One-Pot Chemoselective Synthesis of Arylated Benzo[*h*]quinolines

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Abstract: A one-pot chemoselective synthesis of 2-aminobenzo[*h*]quinolines has been delineated by the reaction of 6-aryl-4-*sec*-amino-2*H*-pyran-2-one-3-carbonitriles and 2-cyanomethylbenzonitrile using sodamide as a base in DMF. The synthesis involves sequential intermolecular C–C and intramolecular C–C and C–N bond formation. This reaction has delivered benzo[*h*]quinolines chemoselectively in excellent yield under microwave irradiation. The structure of one product was confirmed by single-crystal X-ray crystallography.

Key words: chemoselectivity, quinolones, fused-ring systems, nucleophiles

Highly functionalized quinolines and benzoquinolines are an important class of heterocycles. Benzo[*h*]quinoline derivatives exhibit a broad spectrum of pharmacological properties such as anaesthetic,[1a] antiestrogen,[1b] antimalarial,[2] anti-HIV,[3] anticancer;[4] antitubercular;[5] and antimicrobial activities.[6] Benzo[*h*]quinolines have also found application as agrochemicals[7] and fluorescent materials.[8,9] These compounds have wide applications in the preparation of nano and meso structures with enhanced electronic and photonic properties.[10] Various synthetic methods, such as the Skraup[11a] and Doebner–von Miller quinoline syntheses,[11b] Friedland condensations,[12] Diels–Alder reaction,[13] and Vilsmeier methodology,[14] have been reported for the construction of quinolines and fused quinolines. They have also been synthesized by inter- and intramolecular cyclizations by copper-,[15] palladium-,[16] nickel-,[17] and zinc-metal-catalyzed[18] reactions. Recently, Xi et al. have reported the synthesis of quinolines and fused quinolines by reaction of arylisothiocyanates, alkynes, and alkyltriflates.[19] Partially reduced benzo[*h*]quinolines have also been synthesized by condensation reaction of arylidenes and 1-tetralone using ammonium acetate and sodium methoxide.[20] An elegant synthesis of this ring system has also been reported by base-mediated reaction of 5,6-dihydro-2-oxobenzo[*h*]chromenes and various amidines, such as formamidine, *S*-methylisothiourea, and benzamidine.[21] A reaction of 6-methoxy-1-tetralone with methyl propiolate in saturated ammoniacal methanol followed by aromatization, delivered benzo[*h*]quinoline derivatives.[22]

Herein, we report an atom economic and one-pot approach for the construction of highly functionalized benzo[*h*]qninoline motifs. The precursor, 6-aryl-4-*sec*-amino-2-oxo-2*H*-pyran-3-carbonitriles **1** were synthesized in two steps. The first step was the synthesis of 6-aryl-4-methylthio-2-oxo-2*H*-pyran-3-carbonitriles from the reaction of methyl 2-cyano-3,3-bismethylthioacrylate with various aryl/heteroaryl methyl ketones in DMSO using KOH as a base at room temperature while the second step involved amination[23] with various secondary amines in refluxing ethanol to obtain 6-aryl-4-*sec*-amino-2-oxo-2*H*-pyran-3-carbonitriles **1**.[24]

As a model, reaction of 6-(4-chlorophenyl)-4-methylthio-2-oxo-2*H*-pyran-3-carbonitrile with 2-cyanomethylbenzonitrile using NaH, KOH, and $NaNH_2$ as a base in various solvents such as DMF, DMSO, and THF was carried out, but always a complex mixture was obtained possibly due to side reaction involving the SCH_3 substituent, a good leaving group present at C-4 of the lactone. To avoid this side reaction, the methylthio group was replaced with a secondary amine to reduce the electrophilicity of this site.

Thus, 6-(4-chlorophenyl)-4-piperidin-1-yl-2*H*-pyran-2-one-3-carbonitrile and 2-cyanomethylbenzonitrile were used as model substrates to screen various base and solvent combinations at different temperatures to optimize the reaction conditions. Screening of potassium hydroxide as a base in DMF at 20 °C, 40 °C, and 60 °C, led to recovery of starting material without formation of product after 10–15 hours (Table 1, entries 1–3). However, stirring at 70 °C for 50 hours provided the benzo[*h*]quinoline in 50% yield (Table 1, entry 4). Use of higher temperatures did not reduce the reaction time but significantly improved the yields (Table 1, entries 5–7). Replacement of potassium hydroxide with sodamide as a base in DMF afforded 82% yield in 35 hours (Table 1, entry 8). Use of sodium hydride in DMF afforded 50% of desired product (Table 1, entry 9). Changing solvent to DMSO did not furnish the product with potassium hydroxide, sodamide, and sodium hydride as a bases (Table 1, entries 10–12). Therfore, use of sodamide in DMF at 100 °C was taken to be optimal. Thus, stirring an equimolar mixture of a range of 6-aryl-

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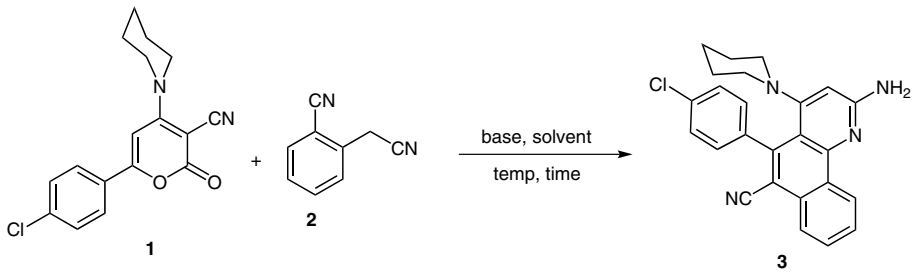
Table 1 Optimization of Reaction Conditions[a]



Entry	Base	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	KOH	DMF	20	10	–
2	KOH	DMF	40	10	–
3	KOH	DMF	60	15	–
4	KOH	DMF	70	50	50
5	KOH	DMF	90	50	60
6	KOH	DMF	100	50	70
7	KOH	DMF	120	50	68
8	$NaNH_2$	DMF	100	35	82
9	NaH	DMF	100	40	50
10	KOH	DMSO	100	30	trace
11	$NaNH_2$	DMSO	100	30	trace
12	NaH	DMSO	100	30	trace

[a] Reaction was performed with 6-(4-chlorophenyl)-2-oxo-4-piperidin-1-yl-2*H*-pyran-3-carbonitrile (**1**, 0.5 mmol) and 2-cyanomethylbenzonitrile (**2**, 0.5 mmol) using base (1.0 mmol) in solvent (4.0 mL).
[b] Isolated yields.

4-sec.amino-2*H*-pyran-2-one-3-carbonitriles and 2-cyanomethylbenzonitrile in DMF using sodamide as a base at 100 °C for 35–50 hours afforded 2-amino-5-aryl-4-*sec*-aminobenzo[*h*]quinoline-6-carbonitriles **3** in good yields (Table 2).

The presence of electron-donating or electron-withdrawing functionality on the aryl group at C-6 of the pyranone ring has no significant effect on yields. However, use of thiophenyl and furyl groups as aryl equivalents required longer duration of reaction, but afforded good yields. The presence of piperidine or morpholine at C-4 of the pyranone equally had no significant effect on yields.

To reduce the time needed for completion of reaction, the strategy was changed from conventional heating to microwave-assisted heating. Thus, a reaction of 6-aryl-2-oxo-4-*sec*-amino-2*H*-pyran-3-carbonitriles **1** and 2-cyanomethylbenzonitrile using sodamide as a base in DMF at 100 °C under microwave-assisted heating afforded an excellent yield of the desired product in 55 minutes (Table 2).

The precursor, 2*H*-pyran-2-one has three electrophilic centers: C-2, C-4, and C-6 in which the latter is highly vulnerable to nucleophilic attack due to extended conjugation with the carbonyl and nitrile groups present at positions 2 and 3. Mechanistically, reaction is possibly initiated though attack of the carbanion generated in situ from 2-cyanomethyl-benzonitrile at C-6 of carbonitrile **1**, leading to the formation of ring-opened intermediate **A**, which may undergo decarboxylation to generate either of the two intermediates **B-1** [*Z*-alkene] or **B-2** [*E*-alkene]. Intermediate **B-1** may cyclize intramolecularly giving intermediate **C** which can further cyclize to yield phenanthridine **4** (Scheme 1, path b). In the case of intermediate **B-2**, cyclization may involve allylic attack of the carbanion on CN-2 to form an intermediate which further undergoes intramolecular sequential cyclization involving nitrile and amino functionalities to produce benzo[*h*]quinolines **3** (Scheme 1, path a). Chemoselective formation of 2-amino-5-aryl-4-*sec*-amino-1-yl-benzo[*h*]quinoline-6-carbonitriles **3** confirms that the reaction follows path a probably due to involvement of the geometrically more stable intermediate **B-2**. The absence of product **4** in the reaction mixture is possibly due to the instability of intermediate **B-1**.

As in an earlier report,[25] if malononitrile was used as the carbanion source, cyclization involved either cyano group, affording 3-amino-5-(piperidin-1-yl)-[1,1′-biphe-

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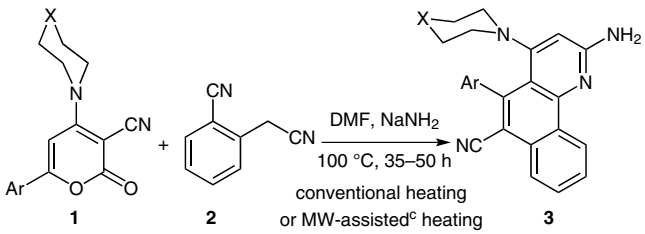
Table 2 Synthesis of 2-Amino-5-aryl-4-*sec*-amino-1-yl-benzo[*h*]quinoline-6-carbonitriles **3**[a,b]



Entry	Compd **3**	Ar	X	Yield (%)[d]	Yield (%)[e]
1	**3a**	Ph	CH_2	75	90
2	**3b**	4-MeC_6H_4	CH_2	65	85
3	**3c**	4-$MeOC_6H_4$	CH_2	71	88
4	**3d**	4-FC_6H_4	CH_2	73	–
5	**3e**	4-ClC_6H_4	CH_2	82	82
6	**3f**	4-BrC_6H_4	CH_2	66	89
7	**3g**	3-BrC_6H_4	CH_2	65	84
8	**3h**	2-furyl	CH_2	82	91
9	**3i**	2-thienyl	CH_2	76	87
10	**3j**	4-$MeOC_6H_4$	O	68	–
11	**3k**	4-ClC_6H_4	O	66	85
12	**3l**	4-BrC_6H_4	O	63	92

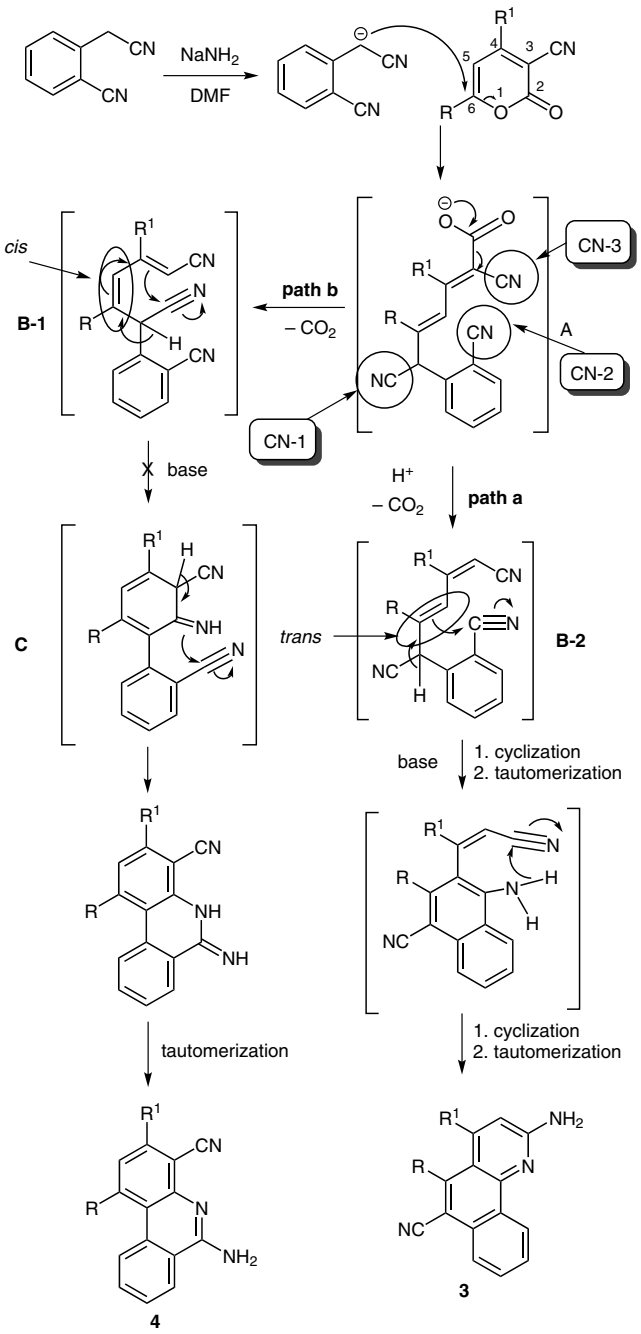
[a] All reactions were performed by heating 6-aryl-4-*sec*-amino-2*H*-pyran-2-one-3-carbonitriles **1** (0.5 mmol) and 2-cyanomethylbenzonitrile (**2**, 0.5 mmol) using sodamide (1.0 mmol) in DMF (4.0 mL) at 100 °C.
[b] All the reactions were performed twice and the average yield is reported.
[c] Reactions were performed by heating **1** (1.0 mmol) and **2** (1.0 mmol) using sodamide (2.0 mmol) in DMF (2.0 mL) at 100 °C under microwave irradiation for 55 min.
[d] Yield obtained through conventional heating.
[e] Yield obtained through microwave-assisted heating.

nyl]-2,4-dicarbonitrile; probably through a similar intermediate as **B-1** (Scheme 2). We proposed that, replacement of either nitrile group with a bulky functional group such as benzonitrile, would force the reaction to follow the path a through intermediate **B-2**.

All the intermediates and final compounds were adequately characterized by spectroscopic analysis,[27] and one of the compound **3l** was further confirmed by single-crystal X-ray analysis.[26]

The ORTEP plot is shown with 30% probability in Figure 1. The asymmetric unit contains two molecules along with chloroform (used as the crystallization solvent) indicating H bonding between the chloroform and the O atom of the morpholine ring.

In conclusion, a novel, efficient, and chemoselective approach for the synthesis of functionalized benzo[*h*]quinolines by base-promoted sequential intermolecular C–C and intramoleculer C–C and C–N bond-formation reactions has been developed. To rationalize the mechanism, we have proposed the involvement of a possible geometrically stable intermediate, which provides chemoselectivity. This procedure is simple, cost effective, and does not require use of expensive metal catalyst. The reaction can be performed by conventional heating or under microwave irradiation, providing excellent yields of 2-amino-5-aryl-4-*sec*-aminobenzo[*h*]quinoline-6-carbonitriles.



Scheme 1 Plausible mechanism for synthesis of 2-amino-5-aryl-4-*sec*-amino-benzo[*h*]quinoline-6-carbonitriles

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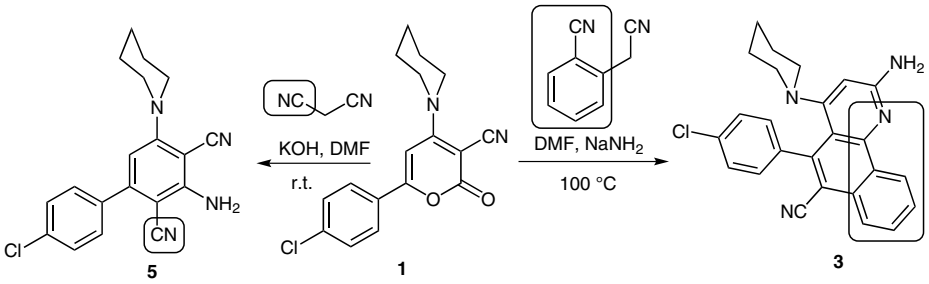

Scheme 2 Comparison of reaction of malononitrile vs. 2-cyanomethylbenzonitrile with 2-pyranone

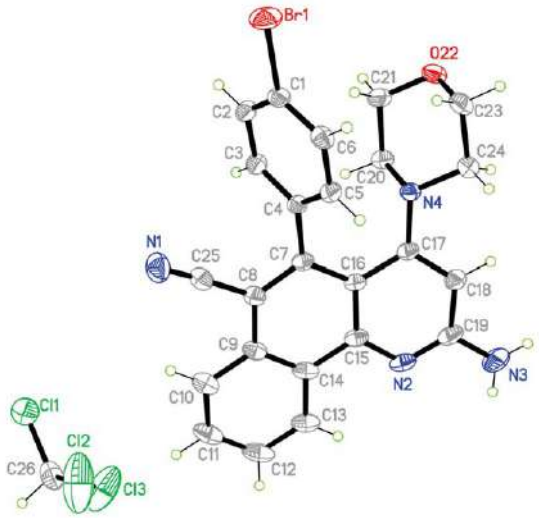

Figure 1 ORTEP diagram of **3l** showing the X-ray molecular structure at 30% probability with atom-numbering scheme. Solvent of crystallization '$CHCl_3$' has been found in the crystal structure.

Acknowledgment

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(26) **Crystal Data for 3l (CCDC 994354)**
$C_{24}H_{19}BrN_4O$, $CHCl_3$, triclinic, space group: *P*-1, *a* = 12.4071(5), *b* = 13.8990(6), *c* = 15.3973(7) Å, *α* = 108.420(4)°, *β* = 93.430(4)°, *γ* = 113.596(4)°, *V* = 2254.92 (18) Å^3, *T* = 293(2) K, *Z* = 2, *m* = 2.026 mm^{-1}, *F*(000) = 1052.0, D_c = 1.529 Mg m^{-1}, colorless rectangular crystal, crystal size: 0.26 × 0.20 × 0.11 mm, *R*1 =0.0712 for 7159 $F_0 > 4\sigma(F_0)$ and 0.1111 for all 10874 data and 593 parameters with goodness of fit GooF = 1.023. Unit cell determination and intensity data collection (2*θ* range = 8-133.2°) was performed with 88.4% completeness at 293(2) K. Structure solutions by direct methods and refinements by full-matrix least-squares methods on *F*2. CCDC 994354 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(27) **General Procedure for the Synthesis of 2-Amino-5-aryl-4-*sec*-amino-1-yl-benzo[*h*]quinoline-6-carbonitriles 3a–3l by Conventional Heating**
A mixture of 6-aryl-2-oxo-4-*sec*-amino-1-yl-2*H*-pyran-3-carbonitrile (0.5 mmol), 2-cyanomethylbenzonitrile (0.5 mmol, 71.0 mg), and $NaNH_2$ (1.0 mmol, 39.0 mg) in dry DMF (4.0 mL) was stirred at 100 °C for 35–50 h. After completion of reaction, the mixture was poured onto crushed ice followed by neutralization with 10% HCl. The solid material formed was filtered, washed with water, dried, and purified by silica gel column chromatography using hexane–EtOAc (7:3) as eluent.

General Procedure for the Microwave-Assisted Synthesis of 2-Amino-5-aryl-4-piperidine-1-yl-benzo[*h*]quinoline-6-carbonitriles 3a–3l (Except 3d and 3j)
A mixture of 2-oxo-6-aryl-4-piperidin-1-yl-2*H*-pyran-3-carbonitrile (1.0 mmol), 2-cyanomethylbenzonitrile (1.0 mmol, 142.0 mg), and $NaNH_2$ (2.0 mmol, 78.0 mg) in dry DMF (2.0 mL) was heated at 100 °C for 55 min under microwave irradiation. Completion of reaction was monitored by TLC. After completion, the reaction mixture was poured onto crushed ice and neutralized with 10% HCl. The precipitate obtained was filtered, washed with H_2O, dried, and purified by silica gel column chromatography using hexane–EtOAc (7:3) as eluent.

2-Amino-5-phenyl-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3a)
Yield 75% (142.0 mg); R_f = 0.28 (30% EtOAc–hexane); orange solid; mp 140–142 °C. IR (KBr): 3338, 3050, 2941, 2854, 2212 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.58–0.71 (m, 2 H, CH_2), 1.20–1.41 (m, 4 H, CH_2), 2.32–2.42 (m, 2 H, CH_2), 2.83–2.94 (m, 2 H, CH_2), 4.88 (s, 2 H, NH_2), 6.28 (s, 1 H, ArH), 7.37–7.44 (m, 3 H, ArH), 7.47–7.53 (m, 2 H, ArH), 7.62–7.74 (m, 2 H, ArH), 8.23 (d, *J* = 8.0 Hz, 1 H, ArH), 9.08 (d, *J* = 7.3 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4, 24.5, 52.7, 98.9, 105.6, 112.6, 118.6, 125.0, 125.2, 126.9, 127.2, 127.9, 129.2, 130.0, 130.2, 131.6, 138.8, 145.0, 150.7, 158.9, 161.3. ESI-HRMS: *m/z* calcd for $C_{25}H_{22}N_4$: 379.1917 [M + H$^+$]; found: 379.1916.

2-Amino-4-piperidin-1-yl-5-*p*-tolyl-benzo[*h*]quinoline-6-carbonitrile (3b)
Yield 65% (128.0 mg); R_f = 0.25 (30% EtOAc–hexane); orange solid; mp 182–184 °C. IR (KBr): 3369, 2926, 2855, 2209 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19–1.46 (m, 6 H, CH_2), 2.35–2.52 (m, 5 H, CH_2, CH_3), 2.87 (d, *J* = 11.7 Hz, 2 H, CH_2), 5.03 (s, 2 H, NH_2), 6.27 (s, 1 H, ArH), 7.20–7.28 (m, 2 H, ArH), 7.39 (d, *J* = 8.0 Hz, 2 H, ArH), 7.62–7.76 (m, 2 H, ArH), 8.24 (d, *J* = 7.3 Hz, 1 H, ArH), 9.10 (d, *J* = 8.0 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 23.4, 24.5, 52.6, 98.5, 105.3, 112.5, 118.8, 125.0, 125.2, 126.9, 127.8, 129.2, 129.7, 130.1, 131.6, 135.7, 137.7, 145.2, 150.4, 158.7, 161.1. ESI-HRMS: *m/z* calcd for $C_{26}H_{24}N_4$: 393.2074 [M + H$^+$]; found: 393.2074.

2-Amino-5-(4-methoxyphenyl)-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3c)
Yield 71% (145.0 mg); R_f = 0.14 (30% EtOAc–hexane); orange solid; mp 180–182 °C. IR (KBr): 3437, 3171, 2924, 2852, 2208 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.60–0.80 (m, 2 H, CH_2), 1.20–1.46 (m, 4 H, CH_2), 2.36 (t, *J* = 10.9 Hz, 2 H, CH_2), 2.86 (d, *J* = 11.9 Hz, 2 H, CH_2), 3.85 (s, 3 H, OCH_3), 4.96 (s, 2 H, NH_2), 6.23 (s, 1 H, ArH), 6.93 (d, *J* = 8.7 Hz, 2 H, ArH), 7.42 (d, *J* = 8.7 Hz, 2 H, ArH), 7.55–7.74 (m, 2 H,ArH), 8.21 (d, *J* = 7.3 Hz,1 H, ArH), 9.09–9.11 (m, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4, 24.6, 52.6, 53.3, 98.4, 105.1, 112.3, 112.5, 118.9, 125.0, 125.1, 126.7, 129.1, 129.8, 131.1, 131.5, 131.6, 144.8, 150.7, 158.8, 159.5, 160.9. ESI-HRMS: *m/z* calcd for $C_{26}H_{24}N_4O$: 409.2023 [M + H$^+$]; found: 409.2000.

2-Amino-5-(4-fluorophenyl)-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3d)
Yield 73% (145.0 mg); R_f = 0.24 (30% EtOAc–hexane); orange solid; mp 203–205 °C. IR (KBr): 3341, 2926, 2853, 2208 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.63–0.83 (m, 2 H, CH_2), 1.17–1.50 (m, 4 H, CH_2), 2.30–2.52 (m, 2 H, CH_2), 2.83–2.90 (m, 2 H, CH_2), 4.90 (s, 2 H, NH_2), 6.28 (s, 1 H, ArH), 7.05–7.18 (m, 2 H, ArH), 7.44–7.52 (m, 2 H, ArH), 7.62–7.77 (m, 2 H, ArH), 8.22 (d, *J* = 8.0 Hz, 1 H, ArH), 9.10 (d, *J* = 7.3 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3, 24.6, 52.7, 98.8, 105.8, 112.3, 114.2 (d, J_{C-F} = 22.0 Hz), 118.5, 125.0, 125.2, 127.2, 129.4, 131.5, 131.9 (d, J_{C-F} = 7.6 Hz), 134.6, 134.7, 143.7, 150.2, 158.7, 161.0, 162.6 (d, J_{C-F} = 250.1 Hz). ESI-HRMS: *m/z* calcd for $C_{25}H_{21}FN_4$: 397.1823 [M + H$^+$]; found: 397.1823.

2-Amino-5-(4-chlorophenyl)-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3e)
Yield 82% (169.0 mg); R_f = 0.25 (30% EtOAc–hexane); golden solid; mp 127–129 °C. IR (KBr): 3474, 3151, 2929, 2853, 2207 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.66–0.77 (m, 2 H, CH_2), 1.22–1.48 (m, 4 H, CH_2), 2.35–2.45 (m, 2 H, CH_2), 2.81–2.91 (m, 2 H, CH_2), 4.91 (s, 2 H, NH_2), 6.29 (s, 1 H, ArH), 7.37–7.47 (m, 4 H, ArH), 7.62–7.75 (m, 2 H, ArH), 8.21 (d, *J* = 8.0 Hz, 1 H, ArH), 9.08 (d, *J* = 7.3 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3, 24.5, 52.6, 99.1, 105.4, 112.3, 118.4, 125.1, 125.1, 127.1, 127.3, 129.3, 130.0, 131.4, 131.4, 133.8, 137.2, 143.5, 150.7, 158.9, 160.9. ESI- HRMS: *m/z* calcd for $C_{25}H_{21}ClN_4O$: 413.1527 [M + H$^+$]; found: 413.1527.

2-Amino-5-(4-bromophenyl)-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3f)
Yield 66% (151.0 mg); R_f = 0.26 (30% EtOAc–hexane); light yellow solid; mp 216–218 °C. IR (KBr): 3368, 2924, 2853, 2209 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.60–0.82 (m, 2 H, CH_2), 1.22–1.50 (m, 4 H, CH_2), 2.32–2.51 (m, 2 H, CH_2), 2.81–2.89 (m, 2 H, CH_2), 4.90 (s, 2 H, NH_2), 6.29 (s, 1 H, ArH), 7.38 (d, *J* = 8.7 Hz, 2 H, ArH), 7.56 (d, *J* = 8.7 Hz, 2 H, ArH), 7.63–7.76 (m, 2 H, ArH), 8.22 (d, *J* = 8.0 Hz, 1 H, ArH), 9.10 (m, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3, 24.6, 52.7, 99.1, 105.4, 112.3, 118.4, 122.0, 125.1, 125.2, 127.2, 129.3, 130.1, 130.3, 131.4, 131.8, 137.7, 143.5, 150.7, 159.0, 161.0. ESI-HRMS: *m/z* calcd for $C_{25}H_{21}BrN_4$: 457.1022 [M + H$^+$]; found: 457.1024.

