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Synthesis of bridgedhead azolo[3,2-*a*]pyrimidines and imidazo[2,1-*b*]thiazines through ring transformation of 2*H*-pyran-2-ones☆

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Abstract—Suitably functionalized 3-carbomethoxy/cyano-2*H*-pyran-2-ones are excellent synthons for the synthesis of arenes and heteroarenes of therapeutic importance. The compounds 6-aryl-3-cyano-4-methylsulfanyl-2*H*-pyran-2-ones have been transformed into bridgedhead azolopyrimidines and imidazothiazines through thermal and base-induced ring transformation reactions with aminoazoles and imidazolidin-2-thiones, respectively.

1. Introduction

Bridgedhead azolopyrimidines, azolothiazines and their isosteres occupy a unique place in medicinal chemistry due to their wide application as drug and drug-intermediates. Diverse pharmacological activities such as antiviral,[1] antimicrobial,[2–4] antiinflammatory,[5] cardiotonic,[6] diuretic,[7] antirheumatic,[8] antidepressant,[9] immunomodulator,[10] antileishmanial,[11] antiarthretic,[12] antihypertensive,[13] and various others[14–18] are associated with functionalized thiazolo[3,2-*a*]pyrimidine, thiadiazolo[3,2-*a*]pyrimidine and imidazo[2,1-*b*]thiazine derivatives. The wide-range of biological activities associated with these classes of compounds prompted chemists to develop an efficient, general synthesis.

Our prime objective was to develop an innovative and economical route for the synthesis of these heterocycles, which could offer scope for substituent variation and structural modification. The literature procedures for the synthesis of the thiazolo[3,2-*a*]pyrimidine ring system usually involve the cyclocondensation of 2-thiouracil with either α-haloalkylesters[18] or α-haloketones.[6b] A reaction of 2-aminothiazole with allene-1,3-dicarboxylic ester,[19] Meldrum's acid,[20] malonic ester,[10a] or methyl acetoacetate separately[21] led to the synthesis of thiazolo[3,2-*a*]pyrimidine derivatives. Further, these have also been synthesized from the reaction of 2-aminothiazoline with acetylenic carboxylate.[22] In addition, a reaction of 2-thioxo-1,2,3,4-tetrahydropyrimidine with phenacyl bromide[23] in glacial acetic acid also afforded the desired class of compound. Recently, these compounds have been prepared from the reaction of 2-imino-4-thiazolidinones with activated nitriles.[24]

Thiadiazolo[3,2-*a*]pyrimidines have been synthesized earlier either by Michael addition followed by sequential cyclocondensation reaction of the benzylidene oxazolone and aminoarylthiadiazole[3d] or by inter-molecular condensation of aminothiadiazole with malonic acid followed by intramolecular cyclization in presence of dehydrating agent.[4] These compounds have also been obtained from the reaction of aminothiadiazoles with bis(2,4,6-trichlorophenyl)malonate[3c] or with ethyl arylideneacetoacetate[6b] separately. Cyclization of thiadiazolylbutanamides has also afforded the target compounds.[25]

Earlier, imidazo[2,1-*b*]thiazine derivatives have been prepared either by cyclization of substituted *N*-alkyl-2-thioimidazolidines in the presence of methyl sulfonic acid[4c] or by cyclocondensation reaction of thiohydantoin with haloalkanes[26] under an inert atmosphere. They have also been prepared from the reaction of imidazol-2-thione with dimethyl acetylenedicarboxylate[27] or the condensation of thiourea with β-propiolactam[28] or unsaturated acid chlorides.[29] Recently, they have been synthesized by Michael type of reaction of benzylidene-5-oxazolone with imidazolidinone[3e] and by base-catalyzed cyclization of cyanomethyl derivative of 2-mercaptoimidazole.[30]

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Keywords: azolo[3,2-*a*]pyrimidine; imidazo[2,1-*b*]thiazines; 2*H*-pyran-2-one.
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The reported procedures for the synthesis of these classes of heterocycles did not offer an easy access to substituent variation at different positions in their ring skeleton. Our methodology is very simple, convenient and economical and provides flexibility of introducing various functionalities into the molecular architecture.

