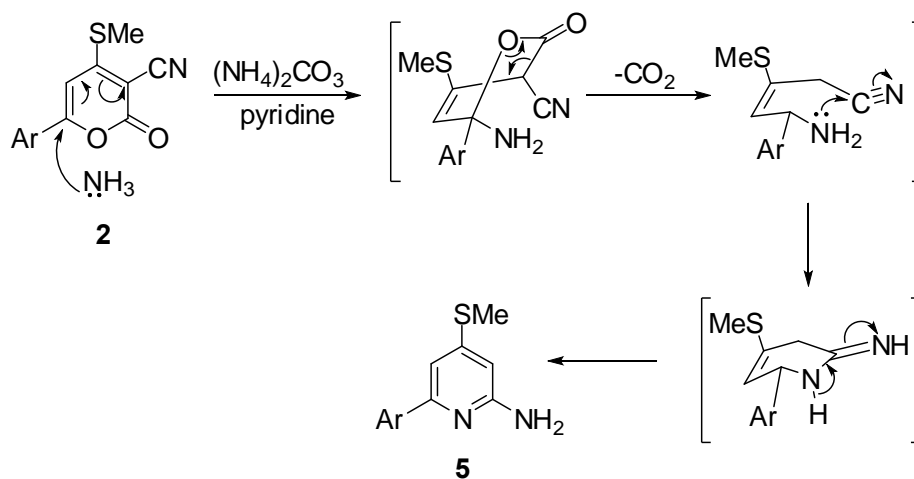
Thus, a mixture of 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**) and arylamidine (**3**) was stirred in DMF in the presence of powdered KOH at room temperature for 3-4 h. The progress of the reaction was monitored by TLC. Thereafter, reaction mixture was poured onto crushed ice with vigorous stirring and neutralized with 10% aqueous HCl. The resulting precipitate was filtered, washed with water and dried. The crude product was purified by column chromatography.



Scheme 2. A plausible mechanism for the formation of 2-(2,6-diarylpyrimidin-4-yl)acetonitriles (**4**)

The major product isolated in moderate yield was identified as (2,6-diarylpyrimidin-4-yl)acetonitrile. As evident from the topography of 2*H*-pyran-2-ones (**2**), that the C-2, C-4, and C-6 positions are electrophilic in nature but position C-6 is highly susceptible to nucleophilic attack due to an extended conjugation and the presence of an electron-withdrawing $-\text{CN}$ substituent at position 3 of the pyran ring. The reaction of **2** with arylamidine has possibly been initiated by the attack of the amino group of amidine at C-6 of the pyran ring with concomitant loss of carbon dioxide followed by recyclization with elimination of the methylmercaptan to yield 2, 6-diaryl-(pyrimidin-4-yl)acetonitrile (**4**) as a major product, Scheme 2.

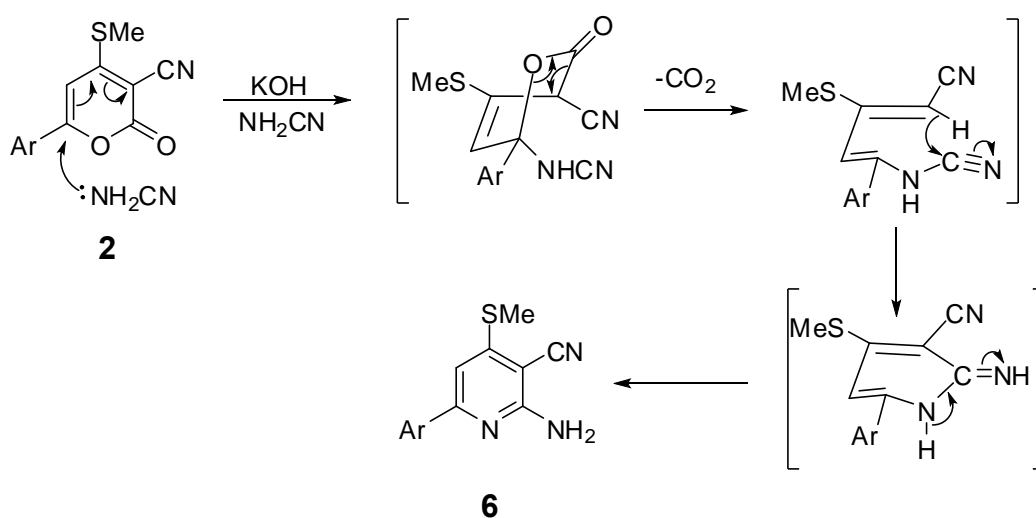
We have also synthesized some highly congested pyridines using two different protocols. 2-amino-4-(methylsulfanyl)-6-arylnicotinonitrile (**5**) was prepared by the reaction of