2-Amino-5-(3-bromophenyl)-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3g)
Yield 65% (149.0 mg); R_f = 0.23 (30% EtOAc–hexane); yellow solid; mp 204–206 °C. IR (KBr): 3368, 3199, 3058, 2936, 2854, 2210 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ =

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0.40–0.62 (m, 1 H, CH_2), 0.76–0.95 (m, 1 H, CH_2), 0.95–1.10 (m, 1 H, CH_2), 1.16–1.30 (m, 1 H, CH_2), 1.33–1.51 (m, 2 H, CH_2), 2.28 (t, *J* = 10.9 Hz, 1 H, CH_2), 2.50 (t, *J* = 10.9 Hz, 1 H, CH_2), 2.80 (d, *J* = 11.7 Hz, 1 H, CH_2), 2.95 (d, *J* = 11.7 Hz, 1 H, CH_2), 4.95 (s, 2 H, NH_2), 6.32 (s, 1 H, ArH), 7.29–7.38 (m, 1 H, ArH), 7.49–7.60 (m, 3 H, ArH), 7.63–7.76 (m, 2 H, ArH), 8.23 (d, *J* = 8.0 Hz, 1 H, ArH), 9.10 (d, *J* = 7.3 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3, 24.4, 51.9, 53.4, 99.6, 105.4, 112.3, 118.3, 121.0, 125.1, 127.2, 128.4, 128.8, 129.2, 130.0, 130.7, 131.3, 133.3, 140.6, 142.9, 150.6, 159.0, 161.0. ESI-HRMS: *m/z* calcd for $C_{25}H_{21}BrN_4$: 457.1022 [M + H^+]; found: 457.1023.

2-Amino-5-furan-2-yl-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile (3h)

Yield 82% (151.0 mg); R_f = 0.60 (40% EtOAc–hexane); brown solid; mp 212–214 °C. IR (KBr): 3356, 2926, 2856, 2212 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90–1.25 (m, 4 H, CH_2), 1.26–1.45 (m, 2 H, CH_2), 2.36 (t, *J* = 10.6 Hz, 2 H, CH_2), 2.96 (d, *J* = 10.2 Hz, 2 H, CH_2), 4.87 (s, 2 H, NH_2), 6.25 (s, 1 H, ArH), 6.51–6.58 (m, 1 H, ArH), 6.86 (d, *J* = 2.5 Hz, 1 H, ArH), 7.46 (s, 1 H, ArH), 7.57–7.70 (m, 2 H, ArH), 8.17 (d, *J* = 7.3 Hz, 1 H, ArH), 9.00 (d, *J* = 8.0 Hz, 1 H, ArH). ^{13}C (100 MHz, $CDCl_3$): δ = 23.7, 25.0, 53.1, 99.1, 105.2, 111.0, 111.2, 112.9, 118.1, 125.0, 125.4, 127.4, 129.2, 130.4, 131.3, 133.0, 142.5, 150.3, 150.9, 159.2, 161.5. ESI-HRMS: *m/z* calcd for $C_{23}H_{20}N_4O$: 369.1710 [M + H^+]; found: 369.1689.

2-Amino-4-piperidin-1-yl-5-thiophen-2-yl-benzo[*h*]quinoline-6-carbonitrile (3i)

Yield 76% (146.0 mg); R_f = 0.64 (40% EtOAc–hexane); orange solid; mp 218–220 °C. IR (KBr): 3394, 2925, 2853, 2215 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80–1.10 (m, 2 H, CH_2), 1.21–1.52 (m, 4 H, CH_2), 2.37 (t, *J* = 10.9 Hz, 2 H, CH_2), 2.96 (d, *J* = 11.7 Hz, 2 H, CH_2), 4.95 (s, 2 H, NH_2), 6.28 (d, *J* = 1.4 Hz, 1 H, ArH), 7.11–7.16 (m, 1 H, ArH), 7.42–7.47 (m, 1 H, ArH), 7.49–7.53 (m, 1 H, ArH), 7.61–7.74 (m, 2 H, ArH), 8.21 (d, *J* = 8.0 Hz, 1 H, ArH), 9.06 (d, *J* = 8.0 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4, 24.8, 52.8, 99.4, 106.1, 113.5, 118.3, 125.0, 125.3, 125.6, 127.1, 127.3, 128.0, 129.2, 130.2, 131.4, 137.0, 141.0, 150.3, 159.1, 161.2. ESI-HRMS: *m/z* calcd for $C_{23}H_{20}N_4S$: 385.1481 [M + H^+]; found: 385.1457.

2-Amino-5-(4-methoxyphenyl)-4-morpholin-4-yl-benzo[*h*]quinoline-6-carbonitrile (3j)

Yield 68% (140.0 mg); R_f = 0.15 (40% EtOAc–hexane); orange solid; mp 278–280 °C. IR (KBr): 3357, 2925, 2854, 2209 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.55–2.72 (m, 4 H, CH_2), 2.77–2.83 (m, 2 H, CH_2), 3.46–3.58 (m, 2 H, CH_2), 3.87 (s, 3 H, OCH_3), 4.94 (s, 2 H, NH_2), 6.27 (s, 1 H, ArH), 6.95–7.00 (m, 2 H, ArH), 7.39–7.47 (m, 2 H, ArH), 7.57–7.75 (m, 2 H, ArH), 8.22 (d, *J* = 8.0 Hz, 1 H, ArH), 9.06–9.11 (m, 1 H, ArH). ^{13}C (100 MHz, $CDCl_3$): δ = 51.5, 55.3, 65.7, 98.6, 106.0, 112.0, 112.8, 118.6, 125.1, 125.2, 127.0, 129.4, 129.8, 131.2, 131.5, 131.6, 144.1, 150.8, 158.7, 159.8, 160.0. ESI-HRMS: *m/z* calcd for $C_{25}H_{22}N_4O_2$: 411.1816 [M + H^+]; found: 411.1816.

2-Amino-5-(4-chlorophenyl)-4-morpholin-4-yl-benzo[*h*]quinoline-6-carbonitrile (3k)

Yield 66% (137.0 mg); R_f = 0.21 (40% EtOAc–hexane); golden solid; mp 258–260 °C. IR (KBr): 3351, 2924, 2853, 2211 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.56–2.60 (m, 4 H, CH_2), 2.71–2.79 (m, 2 H, CH_2), 3.50–3.60 (m, 2 H, CH_2), 4.97 (s, 2 H, NH_2), 6.30 (s, 1 H, ArH), 7.36–7.51 (m, 4 H, ArH), 7.63–7.78 (m, 2 H, ArH), 8.22 (d, *J* = 8.0 Hz, 1 H, ArH), 9.09 (d, *J* = 8.0 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.5, 65.6, 99.2, 106.2, 112.0, 118.1, 125.2, 125.3, 127.4, 127.6, 129.6, 130.0, 131.4, 131.4 134.3, 137.4, 142.8, 151.0, 158.9, 159.9. ESI-HRMS: *m/z* calcd for $C_{24}H_{19}ClN_4O$: 415.1320 [M + H^+]; found: 415.1326.

2-Amino-5-(4-bromophenyl)-4-morpholin-4-yl-benzo[*h*]quinoline-6-carbonitrile (3l)

Yield 63% (145.0 mg); R_f = 0.22 (40% EtOAc–hexane); orange solid; mp 260–262 °C. IR (KBr): 3340, 2925, 2855, 2209 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57–2.68 (m, 4 H, CH_2), 2.70–2.76 (m, 2 H, CH_2), 3.49–3.59 (m, 2 H, CH_2), 5.00 (s, 2 H, NH_2), 6.30 (s, 1 H, ArH), 7.34–7.40 (m, 2 H, ArH), 7.56–7.62 (m, 2 H, ArH), 7.64–7.77 (m, 2 H, ArH), 8.22 (d, *J* = 7.3 Hz, 1 H, ArH), 9.07–9.12 (dd, *J* = 0.9 Hz, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.5, 65.6, 99.3, 106.1, 112.0, 118.1, 122.4, 125.1, 125.3, 127.4, 129.6, 130.0, 130.6, 131.4, 131.6, 137.9, 142.8, 150.8, 158.9, 159.9. ESI-HRMS: *m/z* calcd for $C_{24}H_{19}BrN_4O$: 459.0815 [M + H^+]; found: 459.0816.

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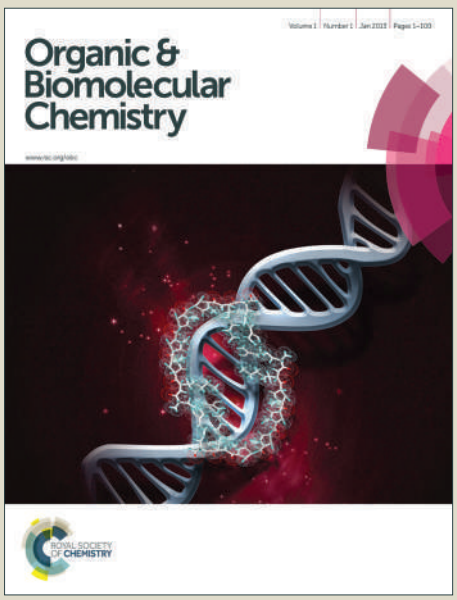

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ARTICLE TYPE

Synthesis of 1-amino-2-aroyl/acetylnaphthalenes through base mediated one pot inter and intramolecular C-C bond formation strategy

Surjeet Singh,[a] Pratik Yadav,[a] Satya Narayan Sahu,[a] Ismail Althagafi,[b] Abhinav Kumar,[c] Brijesh Kumar,[d] Vishnu Ji Ram[c] and Ramendra Pratap[a,]*

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A new precursor 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile has been synthesized by reaction of 2-cyanomethylbenzonitrile, carbon disulfide and methyl iodide under basic conditions. Reaction of 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile with various functionalized aryl/heteroaryl methyl ketones or acetone under basic condition afforded 4-amino-3-aroyl/heteroaroyl/acetyl-2-methylsulfanylnapthalene-1-carbonitriles in good yields through (5C+1C) annulations strategy which involves sequential intermolecular followed by intramolecular C-C bond formation reactions. Structure of the product was confirmed by single crystal X-ray crystallography.

Introduction

Ketenedithioacetals are known as versatile precursors, for their broad synthetic applications.[1] Their synthetic utility has been widely explored for the construction of various aromatic and heteroaromatic along with nonaromatic ring systems of medicinal and synthetic importance.[2] A large variety of ketenedithiacetals are reported for their application in substitution, elimination and addition reactions;[1] synthesis of various functionalized 2*H*-pyran-2-ones;[3] partially reduced coumarin;[3] pyrazoles;[3] oxazoles;[3] thiophenes;[3] pyridines;[3] pyrimidines[3] and fluorescent[4] compounds. The broad synthetic potential of these synthons gave us enthusiasm to further investigate their chemistry.

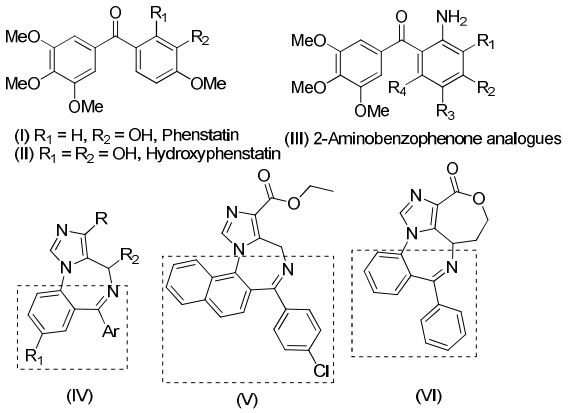
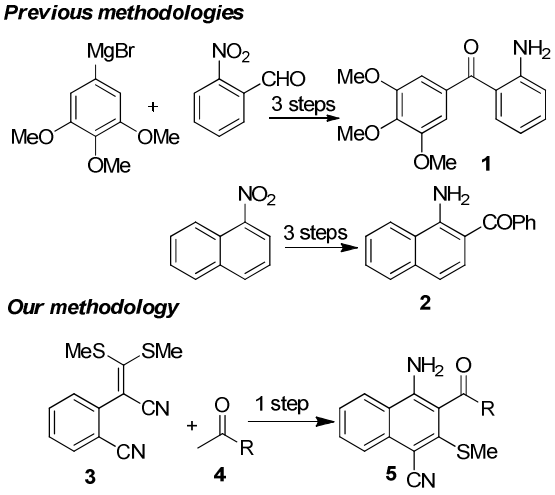


Fig. 1: Structure of phenstatin **I**, hydroxyphenstatine **II**, 2-aminobenzophenone analogues **III** 3-substituted 6-aryl-4*H*-imidazo-[1,5-*a*]benzodiazepines and related compound (**IV-VI**).

Functionally loaded diaryl ketones are present as the structural motif in various synthetically and biologically important molecules and natural products.[5] α-Aminodiaryl ketones and molecules embedded with these molecular skeletons found application as antitubulin agents, e.g. Phenstatin **I**,[6] Hydroxyphenstatine[6] (**II**) and 2-aminobenzophenone analogues (**III**).[7] 2-Amino-1-aroylnaphthalene and 2-hydroxy-1-aroylnaphthalene also exhibit good anti proliferative activity against human cancer cell, comparable to the potency of colchine (Fig. 1).[8]

3-Substituted 6-phenyl-4*H*-imidazo[1,5-*a*][1,4]benzodiazepines (**IV**) and related compounds (**V-VI**) embedded with o-aminatedphenyl aryl ketones are reported as central benzodiazepine receptor (CBR) ligands as shown in Figure 1.[9]



Scheme 1: Reported methodologies versus our methodology.

Extensive literature survey, concluded that very limited methodologies are available for the synthesis of *o*-aminoaryl aryl ketones. 2-Aminobenzophenone analogues have been prepared in three steps by Liou *et al.*[7] The first step was synthesis of benzhydrol derivatives via coupling of (3,4,5-

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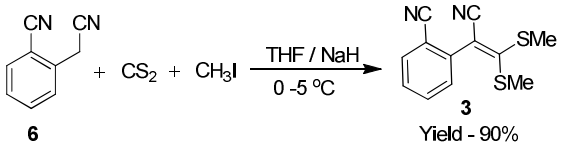
trimethoxyphenyl)magnesium bromide with various substituted 2-nitrobenzaldehydes, which, on oxidation with pyridinium dichromate (PDC), followed by nitro group reduction, provided functionalized α-aminobenzophenones. Synthesis of the α-aminonaphthophenones was also reported by Zhang *et al*.[10] The required precursor 1-amino-2-naphthonitrile for the synthesis of α-aminonaphthophenones has been synthesized by regioselective cyanation of l-nitronaphthalene.[11] Reaction of aryl magnesium halides with 1-amino-2-naphthonitrile followed by hydrolysis provided the α-nitronaphthophenones, which, upon concomitant reduction, gave α-aminonaphthophenones in overall poor yield.

Most of the previously reported methodologies required a multistep reaction approach, use of expensive reagents, harsh reaction conditions, naphthyl ring containing precursors and provided overall low yields. [10,11] 5+1 Annulation strategy for the construction of various kind of nuclei has been reported earlier.[11] Zhang *et al* have reported the 5C+1C/N cyclization strategy for the synthesis of benzene nucleus from ketenedithioacetals.[11b] Liu and co-worker have also used 5C+1C cyclization for the synthesis of highly crowded cyclohexenone.[11] We have made first attempt to synthesized naphthalene nucleus using 5C+1C cyclization strategy.

Results and Discussion

We have chosen 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile as a synthetic key precursor for the construction of multifunctional naphthalene rings. This was synthesized by reaction of 2-cyanomethylbenzonitrile, carbon disulfide and methyl iodide under basic conditions (Scheme 2). We have screened some alkaline solvent combinations such as NaH/THF, K_2CO_3/DMF, NaOEt/Ethanol and KO^{t}Bu/THF for the synthesis of the desired precursor and NaH/THF was found to be the best combination.



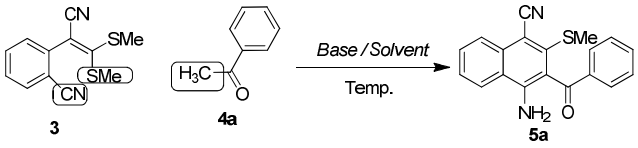
Scheme 2: Synthesis of 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile

Earlier report[3] shows that methylthio group of ketenedithioacetals act as excellent leaving group, can be employed for the development of new molecular make-ups. We wish to use carbon nucleophiles to replace the methylthio group of 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile followed by utilization of the nitrile group at the ortho position in the benzene ring for concomitant cyclization.

Taking into account the above concept, we have used 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile and acetophenone as model substrates to screen various reaction conditions (Table 1). We have started the screening with use of sodium hydride in THF and isolated the desired compound with 55% yield upon reacting for 20 hours at room temperature (entry 1). We shifted to a polar solvent, DMF, in lieu of THF in combination of NaH, but little change was observed (entry 2). We have also tested potassium hydroxide and sodamide in DMF under similar reaction conditions and got better results in the case of potassium hydroxide than sodamide. For further improvement, we carried out the reaction in DMSO with KOH at room temperature, and surprisingly the reaction completed in 2 hours with 81 % yield (entry 5). This result proves that DMSO is best solvent for screening of various bases. Probably the presence of CHO group in DMF hindered the formation of desired product due some side reactions with acetophenone. We screened sodium hydride, sodamide and sodium hydroxide in DMSO, but no base was better than potassium hydroxide (entry 6, 7 and 8). We have checked the influence of temperature using potassium hydroxide as a base in dimethyle sulfoxide and no exciting results were obtained (entry 9 and 10). We have also evaluated the effect of excess of potassium hydroxide on the reaction, and observed the lower yield of desired product (entry 11 and 12). We proposed that, excess of base enhances the possibility of side reactions of the product and lower the yield. Thus stirring of one equivalent of 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile **3** with 1.1 equivalent of aryl methyl ketones **4** and two equivalent of potassium hydroxide in DMSO at room temperature, followed by proper work-up and purification provides multifunctional naphthalenes **5** in good yield.

With these optimized reaction conditions, we have synthesized various highly functionalized aryl naphthyl ketones (Scheme 3). We have used various acetophenones **4** containing electron donor and acceptor groups. It has been observed that the presence of these groups in the aryl ring negatively affects the yields of the desired product. Interestingly, we observed that use of *p*-chloro/fluoroacetophenone, provides the desired product 4-amino-3-(4-chloro/fluoro-benzoyl)-2-(methylthio)-1-naphthonitrile as a major product and 4-amino-2-(methylthio)-3-(4-(methylthio)benzoyl)-1-naphthonitrile as a minor product

Table 1: Optimization of reaction conditions[a]



Entry	Base	Solvent	Temp(°C)[c]	Time(hrs)	Yield(%)[b]
1	NaH	THF	RT	20	55
2	NaH	DMF	RT	20	65
3	KOH	DMF	RT	20	70
4	$NaNH_2$	DMF	RT	20	26
5	KOH	DMSO	RT	2	81
6	NaH	DMSO	RT	2	70
7	$NaNH_2$	DMSO	RT	2	70
8	NaOH	DMSO	RT	2	65
9	KOH	DMSO	60	2	65
10	KOH	DMSO	90	1.5	55
11	KOH	DMSO	RT	2	70[d]
12	KOH	DMSO	RT	2	66[e]

a). All the reactions were carried out by using **3** (0.5 mmol), **4a** (0.55 mmol), base (1.0 mmol) and 4.0 mL of solvent; b) Yield reported are after purification through column chromatography; c) RT is room temperature and it was ranging from 25-30 °C; d) Reaction was carried out using base KOH 3 equivalent (1.5 mmol); e) Reaction was carried out using base KOH 4 equivalent (2.0 mmol).

by an unusual nucleophilic substitution of fluoro/chloro in the aryl ring due to *in situ* generated methylthio nucleophile, while use of *o/p*-bromoacetophenone afforded the only desired product without any formation of product **7**. Probably, bigger size of bromein prevents the nucleophilic attack of methylthio group.

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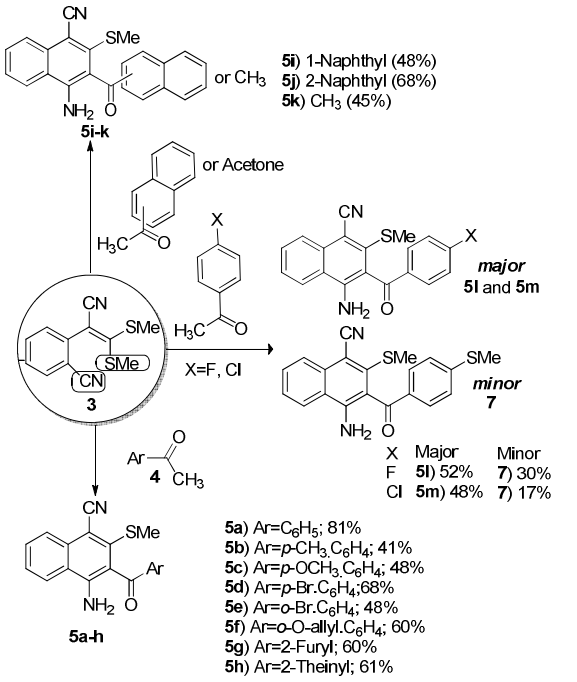
Use of *o*-substituted acetophenone gave low to moderate yield of aryl naphthyl ketone, probably due to steric hindrance. We tried 2-hydroxyacetophenone as a nucleophile source and ended up with a complex reaction mixture, but use of 2-allyloxyacetophenone yielded the desired product in moderate yield. Apart from functionalized acetophenones, we have also used 2-acetylfuran and 2-acetylthiophene as a nucleophile source and isolated the desired product in moderate yield. We have successfully synthesized dinaphthyl ketone by using acetonaphthone as a nucleophile source in good yield. Interestingly, we have also used acetone as a nucleophile source and successfully synthesized highly functionalized acetonaphthone, which is a very interesting precursor and very difficult to synthesized by reported literature procedures.

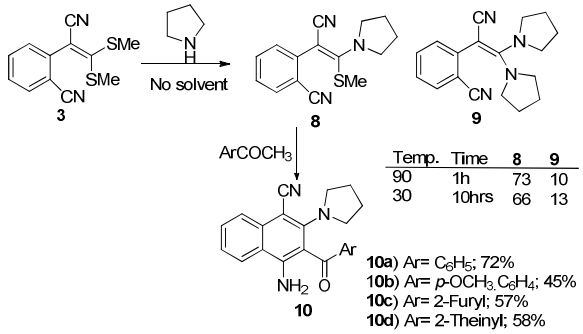
In order to further enhance the scope of this reaction, we have planned to replace the methylthio group with a secondary amine,



Scheme 3: Synthesis of various 4-amino-3-aroyl/heteroaroyl/acetyl-2-methylsulfanylnapthalene-1-carbonitriles (**5a-m** and **7**)

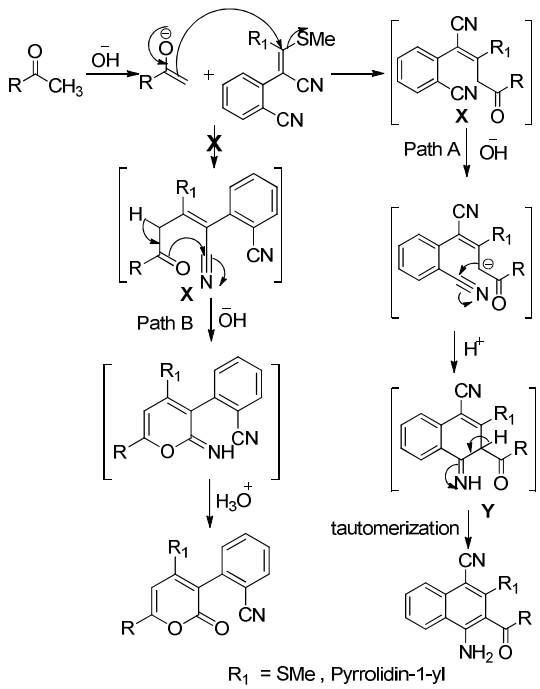
before 5C+1C annulations. We have tested various reaction conditions for the synthesis of 2-(1-cyano-2-(methylthio)-2-(pyrrolidin-1-yl)vinyl)benzonitrile, but failed to obtained a selective route to monoamination. Reaction of 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile and excess of pyrrolidine at 30 °C yielded a mixture of 2-(1-cyano-2-(methylthio)-2-(pyrrolidin-1-yl)vinyl)benzonitrile as a major product and 2-(1-cyano-2,2-di(pyrrolidin-1-yl)vinyl)benzonitrile as a minor product (Scheme 3). At 90ºC, the monoaminated product was isolated in 73% yield, while continuation of the reaction for longer provided the diaminated product in excess. Six membered secondary amines yielded a major diaminated product due to more nucleophilic nature of nitrogen, which was not a suitable precursor for the synthesis of naphthalene.

We have taken 2-(1-cyano-2-(methylthio)-2-(pyrrolidin-1-yl)vinyl)benzonitrile as a precursor and preformed the reaction with various functionalized aryl/heteroaryl methyl ketones, using KOH as a base in DMSO at room temperature and successfully obtained naphthalene bearing a pyrrolidine group in lieu of the methylthio group.



Scheme 4: Synthesis of 2-(1-cyano-methylsulfanyl-2-pyrrolidine-1-1yl-vinyl)-benzonitrile, 2-(1-cyano-methylsufanyl-2,2-di-pyrrolidine-1-yl-vinyl)-benzonitrile and 4-amino-3-aroyl/heteroaroyl/acetyl-2-pyrrolidin-1-yl-1-carbonitriles

Mechanistically, the reaction is possibly initiated by a nucleophilic substitution at C-2 of 2-(1-cyano-2,2-bis(methylthio)vinyl)benzonitrile by an *in situ* generated nucleophile from acetophenone with loss of the methylthio group, which leads to the formation of intermediate **X** (Scheme 5). In presence of excess base, the carbanion generated in α position to the carbonyl group, which attacks intramolecularly at the nitrile group present in ortho position, with formation of intermediate **Y** (Path A). Intermediate **Y** undergoes tautomerisation to yield the desired product. Mechanistically, there was also the possibility for the formation of 2-pyranone (Path B), but the aryl naphthyl ketone has been regioselectively isolated. We proposed that C-C bond formation by attack of the carbanion at the nitrile group present in the aryl ring is more facile than C-O bond formation due to reaction of the enolate oxygen with the other nitrile group.



Scheme 5: Proposed mechanism for synthesis of 4-amino-3-aroyl/heteroaroyl/acetyl-2-methylsulfanylnapthalene-1-carbonitriles.

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In order to prove the mechanism, we have made various attempt to isolate the intermediate X, but failed. We performed the reaction using a ketone/base ratio of 2:1, but we got a mixture of products with the starting material and without any trace of intermediate. This concludes that, as soon as intermediate X forms in the reaction mixture, it immediately undergoes cyclization due to the formation of activated methylene group, which is more reactive the methyl group and cannot be isolated. We have also attempted the reaction to check that proton on amino group is coming from methyl group of aryl methyl ketone or after acidic work-up. We have performed two parallel reactions of **3** and acetone-d6 and acetone in DMSO-d6 in presence of potassium hydroxide. Reaction containing acetone shows additional peak at ~5.98 ppm in comparison to the mixture containing acetone-d6, which confirms that proton on amino group is coming from methyl group of aryl methyl ketone (See SI; Figure 1).

X-ray structural analysis

The structure of one of the products 4-amino-3-(4-methoxybenzoyl)-2-(pyrrolidin-1-yl)-1-naphthonitrile **10b** have been confirmed by X-ray crystallography (Fig. 3).[§] Compound **10b** crystallized in *P*-1 space group having two molecules in the triclinic unit cell. The naphthalene and the anisole rings are planar and the dihedral angle between the planes formed by the fused naphthalene and anisyl rings is 52.47°. The five membered pyrrolidine ring adopts a puckered half-chair conformation to relieve the strain resulting from the eclipsed orientation of the hydrogens and substituents on the adjacent carbon atoms. The proton H1b forms an intramolecular hydrogen bond with carbonyl oxygen O1 having an H1b···O1 interaction length of 1.891 Å with N1–H1b···O1 bond angle of 138.35°.