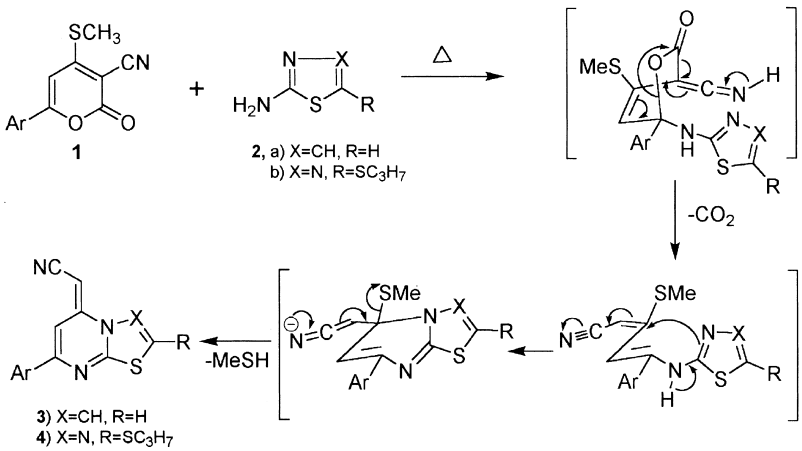
In this paper, we report a new convenient synthesis of thiazolo[3,2-*a*]pyrimidines (**3a**–**h**) and thiadiazolo[3,2-*a*]pyrimidines (**4a**–**g**) through thermally-induced ring transformation of suitably functionalized 2*H*-pyran-2-ones (**1**) with 2-aminoazoles (**2**). Under similar reaction conditions, a reaction of **1** with imidazolidin-2-thione (**5**) did not yield imidazo[2,1-*b*]thiazines (**6a**–**h**), but base-catalyzed ring transformations afforded the desired products in good yields.

2. Results and discussion

Over the last few years, we have been involved in exploring the synthetic potential and limitations of 3-carbomethoxy/cyano-4-methylsulfanyl-2*H*-pyran-2-ones as a novel synthon for generating molecular diversity. Several innovative routes for the synthesis of arenes[31] and heteroarenes[32] have been developed through ring transformation of suitably functionalized 2*H*-pyran-2-ones with various nucleophiles. The advantage of the procedure lies in creation of diverse pharmacologically active entities by a very convenient and economical method, which is normally difficult by conventional routes.

The 2*H*-pyran-2-ones (**1**) used as a parent precursor have been prepared by the reaction of methyl 2-cyano-3,3-dimethylthioacrylate with acetophenone as described earlier.[33] The unique features of lactone **1** is the presence of three electrophilic centres; C_2, C_4 and C_6 in which latter is highly susceptible to nucleophiles due to the extended conjugation and the presence of the electron withdrawing substituent at position 3. Our approach to synthesize thiazolo[3,2-*a*]pyrimidine (**3**) and thiadiazolo[3,2-*a*]pyrimidine (**4**) involves the fusion of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-one (**1**) with 2-aminothiazole (**2a**) or 2-aminothiadiazole (**2b**), respectively, at 100–130°C without using any solvent (Scheme 1). The reaction is possibly initiated by attack of the nitrogen nucleophile on the highly vulnerable electrophilic center C_6, followed by decarboxylation and ring opening. The ring opened intermediate thus generated in situ re-cyclizes involving C_4 of the pyran ring and the ring nitrogen of **2a** or **2b**, followed by the elimination of methyl mercaptan to yield [7-arylthiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (**3a**–**h**) and [7-aryl-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (**4a**–**g**) in good yields (Scheme 1).