Scheme 3. A plausible mechanism for the synthesis of 2-amino-4-(methylsulfanyl)-6-arylnicotinonitrile (**5**)

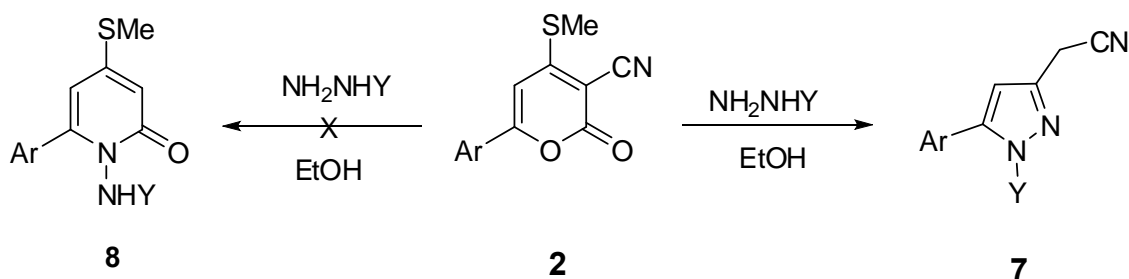
6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**) with ammonium carbonate. The reaction is possibly initiated through Michael addition of NH_3 at C-6 of the pyran ring with concomitant loss of carbon dioxide followed by recyclization to yield 2-amino-4-(methylsulfanyl)-6-arylnicotinonitrile (**5**), Scheme 3.

In another attempt 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**) was treated with cyanamide in DMF using powdered KOH as a base. The reaction was carried under nitrogen atmosphere for 48 hours to yield 2-amino-6-aryl-4-methylsulfanylpuridine (**6**) in good yield, Scheme 4.



Scheme 4. A plausible mechanism for the synthesis of 2-amino-6-aryl-4-methylsulfanylpuridine (**6**)

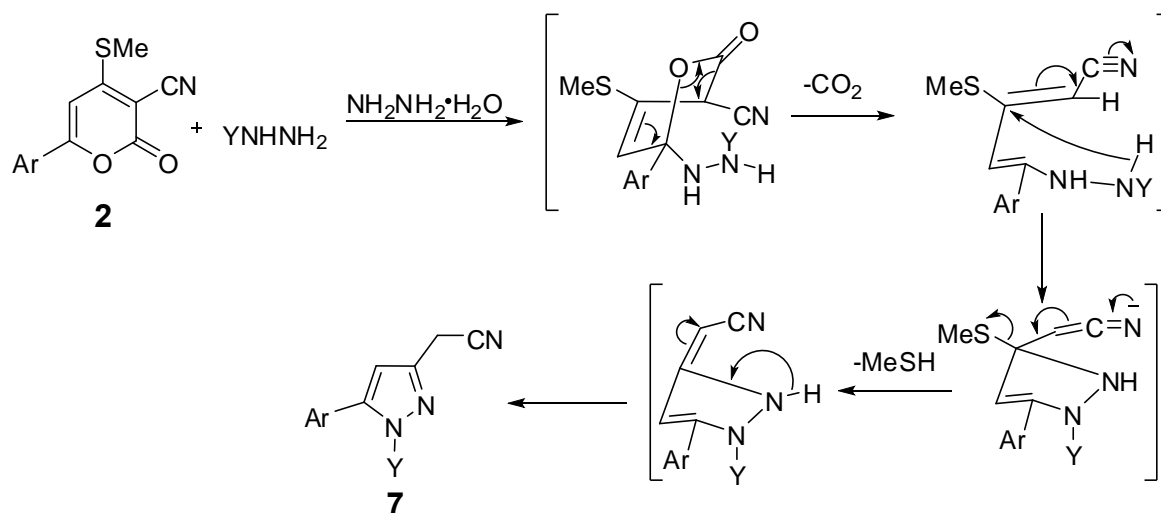
We wanted to make pyridones (**8**) from the reaction of lactone **2** and hydrazine in ethanol at reflux temperature for 4-6 hours but in lieu of anticipated product **8**, 5(3)-aryl-3(5)-cyanomethylpyrazoles (**7**) were isolated in good yields, Scheme 5.