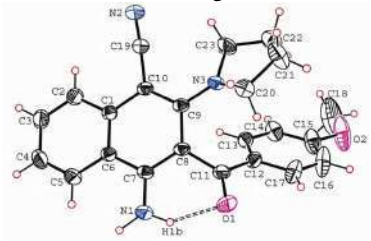

Fig. 2. ORTEP diagram of **10b** at 30% probability with atom numbering scheme. Only one molecule of the asymmetric unit comprising of two molecules is presented.

The compound displayed intermolecular N–H···N≡C interaction (Fig. 3) to form a one dimensional chain having an N···H interaction distance of 2.091 Å and interaction angle of 159.39° (symm. op. -1+*x,y,z*). Quantum chemical DFT calculations for the dimer held by N–H···N≡C interaction yielded the interaction energy of -8.18 kcal mol^{-1}. Additionally the atoms-in-molecules (AIM) theory calculations indicated the bond critical points between the H and N atoms, which also confirm the presence of this interaction between two molecules (see SI). The values of electron density (ρ) +0.019733; Laplacian (∇^2ρbcp) +0.059176; bond ellipticity (ε) +0.018129 and total energy density (H) +0.014103 at the bond critical point indicated the real interaction. The bond ellipticity (ε) measuring the extent to which the density is preferentially accumulated in a given plane of the bond path indicated that these N–H···N≡C interactions are not cylindrically symmetrical in nature.

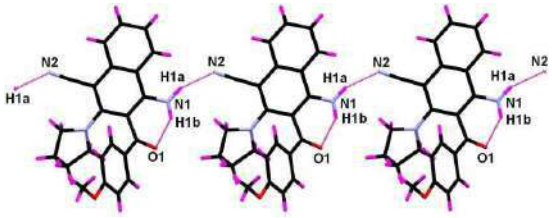

Fig. 3 One dimensional chain held by intermolecular N–H···N≡C interactions (symm. op. -1+*x,y,z*).

Conclusion

In conclusion, we have developed an economical, metal free one step (5+1) annulation strategy for the synthesis of 4-amino-3-aroyl/acetyl-2-methylsulfanyl/secamino-napthalene-1-carbonitriles. The precursor required for the synthesis of 4-amino-3-aroyl/acetylnapthalenes is easily accessible in one step in moderate to good yield. This synthesis is also atomically economical. We have not used any harsh reaction conditions and the structure was confirmed unambiguously by X-ray crystallography.

Experimental section

General remarks: We have used commercially available reagents without purification. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR and 100MHz NMR spectrometer and $CDCl_3$ was used as solvent. Chemical shifts are reported in parts per million shift (δ-value) from ($CDCl_3$) (δ 7.24 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet; bs, broad singlet and bm, broad multiplet. Coupling constants (*J*) are given in hertz (Hz). Infrared (IR) spectra was recorded on a Perkin-Elmer AX-1 spectrophotometer and reported in wave number (cm^{-1}). HRMS reported are showing the peak for M+H$^+$. Room temperature was ranging from 25-30 ºC during the reactions.

General procedure for the synthesis of 2-(1-cyano-2,2-bismethylsulfanylvinyl)benzonitrile 3: To a well dried 100 mL RB flask added THF (40.0 mL) and sodium Hydride [60% dispersion in mineral oil] (30.0 mmol, 1.20 g) and cooled on ice-bath. 2-Cyanomethyl-benzonitrile (15.0 mmol, 2.130 g) was added drop wise to the pre-cold basic solution. After complete addition, stirred the reaction mixture for one hour followed by drop-wise addition of carbondisulphide (16.5 mmol, 0.995mL) at 0-5 ^{0}C. Reaction mixture was further stirred for another hour followed by drop-wise addition of methyl iodide (33.0 mmol, 2.055 mL) over a period of 30 minutes. The reaction mixture was stirred for one hour. After completion, excess of THF was removed under reduced pressure. The mixture was poured onto ice-water with vigorous stirring, filtered the obtained precipitate and dried under vacuum. Compound was purified by recrystallization from 2% acetone in hexane.

2-(1-cyano-2,2-bis-methylsufanyl-vinyl)-benzonitrile 3: Yield: 90% (3.321 g) ; 0.42 R_f (20% ethylacetate-hexane), light yellow solid, mp: 82-84 ^{0}C; IR (KBr): 2925, 2853, 2226, 2200 cm^{-1}; ^{1}H NMR (400 MH_Z , $CDCl_3$): δ 2.41 (s, 3H, -SCH_3), 2.64 (s, 3H, -

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SCH_3), 7.43-7.49 (m, 2H, ArH), 7.61-7.66 (m, 1H, ArH), 7.70 (d, J = 8.0 Hz, 1H, Ar-H); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 18.0, 18.8, 107.1, 112.8, 116.9, 117.1, 129.1, 130.5, 133.2, 133.3, 137.8, 165.1; HRMS (ESI) calculated for $C_{12}H_{10}N_2S_2$, 247.0358 ($M+H^+$); found for *m/z*, 247.0358.

General procedure for the synthesis of 4-amino-3-aroyl-2-methylsulfanyl-napthalene-1-carbonitrile: To a 25 mL RB flask, a mixture of 2-(1-cyno-2,2-bismethylsulfanyl-vinyl)-benzonitrile (0.5 mmol, 0.123g), aryl/alkyl methyl ketone (0.55 mmol), and powdered KOH (1 mmol, 0.056g) in dry DMSO (4.0 mL) was stirred at room temperature for 2 h under dry condition. After completion (monitored by TLC) of reaction, the mixture was poured onto ice-water with constant stirring followed by neutralization with 10% HCl. The obtained precipitate was filtered off and dried. The crude product was purified by silica gel column chromatography using 15% ethylacetate in hexane as an eluent.

4-Amino-3-benzoyl-2-methylsulfanyl-napthalene-1-carbonitrile 5a: Yield: 81% (0.129 g); 0.28 R_f (20% ethylacetate-hexane), light brown solid mp: 166-168 ^{0}C; IR (KBr): 3372, 2921, 2205, 1638, 1248, 763 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.35 (s, 3H, -SCH_3), 5.37 (s, 2H, -NH_2), 7.39-7.47 (m, 2H, ArH), 7.53-7.63 (m, 2H, ArH), 7.69-7.76 (m, 3H, ArH), 7.84 (d, J = 8.0 Hz, 1H, ArH), 8.21 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.5, 104.6, 117.2, 120.5, 121.6, 121.6, 126.0, 127.0, 128.7, 129.1, 130.0, 133.5, 134.5, 138.5, 140.6, 145.3, 196.8; HRMS (ESI) calculated for $C_{19}H_{14}N_2OS$, 319.0900 ($M+H^+$); found for *m/z*, 319.0889.

4-Amino-3-(4-methyl-benzoyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5b: Yield: 41% (0.068 g); 0.27 R_f (20% ethylacetate-hexane), light yellow, mp: 170-172 ^{0}C; IR (KBr): 3367, 2926, 2854, 2206, 1627, 1242, 752 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.37 (s, 3H, -SCH_3), 2.40 (s, 3H, -CH_3), 5.27 (s, 2H, -NH_2), 7.21-7.25 (m, 2H, ArH), 7.53-7.61 (m, 1H, ArH), 7.63 (d, J = 8.0 Hz, 2H, ArH), 7.69-7.75 (m, 1H, ArH), 7.83 (d, J = 8.0 Hz, 1H, ArH), 8.20 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.5, 21.7, 104.3, 117.3, 120.9, 121.6, 125.9, 126.9, 129.3, 129.4, 129.9, 134.4, 135.7, 140.3, 144.8, 145.0, 196.3; HRMS (ESI) calculated for $C_{20}H_{16}N_2OS$, 333.1056 ($M+H^+$); found for *m/z*, 333.1044.

4-Amino-3-(4-methoxy-benzoyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5c: Yield: 48% (0.084 g); 0.24 R_f (20% ethylacetate-hexane), Brown solid, mp: 131-133^{0}C; IR (KBr): 3362, 2933, 2207, 1630, 1594, 1259, 752 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.40 (s, 3H, -SCH_3), 3.85 (s, 3H, -OCH_3), 5.19 (s, 2H, -NH_2), 6.90 (d, J = 8.8 Hz, 2H, Ar-H), 7.54-7.62 (m, 1H, ArH), 7.67-7.76 (m, 3H, ArH), 7.82 (d, J = 8.0 Hz, 1H, ArH), 8.20 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.6, 55.5, 104.4, 114.0, 117.3, 121.3, 121.5, 121.6, 126.0, 126.9, 129.8, 130.9, 131.8, 134.4, 140.2, 144.7, 164.2, 195.1; HRMS (ESI) calculated for $C_{20}H_{16}N_2O_2S$, 349.1005 ($M+H^+$); found for *m/z*, 349.0990.

4-Amino-3-(4-bromo-benzoyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5d: Yield: 68% (0.135 gm); 0.26 R_f (20% ethylacetate-hexane); light yellow solid, mp: 152-154 ^{0}C; IR (KBr): 3361, 2924, 2207, 1638, 1249, 749 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.37 (s, 3H, -SCH_3), 5.45 (s, 2H, -NH_2), 7.51-7.69 (m, 5H, ArH), 7.70-7.78 (m, 1H ,ArH), 7.83 (d, J = 8.0 Hz, 1H, ArH), 8.21 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.6, 104.7, 117.1, 119.6, 121.6, 121.6, 126.1, 127.2, 128.7, 130.2, 130.5, 132.0, 134.5, 137.5, 140.5, 145.6, 195.7; HRMS (ESI) calculated for $C_{19}H_{13}BrN_2OS$, 397.0005 ($M+H^+$); found for *m/z*, 396.9983.

4-Amino-3-(2-bromo-benzoyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5e: Yield 48% (0.095 g); 0.26 R_f (20% ethylacetate-hexane); yellow solid, mp: 188-190 ^{0}C; IR (KBr): 3369, 2925, 2211, 1609, 1245, 757 cm^{-1}; ^{1}H NMR (400 MH_Z , $CDCl_3$): δ 2.23 (s, 3H, -SCH_3), 6.56 (s, 2H, -NH_2), 7.15-7.20 (m, 1H, ArH), 7.23-7.29 (m, 2H, ArH), 7.57-7.67 (m, 2H, ArH), 7.74 (t, J = 7.7 Hz, 1H, ArH), 7.90 (d, J = 8.0 Hz, 1H, ArH), 8.17 (d, J = 8.8 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.4, 105.2, 117.1, 118.0, 121.3, 121.8, 121.9, 126.1, 126.9, 127.2, 130.1, 130.8, 131.7, 134.2, 134.6, 142.4, 142.6, 148.9, 196.7; HRMS (ESI) calculated for $C_{19}H_{13}BrN_2OS$, 397.0005 ($M+H^+$); found for *m/z*, 397.0007.

3-(2-Allyloxy-benzoyl)-4-amino-2-methylsulfanyl-napthalene-1-carbonitrile 5f: Yield: 60% (0.112 g); 0.37 R_f (40% ethylacetate-hexane), light yellow, mp: 165-167 ^{0}C; IR (KBr): 3372, 2929, 2208, 1610, 1240, 757 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.26 (s, 3H, -SCH_3), 4.29-4.33 (m, 2H , -CH_2-), 4.78-4.86 (dd, J = 1.4 Hz, 1H, CH), 4.96-5.06 (m, 1H, CH), 5.32-5.46 (m, 1H, CH), 5.88 (s, 2H, -NH_2), 6.85 (d, J = 8.0 Hz, 1H, ArH), 6.99 (t, J = 7.7 Hz, 1H, ArH), 7.38-7.47 (m, 1H, ArH), 7.56 (t, J = 7.7 Hz, 1H, ArH), 7.60-7.64 (m, 1H, ArH), 7.69 (t, J = 7.7 Hz, 1H, ArH), 7.84 (d, J = 8.8 Hz, 1H, ArH), 8.15 (d, J = 8.8 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.2, 69.1, 104.2, 112.7, 117.4, 117.7, 120.7, 121.7, 122.0, 122.2, 125.9, 126.7, 129.9, 130.0, 130.9, 131.8, 133.7, 134.3, 141.6, 146.1, 157.4, 196.0; HRMS (ESI) calculated for $C_{22}H_{18}N_2O_2S$, 375.1162 ($M+H^+$); found for *m/z*, 375.1161.

4-Amino-3-(furan-2-carbonyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5g: Yield: 60% (0.092 g); 0.30 R_f (40% ethylacetate-hexane), dark green solid, mp: 196-98 ^{0}C; IR (KBr): 3371, 2925, 2209, 1618, 1298, 756 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.46 (s, 3H, -SCH_3), 5.46 (s, 2H, -NH_2), 6.53-6.57 (dd, J = 1.4 Hz, 1H, ArH), 7.03 (d, J = 3.6 Hz, 1H, ArH), 7.55-7.64 (m, 2H, ArH), 7.69-7.76 (m, 1H, ArH), 7.83 (d, J = 8.0 Hz, 1H, ArH), 8.19 (d, J = 8.05 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.0, 100.0, 112.9, 117.6. 119.5, 120.6, 121.4, 123.8, 124.4, 126.3, 130.2, 134.1, 139.2, 146.6, 148.6, 152.8, 182.1; HRMS (ESI) calculated for $C_{17}H_{12}N_2O_2S$, 309.0692 ($M+H^+$); found for *m/z*, 309.0677.

4-Amino-2-methylsulfanyl-3-(thiophene-2-carbonyl)-napthalene-1-carbonitrile 5h: Yield: 61% (0.099 g); 0.31 R_f (30% ethylacetate-hexane), yellow solid mp: 173-175 ^{0}C; IR (KBr): 3362, 2929, 2207, 1624, 1271, 727 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 2.47 (s, 3H, -SCH_3), 5.24 (s, 2H, -NH_2), 7.06-7.10 (m, 1H, ArH), 7.32-7.37 (m, 1H, ArH), 7.56-7.63 (m, 1H, ArH), 7.69-7.76 (m, 2H, ArH), 7.82 (d, J = 8.8 Hz, 1H, ArH), 8.21 (d, J = 8.0 Hz,1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 20.9, 104.5, 117.2, 121.2, 121.5, 121.6, 126.0, 127.0, 128.3, 130.0, 134.4, 134.8, 135.5, 140.2, 144.7, 145.1, 188.3; HRMS (ESI) calculated for $C_{17}H_{12}N_2OS_2$, 325.0464 ($M+H^+$); found for *m/z*, 325.0450.

4-Amino-2-methylsulfanyl-3-(naphthalene-1-carbonyl)-napthalene-1-carbonitrile 5i: Yield: 48% (0.088 g); 0.25 R_f

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(20% ethylacetate-hexane), orange solid, mp: 187-189 ^{0}C; IR (KBr): 3372, 2925, 2210, 1609, 1240, 759 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 2.12 (s, 3H, -SCH$_3$), 5.95 (s, 2H, -NH$_2$), 7.22-7.35 (m, 2H, ArH), 7.55-7.71 (m, 4H ,ArH), 7.90 (d, *J* = 8.0 Hz, 2H, ArH), 7.95 (d, *J* = 8.0 Hz, 1H, ArH), 8.19 (d, *J* = 8.0 Hz, 1H, ArH), 8.78 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 20.3, 104.9, 117.2, 121.1, 121.6, 121.8, 124.0, 126.0, 126.7, 127.1, 128.2, 128.5, 128.8, 130.3, 130.7, 133.1, 134.0, 134.6, 137.6, 141.9, 146.8, 198.9; HRMS (ESI) calculated for $C_{23}H_{16}N_2OS$, 369.1056 (M+H$^+$); found for *m/z*, 369.1038.

4-Amino-2-methylsulfanyl-3-(naphthalene-2-carbonyl)-napthalene-1-carbonitrile 5j: Yield: 68% (0.125 g); 0.25 R$_f$ (20% ethylacetate-hexane), yellow solid, mp: 192-193 ^{0}C; IR (KBr): 3372, 2925, 2208, 1617, 1291, 754 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 2.34 (s, 3H, -SCH$_3$), 5.38 (s, 2H, -NH$_2$), 7.47-7.53 (m, 1H, ArH), 7.55-7.66 (m, 2H ,ArH), 7.75 (t, *J* = 7.3 Hz, 1H, ArH), 7.82 (d, *J* = 8.0 Hz, 1H, ArH), 7.85-7.90 (m, 2H, ArH), 7.90-7.96 (m, 2H, ArH), 8.07 (s, 1H, ArH), 8.25 (d, *J* = 8.0Hz, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 20.6, 104.7, 117.2, 120.8, 121.6, 121.7, 124.3, 126.1, 126.9, 127.0, 127.8, 128.8, 129.6, 130.0, 131.1, 132.4, 134.5, 135.8, 135.9, 140.6, 145.4, 196.7; HRMS (ESI) calculated for $C_{23}H_{16}N_2OS$, 369.1056 (M+H$^+$); found for *m/z*, 369.1033.

3-Acetyl-4-amino-2-methylsulfanyl-napthalene-1-carbonitrile 5k: Yield: 45% (0.058 gm); 0.35 R$_f$ (20% ethylacetate-hexane), light brown solid, mp: 140-142 ^{0}C; IR (KBr): 3373, 2925, 2854, 2210, 1611, 1234, 757 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 2.56 (s, 3H, -SCH$_3$), 2.70 (s, 3H, -CH$_3$), 6.04 (s, 2H, -NH$_2$), 7.48-7.60 (m, 1H, ArH), 7.65-7.72 (m, 1H, ArH), 7.83 (d, *J* = 8.8 Hz, 1H, ArH), 8.14 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 20.7, 32.6, 104.5, 117.2, 120.9, 121.7, 122.0, 126.0, 127.0, 130.3, 134.1, 140.5, 145.7, 204.1; HRMS (ESI) calculated for $C_{14}H_{12}N_2OS$, 257.0743 (M+H$^+$); found for *m/z*, 257.0730.

4-Amino-3-(4-fluoro-benzoyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5l: Yield: 52% (0.087 g); 0.30 R$_f$ (20% ethylacetate-hexane), yellow solid, mp: 144-146 ^{0}C; IR (KBr): 3328, 2929, 2209, 1611, 1228, 757 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 2.37 (s, 3H, -SCH$_3$), 5.49 (s, 2H, -NH$_2$), 7.10 (t, *J* = 8.79Hz, 2H, ArH), 7.60 (t, *J* = 7.3 Hz, 1H, ArH), 7.70-7.78 (m, 3H, ArH), 7.83 (d, *J* =8.0 Hz, 1H, ArH), 8.21 (d, *J* = 8.8 Hz, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 20.5, 104.6, 115.6 (d, $J_{C\text{-}F}$ = 22.0 Hz), 117.1, 120.1, 121.6, 126.6, 127.1, 130.1, 131.8 (d, $J_{C\text{-}F}$ = 9.6 Hz), 134.4, 134.8, 134.9, 140.4, 145.3, 166.0 (d, $J_{C\text{-}F}$ = 253.9Hz), 195.2; HRMS (ESI) calculated for $C_{19}H_{13}FN_2OS$, 337.0805 (M+H$^+$); found for *m/z*, 337.0789.

4-Amino-3-(4-chloro-benzoyl)-2-methylsulfanyl-napthalene-1-carbonitrile 5m: Yield: 48% (0.085 g); 0.31 R$_f$ (20% ethylacetate-hexane), orange solid, mp: 135-137 ^{0}C; IR (KBr): 3377, 2925, 2210, 1620, 1261, 757 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 2.37 (s, 3H, -SCH$_3$), 5.42 (s, 2H, -NH$_2$), 7.39 (d, *J* = 8.8 Hz, 2H, ArH), 7.57-7.67 (m, 3H ,ArH), 7.71-7.77 (m, 1H, ArH), 7.83 (d, *J* = 8.8 Hz, 1H, ArH), 8.21 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 20.5, 104.4, 117.1, 119.6, 121.6, 121.6, 126.0, 127.1, 129.0, 130.2, 130.4, 134.4, 136.9, 139.9, 140.4, 145.6, 195.6; HRMS (ESI) calculated for $C_{19}H_{13}ClN_2OS$, 353.0510 (M+H$^+$); found for *m/z*, 353.0490.

4-Amino-2-methylsulfanyl-3-(4-methylsulfanyl-benzoyl)-napthalene-1-carbonitrile 7: Yield: 30% (0.055 g); 0.30 R$_f$ (30% ethylacetate-hexane), yellow solid, mp: 137-139 ^{0}C; IR (KBr): 3375, 2919, 2206, 1636, 1248, 755 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 2.40 (s, 3H, -SCH$_3$), 2.50 (s, 3H, -SCH$_3$), 5.28 (s, 2H, -NH$_2$), 7.20-7.26 (m, 2H, ArH), 7.56-7.68 (m, 3H ,ArH), 7.70-7.77 (m, 1H, ArH), 7.83 (d, *J* = 8.8 Hz, 1H, ArH) , 8.22 (d, *J* = 8.8 Hz, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 14.6, 20.6, 104.4, 117.2, 120.7, 121.5, 124.9, 126.0, 127.0, 129.6, 129.9, 134.3, 134.4, 140.3, 145.0, 147.1, 195.6; HRMS (ESI) calculated for $C_{20}H_{16}N_2OS_2$, 365.0777 (M+H$^+$); found for *m/z*, 365.0780.

General procedure synthesis of 2-(1-cyano-2-methylsulfanyl-2-pyrrolidine-1-yl-vinyl)-benzonitrile. A mixture of 2-(1-cyno-2,2-bismethylsulfanyl-vinyl)-benzonitrile (1 mmol, 0.246g), pyrrolidine (as a solvent 5.0 mL) was stirred at 90 °C temperature for 1h. After completion (monitored by TLC) of reaction, the mixture was poured onto ice-water with constant stirring followed by neutralization with 10% HCl. The obtained precipitate was filtered off and dried over Na_2SO_4. Crude contains both mono and diaminated product. The crude product was purified by silica gel column chromatography using 20% ethylacetate-hexane as an eluent for monoaminated product and 25% ethyl acetate in hexane as an eluent for diaminated product.

2-(1-Cyano-2-methylsulfanyl-2-pyrrolidine-1-yl-vinyl)-benzonitrile 8: 2-(1-Cyano-2-methylsulfanyl-2-pyrrolidine-1-yl-vinyl)-benzonitrile 8: Yield: 73% (0.196 gm); red, 0.32 R$_f$ (20% ethylacetate-hexane), mp: 191-193 ^{0}C; IR (KBr) 2924, 2853, 2220, 2181, 1514, 1252, 761 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 1.83-1.93 (bm, 4H , -CH$_2$-), 2.56 (s, 3H , -SCH$_3$), 3.10-3.60 (bm, 4H, -CH$_2$-), 7.15-7.22 (m, 1H, ArH), 7.45-7.58 (m, 3H, ArH); ^{13}C NMR (100 MH$_Z$ CDCl$_3$): δ 18.9, 25.3, 52.6, 111.7, 118.0, 122.1, 125.7, 129.6, 132.6, 132.8, 141.4, 165.6; HRMS (ESI) calculated for $C_{15}H_{15}N_3S$, 270.1059 (M+H$^+$); found for *m/z*, 270.1059.

2-(1-Cyano-2,2-di-pyrrolidine-1-yl-vinyl)-benzonitrile 9: Yield: 10% (0.029 gm); 0.30 R$_f$ (10% ethylacetate-hexane), light red, mp: 120-122 ^{0}C; IR (KBr): 2925, 2869, 2181, 1537, 1295, 756, cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 1.92-2.00 (m, 8H , -CH$_2$-), 3.76-3.87 (m, 8H, -CH$_2$-), 7.00-7.08 (m, 1H, ArH), 7.40-7.50 (m, 1H, ArH), 7.78 (d, *J* = 8.0 Hz, 1H, ArH), 7.96 (d, *J* = 8.0, 1H, ArH); ^{13}C NMR (100 MH$_Z$, CDCl$_3$): δ 25.5, 25.8, 48.7, 51.2, 69.2, 113.7, 120.5, 121.8, 122.5, 126.2, 130.6, 141.9, 155.5, 157.1.

General procedure synthesis of 4-amino-3-aroyl-2-pyrrolidin-1-yl-napthalene-1-carbonitriles: A mixture of 2-(1-cyano-2-methylsulfanyl-2-pyrrolidine-1-yl-vinyl)-benzonitrile (0.5 mmol, 0.134 g), ketone (0.55 mmol), and powdered KOH (1 mmol, 0.056 g) in dry DMSO (4.0 mL) was stirred at room temperature for 2 h. After completion (monitored by TLC) of reaction, the mixture was poured onto ice-water with constant stirring followed by neutralization with 10% HCl. The obtained precipitate was filtered, dried and purified by silica gel column chromatography using 20% ethylacetate-hexane as an eluent.

4-Amino-3-benzoyl-2pyrrolidin-1-yl-napthalene-1-carbonitrile 10a: Yield: 72% (0.123 g); 0.32 R$_f$ (20% ethylacetate-hexane), brown solid, mp: 192-194 ^{0}C; IR (KBr): 3325, 2925, 2855, 2192, 1608, 1256, 755 cm^{-1}; ^{1}H NMR (400 MH$_Z$, CDCl$_3$): δ 1.32-1.37 (m, 4H ,-CH$_2$-), 3.39-3.45 (m, 4H, -CH$_2$-), 6.42 (s, 2H, -NH$_2$), 7.31-7.39 (m, 3H, ArH), 7.44-7.51 (m, 1H ,ArH), 7.54-7.65 (m, 3H, ArH), 7.73 (d, *J* = 8.0 Hz, 1H, ArH),

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8.03 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 25.2, 51.8, 109.2, 118.7, 120.4, 121.6, 123.7, 124.8, 128.0, 128.7, 130.6, 132.2, 136.7, 139.9, 149.2, 153.4, 197.0; HRMS (ESI) calculated for $C_{22}H_{19}N_3O$, 342.1601 ($M+H^+$); found for *m/z*, 342.1601.

4-Amino-3-(4-methoxy-benzoyl)-2-pyrrolidin-1-yl-napthalene-1-carbonitrile 10b: Yield: 45% (0.083 g); 0.31 R_f (20% ethylacetate-hexane), light yellow, mp: 197-199 ^{0}C; IR (KBr): 3351, 2924, 2191, 1594, 1251, 763 cm^{-1}; ^{1}H NMR (400 MH_Z , $CDCl_3$): δ 1.42-1.47(m, 4H , $-CH_2-$), 3.44-3.50 (m, 4H, $-CH_2-$), 3.83 (s, 3H, $-OCH_3$), 6.17 (s, 2H, $-NH_2$) , 6.84 (d, J = 8.8 Hz, 2H, ArH), 7.29-7.35 (m, 1H ,ArH), 7.57-7.63 (m, 3H, ArH), 7.70 (d, J = 8.0 Hz, 1H, ArH), 8.03 (d, J = 8.8 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 25.4, 51.9, 55.4, 82.8, 109.3, 113.3, 118.7, 120.6, 121.6, 123.5, 124.7, 130.4, 131.2, 132.0, 136.6, 148.5, 153.1, 163.1, 195.8; HRMS (ESI) calculated for $C_{23}H_{21}N_3O_2$, 372.1707 ($M+H^+$); found for *m/z*, 372.1684.