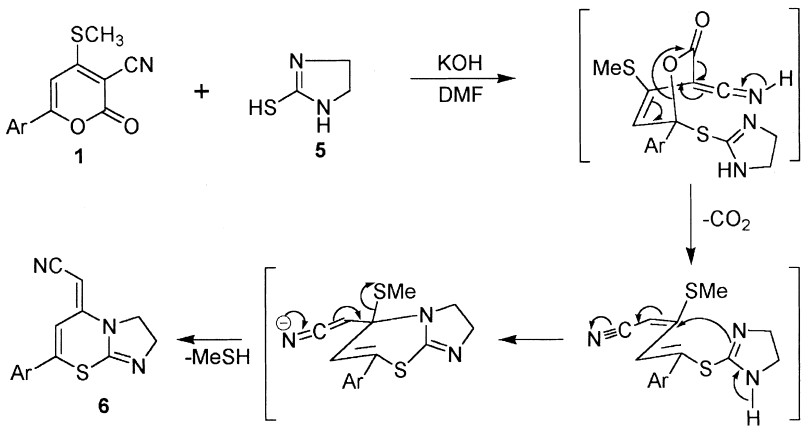
Similarly, a reaction of 2*H*-pyran-2-one (**1**) with imidazolidin-2-thione (**5**) was carried out at 100°C by direct fusion but the reaction did not occur smoothly and, afforded a mixture of compounds possibly due to competitive reaction at both the N,S-nucleophilic centers. It is obvious that sulfur is a better nucleophile than nitrogen and thus at ambient temperature reaction does not afford the nitrogen nucleophile-induced product. The reaction of 2*H*-pyran-2-one with **5** in the presence of powdered KOH in DMF at room temperature was carried out, which afforded the expected product (**6**) in good yield. The plausible mechanism of the reaction is depicted in Scheme 2. The reaction is initiated by attack of the sulfur nucleophile at C_6 of the pyran ring, followed by decarboxylation, ring opening and recyclization involving C_4 of **1** and the ring nitrogen of the imidazole to yield 2-[7-aryl-2,3-dihydro-5*H*-imidazo-[2,1-*b*][1,3]-thiazin-5-ylidene]acetonitrile (**6a**–**h**) in good yields.



3	Ar	Yield (%)
a	3-ClC_6H_4	77
b	4-ClC_6H_4	74
c	4-FC_6H_4	75
d	4-BrC_6H_4	76
e	3-$NO_2C_6H_4$	71
f	4-$NO_2C_6H_4$	78
g	2-furyl	75
h	2-thienyl	78

4	Ar	Yield (%)
a	3-ClC_6H_4	72
b	4-ClC_6H_4	75
c	4-BrC_6H_4	74
d	4-$CH_3OC_6H_4$	73
e	4-$CH_3C_6H_4$	74
f	3-pyridyl	73
g	4-pyridyl	73

Scheme 1.



6	Ar	Yield (%)
a	3-ClC_6H_4	73
b	4-ClC_6H_4	73
c	4-FC_6H_4	74
d	4-BrC_6H_4	72
e	3-$NO_2C_6H_4$	67
f	4-$NO_2C_6H_4$	70
g	2-furyl	74
h	2-thienyl	77

Scheme 2.

The configuration of geometrical isomers in **3**, **4** and **6** was also ascertained by ^{1}H NOE experiments. The ^{1}H NMR spectrum for compound **3b** showed two singlets at δ 4.24 (=CH–CN), 7.18 (H6) and a doublet at δ 7.12 (H3). Selective pre-irradiation of the methine proton resonance at δ 4.24 enhances the signal intensity at δ 7.12 for H3 proton without any change in the signal intensity for H6 proton, confirming the *trans* configuration of the isolated compound. Similarly, the ^{1}H NMR spectrum of [7-(4-bromophenyl)-2-propylthio-1,3,4-thiadiazolo-[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (**4k**) showed two singlets at δ 4.76 (=CH–CN) and 7.09 (H6 proton). Selective pre-irradiation of the methine proton in NOE experiment did not affect the intensity of H6 proton, confirming the *E*-configuration of the isolated compound. The *E*-geometry of the isolated compounds was in accord with our past observation from X-ray diffraction of a similar type of ring-transformed product of 2*H*-pyran-2-one and cyclic ketene aminal.[34]

In summary, we have described an efficient and convenient procedure for the preparation of thiazolo[3,2-*a*]pyrimidines, thiadiazolo[3,2-*a*]pyrimidines and imidazo[2,1-*b*]thiazines through ring transformation reactions of 2*H*-pyran-2-ones.

3. Experimental

3.1. General

Melting points were determined on Büchi-530 capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Brucker WM 300 MHz spectrometer in deuterated solvents with TMS as internal reference. IR spectra of all the compounds were recorded on Perkin–Elmer AC-1 spectrophotometer. Mass spectra of all compounds were measured with Jeol JMS-D 300 spectrometer (70 eV). Microanalyses were determined on Carlo Erba EA-1108 element analyzer within $\pm$0.5% of the theoretical values. Thin layer chromatography was performed on 7 cm×3 cm precoated silica gel plastic plates. For column chromatography silica gel of 60–120 mesh from Acme Synthetic Chemicals, Bombay, India was used.