Scheme 5

5-Aryl-3-cyanomethyl-1*H*-pyrazoles (**7**) and their 1-methyl derivatives are often used as precursors for the synthesis of 3-(2-aminoethyl)-5-phenyl-1*H*-pyrazoles and their 1-methyl analogs, which are known to have gastric secretion stimulatory activity without producing any pharmacological action towards histamine.³⁸

The reported procedures for the synthesis of these pyrazole derivatives are multistep and cumbersome.³⁹ In search of novel methodology, our attention was drawn to a report⁴⁰ describing the synthesis of different pyrazoles by reaction of different hydrazines 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**) with hydrazine. 2-Pyranones have three electrophilic centers C-2, C-4 and C-6 in which C-4 and C-6 are more vulnerable to nucleophilic attack. Depending upon the attack of nucleophile either at C-4 or C-6 position, there are possibilities for the formation of two different products. Attack by hydrazine at C-6 leads to the formation of pyrazoles (**7**) in good yields. The plausible mechanism of the reaction is depicted in Scheme 6.



Scheme 6. A plausible mechanism for the synthesis of 5(3)-aryl-3(5)-cyanomethyl-1*H*-pyrazoles (**7**)

Table 1

Product	Compound	Mp (°C)	Yield (%)
4a		144-146	67
4b		120-122	70
4c		155-157	57

continued...

4d		168-170	58
5a		180-182	76
5b		170-172	74
6a		145-147	75
6b		153-155	72
7a		260-262	85
7b		280-283	85
7c		>300	74
7d		>300	69

CONCLUSION

In conclusion, one-pot regioselective synthesis of 2,6-diarylpyrimidines (**4**), 2,6-disubstituted pyridines (**5** and **6**) and 5-aryl-3-cyanomethyl-1*H*-pyrazoles (**7**) through base catalyzed ring transformation of suitably functionalized 2*H*-pyran-2-ones by arylamidines, cyanamide, ammonium carbonate and hydrazines respectively have been developed. Our synthetic strategy for the regioselective synthesis of 2,6-diarylpyrimidines and 2,6-disubstituted pyridines and pyrazoles is highly facile. The procedure is extremely simple, efficient and economically viable. The protocol provides a new avenue for the construction of functionalized pyrimidines, pyridines and pyrazoles which can be further exploited for the synthesis of novel heterocycles.

EXPERIMENTAL

Materials and methods: The reagents and the solvents used in this study were of analytical grade and used without further purification. The melting points were determined on an electrically heated Townson Mercer melting point apparatus and are uncorrected. Commercial reagents were used without purification. ¹H and ¹³C NMR spectra were measured on a Bruker WM-300 (300 MHz) using CDCl₃ and DMSO-*d*₆ solvents. Chemical shift are reported in parts per million shift (δ -value) from Me₄Si (δ 0 ppm for ¹H) or based on the middle peak of the solvent (CDCl₃) (δ 77.00 ppm for ¹³C NMR) as the internal standard. Signal patterns are indicated as s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet. Coupling constant (*J*) are given in Hertz. Infrared (IR) spectra were recorded on a Perkin-Elmer AX-1 spectrophotometer in KBr disc and reported in wave number (cm⁻¹). Fast-atomic bombardment (FAB) and ESIMS spectrometers were used for mass spectra analysis. ¹³C NMR for those compounds which are poorly soluble in DMSO-*d*₆ is not reported.

General procedure for the synthesis of *N*-(3/4-(6-(cyanomethyl)-2-arylpyrimidin-4-yl)phenyl)-acetamide (4**):** A mixture of 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (**2**, 1mmol) and arylamidine (**3**, 1mmol) was stirred in DMF in the presence of powdered KOH (1.2 mmol) at room temperature for 3-4 h. The progress of the reaction was monitored by TLC. Thereafter, reaction mixture was poured onto crushed ice with vigorous stirring and neutralized with 10% aqueous HCl. The resulting precipitate was filtered, washed with water and dried. The crude product was purified by column chromatography using CHCl₃: MeOH as eluent.