4-Amino-3-(furan-2-carbonyl)-2-pyrrolidin-1-yl-napthalene-1-carbonitrile 10c: Yield: 57% (0.094 g); 0.21 R_f (20% ethylacetate-hexane), orange solid, mp: 170-172 ^{0}C; IR (KBr): 2926, 2225, 1618, 1227, 757 cm^{-1}; ^{1}H NMR (400 MH_Z , $CDCl_3$): δ 1.62-1.67 (m, 4H , $-CH_2-$), 3.58-3.64 (m, 4H,- CH_2-), 6.23 (s, 2H, $-NH_2$), 6.45-6.48 (dd, J = 2.2 Hz, 1H, ArH), 6.91 (d, J = 2.9 Hz, 1H, ArH), 7.26-7.33 (m, 1H, ArH), 7.52-7.62 (m, 2H, ArH), 7.68 (d, J = 8.8 Hz, 1H, ArH), 8.00 (d, J = 8.8 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 25.7, 52.2, 82.3, 108.0, 112.1, 117.8, 118.3, 120.7, 121.6, 123.4, 124.7, 130.7, 137.0, 146.2, 148.7, 152.7, 153.6, 183.5; HRMS (ESI) calculated for $C_{20}H_{17}N_3O_2$, 332.1394 ($M+H^+$); found for *m/z*, 332.1396 .

4-Amino-2-pyrrolidin-1-yl-3-(thiophene-2-carbonyl)-napthalene-1-carbonitrile 10d: Yield: 58% (0.101 g); 0.30 R_f (20% ethylacetate-hexane), yellow solid, mp: 171-173 ^{0}C; IR (KBr): 3349, 2925, 2854, 2190, 1597, 1253, 759 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ 1.57-1.67 (m, 4H , $-CH_2-$), 3.59-3.65 (m, 4H, $-CH_2-$), 6.09 (s, 2H, $-NH_2$), 6.99-7.04 (m, 1H, ArH), 7.27-7.36 (m, 2H, ArH), 7.56-7.62 (m, 2H, ArH), 7.68 (d, J = 8.0 Hz, 1H, Ar-H), 8.02 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ 25.6, 52.2, 82.5, 109.0, 118.3, 120.6, 121.6, 123.4, 124.6, 127.6, 130.5, 133.0, 133.3, 136.8, 145.3, 148.0, 152.2, 188.5; HRMS (ESI) calculated for $C_{20}H_{17}N_3OS$, 348.1165 ($M+H^+$); found for *m/z*, 348.1147.

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§ Crystal data for **10b** (CCDC 967742): $C_{23}H_{21}N_3O_2$, FW= 371.43, Triclinic, P -1, a = 9.094(5) Å, b = 13.650(5) Å, c = 16.253(5) Å, α = 80.99(3), β = 85.10(3), γ = 72.87(4) V = 1902.6(14) Å^3, T = 298(2) K, Z = 4, μ, mm^{-1} = 0.084, d_{calc}, g cm^{-3} = 1.297, R_1 [$I > 2\sigma(I)$] = 0.0787, wR_2 = 0.1529, R_1 [all data] = 0.1815, wR_2 = 0.2068, S = 1.010.

† Electronic Supplementary Information (ESI) available: Crystallographic and Computations details and CIF file for **10b**. See DOI: 10.1039/b000000x/

† Electronic Supplementary Information (ESI) available: [All the proton and ^{13}C NMR spetra are given in SI]. See DOI: 10.1039/b000000x/

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Microwave assisted base dependent regioselective synthesis of partially reduced chromenes, isochromenes and phenanthrenes†‡

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We have reported a microwave assisted base directed regioselective synthesis of partially reduced chromenes, isochromenes and phenanthrenes. Functionalized 4-(piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]-chromen-2-one-3-carbonitriles have been used as precursors, which on reaction with functionalized acetophenones in the presence of KOH in DMF under microwave irradiation yield (*Z*)-2-(2-aryl-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitriles. The use of NaH in DMF provides 3-aryl-1-(piperidin-1-yl)-9,10-dihydro phenanthrene-2-carbonitriles in excellent yield regioselectively. The use of cyclohexanone as a nucleophile source yields (*Z*)-2-(3,4,7,8-tetrahydro-1*H*-naphtho[2,1-*c*]chromen-6(2*H*)-ylidene)acetonitriles. The structure and geometry of isochromene have been proved without any ambiguity by single crystal X-ray diffraction.

Introduction

The development of a new approach for the preparation of biologically active molecules constitutes a great challenge in modern organic chemistry. This challenge has led to growing interest in the field of microwave-enhanced procedures due to great reaction control and high reaction rates. Therefore, microwave-assisted organic synthesis (MAOS) is an invaluable technique for medicinal chemistry and drug discovery applications.[1,2]

Chromenes and isochromene are well known structural motifs that are frequently encountered in bioactive natural products.[3] They are also considered to be a venerable pharmacophore and exhibit a wide range of biological activities such as anti-HIV,[4] anticancer,[5] antihypertensive,[6] insecticidal,[7] and antifungal.[8] Seselin **i** and lonchocarpene **ii** are used as anticancer agents,[9,10] whereas acolbifene **iii**, LG120746 **iv** and **v** are a class of selective estrogen receptor modulators and progesterone receptor modulators, respectively (Fig. 1).[11,12] In addition, cannabinol **vi** has affinity towards CB1 and CB2 receptors, while moracin D **vii** is currently known as an antifungal agent (Fig. 1).[8,13] Apart from this, phenanthrenes have also drawn great attention because of their wide presence in natural products as well as their applications in medicinal chemistry and materials science.[14]

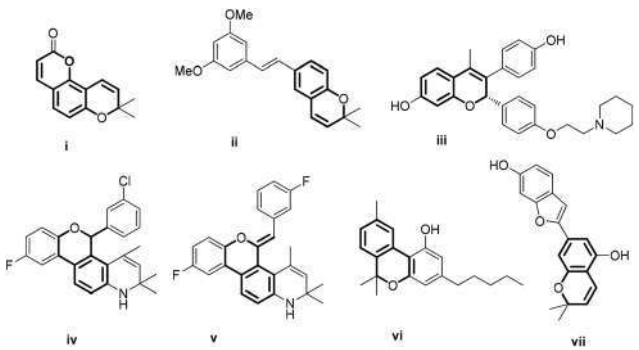

Fig. 1 Some natural products and biologically potent molecules containing chromene and isochromene skeletons.

Among the various functionalized chromenes, 2-ylidene-chromene is a very good progesterone receptor modulator.[12] Recently, Yanai *et al.* have reported a triple carbon acid (KSAs) catalysed synthesis of ylidene-isochromenes *via* reaction of lactones with ketene silyl acetals,[15] whereas Pal *et al.* used $AlCl_3$/Pd/C–Cu as a catalyst[16] (Scheme 1). Organolithium reagents[17] and Grignard reagents[18] were also used to construct this chromene skeleton. However, some protocols suffer from certain drawbacks, such as the use of moisture and air sensitive reagents, low yields and prolonged reaction time.[16–18]

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† This manuscript is dedicated to Dr Vishnu Ji Ram on his 72nd birthday.

‡ Electronic supplementary information (ESI) available: All the proton and ^{13}C NMR spectra are given in ESI. CCDC 959771. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ob41962b

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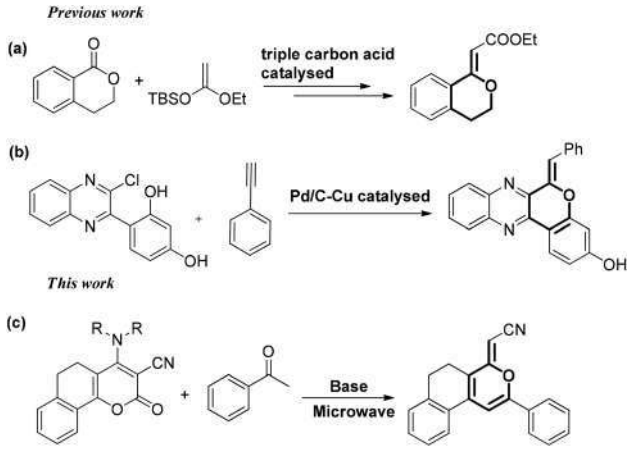
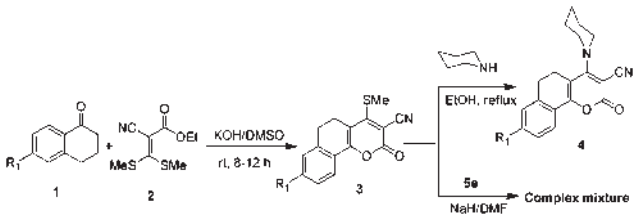


Scheme 1 Synthesis of 2-ylidene-chromenes and isochromenes using various catalysts.

These interesting versatile pharmaceutical activities of 2-ylidene chromene have prompted us towards the improved synthesis of this skeleton. As a part of our continual work towards exploring the synthetic utility of functionalized 2-oxabenzochromene for the synthesis of various biologically important aromatic nucleuses, we wish to report herein a simple and efficient base catalysed microwave assisted regioselective synthesis of isochromene, chromenes and dihydrophenanthrene. The synthesized compounds contain both an exocyclic double bond and an aryl ring attached to the chromene ring, which were important for pharmaceutical activity.[12]

Results and discussion

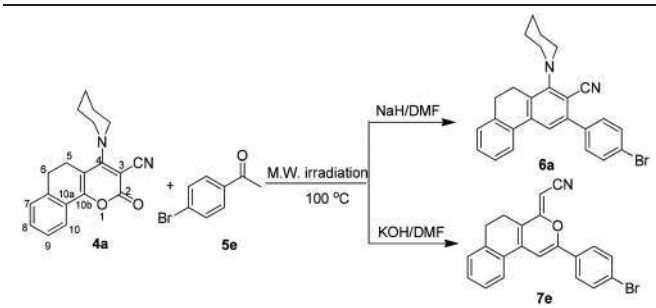
For the synthesis of chromene, isochromenes and dihydrophenanthrenes, 4-(piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]-chromen-2-one-3-carbonitrile **4a** has been taken as a precursor. This precursor was synthesized in three steps. The first step was synthesis of ethyl 2-cyano-3,3-dimethylthioacrylate **2**[19] by reaction of ethyl cyanoacetate, carbon disulphide and methyl iodide under basic conditions, which on reaction with various 1-tetralones gives 4-(methylthio)-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **3**.[20] We have tested compound **3** as a precursor for the synthesis of chromenes and dihydrophenanthrenes under various reaction conditions at different temperatures, but fail to achieve the desired product and end up with formation of a complex mixture. We assume that the presence of the SMe group at position 4 is the most probable reason for the formation of a complex mixture, as the SMe group acts as a good leaving group and is responsible for side reactions, and decomposed at high temperature.[20] Therefore in order to reduce the probability of side reactions, SMe has been replaced by piperidine, a secondary amine to reduce the electrophilicity of C-4. 4-(Piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]chromen-2-one-3-carbonitrile **4** was synthesised by amination of **3** with piperidine in boiling ethanol (Scheme 2).[20]



Scheme 2 Synthesis of 4-(piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]-chromen-2-ones **4**.

In search of better reaction conditions to achieve our goal, 4-(piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]chromen-2-one-3-carbonitrile **4a** and 4-bromoacetophenone **5e** were taken as model substrates. We have screened various base–solvent combinations at various temperatures using conventional heating as well as microwave mediated heating. The use of NaH–DMF at room temperature and 100 °C yields dihydrophenanthrene regioselectively, without the formation of **7e** (Table 1, entries 1 and 2). Previously, Ram *et al.* have already reported the regioselective synthesis of dihydrophenanthrenes using KOH–DMF at room temperature.[20] We checked the effect of temperature on the earlier reported reaction and surprisingly got the mixture of dihydrophenanthrene **6a** and isochromenes **7e** (Table 1, entry 3). We envisioned that **7e** might be synthesized regioselectively under appropriate reaction conditions. With the earlier results, we were encouraged to perform further

Table 1 Effect of base and solvent on the synthesis of **6a** and **7e**[a]



Entry	Base[b]	Solvent	Condition	Yield of **6a**[c] (%)	Yield of **7e**[c] (%)
1	NaH	DMF	rt[d]	75	—
2	NaH	DMF	100 °C[e]	78	—
3	KOH	DMF	100 °C[e]	35	43
4	$NaNH_2$	DMF	100 °C[e]	32	40
5	$KOBu^t$	DMF	100 °C[e]	73	Trace
6	KOH	DMF	M.W.[f]	—	82
7	$KOBu^t$	DMF	M.W.[f]	76	—
8	NaH	DMF	M.W.[f]	90	—
9	$NaNH_2$	DMF	M.W.[f]	Mixture	
10	NaH	THF	M.W.[f]	—	—
11	KOH	DMSO	M.W.[f]	Trace	48

[a] The reaction was conducted with 2-oxo-4-(piperidin-1-yl)-5,6-dihydro-2-benzo[*h*]chromene-3-carbonitrile **4a** (0.5 mmol) and 4-bromoacetophenone **5e** (0.5 mmol). [b] 0.75 mmol (1.5 eq.). [c] Yield of isolated product. [d] Reaction time 4 hours. [e] Reaction time 1 hour. [f] Under a microwave reactor at 100 °C at a maximum applied power of 200 W, 15 minutes.

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optimization through various bases (KOH, $NaNH_2$, and $KOBu^t$) in different solvents (DMF, DMSO and THF). It was found that the use of KOH and $NaNH_2$ resulted in the desired product **7e** in 43% and 40% yield, whereas $KOBu^t$ did not give satisfactory results and only **6a** was obtained as a major product. In view of the previously reported organic synthesis to achieve high regioselectivity,[21] we turned our attention to a microwave assisted procedure. In order to elaborate our study, the previously used bases were further screened to synthesize **7e** under microwave irradiation.

Surprisingly, when we carried out the reaction under microwave conditions (100 °C, at a maximum applied power of 200 watts), interesting results were obtained. The use of KOH with DMF yielded **7e** as an exclusive product (Table 1, entry 6). Whereas $KOBu^t$ and NaH were found to be inefficient at producing the desired product, **6a** was obtained in 76% and 90% yield respectively. A complex mixture of **6a** and **7e** was found when we used $NaNH_2$ as a base. Furthermore, we performed the reaction in THF and DMSO with NaH and KOH to investigate the solvent effect under microwave conditions. The desired product **7e** was obtained in moderate yield in DMSO. However neither **6a** nor **7e** was observed in THF. Thus KOH and NaH were found to be the best bases in DMF for the regioselective synthesis of isochromene **7e** and dihydrophenanthrene **6a**, respectively.

Under these optimized reaction conditions, the generality of this procedure has been examined. Various functionalized isochromenes **7a–g** were synthesized in very good yields (Table 2).

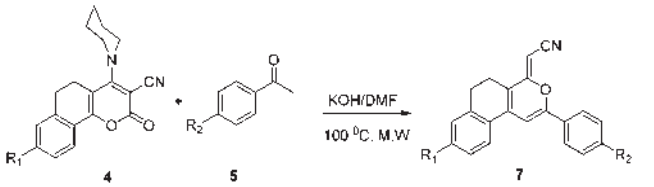
The structure and geometry of isochromene have been confirmed unambiguously by spectroscopic techniques and single crystal X-ray crystallography. The ^1H NMR spectrum of the desired product **7** exhibits a low δ value for proton (~4.40 ppm) at the carbon adjacent to the nitrile group due to the high shielding effect of pyran oxygen.[22] To assess the contribution of heteroaryl methyl ketone and aliphatic ketone as cyclohexanone to further expand the scope of the present methodology, isochromenes **9a–b** and chromenes **11a–b** were also synthesized and the results of this study are summarized in Tables 3 and 4.

All the ketone (aromatic and heteroaromatic) derivatives showed equal ease towards the product formation with 2-oxo-4-(piperidin-1-yl)-5,6-dihydro-2-benzo[*h*]chromene-3-carbonitriles **4**. It is noteworthy that the yield of chromenes **11a–b** was slightly lower.

Dihydrophenanthrenes **6a–c** were also synthesised using NaH and DMF under microwave conditions in good to excellent yields (Table 5). It has been observed that the yield of **6** is very high and the reaction requires much less time as compared to the conventional approach.

The molecular make up of precursor **4** reveals that it possesses three electrophilic centers C-2, C-4, and C-10b. Among them C-10b is highly susceptible to nucleophilic attack because of extended conjugation due to the presence of an electron withdrawing CN substituent at C-3 in the chromene

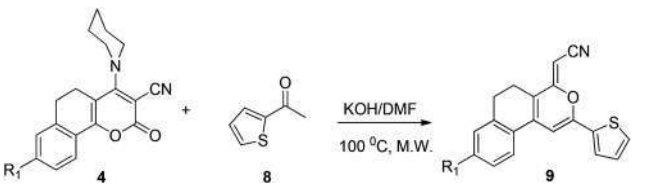
Table 2 Synthesis of (*Z*)-2-(2-aryl-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitriles **7**[a]



7	R_1	R_2	Yield (%)
a	H	H	77
b	H	OMe	79
c	H	F	84
d	H	Cl	80
e	H	Br	82
f	OMe	Br	85
g	OMe	OMe	78

[a] Reactions were performed under microwave irradiation at 100 °C and at a maximum applied power of 200 W for 15 minutes by use of **4** (0.5 mmol), **5** (0.5 mmol) and KOH (0.75 mmol) in 2.0 mL DMF.

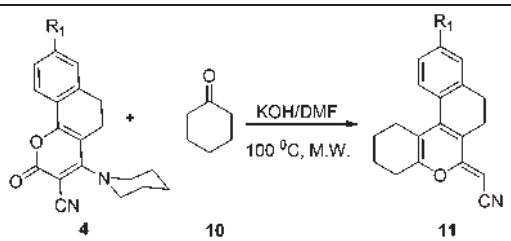
Table 3 Synthesis of (*Z*)-2-(2-(thiophen-2-yl)-5,6-dihydro-4*H*-benzo-[*f*]isochromen-4-ylidene)acetonitriles **9**[a]



9	R_1	Yield (%)
a	H	78
b	OMe	76

[a] Reactions were performed under microwave irradiation at 100 °C and at a maximum applied power of 200 W for 15 minutes by use of **4** (0.5 mmol), **8** (0.5 mmol), and KOH (0.75 mmol) in 2.0 mL DMF.

Table 4 Synthesis of (*Z*)-2-(3,4,7,8-tetrahydro-1*H*-naphtho [2,1-*c*]-chromen-6(2*H*)-ylidene)acetonitriles **9**[a]



11	R_1	Yield (%)
a	H	72
b	OMe	69

[a] Reactions were performed under microwave irradiation at 100 °C and at a maximum applied power of 200 W for 15 minutes by use of **4** (0.5 mmol), **10** (0.5 mmol), and KOH (0.75 mmol) in 2.0 mL DMF.

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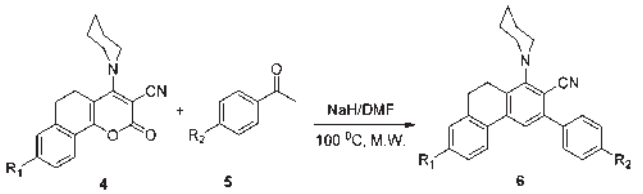
Table 5 Synthesis of 3-phenyl-1-(piperidin-1-yl)-9,10-dihydro phenanthrene-2-carbonitriles **6**[a]



6	R_1	R_2	Yield (%)
a	H	Br	90
b	H	OMe	86
c	OMe	Br	87

[a] Reactions were performed under microwave irradiation at 100 °C and at a maximum applied power of 200 W for 15 minutes by use of **4** (0.5 mmol), **5** (0.5 mmol), and NaH 0.75 mmol in 2.0 mL DMF.

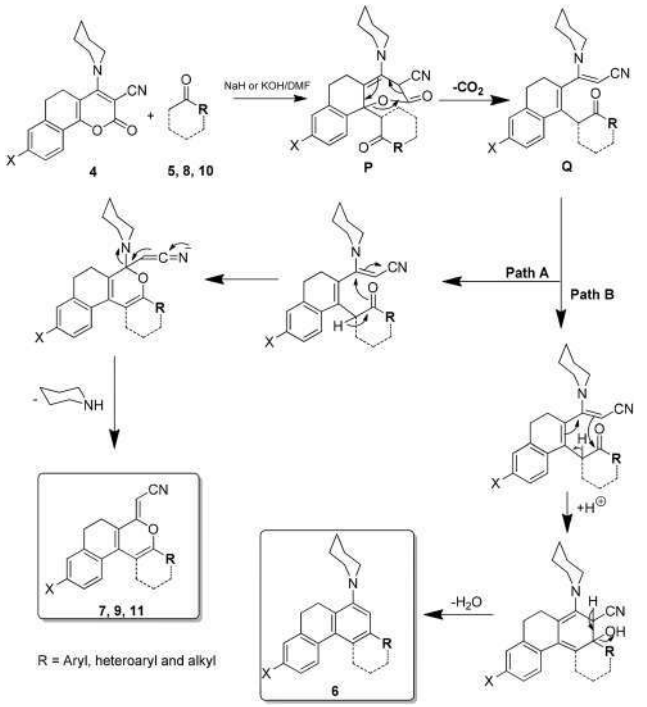
ring. Keeping this fact in mind we hypothesized the mechanism of our reaction as shown in Scheme 3. The reaction commences with the formation of intermediate **P** by a nucleophilic attack of carbanion generated *in situ* at the C-10b position of **4**. **P** undergoes decarboxylation to form **Q**. Thereafter the reaction may follow either path **A** for the formation of chromene or isochromene derivatives **7**, **9**, **11** *via* elimination of piperidine through SNi reaction of enolate formed in the presence of a base or path **B** to yield dihydrophenanthrene **10** *via* cyclization involving C-3 of chromene and the carbonyl group of ketone followed by aromatization *via* dehydration. One of the key differences between the conventional approach and the microwave assisted approach is regioselectivity for the product formation (Table 1, entries 3 and 6). We proposed that fast and uniform heating in microwave is responsible for regioselectivity, which is difficult through conventional heating. On the basis of the obtained regioselectivity, we propose that KOH stabilized the enolate form at high temperature, while NaH stabilized the keto form at both high and low temperatures.

X-ray structural analysis

X-ray diffraction studies[23] of (*Z*)-2-(2-(4-bromophenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (**7e**) showed that the compound has a non-planarity induced chirality due to distortion in the aromatic rings. The conformation is shown as an ORTEP diagram in Fig. 2.

The X-ray studies further showed that the terminal rings A and C are nearly planar, while the central ring B adopts a half chair conformation. The average mean plane angle (torsion angle) for the twist between the terminal rings A and C is 17.8°.

The X-ray studies further confirmed that the *Z* geometry of the molecule and the nitrile group is present at the *syn* position to oxygen in the ring C (Fig. 2a). Crystal packing of (*Z*)-2-(2-(4-bromophenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (**7e**) has shown some significant intermolecular interactions. It has been observed that moderate hydrogen bonding interaction (C–H···Br = 2.991 Å) occurs between the bromo (Br1) group and *ortho* hydrogen (H3) of ring D with the neighbouring molecules (Fig. 2b). This molecule also



Scheme 3 A plausible mechanism for the synthesis of isochromenes **7** and **9**, chromenes **11** and dihydrophenanthrenes **6**.

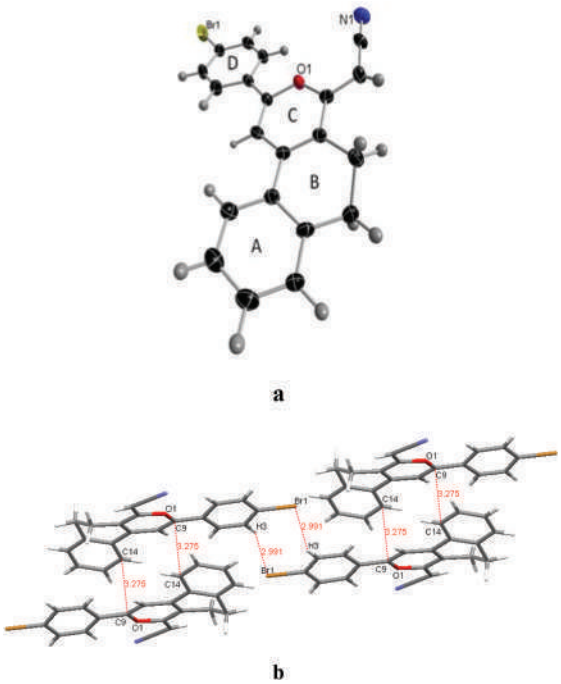


Fig. 2 (a) ORTEP diagram of (*Z*)-2-(2-(4-bromophenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (**7e**); (b) capped stick model of **7e** showing intermolecular interactions.

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exhibits weak pi interaction (C9···C14 = 3.275 Å) between rings C and A of neighbouring molecules.

Conclusion

In summary, we have developed a simple, efficient, non-catalytic regioselective synthesis of biologically important chromene, isochromene and dihydrophenanthrene derivatives from 2-oxabenzo[*h*]chromene under microwave irradiation. Our protocol avoids the use of expensive, moisture and air sensitive metal catalysts, organometallic reagents and ligands. Microwave irradiation played a major role in achieving regioselectivity and high yields. Thus, formation of two products from a single reaction can be performed in a regioselective manner *via* a cascade route using different bases. The structure of isochromene has also been confirmed unambiguously by spectroscopic analysis and X-ray diffraction study.

Experimental section

General remarks

Commercially available reagents were used without purification. ^{1}H and ^{13}C NMR spectra were taken on a 400 MHz NMR spectrometer and $CDCl_3$ was used as a solvent. Chemical shifts are reported in parts per million shift (δ-value) from ($CDCl_3$) (δ 7.24 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet; bs, broad singlet; bm, broad multiplet. Coupling constants (J) are given in hertz (Hz). Infrared (IR) spectra were recorded on a Perkin-Elmer AX-1 spectrophotometer and reported in wave number (cm^{-1}). All the reactions were performed on a CEM microwave synthesizer. The reaction was performed at a constant temperature of 100 °C for 15 min with a maximum applied power of 200 W in a microwave synthesizer.

General procedure for the synthesis of (*Z*)-2-(2-aryl-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitriles (7a–k), (*Z*)-2-(2-(thiophen-2-yl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)-acetonitriles (9a–b), (*Z*)-2-(3,4,7,8-tetrahydro-1*H*-naphtho[2,1-*c*]-chromen-6(2*H*)-ylidene)acetonitrile (11a–b)

A dried microwave vial containing an equimolar mixture of 4-(piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]chromen-2-one-3-carbonitriles **4** (0.5 mmol) and functionalized acetophenones **5** or 2-acetylthiophene **8** or cyclohexanone **10** (0.5 mmol), potassium hydroxide (0.75 mmol) and DMF (2.0 mL) was placed in a microwave reactor for 15 minutes at 100 °C with a maximum applied power of 200 W. Completion of the reaction was monitored by TLC. After the completion, the reaction mixture was poured onto crushed ice with vigorous stirring followed by neutralization with 10% HCl. The precipitate obtained was filtered, dried and purified using 20% ethyl acetate in hexane as an eluent.

(*Z*)-2-(2-Phenyl-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)-acetonitrile (7a). Red solid; yield: 84%; melting point: 155–157 °C; IR (film): 2926 (CH), 2195 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (t, J = 8.0 Hz, 2H), 2.90 (t, J = 8.0 Hz, 2H), 4.40 (s, 1H), 6.84 (s, 1H), 7.31–7.34 (m, 2H), 7.39–7.49 (m, 4H), 7.57–7.59 (m, 1H), 7.83–7.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.2, 63.9, 97.6, 118.7, 121.2, 123.9, 124.9, 125.1, 127.2, 128.3, 128.9, 129.8, 130.3, 131.4, 134.9, 137.0, 155.2, 166.0; *m*/*z* (CI) 320 (M + 23, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{21}H_{16}NO$: 298.1232; found: 298.1226.