3.2. Synthesis of [7-arylthiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3a–h). General procedure. A mixture of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-ones (**1**, 1 mmol) and 2-aminothiazole (**2a**, 100 mg, 1 mmol) was fused at 100°C for four hours. The fused product was dissolved in chloroform and purified by silica gel column chromatography using chloroform/hexane (3:2) as eluent.

3.2.1. [7-(3-Chlorophenyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3a). Light brown powder; mp 179–181°C; [Found: C, 58.52; H, 2.54; N, 14.43. $C_{14}H_8ClN_3S$ requires C, 58.84; H, 2.82; N, 14.70%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 8.02 (1H, s, Ph), 7.84 (1H, d, *J*=8.2 Hz, Ph), 7.44–7.42 (1H, m, Ph), 7.24 (1H, d, *J*=8.2 Hz, Ph), 7.12 (1H, s, C*H*–C=CHCN), 7.10 (1H, d, *J*=5.1 Hz, S–C*H*), 7.06 (1H, d, *J*=5.1 Hz, S–CH=C*H*), 4.22 (1H, s, C*H*CN); *m*/*z* (EI) 287 (M^++2, 52), 286 (M^++1, 23), 285 (M^+, 100), 221 (43%).

3.2.2. [7-(4-Chlorophenyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3b). Light brown powder; mp 179–180°C; [Found: C, 58.36; H, 2.39; N, 14.28. $C_{14}H_8ClN_3S$ requires C, 58.84; H, 2.82; N, 14.70%]; ν_{max} (KBr) 2200 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.66 (2H, d, *J*=8.2 Hz, Ph), 7.52 (2H, d, *J*=8.2 Hz, Ph), 7.18 (1H, s, C*H*–C=CHCN), 7.16 (1H, d, *J*=5.1 Hz, S–C*H*), 7.12 (1H, d, *J*=5.1 Hz, S–CH=C*H*), 4.24 (1H, s, C*H*CN); *m*/*z* (EI) 287 (M^++2, 49), 286 (M^++1, 22), 285 (M^+, 100%).

3.2.3. [7-(4-Fluorophenyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3c). Yellow powder; mp183–185°C; [Found: C, 62.02; H, 2.73; N, 15.42. $C_{14}H_8FN_3S$ requires C,

62.43; H, 2.99; N, 15.60%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 8.04–8.02 (2H, m, Ph), 7.20 (1H, s, C*H*–C═CHCN), 7.16 (2H, t, *J*=6.2 Hz, Ph), 7.08 (1H, d, *J*=5.2 Hz, S–C*H*), 7.04 (1H, d, *J*=5.2 Hz, S–CH═C*H*), 4.18 (1H, s, C*H*CN); *m/z* (EI) 269 (M^+, 52%).

3.2.4. [7-(4-Bromophenyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3d). Light brown powder; mp 200–201°C; [Found: C, 50.69; H, 1.98; N, 12.38. $C_{14}H_8BrN_3S$ requires C, 50.92; H, 2.44; N, 12.72%]; ν_{max} (KBr) 2200 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.96 (2H, d, *J*=8.4 Hz, Ph), 7.60 (2H, d, *J*=8.4 Hz, Ph), 7.12 (1H, s, C*H*–C═CHCN), 7.10 (1H, d, *J*=5.1 Hz, S–C*H*), 7.04 (1H, d, *J*=5.1 Hz, S–CH═C*H*), 4.26 (1H, s, C*H*CN); *m/z* (EI) 331 (M^++2, 32), 286 (M^++1, 14), 329 (M^+, 72), 183 (13%).

3.2.5. [7-(3-Nitrophenyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3e). Light brown powder; mp 234–235°C; [Found: C, 56.31; H, 2.42; N, 18.48. $C_{14}H_8N_4O_2S$ requires C, 56.75; H, 2.72; N, 18.90%]; ν_{max} (KBr) 2215 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 8.92 (1H, s, Ph), 7.80 (1H, d, *J*=8.0 Hz, Ph), 7.74–7.72 (1H, m, Ph), 7.68 (1H, d, *J*=8.0 Hz, Ph), 7.12 (1H, s, C*H*–C═CHCN), 7.10 (1H, d, *J*=5.0 Hz, S–C*H*), 7.06 (1H, d, *J*=5.0 Hz, S–CH═C*H*), 4.28 (1H, s, C*H*CN); *m/z* (EI) 296 (M^+, 79), 261 (35), 249 (24), 221 (21%).