***N*-(4-(6-(Cyanomethyl)-2-phenylpyrimidin-4-yl)phenyl)acetamide (**4a**):** Yellow solid, IR (KBr) cm⁻¹: 3377 (>N-H), 2922 (-CH₂), 2223 (-CN), 1628 (>C=O, NHCO); ¹H NMR (300 MHz, DMSO-*d*₆): δ 2.09 (s, 3H, CH₃), 3.57 (s, 2H, CH₂), 6.82 (s, 1H, Ar-H), 7.14 (s, 3H, Ar-H), 7.72 (m, 3H, Ar-H), 8.00 (m, 3H, Ar-H), 10.32 (s, 1H, NH); ESI-HRMS: *m/z* calcd for C₂₀H₁₆N₄O: 328.1324 (M⁺); found: 328.1324 (M⁺).

***N*-3-(6-(Cyanomethyl)-2-phenylpyrimidin-4-yl)phenylacetamide (4b):** Yellow solid, IR (KBr) cm^{-1} : 3323 (>N-H), 3003 (CH_2), 2224 (-CN), 1586 (>C=O, NHCO); ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 2.08 (s, 3H, CH_3), 3.73 (s, 2H, CH_2), 7.18 (s, 2H, Ar-H), 7.51 (m, 2H, Ar-H), 7.78 (m, 2H, Ar-H), 7.87 (m, 2H, Ar-H), 8.12 (m, 2H, Ar-H), 10.19 (s, 1H, NH); ESI-HRMS: m/z calcd for $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}$: 328.1324 (M^+); found: 328.1306 (M^+).

***N*-4-(6-(Cyanomethyl)-2-(pyridin-4-yl)pyrimidin-4-yl)phenylacetamide (4c):** Brown solid, IR (KBr) cm^{-1} : 3455 (>N-H), 2922 (- CH_2), 2199 (-CN), 1660 (>C=O, NHCO); ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 2.06 (s, 3H, CH_3), 3.99 (s, 2H, - CH_2), 6.83 (s, 1H, Ar-H), 7.79 (d, $J = 9$ Hz, 2H, Ar-H), 8.01 (d, $J = 9$ Hz, 2H, Ar-H), 8.15 (d, $J = 6$ Hz, 2H, Ar-H), 8.35 (d, $J = 2$ Hz, 2H, Ar-H), 10.24 (s, 1H, NH); ESI-HRMS: m/z calcd for $\text{C}_{19}\text{H}_{15}\text{N}_5\text{O}$: 329.1277 (M^+); found: 329.1274 (M^+).

***N*-3-(6-(Cyanomethyl)-2-(pyridin-4-yl)pyrimidin-4-yl)phenylacetamide (4d):** Light brown solid, IR (KBr) cm^{-1} : 3450 (>N-H), 2930 (- CH_2), 2238 (-CN), 1632 (>C=O, NHCO); ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 2.06 (s, 3H, CH_3), 3.99 (s, 2H, - CH_2), 6.85 (s, 1H, Ar-H), 7.30 (m, 1H, Ar-H), 7.50 (m, 3H, Ar-H), 7.94 (m, 3H, Ar-H), 8.12 (s, 1H, Ar-H), 10.24 (s, 1H, NH); ESI-HRMS: m/z calcd for $\text{C}_{19}\text{H}_{15}\text{N}_5\text{O}$: 329.1277 (M^+); found: 329.1276 (M^+), 330.1312.

General procedure for the synthesis of *N*-(3/4-(6-amino-4-(methylsulfanyl)pyridin)-2-yl)phenylacetamide (5): A mixture of 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (2,1 mmol) and ammonium carbonate (1 mmol) was refluxed in pyridine (10 mL) for 6-8 h. The progress of the reaction was monitored by TLC, The reaction mixture reduced to half by evaporating the excess pyridine. Thereafter it was poured onto crushed ice with vigorous stirring and neutralized with 10% aqueous HCl. The resulting precipitate was filtered, washed with water and dried. The crude product was purified by column chromatography using CHCl_3 : MeOH as eluent.