(*Z*)-2-(2-(4-Methoxyphenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (7b). Red solid; yield: 79%; melting point: 190–192 °C; IR (film): 2933 (CH), 2192 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (t, J = 8.0 Hz, 2H), 2.88 (t, J = 8.0 Hz, 2H), 3.84 (s, 1H), 4.35 (s, 1H), 6.71 (s, 1H), 6.95 (d, J = 6.4 Hz, 2H), 7.22–7.32 (m, 4H), 7.83 (d, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 27.2, 55.4, 63.2, 96.0, 114.3, 119.0, 120.0, 123.8, 123.9, 126.6, 127.1, 128.2, 129.7, 130.5, 135.2, 137.0, 155.2, 161.3, 166.2; HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{22}H_{18}NO_2$: 328.1338; found: 328.1330.

(*Z*)-2-(2-(4-Fluorophenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (7c). Red solid; yield: 84%; melting point: 188–190 °C; IR (film): 2927 (CH), 2193 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (t, J = 7.7 Hz, 2H), 2.90 (t, J = 7.7 Hz, 2H), 4.41 (s, 1H), 6.78 (s, 1H), 7.12–7.17 (m, 2H), 7.26–7.34 (m, 3H), 7.56–59 (m, 1H), 7.86–7.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.2, 64.1, 97.3, 116.1 (d, J = 20 Hz, 2C), 118.7, 121.0, 123.9, 127.0, 127.1 (d, J = 10 Hz, 2C), 127.6, 128.3, 129.9, 130.3, 134.9, 137.0, 154.2, 164.0 (d, J = 250 Hz, 1C), 166.0; *m*/*z* (CI) 316 (M + 1, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{21}H_{15}FNO$: 316.1138; found: 316.1132.

(*Z*)-2-(2-(4-Chlorophenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (7d). Red solid; yield: 80%; melting point: 192–194 °C; IR (film): 2924 (CH), 2194 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (t, J = 7.6 Hz, 2H), 2.85 (t, J = 7.6 Hz, 2H), 4.37 (s, 1H), 6.77 (s, 1H), 7.18–7.29 (m, 3H), 7.36 (d, J = 8.0 Hz, 2H), 7.51–7.53 (m, 1H), 7.76–7.78 (d, J = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.1, 29.7, 64.4, 97.9, 118.6, 121.5, 123.9, 126.2, 127.2, 128.3, 129.2, 129.8, 130.0, 130.2, 136.3, 136.9, 154.0, 165.8; *m*/*z* (CI) 332 (M + 1, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{21}H_{15}ClNO$: 332.0842; found: 332.0835.

(*Z*)-2-(2-(4-Bromophenyl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (7e). Red solid; yield: 82%; melting point: 190–192 °C; IR (film): 2929 (CH), 2195 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (t, J = 7.6 Hz, 2H), 2.90 (t, J = 7.6 Hz, 2H), 4.41 (s, 1H), 6.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.1, 64.4, 97.9, 118.6, 121.5, 123.8, 124.6, 126.3, 126.5, 127.2, 128.3, 130.0, 130.2, 132.1, 134.7, 136.9, 154.0, 165.8; *m*/*z* (CI) 376 (M + 1, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{21}H_{15}BrNO$: 376.0337; found: 376.0323.

(*Z*)-2-(2-(4-Bromophenyl)-8-methoxy-5,6-dihydro-4*H*-benzo[*f*]-isochromen-4-ylidene)acetonitrile (7f). Red solid; yield: 80%; melting point: 228–230 °C; IR (film): 2923 (CH), 2188 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (t, J = 7.8 Hz, 2H), 2.87 (t, J = 7.8 Hz, 2H), 3.84 (s, 3H), 4.35 (s, 1H), 6.77–6.78 (m,

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1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.6, 55.4, 63.2, 97.9, 112.3, 114.0, 118.9, 119.4, 123.1, 124.6, 125.5, 126.4, 130.4, 132.1, 134.7, 139.1, 153.9, 161.0, 165.9; *m*/*z* (CI) 428 (M + 23, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{22}H_{17}BrNO_2$: 406.0437; found: 406.0443.

(*Z*)-2-(8-Methoxy-2-(4-methoxyphenyl)-5,6-dihydro-4*H*-benzo[*f*]-isochromen-4-ylidene)acetonitrile (7g). Red solid; yield: 78%; melting point: 156–158 °C; IR (film): 2935 (CH), 2192 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (t, *J* = 8.0 Hz, 2H), 2.81 (t, *J* = 8.0 Hz, 2H), 3.78–3.79 (m, 6H), 4.24 (s, 1H), 6.62 (s, 1H), 6.71 (d, *J* = 2.8 Hz, 1H), 6.77 (dd, *J* = 8.8 Hz, *J* = 2.8 Hz, 1H), 6.90 (d, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 27.7, 55.4, 62.1, 94.0, 112.2, 113.9, 114.3, 117.9, 119.4, 123.4, 124.0, 125.6, 126.6, 135.3, 139.2, 155.1, 160.8, 161.3, 166.3; HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{23}H_{20}NO_3$: 358.1443; found: 358.1438.

(*Z*)-2-(2-(Thiophen-2-yl)-5,6-dihydro-4*H*-benzo[*f*]isochromen-4-ylidene)acetonitrile (9a). Red solid; yield: 78%; melting point: 162–164 °C; IR (film): 2925 (CH), 2197 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (t, *J* = 8.0 Hz, 2H), 2.84 (t, *J* = 8.0 Hz, 2H), 4.34 (s, 1H), 6.58 (s, 1H), 7.04 (t, *J* = 4.8 Hz, 1H), 7.16–7.18 (m, 1H), 7.25–7.29 (m, 2H), 7.34 (d, *J* = 4.8 Hz, 1H), 7.48–7.50 (m, 1H), 7.59 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 27.2, 64.3, 96.9, 118.5, 120.7, 123.9, 126.8, 127.2, 127.7, 128.3, 129.9, 130.2, 134.9, 135.1, 136.9, 151.1, 165.6; *m*/*z* (CI) 326 (M + 23, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{19}H_{13}NOS$: 304.0796; found: 304.0786.

(*Z*)-2-(8-Methoxy-2-(thiophen-2-yl)-5,6-dihydro-4*H*-benzo[*f*]-isochromen-4-ylidene)acetonitrile (9b). Red solid; yield: 76%; melting point: 180–182 °C; IR (film): 2924 (CH), 2192 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (t, *J* = 7.8 Hz, 2H), 2.86 (t, *J* = 7.8 Hz, 2H), 3.83 (s, 3H), 4.32 (s, 1H), 6.59 (s, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 6.82 (dd, *J* = 8.8 Hz, *J* = 2.0 Hz, 1H), 7.08–7.10 (m, 1H), 7.37–7.38 (m, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 7.62–7.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.6, 55.4, 63.0, 96.9, 112.3, 114.0, 118.5, 118.7, 123.1, 125.6, 126.7, 127.6, 128.2, 134.9, 135.2, 139.1, 151.0, 160.9, 165.7; HRMS (*m*/*z*): [M]+ calcd for $C_{20}H_{15}NO_2S$: 333.0823; found: 333.0879.

(*Z*)-2-(3,4,7,8-Tetrahydro-1*H*-naphtho[2,1-*c*]chromen-6(2*H*)-ylidene)acetonitrile (11a). Viscous red liquid; yield: 72%; IR (film): 2928 (CH), 2194 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60–1.66 (m, 2H), 1.83–1.87 (m, 2H), 2.25 (t, *J* = 7.4 Hz, 2H), 2.57 (t, *J* = 6.4 Hz, 4H), 2.73 (t, *J* = 7.4 Hz, 2H), 4.28 (s, 1H), 7.21–7.28 (m, 3H), 7.49–7.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 22.8, 23.2, 27.5, 27.8, 28.1, 61.8, 110.4, 119.3, 123.2, 126.2, 127.4, 127.8, 128.8, 131.1, 138.1, 138.9, 155.0, 165.8; HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{19}H_{18}NO$: 276.1388; found: 276.1383.

(*Z*)-2-(10-Methoxy-3,4,7,8-tetrahydro-1*H*-naphtho[2,1-*c*]-chromen-6(2*H*)-ylidene)acetonitrile (11b). Viscous red liquid; yield: 69%; IR (film): 2927 (CH), 2192 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.61–1.63 (m, 2H), 1.81 (t, *J* = 6.0 Hz, 2H), 2.21 (t, *J* = 7.4 Hz, 2H), 2.54 (t, *J* = 6.0 Hz, 4H), 2.69 (t, *J* = 7.4 Hz, 2H), 3.81 (s, 3H), 4.19 (s, 1H), 6.73–6.76 (m, 2H), 7.43 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 22.6, 23.2, 27.5, 27.9, 28.6, 55.3, 60.7, 110.4, 111.2, 113.6, 119.6, 121.3, 123.9, 130.0, 138.1, 141.1, 155.0, 159.8, 165.9; *m*/*z* (CI) 306 (M + 1, 100%); HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{20}H_{20}NO_2$: 306.1489; found: 306.1496.

General procedure for the synthesis of 3-aryl-1-(piperidin-1-yl)-9,10-dihydrophenanthrene-2-carbonitriles (6a–c)

A dried microwave vial containing an equimolar mixture of 4-(piperidin-1-yl)-5,6-dihydro-2*H*-benzo[*h*]chromen-2-ones **4** (0.5 mmol) and different acetophenones **5** (0.5 mmol) with NaH (0.75 mmol) and DMF (2 mL) was placed in a microwave reactor for 15 minutes at 100 °C. The reaction was monitored by TLC and after completion the reaction mixture was poured onto crushed ice and neutralized by 10% HCl with vigorous stirring. The precipitate was filtered, dried and purified using 20% ethyl acetate in hexane as an eluent. Compounds **6a** and **6b** have been reported in earlier literature.[20]

3-(4-Bromophenyl)-7-methoxy-1-(piperidin-1-yl)phenanthrene-2-carbonitrile (6c). Off white solid; yield: 87%; melting point: 168–170 °C; IR (film): 2924 (CH), 2213 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.73 (br, 6H), 2.81 (t, *J* = 8.0 Hz, 2H), 2.91 (t, *J* = 8.0 Hz, 2H), 3.26 (br, 4H), 3.84 (s, 3H), 6.79–6.84 (m, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 24.1, 26.8, 28.9, 52.0, 55.4, 105.8, 112.7, 113.3, 118.7, 120.5, 122.7, 126.1, 126.5, 130.6, 131.7, 133.9, 138.0, 139.8, 140.1, 144.2, 154.8, 160.2; HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{27}H_{25}BrN_2O$: 473.1229; found: 473.1223.

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23 Crystal data for $C_{21}H_{14}BrNO$: a red crystal (0.11 × 0.10 × 0.03 mm) was mounted on a capillary tube for indexing and intensity data collection at 293(2) K on an Oxford Xcalibur Sapphire3 CCD single-crystal diffractometer (Mo Kα radiation, λ = 0.71073 Å). Routine Lorentz and polarization corrections were applied, and an absorption correction was performed using the ABSCALE 3 program [CrysAlis Pro software system, Version 171.34; Oxford Diffraction Ltd, Oxford, UK, 2011]. Patterson methods were used to locate the heavy metal atoms (SHELXS-86), and the remaining atoms were located from successive Fourier maps (SHELXL-97). All the non-hydrogen atoms were refined anisotropically; hydrogen atoms were located at calculated positions using a riding model. All hydrogen atoms were calculated after each cycle of refinement using a riding model, with C–H = 0.93 Å + U_{iso}(H) = 1.2 U_{eq}(C) for aromatic H atoms, and with C–H = 0.97 Å + U_{iso}(H) = 1.2 U_{eq}(C) for methylene H atoms. Crystal data: $C_{21}H_{14}BrNO$; M_r = 376.25, crystal system: triclinic; space group $P\bar{1}$, a = 7.3715(4) Å, b = 9.3781(7) Å, c = 12.8371(12) Å, α = 96.360(7)°, β = 99.202(7)°, γ = 111.905(6)°, V = 798.57(10) Å^3, Z = 2, ρ_{calcd} = 1.565 g cm^{-3}, μ = 2.580 mm^{-1}, F(000) = 380, R_1 = 0.0759 and wR_2 = 0.2085 for $I > 2\sigma(I)$ and 226 parameters, R_1 = 0.0892 and wR_2 = 0.2198, gof = 1.097 for all data. CCDC (Deposit no. 959771) contains the supplementary crystallographic data.

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RSC Advances

PAPER

Substituent dependent tunable fluorescence in thieno[3,2-*c*]pyrans†

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A series of thieno[3,2-*c*]pyrans were designed and synthesized by L-proline catalyzed reaction of 6-aryl/5,6-diaryl-4-methylthio-2*H*-pyrane-2-one-3-carbonitriles or 4-(methylthio)-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile and methylthioglycolate in good yields. These thieno[3,2-*c*]pyrans exhibit substituent dependent fluorescence. The 6-aryl-thieno[3,2-*c*]pyrans **3a–3e** exhibit high fluorescence quantum yields (95%) with large Stokes shifts, whereas the 6,7-di-substituted-thieno[3,2-*c*]pyrans **3f–3h** show poor fluorescence in solution and exhibit an aggregation-induced emission (AIE). Interestingly, fused 6,7-di-substituted-thieno[3,2-*c*]pyran is highly fluorescent in the solution state, which reveals that restricted intramolecular rotation is the cause for AIE in **3f–3h**.

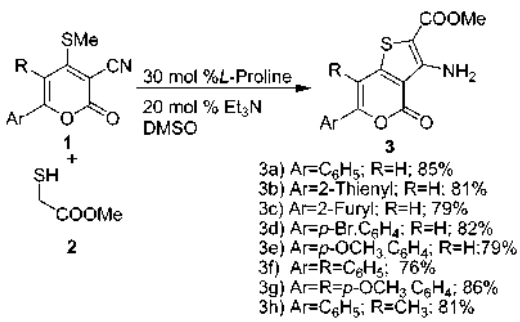
Organic light-emitting materials are of wide interest due to their applications in organic field effect transistors (OFETs), organic light-emitting diodes (OLEDs), and organic photovoltaics (OPVs) and bioimaging.[1] Design and synthesis of efficient light emitters in solution as well as in the solid state has gained momentum.[2] Conventional fluorophores are poorly emissive in the solid state due to aggregation caused quenching (ACQ). To overcome ACQ Tang *et al.* introduced the concept of aggregation induced emission (AIE).[3] Thiophene and fused thiophenes (thienothiophene, dithienothiophene) have been explored in OFETs, and OPV's.[4,5] The thieno[3,2-*c*]pyran is a thiophene and pyranone fused ring system. Thieno[3,2-*c*]pyrans are known for antileishmanial and antifungal activities.[6,7]

Few reports on the synthesis of pyranothiophenes are available and their photophysical properties are unexplored. In this paper we wish to report substituent dependent variation in photonic properties of various functionalized thieno[3,2-*c*]-pyrans. They could be synthesized by reaction of 6-aryl/5,6-diaryl-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitriles and methyl thioglycolate using an organocatalytic approach. The required precursors were synthesized by reaction of ethyl 2-cyano-3,3-dimethylthioacrylate and various acetophenones or deoxybenzoin/anisoin in the presence of potassium hydroxide in DMSO.[8]

Synthesis of functionalized 6-aryl/5,6-diaryl-thieno[3,2-*c*]pyrans **3a–3h** were carried out by the 6-aryl/5,6-diaryl-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitriles and methyl thioglycolate in presence of L-proline (30 mol%) and Et_3N (20 mol%) in DMSO at 90 °C (Table 1). For further derivatisation 4-(methylthio)-2-oxo-5,6-dihydro-2*H*-benzo[*h*]-chromene-3-carbonitrile **4** was used as precursor, which react with methyl thioglycolate under similar conditions and afforded methyl 1-amino-11-oxo-5,11-dihydro-4*H*-benzo[*h*]thieno[3,2-*c*]chromene-2-carboxylate in good yield (Scheme 1).

The electronic absorption, and fluorescence spectra of the thieno[3,2-*c*]pyrans **3a–3h** and **5** in dichloromethane solution are shown in Fig. S2,† and their photophysical data are listed in Table 2. The thieno[3,2-*c*]pyrans **3a–3h** and **5** absorbs in 300–450 nm region. Time-dependent DFT calculation was performed

Table 1 L-Proline/Et_3N catalyzed synthesis of thieno[3,2-*c*]pyrans[a,b]



[a] All the reactions were carried out by using **1** (0.5 mmol), **2** (0.6 mmol) and L-proline (30 mol%) + Et_3N (20 mol%) in 4.0 mL of DMSO at 90 °C. [b] All the reactions were performed twice and average yields are reported.

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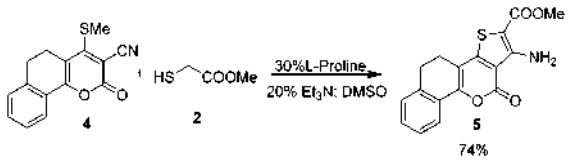
† Electronic supplementary information (ESI) available: This material includes characterization data and ^1H and ^{13}C NMR spectra for all the reported compounds. It also includes detail about thermogravimetric analysis, solvent effect, AIE study and theoretical studies of all the synthesized compounds. See DOI: 10.1039/c4ra11337c



Scheme 1 Synthesis of methyl 1-amino-11-oxo-5,11-dihydro-4*H*-benzo[*h*]thieno[3,2-*c*]chromene-2-carboxylate **5**.

to understand the absorption properties of thieno[3,2-*c*]-pyrans. The contributions of the molecular orbitals involved in the UV-vis transitions were determined on the basis of their oscillator strengths (*f*). The TD-DFT calculation shows that, the lower-energy bands (350–450 nm) in the absorption spectra show a preferential contribution from HOMO → LUMO and HOMO−1 → LUMO transitions (Table S4†).

The photophysical properties of the thieno[3,2-*c*]pyrans can be tuned by varying the substituents. The replacement of phenyl unit with thiophene results in 15 nm red shift in the absorption spectra. The heterocyclic substituent thiophene and furan on pyranothiophene show high extinction coefficient and the trend in ε follows the order **3b** > **3c** > **5** > **3e** > **3d** > **3g** > **3a** >**3f** > **3h**. The fluorescence spectra of thieno[3,2-*c*]pyrans in dichloromethane show emission from 464 nm to 500 nm. The 6-aryl-thieno[3,2-*c*] pyrans (**3a–3e**) show high fluorescence quantum yields up to 95%, with large Stokes shifts ~4720 cm^{-1}. The sensitivity of 6-aryl-thieno[3,2-*c*]pyrans towards solvent polarity were investigated. The absorption spectra show solvent independent nature, whereas emission was found to be solvent dependent. The bathochromic shift in the fluorescence spectra with solvent polarity suggests the polar nature of the excited state. The solvent dependence was confirmed by the Lippert–Mataga plot, which shows a linear correlation of the Stokes shift with solvent polarity (Fig. S4 and S6†).[9]

The poor quantum yields of the thieno[3,2-*c*]pyrans **3f–3h** suggest the possibility of molecular rotation within the molecule.[3d,10] The excited state energy of these molecules were dissipated by the molecular rotation, which results in weak-fluorescent nature of these thieno[3,2-*c*]pyrans (**3f–3h**) in the solution state. The aggregation induced emission study was performed by making the small aggregates, using THF–water mixtures, with the increasing percentage of water in THF (Fig. 1). The fluorescence intensity of **3f** in THF was increased by 200 folds in the aggregate suspension (98% aqueous mixture). In the solid state (aggregates) the molecular rotation was ceased and the fluorescence was restored.[3d] Similar study was performed on **3g** and **3h**. The **3g** exhibits aggregation induced emission with 20 fold increase in fluorescence intensity. In **3h** fluorescence intensity was increased upto 40% of water fraction and get almost constant upto 90% of water fraction and after that fluorescence intensity was decreased by increase in water fraction (98%). To confirm the AIE in 6,7-disubstitued thieno [3,2-*c*]pyrans, we synthesized fused 6,7-disubstitued thieno[3,2-*c*]pyran **5**. The high fluorescence quantum yield (95%) in the solution was observed for **5** which confirms the RIR (restricted intramolecular rotation) is the main cause for low fluorescence quantum yields in the 6,7-disubstitued thieno[3,2-*c*]pyrans.

The thermal stability is one of key requirement for various practical applications. The thieno[3,2-*c*]pyrans **3a–3h** and **5** shows thermal decomposition (T_d) temperature corresponding to 5% weight loss in nitrogen atmosphere in the range of 230–290 °C (Fig. S1†). The 6,7-di-substituted-thieno[3,2-*c*]pyrans (**3f–3h**, and **5**) shows higher thermal stability compared to 6-aryl-thieno[3,2-*c*]pyrans (**3a–3e**).

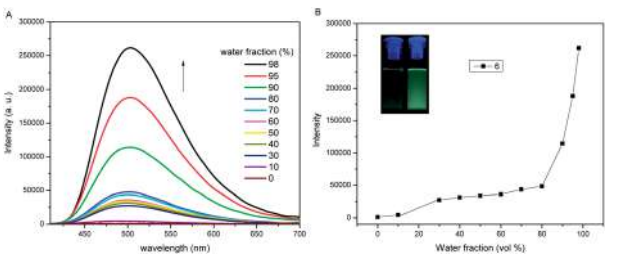


Fig. 1 (A) Fluoroscence spectra of **3f** in THF–water mixtures with different water fractions. (B) Plot of PL peak intensity at 502 nm *vs.* water fraction of the aqueous mixture. Luminogen concentration: 20 μm; excitation wavelength: 370 nm. Inset: solution of **3f** in THF (fw = 0%) and its suspension in a THF–water mixture with fw = 98%; photographs taken under UV illumination.

Table 2 Photophysical and thermal properties of the thieno[3,2-*c*]pyrans **3a–3h** and **5**

Compound	λ_{max} [nm] (ε^a [L mol^{-1} cm^{-1}])	$\lambda_{em}{}^a$ (nm)	Stokes shift (cm^{-1})	$\Phi_f{}^b$ (%)	Optical band gap (eV)	Theoretical band gap^c (eV)	T_d (°C)
3a	326 (16 026), 390 (21 745)	478	4721	88.89	2.83	3.40	267
3b	340 (17 994), 354 (18 766), 405 (31 021)	498	4611	73.63	2.71	3.24	246
3c	334 (18 160), 350 (20 519), 400 (30 256)	477	4036	95.95	2.78	3.32	245
3d	330 (17 562), 395 (22 146)	485	4698	72.50	2.75	3.29	—
3e	346 (14 759), 396 (25 609)	476	4244	54.88	2.80	3.40	232
3f	328 (12 620), 384 (19 581)	—	—	—	2.88	3.48	273
3g	276 (18 147), 390 (27 507)	—	—	—	2.84	3.46	289
3h	322 (16 740), 375 (22 099)	464	5299	7.98	2.95	3.56	258
5	337 (13 243), 353 (16 378), 399 (28 432)	476	4054	95.76	2.80	3.38	271

^{a} Measured in dichloromethane. ^{b} The fluorescence quantum yields were calculated by using 9,10-diphenylanthracence as a standard in ethanol solution (λ_{ex} 370 nm). ^{c} Theoretical values at B3LYP/6-31G(d) level.

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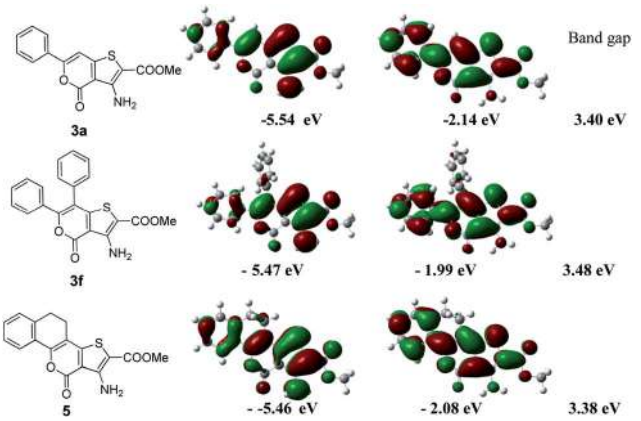

Fig. 2 HOMO and LUMO frontier molecular orbitals of Thieno[3,2-*c*]pyrans **3a**, **3f**, and **5** at the B3LYP/6-31G(d) level.

In order to understand the geometrical and electronic structure of the thieno[3,2-*c*]pyrans, computational calculation was performed using density functional theory (DFT) at the B3LYP/6-31G(d) level using the Gaussian 09 program.[11] The energy minimized structures of the thieno[3,2-*c*]pyrans **3a–3e** and **5** show planar structure whereas the 6,7-disubstituted thieno[3,2-*c*]pyrans **3f–3h** are non-planar (Fig. S7†). The DFT calculated HOMO–LUMO gap values shows good agreement with optical band gap values calculated from the absorption spectra.

The HOMO, and LUMO frontier molecular orbital (FMO) distribution of thieno[3,2-*c*]pyrans **3a**, **3f** and **5** are shown in Fig. 2. The HOMOs and LUMOs are distributed on the whole molecule. The careful observation reveals that the thiophene ring fused with pyranone shows more contribution in the HOMO, whereas pyranone ring and the substituents on it contribute more to the LUMO orbital. The HOMO and LUMO orbitals show similar distribution in 6-aryl-thieno[3,2-*c*]pyran-4-one **3a** and 6,7-di-substituted-thieno[3,2-*c*]pyrans **3f**, and very small contribution from second phenyl ring was observed for pyranothiophene **3f**. The trend in the HOMO–LUMO gap of thieno[3,2-*c*]pyrans follows the order 6,7-di-substituted-thieno [3,2-*c*]pyrans (**3f–3h**) > 6-aryl-thieno[3,2-*c*]pyran-4-one (**3a–3e**) > fused 6,7 diarylated thieno[3,2-*c*]pyran (**5**). This is due to more planar and conjugated structure in fused 6,7 diarylated thieno [3,2-*c*]pyrans **5** compared to 6-aryl-thieno[3,2-*c*]pyran-4-one **3a–3e** and 6,7 diarylated thieno[3,2-*c*]pyrans **3f–3h**.

Conclusions

In conclusion, we have demonstrated a simple, efficient and organocatalytic approach for synthesis of thermally stable thieno[3,2-*c*]pyrans by reaction of 6-aryl/6,7-diaryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles and methylthioglycolate using L-proline in good yields. Photophysical studies of the **3a–3e** and **5** exhibit high fluorescence quantum yields up to 95% with large Stokes shift. Presence of additional aryl ring at position 7 of thieno[3,2-*c*]pyrans shows change in photophysical properties and their studies in different THF–water mixtures shows that they exhibit AIE. The fused 6,7-di-substituted-thieno[3,2-*c*]pyran confirms the RIR is responsible for AIE in 6,7-di-substituted-thieno[3,2-*c*]pyrans. These functionalized thieno[3,2-*c*]pyrans are highly fluorescent and can be used as a fluorescent probes in bioimaging.

Experimental section

General remarks

Commercially available reagents and solvents were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz NMR spectrometer respectively. $CDCl_3$ and DMSO-d_6 were used as solvent for NMR. Chemical shift is reported in ppm considering ($CDCl_3$) δ 7.24 ppm for ^{1}H NMR and δ 77.00 ppm for ^{13}C NMR as an internal standard. Signal patterns are indicated as s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet; br s, broad singlet. Coupling constants (J) are given in hertz (Hz). Infrared (IR) spectra were recorded on AX-1 spectrophotometer and reported as wave number (cm^{-1}). UV-Visible absorption spectra of all compounds were recorded on a Carry-100 Bio UV-Visible Spectrophotometer. HRMS was recorded on Brucker-Daltonics, Micro-TOF-Q II mass spectrometer.