3.2.6. [7-(4-Nitrophenyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3f). Light brown powder; mp 204–205°C; [Found: C, 56.56; H, 2.43; N, 18.51. $C_{14}H_8N_4O_2S$ requires C, 56.75; H, 2.72; N, 18.90%]; ν_{max} (KBr) 2215 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.72 (2H, d, *J*=8.4 Hz, Ph), 7.68 (2H, d, *J*=8.4 Hz, Ph), 7.13 (1H, s, C*H*–C═CHCN), 7.10 (1H, d, *J*=5.1 Hz, S–C*H*), 7.06 (1H, d, *J*=5.1 Hz, S–CH═C*H*), 4.30 (1H, s, C*H*CN); *m/z* (EI) 296 (M^+, 100), 261 (43), 249 (11), 221 (16%).

3.2.7. [7-(2-Furyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]-acetonitrile (3g). Off-white powder; mp 202–203°C; [Found: C, 59.80; H, 3.15; N, 17.68. $C_{12}H_7N_3OS$ requires C, 59.73; H, 2.92; N, 17.41%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.56 (1H, d, *J*=3.2 Hz, O–C*H*), 7.18 (1H, d, *J*=3.2 Hz, O–CH═CH–C*H*), 7.10 (1H, s, C*H*–C═CHCN), 7.06 (1H, d, *J*=5.1 Hz, S–C*H*), 7.02 (1H, d, *J*=5.1 Hz, S–CH═C*H*), 6.59 (1H, t, *J*=2.4 Hz, O–CH═C*H*), 4.16 (1H, s, C*H*CN); *m/z* (EI) 241 (M^+, 56), 211 (19), 196 (11), 179 (21%).

3.2.8. [7-(2-Thienyl)thiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (3h). Light brown powder; mp 178–180°C; [Found: C, 55.89; H, 2.54; N, 16.11. $C_{12}H_7N_3S_2$ requires C, 56.00; H, 2.74; N, 16.32%]; ν_{max} (KBr) 2215 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.46 (1H, d, *J*=5.0 Hz, S–C*H*), 7.28 (1H, d, *J*=5.0 Hz, S–CH═CH–C*H*), 7.12 (1H, s, C*H*–C═CHCN), 7.10 (1H, d, *J*=5.1 Hz, S–C*H*), 7.06 (1H, d, *J*=5.1 Hz, S–CH═C*H*), 7.0–6.98 (1H, m, S–CH═C*H*), 4.16 (1H, s, C*H*CN); *m/z* (EI) 257 (M^+, 100%).

3.3. Synthesis of [7-aryl-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4a–g). General procedure. A mixture of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-ones (**1**, 1 mmol) and 2-amino-5-propylthio-1,3,4-thiadiazole (**2b**, 175 mg, 1 mmol) was fused at 130°C for four hours. The fused reaction product was dissolved in $CHCl_3$ and purified on silica gel column, using chloroform/hexane (1:1) as eluent.

3.3.1. [7-(3-Chlorophenyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4a). Light brown powder; mp 154–155°C; [Found: C, 53.06; H, 3.41; N, 15.26. $C_{16}H_{13}ClN_4S_2$ requires C, 53.25; H, 3.63; N, 15.52%]; ν_{max} (KBr) 2215 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 8.02 (1H, s, Ph), 7.84 (1H, d, *J*=8.2 Hz, Ph), 7.44–7.42 (1H, m, Ph), 7.25 (1H, d, *J*=8.2 Hz, Ph), 7.03 (1H, s, C*H*–C═CHCN), 4.69 (1H, s, C*H*CN), 3.16 (2H, t, *J*=6.2 Hz, S–CH_2), 1.84–1.75 (2H, m, S–CH_2CH_2), 1.03 (3H, t, *J*=6.3 Hz, CH_3); *m/z* (EI) 362 (M^++2, 51), 361 (M^++1, 24), 360 (M^+, 100), 318 (19), 286 (20), 278 (15%).