***N*-4-(6-Amino-4-(methylsulfanyl)pyridin)-2-yl)phenylacetamide (5a):** Brown solid, IR (KBr) cm^{-1} : 3477, 3446 (>N-H), 1610 (>C=O, NHCO); ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 2.09 (s, 3H, CH_3), 2.83 (s, 3H, SCH_3), 4.83 (s, 2H, NH_2), 6.87 (s, 2H, Ar-H), 7.69 (d, $J = 9$ Hz, 2H, Ar-H), 7.89 (d, $J = 9$ Hz, 2H, Ar-H), 10.32 (s, 1H, NH); ESI-HRMS: m/z calcd for $\text{C}_{14}\text{H}_{15}\text{N}_3\text{OS}$: 273.0936 (M^+); found: 273.0966 (M^+).

***N*-3-(6-Amino-4-(methylsulfanyl)pyridin)-2-yl)phenylacetamide (5b):** Brown solid, IR (KBr) cm^{-1} : 3575, 3470 (>N-H), 2322, 1610 (>C=O, NHCO); ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 1.96 (s, 3H, CH_3), 2.93 (s, 3H, SCH_3), 4.49 (s, 2H, NH_2), 6.51 (s, 1H, Ar-H), 7.13 (s, 2H, Ar-H), 7.30 (s, 1H, Ar-H), 7.49 (s, 1H, Ar-H), 7.69 (d, $J = 8.1$ Hz, 1H, Ar-H), 8.164 (d, $J = 8.1$ Hz, 1H, Ar-H) 10.014 (s, 1H, NH); ESI-HRMS: m/z calcd for $\text{C}_{14}\text{H}_{15}\text{N}_3\text{OS}$: 274.0969 ($\text{M}^+ + 1$); found: 274.0968 ($\text{M}^+ + 1$).

General procedure for the synthesis of *N*-(3/4-(6-amino-5-cyano-4-(methylsulfanyl)pyridin)-2-yl)phenylacetamide (6): A mixture of 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles (2,1 mmol) and cyanamide (1 mmol) was stirred in DMF (8 mL) in the presence of powdered KOH (1.2 mmol)

for 48 h under nitrogen atmosphere. The progress of the reaction was monitored by TLC. Thereafter, reaction mixture was poured onto crushed ice with vigorous stirring and neutralized with 10% aqueous HCl. The resulting precipitate was filtered, washed with water and dried. The crude product was purified by column chromatography using CHCl_3 : MeOH as eluent.

***N*-(4-(6-Amino-5-cyano-4-(methylsulfanyl)pyridin)-2-yl)phenyl)acetamide (6a):** Brown solid, IR (KBr) cm^{-1} : 3477, 3446 (>N-H), 2182 (CN), 1610 (>C=O, NHCO); ^1H NMR (300 MHz, DMSO- d_6): δ 1.98 (s, 3H, CH_3), 2.76 (s, 3H, SCH_3), 4.45 (bs, 2H, Ar- NH_2), 6.64 (s, 1H, Ar-H), 7.36 (s, 1H, Ar-H), 7.56 (s, 1H, Ar-H), 7.72 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 10.08 (s, 1H, NHCO); ^{13}C NMR (300 MHz, DMSO- d_6): δ 14.66, 24.04, 88.34, 100.95, 118.88, 119.21, 127.25 (2C), 134.06, 137.33, 151.32, 158.30 (2C), 161.65, 168.88; ESI-HRMS: m/z calcd for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{OS}$: 298.0888 (M^+); found: 298.0883 (M^+).

***N*-(3-(6-Amino-5-cyano-4-(methylsulfanyl)pyridin)-2-yl)phenyl)acetamide (6b):** Brown solid, IR (KBr) cm^{-1} : 3575, 3470 (>N-H), 1610 (>C=O, NHCO); ^1H NMR (300 MHz, DMSO- d_6): δ 1.98 (s, 3H, CH_3), 2.83 (s, 3H, SCH_3), 4.55 (s, 2H, NH_2), 6.60 (s, 1H, Ar-H), 7.73 (s, 1H, Ar-H), 7.87 (s, 3H, Ar-H), 10.08 (s, 1H, NHCO); ^{13}C NMR (100 MHz, DMSO- d_6): δ 14.66, 24.04, 88.34, 100.95, 118.88, 119.21, 120.22, 124.24, 129.55, 135.06, 138.33, 158.30 (2C), 161.65, 168.98; ESI-HRMS: m/z calcd for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{OS}$: 298.0888 (M^+); found: 298.0883 (M^+).