General procedure for the synthesis of 3-amino-2-carbmethoxy-6-aryl-4*H*-thieno[3,2-*c*]pyran-2-one

A mixture of 4-(methylthio)-2-oxo-6-aryl-2*H*-pyran-3-carbonitriles (0.5 mmol) and methyl thioglycolate (0.75 mmol) in 4.0 mL DMSO in presence of triethylamine (20 mol%) and L-proline (30 mol%) was stirred for 8–9 h at 90 °C. Completion of reaction was monitored by TLC. The reaction mixture was poured onto crushed ice with vigorous stirring. Obtained precipitate was filtered, dried and purified by column chromatography by using 1 : 1 hexane : dichloromethane as an eluent.

3-Amino-4-oxo-6-phenyl-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester (3a)

Yield: 85% (128 mg) R_f = 0.32 (50% hexane in dichloromethane); yellow colored floppy solid; mp: 204–206 °C; IR (KBr): 3457, 3351, 1707, 1675, 1573 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 3H, OCH_3), 6.74 (br s, 2H, NH_2), 6.98 (s, 1H, CH), 7.44 (m, 3H, ArH), 7.84 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.4, 98.51, 112.0, 125.6, 128.9, 130.9, 153.0.157.6, 158.4, 164.2; HRMS (ESI): calculated for $C_{15}H_{11}NO_4S$, 324.0301 ($M + Na^+$); found for m/z, 324.0301.

3-Amino-4-oxo-6-thiophen-2-yl-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester (3b)

Yield: 81% (124 mg); R_f = 0.35 (50% hexane in dichloromethane); yellow solid; mp: 212–214 °C, IR (KBr): 3468, 3340, 1725, 1676, 1582 cm^{-1}; ^{1}H NMR(400 MHz, $CDCl_3$): δ 3.84 (s, 3H, OCH_3), 6.73 (br s, 2H, NH_2), 6.84 (s, 1H, CH), 7.12 (t, J = 4.76 Hz, 1H, ArH), 7.46 (d, J = 5.13 Hz, 1H, ArH), 7.60 (d, J = 2.93 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.4, 97.5, 111.5, 127.6, 128.4, 129.1, 134.6, 152.9, 153.3, 157.8, 164.2; HRMS (ESI):

calculated for $C_{13}H_9NO_4S_2$, 329.9865 (M + Na^+); found for *m*/*z* 329.9865.

3-Amino-6-furan-2-yl-4-oxo-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester (3c)

Yield: 79% (115 mg); R_f = 0.27 (50% hexane in dichloromethane); yellow solid; mp: 204–206 °C, IR (KBr): 3475, 3347, 1725, 1677, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 6.54 (m, 1H, ArH), 6.73 (br s, 2H, NH_2), 6.93 (s, 1H, CH), 7.02 (d, J = 3.2 Hz, 1H, ArH), 7.52 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.4, 96.8, 111.5, 112.2, 112.6, 145.0, 146.0, 149.5, 152.7, 157.7, 164.2; HRMS (ESI): calculated for $C_{13}H_9NO_5S$, 314.0094 (M + Na^+); found for *m*/*z* 314.0094.

3-Amino-6-(4-bromo-phenyl)-4-oxo-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester (3d)

Yield: 82% (155 mg); R_f = 0.25 (50% hexane in dichloromethane); yellow solid; mp: 230–232 °C; IR (KBr): 3478, 3362 1708, 1675, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H, OCH_3), 6.73 (br s, 2H, NH_2), 7.00 (s, 1H, CH), 7.59 (d, J = 9.16 Hz, 2H, ArH), 7.69 (d, J = 9.16 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.5, 98.7, 112.2, 125.5, 127.0, 129.8, 132.3, 152.6, 156.5, 158.1, 164.2; HRMS (ESI) calculated for $C_{15}H_{10}$ $BrNO_4S$, 379.9587 (M + H^+); found for *m*/*z* 379.9585.

3-Amino-6-(4-methoxy-phenyl)-4-oxo-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester (3e)

Yield: 79% (130 mg); R_f = 0.19 (50% hexane in dichloromethane); yellow solid; mp: 203–205 °C; IR (KBr): 3481, 3366, 1733, 1685, 1677, 1583 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.72 (br s, 2H, NH_2), 6.87 (s, 1H, CH), 6.94 (d, J = 9.16 Hz, 2H, ArH), 7.77 (d, J = 9.16 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.3, 55.4, 96.9, 111.3, 114.4, 123.3, 127.4, 153.5, 157.7, 158.5, 161.8, 164.3; HRMS(ESI): calculated for $C_{16}H_{13}NO_5S$, 332.0587 (M + H^+); found for *m*/*z* 332.0578.

3-Amino-4-oxo-6,7-diphenyl-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester (3f)

Yield: 76% (143 mg); R_f = 0.28 (50% hexane in dichloromethane); yellow solid; mp: 236–238 °C; IR(KBr):3467, 3345, 1726, 1678 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ 3.80 (s, 3H, OCH_3), 6.76 (br s, 2H, NH_2), 7.20–7.40 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.4, 112.1, 115.4, 128.1, 128.9, 129.2, 129.3, 129.7, 129.8, 131.5, 133.3, 153.9, 157.1, 158.4, 164.3; HRMS (ESI) calculated for $C_{21}H_{15}NO_4S$, 378.0795 (M + H^+) found for *m*/*z* 378.0786.

3-Amino-6,7-bis-(4-methoxy-phenyl)-4-oxo-4*H*-thieno[3,2-*c*] pyran-2-carboxylic acid methyl ester (3g)

Yield: 86% (187 mg); R_f = 0.22 (50% hexane in dichloromethane); yellow solid; mp: 185–187 °C; IR (KBr): 3476, 3359, 1666, 1602 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$): δ 3.76 (s, 3H, OCH3), 3.78 (s, 3H, OCH3), 3.82 (s, 3H, OCH_3), 6.71 (br s, 2H, NH_2), 6.73 (s, 2H, ArH), 6.91 (d, J = 8.79 Hz, 2H, ArH),7.19 (d, J = 8.79 Hz, 2H, ArH), 7.30 (d, J = 6.59 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.3, 55.2, 111.6, 113.5, 113.9, 114.8, 123.9, 125.7, 130.8, 130.9, 153.9, 158.1, 158.5, 159.8, 160.6, 164.4: HRMS (ESI) calculated for $C_{23}H_{19}NO_6S$, 438.1006 (M + H^+); found for *m*/*z* 438.1003.

3-Amino-7-methyl-4-oxo-6-phenyl-4*H*-thieno[3,2-*c*]pyran-2-carboxylic acid methyl ester(3h)

Yield: 89% (140 mg); R_f = 0.31 (50% hexane in dichloromethane); yellow solid; mp: 213–215 °C; IR (KBr): 3488, 3368, 1718, 1670, 1578, 1295 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$):δ 2.24 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.74 (br s, 2H, NH_2), 7.46 (m, ArH, 3H), 7.58 (m, ArH, 2H) ^{13}C NMR (100 MHz, $CDCl_3$):δ 14.3, 51.5, 108.9, 112.1, 128.4, 128.5, 129.0, 130.0, 131.8, 154.6, 156.9, 158.7, 164.3; HRMS (ESI):calculated for $C_{16}H_{13}NO_4S$, 316.0638 (M + H^+); found for *m*/*z* 316.0638.

17-Amino-12-oxo-6,12-dihydro-7*H*-11-oxa-15-thiacyclopenta[*a*] phenanthrene-16-carboxylic acid methyl ester(3i)

Yield: 89% (145 mg); R_f = 0.32 (50% hexane–dichloromethane); yellow solid; mp: 232–234 °C IR (KBr) 3463, 3341, 1708, 1589, 1294 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): δ 2.78 (m, 2H, CH_2), 3.02 (t, J = 7.32 Hz, 2H, CH_2),3.83 (s, 3H, OCH_3) 6.76 (br s, 2H, NH_2),7.32 (m, 3H, ArH), 7.85 (m, 1H, ArH), ^{13}C NMR (100 MHz, $CDCl_3$):δ = 22.5, 26.9, 51.4, 109.1, 123.6, 127.3, 127.4127.9, 130.2, 136.8, 151.4, 154.5, 158.4, 164.3; HRMS (ESI) calculated for $C_{17}H_{13}NO_4S$, 328.0638 (M + H^+); found for *m*/*z* 328.0638.

Acknowledgements

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One pot synthesis of tetrasubstituted thiophenes: [3 + 2] annulation strategy†

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A simple, efficient and economical synthesis of dimethyl 3-amino-5-(2-oxo-2-arylethyl)thiophene-2,4-dicarboxylates has been reported by ring opening of methyl 3-amino-6-aryl-4-oxo-4*H*-thieno[3,2-*c*]-pyran-2-carboxylates by alkoxide ions. Pyranothiophenes have been obtained by the reaction of methyl thioglycolate and 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles in the presence of triethylamine. A one-pot multicomponent protocol for the synthesis of tetrasubstituted thiophenes has been developed by reaction of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles and methyl thioglycolate in the presence of sodium methoxide in excellent yields. The structure of the isolated compound was confirmed by single crystal X-ray diffraction and spectroscopic studies.

Thiophene is one of the important class of heterocyclic scaffolds of biological importance, widely present in various natural products[1] and therapeutics as a substructure. These are very useful as allosteric agonists and modulators of the adenosine A1 receptor 2A3BTs[2] and PD81, 723 [3] (Fig. 1). Besides, they are useful as potent PI3K inhibitors[4] and check point kinase inhibitors.[5] Articaine,[6] a thiophene derivative is commonly used as an anesthetic in dental surgery and also PaTrin-2 inhibitor of the DNA repair enzyme, O6-methylguanine-DNA methyl transferase.[7] Recently, numerous thiophene derivatives are reported to display significant activity towards CB1 receptors with good CB1/CB2 selectivity.[8] Additionally, thiophene scaffolds have wide applications as anthelmintics,[9] antiviral,[10] antitumor,[11] anti-inflammatory,[12] antimicrobials[13] and antiplatelet[14] agents. Further, various thiophene derivatives have broad applications as functional materials in electrically conducting organic materials,[15] semiconductors,[16] light emitting diodes (OLEDs),[17] organic field effect transistors (OFETs),[18] organic solar cells,[19] laser,[20] liquid crystals and molecular wires.[21]

The conventional synthetic approaches for the construction of polysubstituted thiophene scaffold include the Gewald,[22] Paal–Knorr,[23] and Fiesselmann[24] syntheses. There is also one report for the construction of tetrasubstituted thiophenes from the reaction of aroyl isothiocyanates with ethyl bromopyruvate in the presence of enaminone in good to excellent yields.[25] El-Saghier *et al.*[26] have reported numerous highly functionalized thiophene scaffolds *via* ketene *S*,*S*- and *S*,*N*-acetals.[27] Recently, a novel approach to the synthesis of tetrasubstituted thiophenes is reported in two steps from *trans*-2-aroyl-arylcyclopropane-1,1-dicarboxylates and 1,4-dithianes-2,5-diol.[28] Amongst various approaches, modification of pre-existed thiophene ring system through α-metalation or β-halogenation also provided an alternative route to deliver highly functionalized thiophenes.[29] A regioselective synthesis of polysubstituted thiophenes from Baylis–Hillman adducts has been reported by Kim and coworkers.[30] Further, development in the synthetic methodology opened a new avenue for the construction of trisubstitutedthiophenes by reacting β-ketothioesters with dialkyl acetylenedicarboxylates.[31] Recently, thiophenes are prepared by annulation of β-ketothioamides with arylglyoxal and 5,5-dimethyl-1,3-cyclohexanedione in CF_3CH_2OH.[32] Ram *et al.*[33] have also reported an elegant approach to the synthesis of trisubstitutedthiophenes through ring transformation of suitably

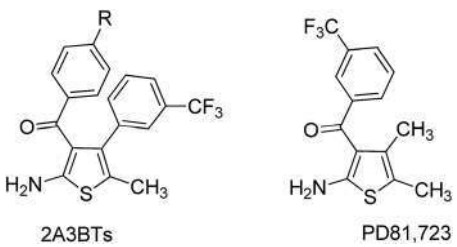

Fig. 1 Biologically active thiophenes.

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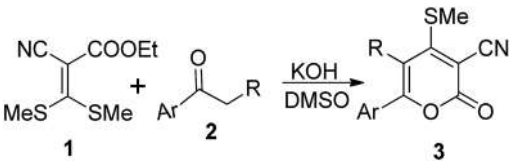


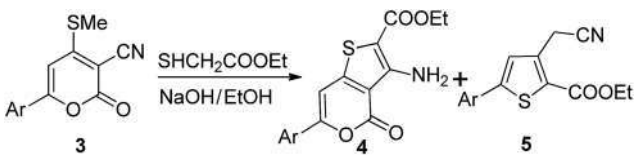
Scheme 1 Synthesis of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles (**3**).

functionalized 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles[34] by alkyl thioglycolate in the presence of NaOH in methanol under reflux condition. Although the existing procedures are very useful for the construction of various thiophene derivatives but most of them suffer with certain limitations of harsh reaction conditions, use of expensive catalysts, long reaction time, multistep approach, use of strong base, difficulty in purification and compatibility of functional groups towards reagents under applied reaction conditions. Therefore, search for highly efficient and economical route was inevitable in view of their wide-ranging applications in the field of material science and pharmaceuticals.

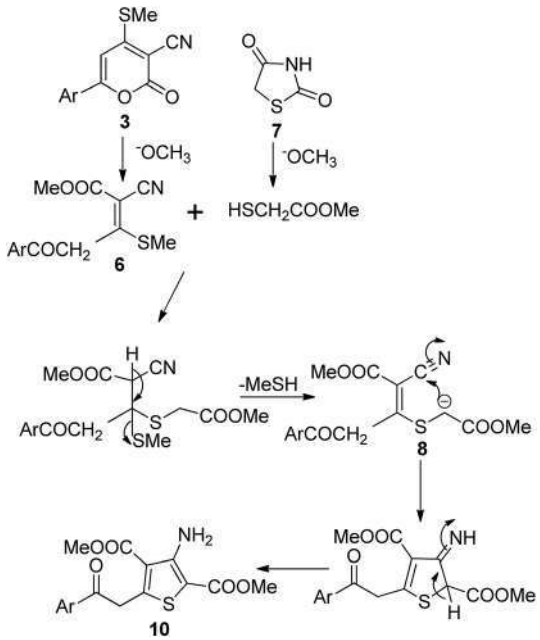
Our quest to develop an efficient and economical protocol for the construction of tetrasubstituted thiophenes did not diminish by using 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles (**3**)[34] as precursors, obtainable from the reaction of ethyl 3,3-dimethylthio-2-cyanoacrylate (**1**) and aryl methyl or aryl aralkyl ketones (**2**) separately, Scheme 1.

From the structural dissection, **3** may be considered as a cyclic ketenehemithioacetal and can be exploited for the construction of thiophene scaffolds. Thus, the reaction of **3** with ethyl thioglycolate in the presence of NaOH in methanol at reflux temperature delivered a mixture of ethyl 3-amino-6-arylthieno[3,2-*c*]pyran-4-one-2-carboxylates (**4**) as major product and trisubstitutedthiophene, ethyl 5-aryl-3-cyanomethyl-2-carboxylates (**5**) in 30–60% yields, Scheme 2.

Therefore, we planned an entirely new synthetic strategy through ring transformation of **3** by oxazolidene-2,4-dione in the presence of CH_3ONa under reflux condition. This reaction after usual workup delivered a complex mixture. However, we succeeded to isolate a compound in poor yield, which was characterized as methyl 3-amino-5-(2-oxo-2-arylethyl)-thiophene-2,4-dicarboxylate by X-ray diffraction and spectroscopic studies. A plausible mechanism of this reaction is depicted in Scheme 3. The ring opening of lactone (**3**) in alkoxide provides methyl 2-cyano-3-methylthio-3-aroylmethylacrylate (**6**), while thiozolidenedione under analogous reaction conditions is reported[35] to give methyl



Scheme 2 Synthesis of ethyl 3-amino-6-arylthieno[3,2-*c*]pyran-4-one-2-carboxylates (**4**) and ethyl 6-aryl-3-cyanomethylthiophen-2-carboxylates (**5**).



Scheme 3 A plausible mechanism for the formation of tetrasubstituted-thiophene (**10**).

thioglycolate *in situ*. Both the reactants **6** and methyl thioglycolate generated *in situ* from thiozolidenedione react under basic conditions at reflux temperature to afford polyfunctionalized thiophene **10**. The first step in the formation of tetrasubstituted thiophene (**10**) is the ring opening of lactone **3** and thiazolidinedione (**7**) in the presence of CH_3ONa to give **6** and methyl thioglycolate, which underwent Michael addition followed by elimination of methyl mercaptan to afford intermediate **8**, which on recyclization produced tetrasubstituted thiophene (**10**), Scheme 3.

Albeit, we succeeded to synthesize tetrasubstituted thiophenes (**10**) in single step but the yield was poor. From careful topographical analysis of **4**, we envisaged that alkoxide mediated ring opening of methyl 3-amino-6-arylthieno[3,2-*c*]pyran-4-one-2-carboxylates (**4**)[33,36] may deliver the desired thiophene in high yield. Therefore, methyl 3-amino-6-arylthieno[3,2-*c*]pyran-4-one-2-carboxylates (**4**) was stirred in freshly prepared solution of CH_3ONa in methanol for 1–2 h at room temperature, which produced ring opened compound, similar in all respect to **10**. It was conspicuous that long duration of stirring provides conversion of **10** to parent compound **4**. Therefore, it was important to monitor the reaction time critically for better yield of **10** (50–80%). For improving the yields of desired product, we modified the reaction conditions using triethylamine in methanol for the ring opening of **4** at 90 °C, but net result was fiasco. Thereafter, ring opening of **4** was conducted in $NaOCH_3$ in DMF at room temperature, which after usual work up gave desired product in excellent yield. Under this condition, the reaction was not reversible and even no trace of starting material was observed on TLC (Table 1). It was interesting to note that the change of solvent from methanol to DMF provided excellent results. We contemplated that the recyclization is more facile in

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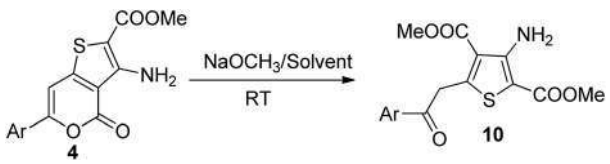
Table 1 Synthesis of tetrasubstituted thiophenes (10)[a]

10	Ar	Yield (%) (in methanol) and (in DMF)	
a	C_6H_5	76[c]	90[b]
b	p-$CH_3 \cdot C_6H_4$	68[c]	88[b]
c	p-$F \cdot C_6H_4$	71[c]	80[b]
d	p-$Cl \cdot C_6H_4$	65[c]	71[b]
e	o-$Cl \cdot C_6H_4$	70[c]	71[b]
f	p-$Br \cdot C_6H_4$	60[c]	70[b]
g	m-$Br \cdot C_6H_4$	50[c]	65[b]
h	2-Naphthyl	65[c]	87[b]
i	1-Naphthyl	68[c]	84[b]
j	p-$OCH_3 \cdot C_6H_4$	65[c]	78[b]
k	3,4-$(OMe)_2 \cdot C_6H_3$	70[c]	80[b]
l	o-$OMe \cdot C_6H_4$	65[c]	80[b]
m	2-Theinyl	65[c]	77[b]
n	2-Furyl	80[c]	83[b]
o	p-$NO_2 \cdot C_6H_4$	78[b]	60[c]

[a] All the reaction were carried out by using **4** (0.5 mmol) and sodium methoxide (1.0 mmol) in a solvent (4 mL) at room temperature. [b] Yields are reported without further purification through column chromatography. [c] Yield are reported after purification through column chromatography.

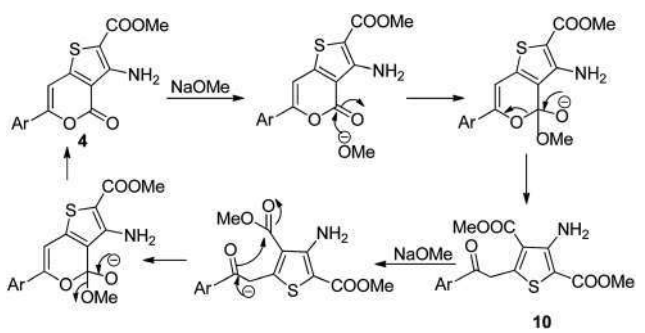


Scheme 4 Synthesis of tetrasubstituted thiophenes **10**.

polar protic solvent rather than in polar aprotic solvent. Thus, DMF was found as a choice of solvent for better yields and clean reaction (Scheme 4).

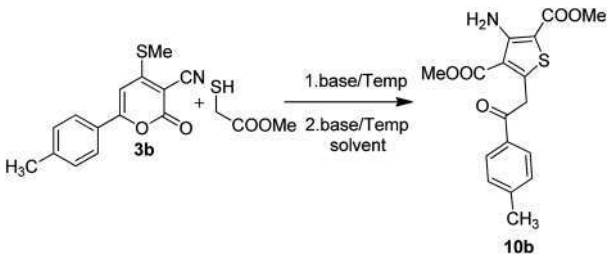
Mechanistically, the ring opening of **4** is initiated with attack of methoxide ion at carbonyl carbon at C4 to form a transition state which stabilized after ring opening to form tetrasubstituted thiophene (**10**). If reaction was not monitored carefully, the formed product **10** in methanol in the presence of methoxide ion cyclized to parent compound **4** in significant amount (Scheme 5).

After success of two steps strategy for the synthesis of tetrasubstituted thiophenes, our prime objective was to synthesize



Scheme 5 A plausible mechanism for the ring opening and ring closure.

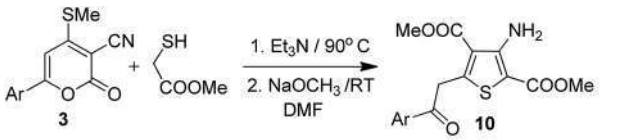
Table 2 Optimization of reaction conditions[a,b,d]



Entry	Solvent	Base 1/t, °C/T, h	Base 1/t, °C/T, h	Yield (%)
1	CH_3OH	Et_3N/rt/24 h	—	—[c]
2	CH_3OH	Et_3N/90/2.5 h	$NaOCH_3$/rt/1.5	60
3	CH_3OH	Et_3N/90/2.5 h	$NaOCH_3$/90/1	62
4	DMF	$NaOCH_3$/90/2 h	$NaOCH_3$/90/4	Complex mixture
5	DMF	Et_3N/rt/40 h	$NaOCH_3$/rt/2	80
6	DMF	Et_3N/90/2.5 h	$NaOCH_3$/rt/2	86

[a] Reactions were carried out by stirring **3b** (0.5 mmol), methyl thioglycolate (0.75 mmol), triethylamine (1.0 mmol) and sodium methoxide (1.0 mmol) at various temperature. [b] 1st and 2nd bases were added sequentially and reaction was carried out for given time at mentioned temperature. [c] Thieno[3,2-*c*]pyran was isolated. [d] Room temperature was ranging between 30–35 °C.

10 in single step using 2-pyranones as a precursor. For one pot synthesis of **10**, optimization of reaction was carried out in various solvents and bases. We conducted our screening by refluxing a mixture of **3b** and methyl thioglycolate in methanol using triethylamine (1.0 mmol) as a base for 24 h which exclusively delivered thieno[3,2-*c*]pyrans (**4**). This indicated that methanol only acts as solvent in the reaction and not as nucleophile (entry 1, Table 2). In other set of experiment, a mixture of lactone **3b**, methyl thioglycolate and triethylamine in methanol was refluxed at 90 °C for 2.5 h. There after, sodium methoxide was added and reaction mixture was stirred further at room temperature for 1.5 h. Usual work-up delivered 60% of desired product (Table 2, entry 2). In another set of experiment, pyranothiophene formed by the reaction of **3b** and methyl thioglycolate using triethylamine in methanol, sodium methoxide was added and ring opening was performed at 90 °C. This reaction afforded 62% of desired product and stirred further for 2.5 h (entry 3, Table 2). In quest for better yield and to avoid reversibility of the reaction, we performed a reaction of **3b** and methyl thioglycolate in the presence of $NaOCH_3$ and DMF at 90 °C, which produced a complex mixture (entry 4, Table 2). In another set of experiment, we performed the reaction using Et_3N in DMF at room temperature for 40 h and thereafter sodium methoxide was added and stirred further for additional 2 h at room temperature. Usual work up afforded 80% of tetrasubstituted thiophene (**10**) (entry 5, Table 2). To reduce the duration of reaction, A mixture of **3b** and methyl thioglycolate was stirred in the presence of triethylamine as a base in DMF at 90 °C for 2.5 h to generate pyranothiophene *in situ*. Thereafter, NaOMe was added and stirred further at room temperature.



10a) Ar=C_6H_5; 87%
10b) Ar=*p*-$CH_3.C_6H_4$; 86%
10c)Ar=*p*-$F.C_6H_4$; 85%
10d)Ar=*p*-$Cl.C_6H_4$; 68%
10e)Ar=*o*-$Cl.C_6H_4$; 70%
10f)Ar=*p*-$Br.C_6H_4$; 62%
10g)Ar=*m*-$Br.C_6H_4$; 55%
10h)Ar=2-naphthyl; 83%
10i)Ar=1-naphthyl; 80%
10j)Ar=*p*-$OCH_3.C_6H_4$; 80%
10k)Ar= *3,4-*$(OCH_3)_2.C_6H_4$; 80%
10l)Ar=*o*-$OCH_3.C_6H_4$; 75%
10m) Ar=2-Theinyl; 70%
10n) Ar=2-Furyl; 77%
10o) Ar=*p*-$NO_2.C_6H_4$; 65%

Scheme 6 One pot approach for the synthesis of tetrasubstituted thiophenes **10**.

Usual work up delivered 86% of the desired product **10** (entry 6, Table 2).

After optimization of reaction condition, we have synthesized various derivatives of tetrasubstituted thiophene in good to excellent yields in one pot (Scheme 6). It was interesting to note that methyl 3-amino-6,7-diaryl-4-oxo-4*H*-thieno[3,2-*c*]-pyran-2-carboxylates (**4**) under similar reaction conditions did not form tetrasubstituted thiophene, possibly the presence of additional aryl group at position 6 stabilized the pyran ring and not allow the ring opening from alkoxide ion.

The presence of various functional group in aryl ring present at position 6 of 2-pyranone does not follow any specific trend on reactivity. The presence of 4-nitrophenyl and 4-bromophenyl ring greatly reduces the yield of tetrasubstituted thiophenes. Overall, it is very difficult to assess the role of aryl ring in the reaction.

The molecular view (ORTEP) for the compounds **10a** with atom numbering scheme is presented in Fig. 2.‡ The compound crystallizes in monoclinic crystal system having P_12_1/C_1 space group with four molecules in the unit cell. The dihedral angle between the two aromatic rings *viz.* thiophene and the phenyl ring is 76.89°. The torsion angles O(1)–C(7)–C(1)–C(6) and O(1)–C(7)–C(8)–C(9) are 170.29(17)° and 30.9(2)°, respectively. The torsion angles associated with the two ester functions and the 1° amine group *viz.* N(1)–C(13)–C(14)–C(15), C(11)–C(10)–C(13)–N(1), C(13)–C(10)–C(11)–O(3) and C(13)–C(14)–C(15)–O(4) are 0.9(3), −0.6(3), −1.4(3) and −3.2(3), respectively. These torsion angle data indicates that N(1), O(4) and O(3) are almost coplanar and the two hydrogens over 1° amine can display intramolecular hydrogen bonding.