3.3.2. [7-(4-Chlorophenyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4b). Light brown powder; mp 199–200°C; [Found: C, 53.12; H, 3.39; N, 15.19. $C_{16}H_{13}ClN_4S_2$ requires C, 53.25; H, 3.63; N, 15.52%]; ν_{max} (KBr) 2192 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.81 (2H, d, *J*=8.2 Hz, Ph), 7.44 (2H, d, *J*=8.2 Hz, Ph), 7.08 (1H, s, C*H*–C═CHCN), 4.75 (1H, s, C*H*CN), 3.18 (2H, t, *J*=6.2 Hz, S–CH_2), 1.86–1.75 (2H, m, S–CH_2CH_2), 1.03 (3H, t, *J*=6.3 Hz, CH_3); *m/z* (EI) 362 (M^++2, 54), 361 (M^++1, 23), 360 (M^+, 100), 317 (26), 285 (24) 276 (35%).

3.3.3. [7-(4-Bromophenyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4c). Light brown powder; mp 168–170°C; [Found: C, 47.08; H, 2.95; N, 13.45. $C_{16}H_{13}BrN_4S_2$ requires C, 47.41; H, 3.23; N, 13.82%]; ν_{max} (KBr) 2195 cm^{-1} δ_H (200 MHz, $CDCl_3$) 7.84 (2H, d, *J*=8.4 Hz, Ph), 7.60 (2H, d, *J*=8.4 Hz, Ph), 7.09 (1H, s, C*H*–C═CHCN), 4.76 (1H, s, C*H*CN), 3.28 (2H, t, *J*=6.2 Hz, S–CH_2), 1.93–1.78 (2H, m, S–CH_2CH_2), 1.06 (3H, t, *J*=6.3 Hz, CH_3); *m/z* (EI) 406 (M^++2, 50), 405 (M^++1, 22), 404 (M^+, 100%).

3.3.4. [7-(4-Methoxyphenyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4d). Light brown powder; mp 210–211°C; [Found: C, 57.03; H, 4.16; N, 15.58. $C_{17}H_{16}N_4OS_2$ requires C, 57.28; H, 4.52; N, 15.72%]; ν_{max} (KBr) 2195 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.88 (2H, d, *J*=8.3 Hz, Ph), 7.03 (1H, s, C*H*–C═CHCN), 6.96 (2H, d, *J*=8.3 Hz, Ph), 4.69 (1H, s, C*H*CN), 3.69 (3H, s, OCH_3), 3.31 (2H, t, *J*=6.2 Hz, S–CH_2), 1.96–1.78 (2H, m, S–CH_2CH_2), 1.06 (3H, t, *J*=6.2 Hz, CH_3); *m/z* (EI) 356 (M^+, 100%).

3.3.5. [7-(4-Methylphenyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4e). Pale yellow powder; mp 145–50°C; [Found: C, 59.69; H, 4.57; N, 16.18. $C_{17}H_{16}N_4S_2$ requires C, 59.97; H, 4.74; N, 16.45%]; ν_{max} (KBr) 2195 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 7.80 (2H, d, *J*=8.1 Hz, Ph), 7.22 (2H, d, *J*=8.1 Hz, Ph), 7.09 (1H, s, C*H*–C═CHCN), 4.71 (1H, s, C*H*CN), 3.28 (2H, t, *J*=6.2 Hz, S–CH_2), 2.40 (3H, s, CH_3), 1.97–1.78 (2H, m, S–CH_2CH_2), 1.06 (3H, t, *J*=6.2 Hz, CH_3); *m/z* (EI) 340 (M^+, 100%).

3.3.6. [7-(3-Pyridyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene] acetonitrile (4f). Reddish brown powder; mp 153–155°C; [Found: C, 54.92; H, 3.82; N, 21.09. $C_{15}H_{13}N_5S_2$ requires C, 55.02; H, 4.00; N, 21.38%]; ν_{max} (KBr) 2195 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 9.04 (1H, s, Py), 8.63 (1H, d, *J*=4.8 Hz, Py), 8.54 (1H, d, *J*=8.0 Hz, Py), 7.56 (1H, dd, *J*=4.8 Hz, Py), 7.09 (1H, s, C*H*–C=CHCN), 4.67 (1H, s, C*H*CN), 3.32 (2H, t, *J*=6.2 Hz, S–CH_2), 1.94–1.78 (2H, m, S–CH_2CH_2), 1.06 (3H, t, *J*=6.2 Hz, CH_3); *m/z* (EI) 327 (M^+, 100), 249 (49%).