General procedure for the synthesis of *N*-(3/4-(3-(cyanomethyl)-1H-pyrazol-5-yl)phenyl)acetamide (7): A mixture of 6-aryl-4-methylsulfanyl-2H-pyran-2-one-3-carbonitriles (2,1 mmol) and hydrazine (1 mmol) was refluxed in ethanol (10 mL) for 3-4 h. The progress of the reaction was monitored by TLC. The reaction mixture cooled to room temperature. The precipitate was filtered, washed with alcohol and dried. The crude product was purified by column chromatography using CHCl_3 : MeOH as eluent.

***N*-(4-(3-(Cyanomethyl)-1H-pyrazol-5-yl)phenyl)acetamide (7a):** Light brown solid, IR (KBr) cm^{-1} : 3377 (>N-H), 1628, 1599 (>C=O, NHCO); ^1H NMR (300 MHz, DMSO- d_6): δ 1.96 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 6.48 (s, 1H, Ar-H), 7.62 (s, 4H, Ar-H), 10.05 (s, 1H, NH), 13.09 (s, 1H, N-H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 16.66, 24.04, 100.95, 188.88, 119.21 (2C), 125.65 (2C), 126.25, 139.33, 145.33, 151.34, 168.48; ESI-HRMS: m/z calcd for $\text{C}_{13}\text{H}_{12}\text{N}_4\text{O}$: 240.1011 (M^+); found: 240.1015 (M^+).

***N*-(3-(3-(Cyanomethyl)-1H-pyrazol-5-yl)phenyl)acetamide (7b):** Brown solid, IR (KBr) cm^{-1} : 3323 (>N-H), 1560 (>C=O, NHCO); ^1H NMR (300 MHz, DMSO- d_6): δ 1.96 (s, 3H, CH_3), 3.88 (s, 3H, CH_2), 6.38 (s, 1H, Ar-H), 7.69 (s, 4H, Ar-H), 10.05 (s, 1H, NH), 13.09 (s, 1H, N-H); ESI-HRMS: m/z calcd for $\text{C}_{13}\text{H}_{12}\text{N}_4\text{O}$: 240.1011 (M^+); found: 240.1010 (M^+).

***N*-(4-(3-(Cyanomethyl)-1-(2,4-dinitrophenyl)pyrazol-5-yl)phenyl)acetamide (7c):** Brown solid, IR (KBr) cm^{-1} : 3323 (>N-H), 1560 (>C=O, NHCO); ^1H NMR (300 MHz, DMSO- d_6): δ 1.96 (s, 3H, CH_3), 3.88 (s, 3H, CH_2), 6.48 (s, 1H, Ar-H), 7.56 (s, 7H, Ar-H), 10.05 (s, 1H, NH); ESI-HRMS: m/z calcd for $\text{C}_{19}\text{H}_{14}\text{N}_6\text{O}_5$: 406.1026 (M^+); found: 406.1022 (M^+).

***N*-(3-(3-(Cyanomethyl)-1-(2,4-dinitrophenyl)pyrazol-5-yl)phenyl)acetamide (7d)**: Light brown solid, IR (KBr) cm^{-1} : 3323 (>N-H), 1560 (>C=O, NHCO); ^1H NMR (300 MHz, DMSO- d_6): δ 1.96 (s, 3H, CH₃), 3.88 (s, 2H, CH₂), 6.48 (s, 1H, Ar-H), 7.56 (s, 7H, Ar-H), 10.05 (s, 1H, NHCO); ESI-HRMS: m/z calcd for C₁₉H₁₄N₆O₅: 406.1026 (M⁺); found: 406.1032 (M⁺).

ACKNOWLEDGEMENTS

Pushyamitra is thankful to CST, UP, India for sponsoring the Project, No. CST/SERPD//D-3433 and Sandeep is thankful to DST, New Delhi for INSPIRE Fellowship [IF10379]. Authors' are also thankful to CDRI SAIF division, Lucknow, India for providing spectroscopic data.

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