The intramolecular N(1)–H(1′)···O(3) and N(1)–H(1″)···O(4) interaction distances and angles are 2.09(2) Å; 130(2)° and 2.21(2) Å; 129(2)°, respectively (Fig. 3). The supramolecular aggregation in **10a** is stabilized by a pair of weak intermolecular

‡ Crystal data for **10a** (CCDC 1038008): $C_{16}H_{15}NO_5S$, formula mass 333.35, monoclinic space group P_12_1/C_1, a = 14.073(5), b = 13.465(5), c = 8.576(5) Å, β = 93.433(5)°, V = 1622.2(13) Å^3, Z = 4, d_{calcd} = 1.365 mg m^{-3}, linear absorption coefficient 0.224 mm^{-1}, F(000) = 696, crystal size 0.27 × 0.25 × 0.18 mm, reflections collected 9249, independent reflections 3729 [R_{int} = 0.0232], final indices [$I > 2\sigma(I)$] R_1 = 0.0466, wR_2 = 0.1110, R indices (all data) R_1 = 0.0628, wR_2 = 0.1207, gof 1.042, largest difference peak and hole 0.233 and −0.232 e Å^{-3}.

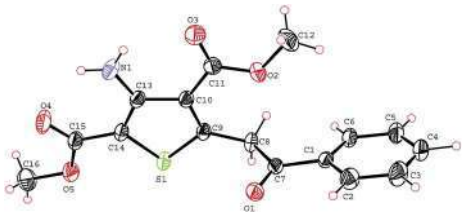


Fig. 2 ORTEP diagram of **10a** at 30% probability with atom numbering scheme.

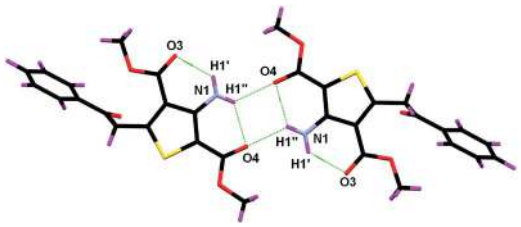


Fig. 3 Centro symmetric dimer held by pair of weak N–H···O interactions (intramolecular N–H···O interaction pairs are also presented).

Table 3 Selected topographical features for various interactions computed at B3LYP/6-31G** level of theory

Interaction Type	ρ_{bcp}	$\nabla^2\rho_{bcp}$	E	H (au)
Intra N–H···O	+0.016769	+0.056219	+0.100692	+0.029323
Intra N–H···O	+0.025872	+0.081472	+0.023475	+0.028191
Inter N–H···O	+0.014931	+0.054220	+0.088161	+0.018966

N–H···O interactions (Fig. 3) that lead to the formation of centro symmetric dimers. The N(1)–H(1″)···O intermolecular interaction distance is 2.199 Å and the N–H···O is non-linear having magnitude of 130.74°.

The analysis of the interaction energy in the crystal structures of **10a** by means of dimer unit bound by pair of N–H···O interactions at the DFT level of theory yields the interaction energy −20.82 kJ mol^{-1} for pair of interaction and −10.41 kJ mol^{-1} for individual N–H···O interaction. To further confirm the nature of these weak interactions, bond critical points (bcp) were calculated for the different dimers by using the Atoms in Molecules theory.[37] The bond critical points observed between the interacting atoms, confirmed the presence of weak non-covalent interactions between the two molecules of **10**. The value of electron density (ρ); Laplacian of the electron density ($\nabla^2\rho_{bcp}$); bond ellipticity (ε) electron density (ρ) and total energy density (H) at the bond critical point for all the three interactions are presented in Table 3. As indicated in the table, the electron density for all the three types of interactions at bond critical point (ρ_{bcp}) are less than +0.10 au which indicates a closed shell hydrogen bonding interactions. Additionally, the Laplacian of the electron density $\nabla^2\rho_{bcp}$ in all the three cases are greater than zero which indicated the depletion of electron density in the region of contact between the H···O atoms. The bond ellipticity (ε) which measures the extent to which the electron density is

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preferentially accumulated in a given plane containing the bond path indicates that all the three interactions are not cylindrically symmetrical in nature.

Conclusions

One pot expeditious, economical and convenient synthesis of dimethyl 3-amino-5-(2-oxo-2-arylethyl)thiophene-2,4-dicarboxylates has been developed for the first time through [3 + 2] donor–acceptor heteroannulation of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles and methyl thioglycolate followed by ring opening using sodium methoxide. We have also demonstrated the ring opening reaction of methyl 3-amino-6-aryl-4-oxo-4*H*-thieno[3,2-*c*]pyran-2-carboxylates in methanol and DMF and given some interesting finding. If we perform ring opening in methanol rather than DMF, it was observed that prolonged stirring of reaction mixture reverted to parent compound **4**. The various functional groups present in thiophene ring at positions 2,3,4,5 are very reactive and can be utilized as precursors for the construction of various fused heterocycles not easily obtainable by conventional route. The mild reaction conditions, easy workup and non-involvement of metal catalyst make this protocol attractive for practical applications.

Experimental section

General remarks

Commercially available reagents and solvents were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz and 100 MHz NMR spectrometer respectively. $CDCl_3$ were used as solvent for NMR. Chemical shift reported in ppm considering ($CDCl_3$) δ 7.24 ppm for ^{1}H NMR and δ 77.00 ppm for ^{13}C NMR as an internal standard. Signal patterns are indicated as s, singlet; d, doublet; dd, doublet of doublet; t, triplet; m, multiplet; br s, broad singlet. Coupling constants (*J*) are given in hertz (Hz). Infrared (IR) spectra were recorded on AX-1 spectrophotometer and reported as wave number (cm^{-1}). Intensity data for **10** were collected at 298(2) K on a Sapphire2-CCD, OXFORD diffractometer system equipped with graphite monochromated Mo Kα radiation λ = 0.71073 Å. The final unit cell determination, scaling of the data, and corrections for Lorentz and polarization effects were performed with CrysAlis RED.[38] The structure was solved by direct methods (SHELXS-97)[39] and refined by a full-matrix least-squares procedure based on F^2.[40] All the calculations were carried out using WinGX system Ver-1.64.[41] All non-hydrogen atoms were refined anisotropically; hydrogen atoms were located at calculated positions and refined using a riding model with isotropic thermal parameters fixed at 1.2 times the U_{eq} value of the appropriate carrier atom.

General procedure for the synthesis of dimethyl 3-amino-5-(2-oxo-2-(aryl)ethyl)thiophene-2,4-dicarboxylate: two steps and one pot approach were established

One pot synthetic approach (method A). A mixture of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles (0.5 mmol), methyl thioglycolate (0.75 mmol) and triethylamine (1.0 mmol) in DMF (4.0 mL) was stirred for 2.5 h at 90 °C. Thereafter, the reaction mixture was brought to room temperature and sodium methoxide (1.0 mmol) was added to the reaction mixture and stirred for additional 2 h at room temperature. The reaction mixture was poured onto crushed ice with vigorous stirring followed by neutralization with 10% HCl. The precipitate obtained was filtered, dried and recrystallized from methanol to obtain the desired product in good to excellent yields.

Ring opening approach in methanol (method B). Methyl 3-amino-6-arylthieno[3,2-*c*]pyran-4-one-2-carboxylates (**4**, 0.5 mmol) obtained by the procedure reported[33] earlier was treated with freshly prepared $NaOCH_3$ solution (23 mg Na in 4.0 mL MeOH) for 1–2 h and completion of reaction was monitored by TLC. After completion, the excess of methanol was removed under reduced pressure followed by addition of cold water. Reaction mixture was neutralized with 10% HCl and filtered the precipitate. The crude product was purified by silica gel column chromatography using 50% dichloromethane in hexane as an eluent.

Ring opening approach in DMF (method C). A mixture of methyl 3-amino-6-arylthieno[3,2-*c*]pyran-4-one-2-carboxylates (**4**, 0.5 mmol) and sodium methoxide (1.0 mmol) in DMF (4.0 mL) was stirred for 1–2 h at room temperature. Completion of reaction was monitored by TLC. Thereafter, the reaction mixture was poured onto crushed ice with vigorous stirring followed by neutralization with 10% HCl. The precipitate obtained was filtered dried and recrystallized from methanol to obtain the pure product.

Dimethyl 3-amino-5-(2-oxo-2-phenylethyl)thiophene-2,4-dicarboxylate (10a). Yield: 87% (144 mg) R_f = 0.32 (1 : 1 hexane in dichloromethane); yellow solid; mp: 142–144 °C; IR (KBr): 3476, 3365, 1685, 1597, 1448, 1326 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.66 (s, 2H, CH_2), 6.83 (br s, 2H, NH_2), 7.49 (t, J = 7.62 Hz, 2H, ArH), 7.58–7.59 (m, 1H, ArH), 7.98 (d, J = 7.32 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.6, 51.2, 51.4, 117.8, 128.0, 128.7, 133.5, 136.2, 151.1, 155.1, 163.4, 164.2, 194.3; HRMS (ESI): calculated for $C_{16}H_{15}NO_5S$, 334.0744 (M + H^+) found for *m*/*z*, 334.0741.

Dimethyl 3-amino-5-(2-oxo-2-(*p*-tolyl)ethyl)thiophene-2,4-dicarboxylate (10b). Yield: 86% (144 mg) R_f = 0.31 (1 : 1 hexane in dichloromethane); white solid; mp: 162–164 °C; IR (KBr): 3478, 3359, 1702, 1687, 1579, 1274 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 3H, CH_3), 3.61 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.64 (s, 2H, CH_2), 6.83 (br s, 2H, NH_2), 7.28 (d, J = 7.93 Hz, 2H, ArH), 7.88 (d, J = 7.93 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 40.5, 51.1, 51.3, 97.7, 117.7, 128.1, 129.4, 133.7, 144.3, 151.3, 155.1, 163.4, 164.2, 193.9; HRMS (ESI): calculated for $C_{17}H_{17}NO_5S$, 348.0900 (M + H^+); found for *m*/*z*, 348.0891.

Dimethyl 3-amino-5-(2-(4-fluorophenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10c). Yield: 85% (149 mg) R_f = 0.21 (1 : 1 hexane in dichloromethane); yellow solid; mp: 152–153 °C; IR (KBr): 3476, 3359, 1702, 1595, 1528, 1273 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.63 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.60 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 7.16 (t, J = 8.77 Hz, 2H ArH), 8.00–8.02 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.5, 51.2, 51.4, 115.9, (d, J = 22.04 Hz), 117.8, 124.9, 128.4, 130.7, (d,

J = 9.58 Hz), 132.6, 150.8, 155.0, 163.3, 164.1, 165.9 (d, J = 255.9), 192.8; HRMS (ESI): calculated for $C_{16}H_{14}FNO_5S$, 352.0649 (M + H^+); found for m/z, 352.0648.

Dimethyl 3-amino-5-(2-(4-chlorophenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10d). Yield: 68% (124 mg) R_f = 0.30 (1 : 1 hexane in dichloromethane); white solid; mp: 147–149 °C; IR (KBr): 3482, 3363, 1701, 1589, 1459, 1273 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.63 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.63 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 7.46 (d, J = 8.54 Hz, 2H ArH), 7.93 (d, J = 8.54 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.5, 51.2, 51.5, 117.8, 129.1, 129.5, 134.5, 140.0, 150.6, 155.0, 163.3, 164.2, 193.2; HRMS (ESI) calculated for $C_{16}H_{14}ClNO_5S$, 368.0354 (M + H^+); found for m/z, 368.0348.

Dimethyl 3-amino-5-(2-(2-chlorophenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10e). Yield: 70% (128 mg) R_f = 0.30 (1 : 1 hexane in dichloromethane); cinnamon solid; mp: 90 °C; IR (KBr): 3461, 3348, 1707, 1664, 1587, 1269 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.69 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.65 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 7.34–7.36 (m, 1H, ArH), 7.38–7.45 (m 2H, ArH), 7.53–7.55 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.6, 51.2, 51.5, 117.8, 127.02, 129.5, 130.7, 131.0, 132.2, 138.2, 150.0, 155.0, 163.4, 164.2, 196.6; HRMS (ESI): calculated for $C_{16}H_{14}ClNO_5S$, 368.0354 (M + H^+); found for m/z, 368.0352.

Dimethyl 3-amino-5-(2-(4-bromophenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10f). Yield: 62% (127 mg) R_f = 0.28 (1 : 1 hexane in dichloromethane); yellow solid; mp: 141–143 °C; IR (KBr): 3475, 3359, 1699, 1599, 1458, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.63 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.62 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 7.63 (d, J = 8.54 Hz, 2H ArH), 7.85 (d, J = 8.54 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.5, 51.2, 51.5, 117.8, 128.7, 129.6, 132.1, 134.9, 150.6, 155.0, 163.3, 164.1, 193.4; HRMS (ESI) calculated for $C_{16}H_{14}BrNO_5S$, 411.9849 (M + H^+); found for m/z, 411.9840.

Dimethyl 3-amino-5-(2-(3-bromophenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10g). Yield: 55% (112 mg) R_f = 0.24 (1 : 1 hexane in dichloromethane); chocolate solid; mp: 134 °C; IR (KBr): 3467, 3350, 1699, 1582, 1517, 1270 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.65 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.63 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 7.37 (t, J = 7.63 Hz, 1H, ArH), 7.72 (d, J = 9.92 Hz, 1H, ArH); 7.91 (d, J = 7.63 Hz, 1H, ArH), 8.11–8.12 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.6, 51.2, 51.5, 117.9, 123.1, 126.6, 130.3, 131.1, 136.3, 137.9, 150.4, 155.0, 163.3, 164.1, 193.0; HRMS (ESI) calculated for $C_{16}H_{14}BrNO_5S$, 411.9849 (M + H^+); found for m/z, 411.9839.

Dimethyl 3-amino-5-(2-(naphthalen-2-yl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10h). Yield: 83% (158 mg) R_f = 0.21 (1 : 1 hexane in dichloromethane); carrot orange solid; mp: 170–172 °C; IR (KBr): 3476, 3361, 1702, 1586, 1529, 1274 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.59 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.80 (s, 2H, CH_2), 6.85 (br s, 2H, NH_2), 7.56–7.62 (m, 2H, ArH), 7.87–8.02 (m, 4H, ArH), 8.53 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.7, 51.2, 51.4, 117.8, 123.7, 126.9, 127.8, 128.7, 129.5, 129.8, 132.4, 133.5, 135.7, 151.2, 155.1, 163.4, 164.2, 194.2; HRMS (ESI): calculated for $C_{20}H_{17}NO_5S$, 384.0900 (M + H^+) found for m/z, 384.0895.

Dimethyl 3-amino-5-(2-(naphthalen-1-yl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10i). Yield: 80% (153 mg) R_f = 0.22 (1 : 1 hexane in dichloromethane); buff solid; mp: 151–153 °C; IR (KBr): 3459, 3346, 1706, 1686, 1586, 1273 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.58 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.74 (s, 2H, CH_2), 6.86 (br s, 2H, NH_2), 7.50–7.55 (m, 3H, ArH), 7.87 (d, J = 8.24 Hz, 1H, ArH); 7.99 (dd, J = 7.33 Hz, 7.79 Hz, 2H, ArH), 8.56 (d, J = 8.24 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.8, 51.2, 51.5, 117.8, 124.2, 125.6, 126.6, 127.6, 128.2, 128.4, 130.0, 133.2, 133.9, 134.7, 151.0, 163.5, 164.2, 197.5; HRMS (ESI) calculated for $C_{20}H_{17}NO_5S$, 384.0900 (M + H^+) found for m/z, 384.0900.

Dimethyl 3-amino-5-(2-(4-methoxyphenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10j). Yield: 80% (144 mg) R_f = 0.17 (1 : 1 hexane in dichloromethane); yellow solid; mp: 142–144 °C; IR (KBr): 3475, 3353, 1700, 1582, 1451, 1278 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.62 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.61 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 6.95 (d, J = 8.54 Hz, 2H ArH), 7.96 (d, J = 9.16 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.3, 51.2, 51.4, 55.5, 113.9, 117.7, 129.2, 130.4, 151.6, 155.1, 163.5, 163.7, 164.2, 192.8; HRMS (ESI) calculated for $C_{17}H_{17}NO_6S$, 364.0849 (M + H^+); found for m/z 364.0847.

Dimethyl 3-amino-5-(2-(3,4-dimethoxyphenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10k). Yield: 80% (157 mg) R_f = 0.18 (1 : 1 hexane in dichloromethane); buff solid; mp: 183–184 °C; IR (KBr): 3475, 3345, 1707, 1590, 1512, 1265 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.64 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3) 4.64 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 6.91 (d, J = 8.39 Hz, 1H, ArH), 7.52–7.53 (m, 1H, ArH), 7.62–7.64 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.2, 51.1, 51.4, 55.9, 56.0, 110.0, 110.1, 117.7, 122.7, 129.3, 149.1, 151.6, 153.5, 155.0, 163.4, 164.2, 192.9; HRMS (ESI): calculated for $C_{18}H_{19}NO_7S$, 394.0955 (M + H^+); found for m/z, 394.0947.

Dimethyl 3-amino-5-(2-(2-methoxyphenyl)-2-oxoethyl)-thiophene-2,4-dicarboxylate (10l). Yield: 75% (136 mg) R_f = 0.18 (1 : 1 hexane in dichloromethane); yellow solid; mp: 115–117 °C, IR (KBr): 3471, 3354, 1690, 1586, 1508, 1274 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.61 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.63 (s, 2H, CH_2), 6.83 (br s, 2H, NH_2), 6.97–7.02 (m, 2H, ArH), 7.48 (t, J = 7.63 Hz, 1H, ArH), 7.70 (d, J = 7.63 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.6, 51.1, 51.2, 55.4, 97.4, 111.4, 117.5, 120.7, 127.2, 130.5, 134.0, 152.1, 155.2, 158.5, 163.5, 164.2, 196.0; HRMS (ESI): calculated for $C_{17}H_{17}NO_6S$, 364.0849 (M + H^+); found for m/z, 364.0847.

Dimethyl 3-amino-5-(2-oxo-2-(thiophen-2-yl)ethyl)thiophene-2,4-dicarboxylate (10m). Yield: 70% (118 mg) R_f = 0.33 (1 : 1 hexane in dichloromethane); white solid; mp: 145–147 °C; IR (KBr): 3481, 3365, 1685, 1589, 1439, 1272 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.59 (s, 2H, CH_2), 6.83 (br s, 2H, NH_2), 7.15 (dd, J = 4.88, 4.88 Hz, 1H, Ar-H), 7.67 (d, J = 4.27 Hz, 1H, ArH), 7.78 (dd, J = 1.22, 1.49 Hz, 1H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.2, 51.2, 51.4, 117.8, 128.2, 132.1, 134.1, 143.0, 150.2, 163.4, 164.2, 187.0; HRMS (ESI): calculated for $C_{14}H_{13}NO_5S_2$, 340.03068 (M + H^+); found for m/z 340.0307.

Dimethyl 3-amino-5-(2-(furan-2-yl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10n). Yield: 77% (124 mg) R_f = 0.25 (1 : 1 hexane in dichloromethane); yellow colored solid; mp: 149–151 °C; IR (KBr): 3481, 3363, 1701, 1587, 1466, 1257 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.53 (s, 2H, CH_2), 6.56 (m, 1H, Ar-H), 6.82 (br s, 2H, NH_2), 7.25 (d, J = 3.66 Hz, 1H, ArH), 7.61 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$):

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δ 40.2, 51.2, 51.4, 112.5, 117.4, 117.8, 146.5, 150.0, 151.9, 155.0, 163.4, 164.2, 183.3; HRMS (ESI): calculated for $C_{14}H_{13}NO_6S$, 324.0536 ($M + H^+$); found for m/z, 324.0536.

Dimethyl 3-amino-5-(2-(4-nitrophenyl)-2-oxoethyl)thiophene-2,4-dicarboxylate (10o). Yield: 65% (122 mg) $R_f = 0.17$ (1 : 1 hexane in dichloromethane); yellow solid; mp: 194–196 °C; IR (KBr): 3467, 3363, 1699, 1608, 1530, 1257 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.61 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.64 (s, 2H, CH_2), 6.74 (br s, 2H, NH_2), 8.09–8.11 (m, 2H, ArH), 8.28–8.30 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.1, 51.3, 51.6, 118.0, 124.0, 129.1, 140.7, 149.8, 150.5, 163.2, 164.1, 193.0; HRMS (ESI): calculated for $C_{16}H_{14}N_2O_7S$, 379.0594 ($M + H^+$); found for m/z, 379.0594.

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Precursor directed regioselective synthesis of partially reduced benzo[*e*]indene through oxidative cyclization and benzo[*h*]quinolines†

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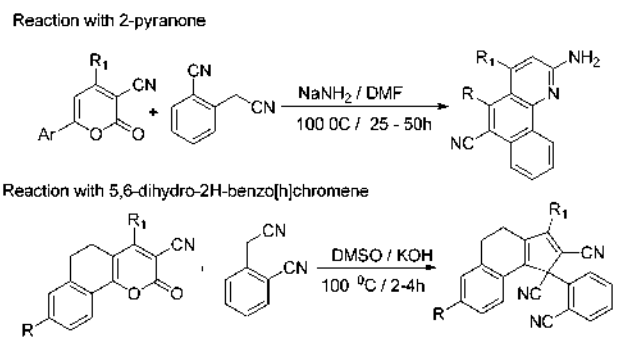
We have reported a simple, unprecedented base promoted synthesis of 7-substituted-1-(2-cyano-phenyl/phenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitriles by reaction of 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles and 2-cyanomethyl-benzonitrile/phenyl-acetonitrile under basic conditions at 100 °C. This reaction involves ring opening of 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile by a carbanion generated *in situ* from 2-cyanomethylbenzonitrile/phenyl-acetonitrile followed by oxidative cyclization to afford the desired product. Alternatively, reaction of 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles and 2-cyanomethyl-benzonitrile under basic conditions provides functionalized benzo[*h*]quinolines. The structure of the synthesized compound was confirmed by single crystal X-ray.

Benzo[*e*]indenes are widely present in nature and well known for their use as a building block in organic synthesis. Indene has broad use in medicine.[1] This skeleton is present as substructure in steroid,[2] hamigeran B[3] and polymers[4] in completely or partially reduced form. Various monosubstituted derivatives of 1*H*-benzo[*e*]indene-1,3-(2*H*)-dione exhibit antiviral activity.[5] Many approaches for the construction of benzo[*e*]-indene as whole or substructure has been reported. Synthesis of indene derivatives has been carried out by reaction of alkynes and phenyl pyrrolidino or morpholino chromium carbene complexes[6] in DMF at 120–125 °C. Another approach used to build indene skeleton involves cyclization of substituted phenyl allylic cations.[7] Indene was also prepared by cycloalkylation procedure, such as; reaction of arylated alkene with phosphorus halide and dehydration of aryl substituted diols.[8–10] It was also synthesized by reaction of *gem*-dihalocyclopropane and benzene in presence of aluminium chloride.[11] Recently, indene was synthesized by metal catalyzed cycloisomerization of 1-alkyl-2-ethynylbenzenes.[12] This reaction can be performed by using $PtCl_2$ or $PtCl_4$ or $[RuCl_2(CO)_3]_2$ as a catalyst at 30–80 °C.[12] Au(I) catalyzed [3 + 3] cycloaddition,[13] and Pd-catalyzed carboannulation of propargyl carbonates[14] also provides functionalized indenes. Ru catalyzed hydroamination followed by Re catalyzed C–H bond activation approach using aryl alkyne as a precursor[15] was also reported for synthesis of indene. Bi *et al.* have established electrocyclization approach for generation of indene.[16]

A careful literature survey confirms that various approach for the synthesis of indene skeleton requires various expensive metal catalyst and harsh reaction conditions. Recently, we have reported the synthesis of benzo[*h*]quinolines by reaction of 2-cyanomethylbenzonitrile and 2-pyranone under basic conditions.[17]

In this connection, we wish to report the use of 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles as a precursor, which changes the course of the reaction to give benzo[*e*]indenes (Scheme 1).

Here, we have studied the comparison of two precursor 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **4** and 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles **4′** using 2-



Scheme 1 Precursor dependent synthesis of functionalized benzo[*h*]-quinoline and 4,5-dihydro-1*H*-benz[e]indene.

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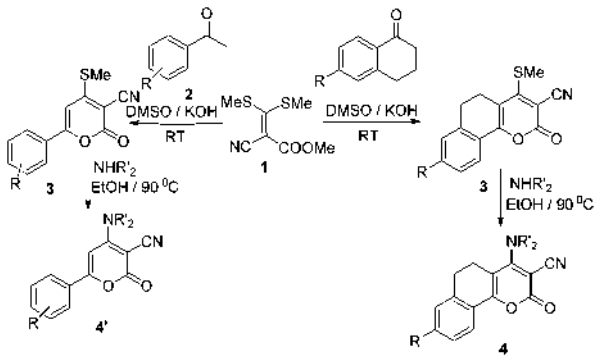
† Electronic supplementary information (ESI) available: Characterization data and ^1H and ^{13}C NMR spectra for all the reported compounds. CCDC 1032257–1046947. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ra13612h

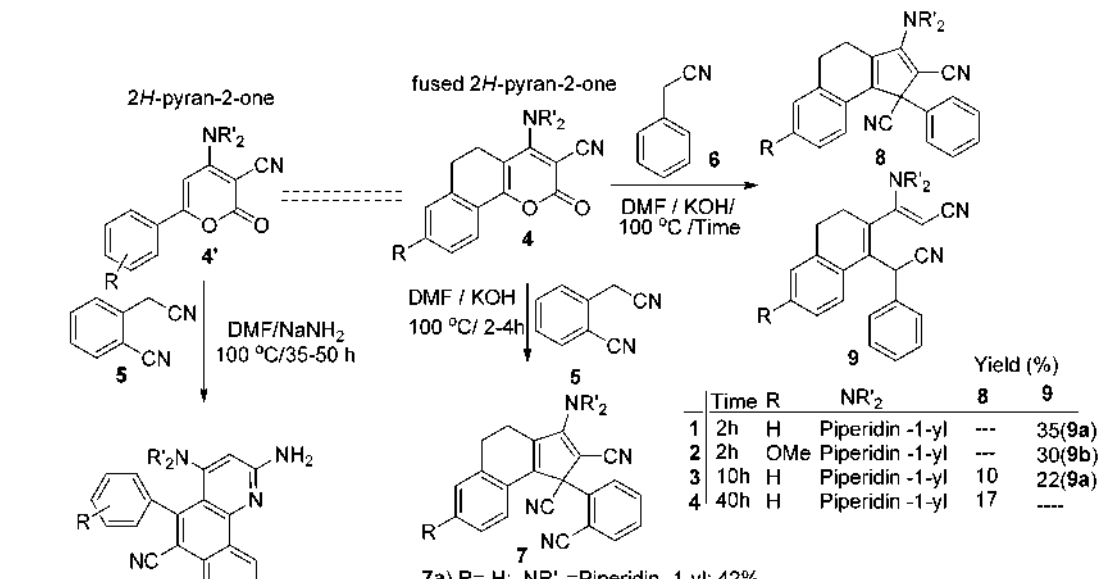


Scheme 2 Synthesis of 8-OMe/*H*-2-oxo-4-*sec* amino-1-yl-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles and 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles.

cyanomethylbenzonitrile as carbanion source. These precursors can be synthesized in two steps. First 8-substituted-4-methylsulfanyl-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **3** and 6-aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles were synthesized by reaction of 2-cyono-3,3-bis-methylthio-acrylic acid methyl ester **1** and 1-teteralone/6-methoxy-1-teteralone and functionalized acetophenones in DMSO in presence of KOH respectively. The compound **3** on amination with various secondary amine in refluxing ethanol provides 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4** and 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles **4′** in good yields (Scheme 2).[18]

Recently, base promoted chemoselective synthesis of benzo[*h*]quinolines[17] was reported by reaction of 6-aryl-4-*sec* amino-2-oxo-2*H*-pyran-3-carbonitriles **4′** and 2-cyanomethylbenzonitrile under basic conditions (Scheme 3). To expand the scope of reaction, we shifted to fused precursor 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **4**. Interestingly, use of 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **4** as a precursor did not followed the same course of reaction and 7-substituted-1-(2-cyano-phenyl)-3-*sec* amino-1-yl-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile was obtained as a product.