3.3.7. [7-(4-Pyridyl)-2-propylthio-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-ylidene]acetonitrile (4g). Reddish brown powder; mp 149–150°C; [Found: C, 55.22; H, 4.26; N, 21.52. $C_{15}H_{13}N_5S_2$ requires C, 55.02; H, 4.00; N, 21.38%]; ν_{max} (KBr) 2195 cm^{-1} (CN); δ_H (200 MHz, $CDCl_3$) 8.72 (2H, d, *J*=6.3 Hz, Py), 7.84 (2H, d, *J*=6.3 Hz, Py), 7.10 (1H, s, C*H*–C=CHCN), 4.73 (1H, s, C*H*CN), 3.29 (2H, t, *J*=6.2 Hz, S–CH_2), 1.97–1.79 (2H, m, S–CH_2CH_2), 1.07 (3H, t, *J*=6.2 Hz, CH_3); *m/z* (EI) 327 (M^+, 59), 285 (20), 284 (19), 253 (20), 226 (12%).

3.4. Synthesis of 2-[7-aryl-2,3-dihydro-5*H*-imidazo-[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6a–h). General procedure. A mixture 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-ones (**1**, 1 mmol) imidazolidin-2-thione (**5**, 102 mg, 1 mmol) and KOH (56 mg, 1 mmol) in dry dimethylformamide (10 mL) was stirred at room temperature for 48 h. After completion of the reaction, mixture was poured into water (100 mL) and acidified with 10% HCl, the solid thus obtained was filtered and crystallized with minimum amount of DMSO.

3.4.1. 2-[7-(3-Chlorophenyl)-2,3-dihydro-5*H*-imidazo-[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6a). Yellow powder; mp >260°C; [Found: C, 58.26; H, 3.21; N, 14.39. $C_{14}H_{10}ClN_3S$ requires C, 58.42; H, 3.50; N, 14.60%]; ν_{max} (KBr) 2195 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 8.02 (1H, s, Ph), 7.42 (1H, d, *J*=8.0 Hz, Ph), 7.23 (1H, t, *J*=6.4 Hz, Ph), 7.12 (1H, s, C*H*–C=CHCN), 7.10 (1H, d, *J*=8.0 Hz, Ph), 5.63 (1H, s, C*H*CN), 4.43 (2H, t, *J*=6.2 Hz, =N–CH_2), 4.13 (2H, t, *J*=6.2 Hz, =N–CH_2CH_2); *m/z* (EI) 289 (M^++2, 35), 288 (M^++1, 17), 287 (M^+, 74), 265 (10), 233 (7%).

3.4.2. 2-[7-(4-Chlorophenyl)-2,3-dihydro-5*H*-imidazo-[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6b). Yellow powder; mp >260°C; [Found: C, 58.24; H, 3.23; N, 14.31. $C_{14}H_{10}ClN_3S$ requires C, 58.42; H, 3.50; N, 14.60%]; ν_{max} (KBr) 2195 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 7.66–7.59 (5H, m, Ph and C*H*–C=CHCN), 5.76 (1H, s, C*H*CN), 3.86–3.72 (4H, m, CH_2CH_2); *m/z* (EI) 289 (M^++2, 48), 288 (M^++1, 23), 287 (M^+, 100%).

3.4.3. 2-[7-(4-Fluorophenyl)-2,3-dihydro-5*H*-imidazo-[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6c). Yellow powder; mp >260°C; [Found: C, 61.69; H, 3.47; N, 15.09. $C_{14}H_{10}FN_3S$ requires C, 61.98; H, 3.72; N, 15.48%]; ν_{max} (KBr) 2200 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 8.14–8.12 (2H, m, Ph), 7.18 (2H, t, *J*=6.3 Hz, Ph), 7.12 (1H, s, C*H*–C=CHCN), 5.68 (1H, s, C*H*CN), 3.85–3.73 (4H, m, CH_2CH_2); *m/z* (EI) 271 (M^+, 100%).

3.4.4. 2-[7-(4-Bromophenyl)-2,3-dihydro-5*H*-imidazo-[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6d). Yellow powder; mp >260°C; [Found: C, 50.36; H, 2.82; N, 12.35. $C_{14}H_{10}BrN_3S$ requires C, 50.61; H, 3.03; N, 12.64%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 7.70 (2H, d, *J*=8.4 Hz, Ph), 7.42 (2H, d, *J*=8.4 Hz, Ph), 7.25 (1H, s, C*H*–C=CHCN), 5.56 (1H, s, C*H*CN), 3.64–3.58 (4H, m, CH_2CH_2); *m/z* (EI) 333 (M^++2, 51), 332 (M^++1, 23), 331 (M^+, 100%).

3.4.5. 2-[7-(3-Nitrophenyl)-2,3-dihydro-5*H*-imidazo[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6e). Yellow powder; mp >260°C; [Found: C, 56.19; H, 3.13; N, 18.34. $C_{14}H_{10}N_4O_2S$ requires C, 56.36; H, 3.37; N, 18.78%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 8.26 (1H, s, Ph), 8.00 (1H, d, *J*=8.0 Hz, Ph), 7.83–7.81 (1H, m, Ph), 7.72 (1H, d, *J*=8.0 Hz, Ph), 7.12 (1H, s, C*H*–C=CHCN), 5.67 (1H, s, C*H*CN), 3.78 (2H, t, *J*=6.2 Hz, =N–CH_2), 3.64 (2H, t, *J*=6.2 Hz, =N–CH_2CH_2); *m/z* (EI) 298 (M^+, 65), 261 (14%).

3.4.6. 2-[7-(4-Nitrophenyl)-2,3-dihydro-5*H*-imidazo[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6f). Yellow powder; mp >260°C; [Found: C, 56.59; H, 3.13; N, 18.45. $C_{14}H_{10}N_4O_2S$ requires C, 56.36; H, 3.37; N, 18.78%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 8.36 (2H, d, *J*=8.4 Hz, Ph), 8.24 (2H, d, *J*=8.4 Hz, Ph), 7.12 (1H, s, C*H*–C=CHCN), 5.64 (1H, s, C*H*CN), 3.94 (2H, t, *J*=6.2 Hz, =N–CH_2), 3.68 (2H, t, *J*=6.2 Hz, =N–CH_2CH_2); *m/z* (EI) 298 (M^+, 100%).

3.4.7. 2-[7-(2-Furyl)-2,3-dihydro-5*H*-imidazo[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6g). Yellow powder; mp >260°C; [Found: C, 59.09; H, 3.38; N, 17.12. $C_{12}H_9N_3OS$ requires C, 59.24; H, 3.72; N, 17.27%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 8.29 (1H, d, *J*=3.2 Hz, O–C*H*), 7.59 (1H, d, *J*=3.2 Hz, O–CH=CH–C*H*), 7.15–7.13 (1H, m, O–CH=C*H*), 7.10 (1H, s, C*H*–C=CHCN), 5.63 (1H, s, C*H*CN), 4.43 (2H, t, *J*=6.2 Hz, =N–CH_2), 4.13 (2H, t, *J*=6.2 Hz, =N–CH_2CH_2); *m/z* (EI) 243 (M^+, 100%).

3.4.8. 2-[7-(2-Thienyl)-2,3-dihydro-5*H*-imidazo[2,1-*b*][1,3]thiazin-5-ylidene]acetonitrile (6h). Yellow powder; mp >260°C; [Found: C, 55.29; H, 3.18; N, 16.05. $C_{12}H_9N_3S_2$ requires C, 55.57; H, 3.49; N, 16.20%]; ν_{max} (KBr) 2210 cm^{-1} (CN); δ_H (200 MHz, DMSO-d_6) 7.79 (1H, d, *J*=5.4 Hz, S–C*H*), 7.56 (1H, d, *J*=5.4 Hz, S–CH=CH–C*H*), 7.22–7.20 (1H, m, S–CH=C*H*), 7.12 (1H, s, C*H*–C=CHCN), 5.94 (1H, s, C*H*CN), 3.92–3.79 (4H, m, CH_2CH_2); *m/z* (EI) 259 (M^+, 69), 206 (24), 187 (28), 160 (15%).

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