To study the effect of base and solvents on reaction, we have chosen 2-oxo-4-piperidin-1-yl-5,6-dihydro-2*H*-benzo[*h*]-chromene-3-carbonitrile and 2-cyanomethylbenzonitrile as model substrates. Initially, 4-methylsulfanyl-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **3** was used as substrate to perform the ring transformation reaction and complex mixture obtained, probably due to presence of methylthio group at position 4. To reduce the electrophilicity at C-4, methylthio group was replaced with secondary amine. We have started the study using sodamide as a base in DMF (entry 1) and DMSO (entry 2) at room temperature and observed complex mixture formation with major unreacted starting material. Then, we



	Time	R	NR'_2	8	9
				Yield (%)	
1	2h	H	Piperidin -1-yl	---	35(**9a**)
2	2h	OMe	Piperidin -1-yl	---	30(**9b**)
3	10h	H	Piperidin -1-yl	10	22(**9a**)
4	40h	H	Piperidin -1-yl	17	----

7a) R= H; NR'_2=Piperidin -1-yl; 42%
7b) R= H; NR'_2= Pyrrolidine -1-yl ; 50%
7c) R= H; NR'_2= 4-Morpholin -1-yl; 40%
7d) R= H; NR'_2= 4-benzylpiperazine -1-yl; 38%
7e) R= OMe; NR'_2=Piperidin -1-yl;40%
7f) R= OMe;NR'_2= 4-Morpholin -1-yl; 37%

11a) R= H; NR'_2=Piperidin -1-yl; 75%
11b) R= 4-Me;NR'_2=Piperidin -1-yl;65%
11c) R= 2-F; NR'_2=Piperidin -1-yl; 60%
11d) R= 4-OMe;NR'_2=4-benzylpiperazine -1-yl;74%

Scheme 3 Synthesis of 7-OMe/*H*-1-(2-cyano-phenyl/phenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitriles, [a]3-[1-(cyano-phenyl-methyl)-6-OMe/*H*-3,4-dihydro-napthalen-2-yl]-3-piperidine-1-yl-acrylonitrile[b] and functionalized benzo[*h*]quinoline.[18] (a) Reactions were performed by stirring 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **4** (0.5 mmol) and 2-cynomethyl-benzonitrile **5** (0.5 mmol) using KOH (0.75 mmol) in DMF (4.0 mL) at 100 °C; (b) reactions were performed by stirring 2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **4** (0.5 mmol) and phenyl-acetonitrile **6** (0.5 mmol) using KOH (0.75 mmol) as a base in DMF (4.0 mL) at 100 °C.

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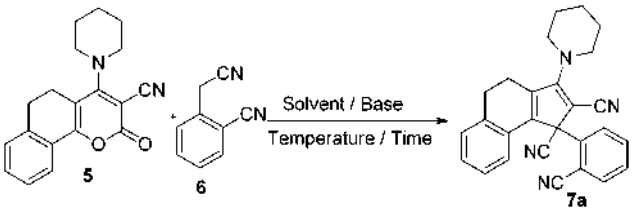
Table 1 Effect of base and solvent on the synthesis of **7a**[a]



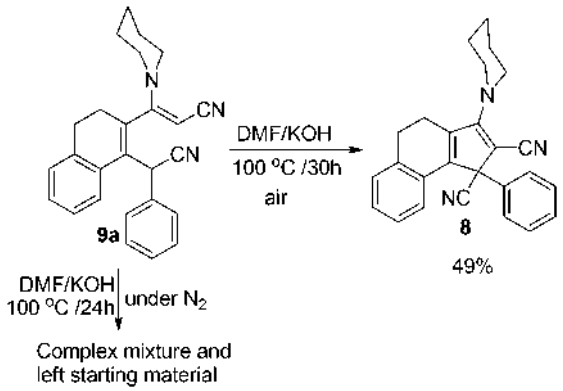
Entry	Base	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	$NaNH_2$	DMF	RT[b]	5 h	Complex mixture
2	$NaNH_2$	DMSO	RT	5 h	Complex mixture
3	$NaNH_2$	DMF	70	4 h	25
4	$NaNH_2$	DMF	100	2 h	40
5	$NaNH_2$	DMSO	100	2 h	35
6	KOH	DMSO	100	2 h	35
7	**KOH**	**DMF**	100	**2 h**	**42**
8	KOH	DMF	120	2 h	35
9	NaH	DMSO	95	2 h	32
10	NaH	DMF	95	2 h	37

[a] Reactions were carried out by stirring 2-oxo-4-piperidin-1-yl-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile (0.5 mmol), 2-cyanomethylbenzonitrile (0.5 mmol), base (0.75 mmol) in solvent (4.0 mL). [b] RT = 25–35 °C.

have performed the reaction **4** and **5** in DMF using sodamide as a base at 70 °C and 25% of desired product was isolated (entry 3), while at 100 °C, 40% of product formed in 2 h (entry 4). Use of sodamide in DMSO at 100 °C afforded 35% of desired product (entry 5). Further optimization was carried out by using KOH as base in DMSO and DMF separately at 100 °C and 35% and 42% of the product isolated respectively (entries 6 and 7). In another experiment, reaction of **4** and **5** was carried out in DMF using KOH as a base at 120 °C and lowering in yield was observed (entry 8). Further reaction was also performed by using sodium hydride as base in DMSO and DMF separately at 100 °C and obtained the desired product in 32% and 37% of yield (entries 9 and 10) (Table 1).

Thus, stirring of a mixture of functionalized 5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4** and 2-cyanomethylbenzonitrile in DMF using potassium hydroxide as a base at 100 °C for 2–4 h provides corresponding product in moderate yield (Scheme 3).

Efficiency of reaction condition as in entry 7 was tested for the synthesis of various 1-(2-cyano-phenyl/phenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile (**7**) derivatives. Surprisingly, When we have used benzyl cyanide *in lieu* of 2-cyanomethylbenonitrile as a carbanion source, under similar reaction condition cyclised product was not obtained after 2 h. Probably, 3-(1-(cyano(phenyl)methyl)-6-substituted-3,4-dihydronaphthalen-2-yl)-3-(piperidin-1-yl)acrylonitriles (**9**) is intermediate for the final product. In order to prove this we have performed the reaction for 10 h and obtained mixture of 3-(1-(cyano(phenyl) methyl)-6-substituted-3,4-dihydronaphthalen-2-yl)-3-(piperidin-1-yl)acrylonitriles (**9**) and proposed cyclized product 1-phenyl-3-(piperidin-1-yl)-4,5-dihydro-1*H*-cyclopenta[*a*]naphthalene-1,2-dicarbonitrile (**8**) in low yield (Scheme 3). Further increase in



Scheme 4 Scheme showing the proposed intermediate and role of aerial oxygen.

duration of reaction up to 40 h afforded regioselectively 1-phenyl-3-(piperidin-1-yl)-4,5-dihydro-1*H*-cyclopenta[*a*]naphthalene-1,2-dicarbonitrile (**8**) in 17% yield. This result concludes that presence of electron withdrawing group at ortho position of benzyl cyanide increase the rate of cyclization. To confirm **9a** as reaction intermediate, an independent reaction was performed and it was stirred in DMF in presence of KOH and 49% of desired product **8** was isolated (Scheme 4). We have further proved the role of aerial oxygen in cyclization by running the above mentioned reaction under nitrogen atmosphere. No desired product formation was observed except formation of complex reaction mixture and left starting material.

Recently, we have reported that use of 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles as precursor afforded 2-amino-5-aryl-4-*sec* amino-1-yl-benzo[*h*]quinoline-6-carbonitriles rather than cyclopentadiene. This reaction also requires longer duration for completion to afford good yield of benzo[*h*]quinoline. If we compare the structure of 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles **4′** and 5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4**, only difference of substitution pattern at position 5 was observed, which change the course of reaction (Fig. 1).

Role of substitution at position 5 can be understood by intermediate involved in the mechanism itself. It is clear from topography of 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles and 5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4**, that position C6 and C10b are more electrophilic in nature respectively and more vulnerable to nucleophilic attack. Mechanistically, if reaction follows path a, ring opening of pyran ring with

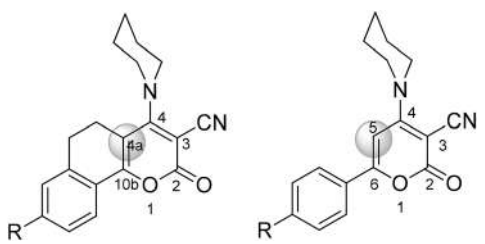
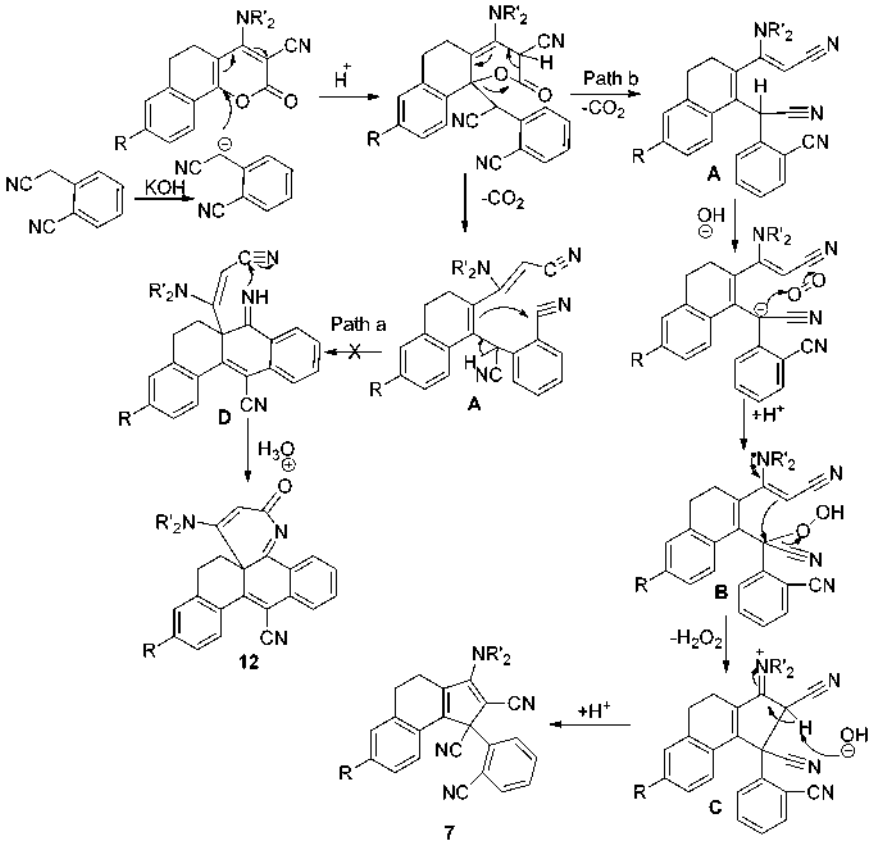


Fig. 1 Structural comparison of precursors 6-aryl-4-*sec* amino-2*H*-pyran-2-one-3-carbonitriles **4′** and 5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4**.



Scheme 5 Mechanistic approach for the synthesis of 1-(2-cyano-phenyl/phenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitriles **7**.

carbanion generated by 2-cyanomethylbenzonitrile resulting in intermediate **A**.

If this intermediate followed the previous pathway seen with the pyrones, a cyclization involving the nitrile group of benzonitrile and C4a of chromone provide the formation of intermediate **D**, which can further cyclize by involving imine generated *in situ* with nitrile present in chromene to result the final product **12**. Product **12** was not formed probably due to involvement of sterically congested and rigid intermediate, which cannot undergo cyclization (path a). According to path b, 2-((2-(1-*sec* amino-2-cyanovinyl)-3,4-dihydronaphthalen-1-yl)-(cyano)methyl)benzonitriles formed by attack of carbanion generated from 2-cyanomethylbenzonitrile at C-10b position of 5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4** followed by decarboxylation. In presence of excess of base, carbanion generated at benzylic carbon of intermediate **A**, which reacts with molecular oxygen, resulting an intermediate **B**. Intermediate **B** undergoes cyclization involving C3 of 5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile **4** and benzylic carbon of 2-cyanomethylbenzonitrile involving loan pair of secondary amine present at C4 position leading the intermediate **C** with loss of peroxide. Intermediate **C** leads to the desired product **7** with loss of proton (Scheme 5). It is clear from the mechanistic discussion that presence of functional group at position 5 of pyran ring change the course of reaction possible due to involvement of steric factor.

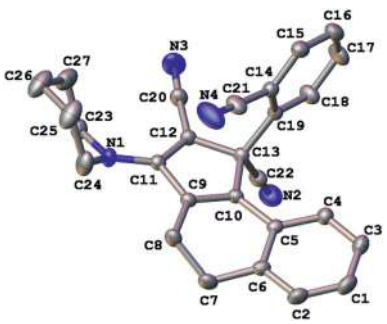


Fig. 2 ORTEP image of **7a** at 30% probability with atom numbering scheme.

Structure of one of the synthesized compound **7a** was confirmed by single crystal X-ray (Fig. 2).[19] From the structure of compound, it is clear that piperidine ring exhibit chair form. Cyclopentadiene and phenyl rings are planar and C7 and C8 push them in different plane due to puckered ring. There is no major interaction present in the molecule.

Conclusions

In summary, we have demonstrated the precursor directed synthesis of 1-(2-cyano-phenyl/phenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitriles in one pot under basic

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condition through aerial oxidation and functionalized benzo[*h*]-quinolines. Intermediate involved in the synthesis of 1-(2-cyano-phenyl/phenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[e]indene-1,2-dicarbonitriles was also isolated. Role of aerial oxygen was also demonstrated by independent reaction. This procedure is metal free and all the required precursors are easily accessible. These molecules could not be synthesized in single step by using available literature method. We have also tried to explain the role of structure of precursor for synthesis of corresponding product.

Experimental section

General remarks

Commercial available reagent and solvent purchased by Sigma Aldrich and Alfa Aesar and used without further purification. IR spectra were recorded on a Perkin-Elmer AX-1 spectroscopy in wave number (cm^{-1}). The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ considering ($CDCl_3$) δ 7.24 ppm for ^1H NMR and δ 77.00 ppm for ^{13}C NMR as an internal standard. Coupling constant J is reported in Hz and internal signal patterns reported as m, multiplet; dd double doublet; t, triplet; d, doublet; s, singlet. HRMS were recorded ESIMS spectrometer.

Intensity data for the white crystal of **7a** was collected at 298(2) K on a OXFORD CrysAlis diffractometer system equipped with graphite monochromated Mo Kα radiation $\lambda = 0.71073$ Å. The final unit cell determination, scaling of the data, and corrections for Lorentz and polarization effects were performed with CrysAlis RED.[20] The structures were solved by direct methods (SHELXS-97)[21] and refined by a full-matrix least-squares procedure based on F2.[22] All the calculations were carried out using WinGX system Ver-1.64.[23]

General procedure for the synthesis of 7-OMe/*H*-1-(2-cyanophenyl)-3-*sec* amino-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile (7a–7f)

A mixture of 8-OMe/*H*-2-oxo-4-*sec* amino-5,6-dihydro-2*H*-benzo-[*h*]chromene-3-carbonitrile (0.5 mmol), 2-cyanomethylbenzonitrile (0.5 mmol, 71.0 mg) and KOH (0.75 mmol, 42.0 mg) in DMF (4.0 mL) was stirred at 100 °C for 2–4 h. Reaction was monitored by TLC. After completion, reaction mixture was poured onto ice-water with constant stirring and then neutralized with 10% HCl. The precipitate obtained was filtered, washed with water and dried over dry sodium sulphate. Crude product was purified on silica-gel column chromatography using 10% ethyl acetate in hexane as an eluent.

1-(2-Cyano-phenyl)-3-piperidine-1-yl-4,5-dihydro-1*H*-benz[*e*] indene-1,2-dicarbonitrile 7a. Yield: 42%, 0.45 R_f (20% ethyl-acetate–hexane), orange solid; mp: 222–224 °C; IR (KBr): 2926, 2854, 2180 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.63–1.82 (m, 6H, $-CH_2-$), 2.64–2.75 (m, 1H, $-CH_2-$), 2.77–2.89 (m, 1H, $-CH_2-$), 2.90–3.01 (m, 1H, $-CH_2-$), 3.03–315 (m, 1H, $-CH_2-$), 3.46–3.62 (m, 4H, $-CH_2-$), 6.81 (d, $J = 7.6$ Hz, 1H, ArH), 6.94–7.02 (m, 1H, ArH), 7.13–7.19 (m, 2H, ArH), 7.43 (t, $J = 7.6$ Hz, 1H, ArH), 7.56–7.61 (dd, $J = 1.5$ Hz, 1H, ArH), 7.72–7.78 (m, 1H, ArH), 8.24 (d, $J = 7.6$ Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 23.7, 26.0, 27.9, 51.0, 55.0, 83.6, 108.8, 116.2, 116.7, 117.6, 123.0, 126.9, 128.1, 128.3, 129.1, 129.3, 129.5, 133.7, 135.2, 136.4, 136.6, 142.3, 142.6, 165.0; HRMS (ESI) calculated for $C_{27}H_{22}N_4$, 403.1917 (MH^+); found for m/z, 403.1896.

1-(2-Cyano-phenyl)-3-pyrrolidin-1-yl-4,5-dihydro-1*H*-benz[*e*] indene-1,2-dicarbonitrile 7b. Yield: 50%, 0.46 R_f (20% ethyl-acetate–hexane), orange solid; mp: 172–174 °C; IR (KBr): 2924, 2854, 2174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 190–2.03 (m, 4H, $-CH_2-$), 2.83–3.20 (m, 4H, $-CH_2-$), 3.72–3.97 (m, 4H, $-CH_2-$), 6.89 (d, $J = 7.6$ Hz, 1H, ArH), 6.95–7.02 (m, 1H, ArH), 7.12–7.18 (m, 2H, ArH), 7.41 (t, $J = 7.6$ Hz, 1H, ArH), 7.56 (d, $J = 7.6$ Hz, 1H, ArH), 7.68–7.77 (m, 1H, ArH), 8.23 (d, $J = 7.6$ Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.7, 25.5, 27.7, 51.3, 55.0, 78.1, 108.8, 116.4, 117.2, 119.4, 123.2, 126.8, 128.0, 128.1, 128.9, 129.3, 129.4, 133.6, 136.0, 136.1, 136.6, 140.9, 142.8, 159.8; HRMS (ESI) calculated for $C_{26}H_{19}N_4$, 389.1761 (MH^+); found for m/z, 389.1741.

1-(2-Cyano-phenyl)-3-morpholin-1-yl-4,5-dihydro-1*H*-benz[*e*] indene-1,2-dicarbonitrile 7c. Yield: 40%, 0.40 R_f (30% ethyl-acetate–hexane), orange solid; mp: 188–190 °C; IR (KBr): 2923, 2853, 2182 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.63–2.74 (m, 1H, $-CH_2-$), 2.76–2.87 (m, 1H, $-CH_2-$), 2.92–3.03 (m, 1H, $-CH_2-$), 3.03–315 (m, 1H, $-CH_2-$), 3.54–3.69 (m, 4H, $-CH_2-$), 3.81–3.88 (m, 4H, $-CH_2-$), 6.79 (d, $J = 7.3$ Hz, 1H, ArH), 6.95–7.03 (m, 1H, ArH), 7.19 (d, $J = 4.4$ Hz, 2H, ArH), 7.44–7.51 (m, 1H, ArH), 7.58–7.63 (m, 1H, ArH), 7.74–7.81 (m, 1H, ArH), 8.25 (d, $J = 8.0$ Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0, 27.8, 50.0, 55.1, 66.5, 85.0, 108.7, 116.2, 116.3, 117.0, 123.0, 127.0, 128.1, 128.2, 129.3, 129.6, 129.6, 133.9, 134.6, 136.3, 136.7, 141.7, 143.1, 164.5; HRMS (ESI) calculated for $C_{26}H_{20}N_4O$, 405.1710 (MH^+); found for m/z, 405.1717.

1-(2-Cyano-phenyl)-3-(4-benzyl-piperazin)-1-yl-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile 7d. Yield: 38%, 0.42 R_f (30% ethylacetate–hexane), orange solid; mp: 186–188 °C; IR (KBr): 2924, 2853, 2183 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.58–2.63 (m, 4H, $-CH_2-$), 2.63–2.73 (m, 1H, $-CH_2-$), 2.76–2.86 (m, 1H, $-CH_2-$), 2.90–3.00 (m, 1H, $-CH_2-$), 3.03–313 (m, 1H, $-CH_2-$), 3.55 (s, 2H, $-CH_2-$), 3.58–3.66 (m, 4H, $-CH_2-$), 6.79 (d, $J = 7.3$ Hz, 1H, ArH), 6.95–7.01 (m, 1H, ArH), 7.16 (d, $J = 4.4$ Hz, 2H, ArH), 7.39–7.35 (m, 5H, ArH), 7.42–7.48 (m, 1H, ArH), 7.57–7.62 (m, 1H, ArH), 7.72–7.79 (m, 1H, ArH), 8.24 (d, $J = 8.0$ Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 27.9, 49.7, 52.7, 55.0, 62.6, 84.3, 108.7, 116.2, 116.6, 117.3, 123.0, 126.9, 127.3, 128.1, 128.2, 128.3, 129.0, 129.2, 129.4, 129.5, 133.8, 134.9, 136.3, 136.7, 137.4, 142.0, 142.9, 164.5; HRMS (ESI) calculated for $C_{33}H_{27}N_5$, 494.2339 (MH^+); found for m/z, 494.2343.

1-(2-Cyano-phenyl)-7-methoxy-3-piperidine-1-yl-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile 7e. Yield: 40%, 0.47 R_f (30% ethylacetate–hexane), orange solid; mp: 119–121 °C; IR (KBr): 2939, 2855, 2179 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.60–1.80 (m, 6H, $-CH_2-$), 2.60–2.73 (m, 1H, $-CH_2-$), 2.74–2.86 (m, 1H, $-CH_2-$), 2.87–299 (m, 1H, $-CH_2-$), 3.00–312 (m, 1H, $-CH_2-$), 3.49–3.60 (m, 4H, $-CH_2-$), 3.72 (s, 3H, $-O-CH_3$), 6.47–6.53 (d,d, $J = 2.2$ Hz, 1H, ArH), 6.69–6.79 (m, 2H, ArH), 7.39–7.46 (m, 1H, ArH), 7.55–7.60 (m, 1H, ArH), 7.70–7.77 (m, 1H, ArH), 8.22 (d, $J = 8.0$ Hz, 1H, ArH); ^{13}C NMR (100 MH, $CDCl_3$): δ 23.0,

23.7, 26.0, 28.4, 50.9, 54.9, 55.1, 82.5, 108.8, 111.5, 114.4, 116.2, 116.9, 117.9, 121.4, 124.4, 129.0, 129.4, 133.6, 135.5, 136.6, 138.6, 139.3, 142.8, 160.4, 165.3; HRMS (ESI) calculated for $C_{28}H_{24}N_4O$, 433.2023 (MH^+); found for *m*/*z*, 433.2023.

1-(2-Cyano-phenyl)-7-methoxy-3-morpholine-1-yl-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile 7f. Yield: 37%, 0.38 R_f (30% ethylacetate–hexane), orange solid; mp: 131–133 °C; IR (KBr): 2941, 2859, 2185 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.60–2.71 (m, 1H, $-CH_2-$), 2.73–2.84 (m, 1H, $-CH_2-$), 2.89–3.00 (m, 1H, $-CH_2-$), 3.01–3.12 (m, 1H, $-CH_2-$), 3.54–3.69 (m, 4H, $-CH_2-$), 3.73 (s, 3H, $-O-CH_3$), 3.79–3.88 (m, 4H, $-CH_2-$), 6.48–6.53 (dd, $J = 2.4$ Hz, 1H, ArH), 6.71–6.75 (m, 2H, ArH), 7.42–7.50 (m, 1H, ArH), 7.60 (d, $J = 7.9$ Hz, 1H, ArH), 7.72–7.80 (m, 1H, ArH), 8.23 (d, $J = 7.93$ Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0, 28.3, 49.9, 55.2, 66.5, 84.0, 108.6, 111.6, 114.6, 116.2, 116.5, 117.3, 121.2, 124.5, 129.2, 129.5, 133.8, 135.0, 136.7, 138.5, 138.7, 143.3, 160.6, 165.0; HRMS (ESI) calculated for $C_{27}H_{22}N_4O_2$, 435.1816 (MH^+); found for *m*/*z*, 435.1808.

General procedure for the synthesis of 1-(phenyl)-3-piperidine-1-yl-4,5-dihydro-1*H*-benz[*e*]indene-1,2-dicarbonitrile 8

A mixture of 2-oxo-4-piperidine-1-yl-5,6-dihydro-2*H*-benzo[*h*]-chromene-3-carbonitrile (0.5 mmol, 153.0 mg), phenylacetonitrile (0.5 mmol, 0.057 mL) and KOH (0.75 mmol, 42.0 mg) in DMF (4.0 mL) was stirred at 100 °C for 40 h. After completion, reaction mixture was poured onto ice-water with vigorous stirring followed by neutralization with 10% HCl. The precipitate obtained was filtered, washed with water and dried over dry sodium sulphate. Crude mixture was purified by silica-gel column chromatography using 10% ethyl acetate in hexane as an eluent: yield: 17%, 0.48 R_f (20% ethylacetate–hexane), orange solid; mp: 207–209 °C; IR (KBr): 2924, 2853, 2182 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.60–1.75 (m, 6H, $-CH_2-$), 2.65–2.80 (m, 2H, $-CH_2-$), 2.90–3.07 (m, 2H, $-CH_2-$), 3.38–3.50 (m, 4H, $-CH_2-$), 6.95–7.07 (m, 2H, ArH), 7.13–7.19 (m, 2H, ArH), 7.27–7.38 (m, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0, 23.7, 25.9, 28.4, 50.8, 54.7, 88.9, 117.6, 117.7, 124.2, 125.6, 127.0, 127.8, 128.6, 128.7, 129.1, 129.4, 133.6, 135.9, 139.3, 144.9, 162.9; HRMS (ESI) calculated for $C_{26}H_{23}N_3$, 378.1965 (MH^+); found for *m*/*z*, 378.1953.

General procedure synthesis of 3-(1-(cyano(phenyl)methyl)-6-OMe/*H*-3,4-dihydronaphthalen-2-yl)-3-(piperidin-1-yl) acrylonitrile (9a and 9b)

A mixture of 2-oxo-4-piperidine-1-yl-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitrile (0.5 mmol, 153.0 mg), phenylacetonitrile (0.5 mmol, 0.057 mL) and KOH (0.75 mmol, 42.0 mg) in DMF (4.0 mL) was stirred at 100 °C for 2 h. After completion, reaction mixture was poured onto ice-water with vigorous stirring followed by neutralization with 10% HCl. The precipitate obtained was filtered, washed with water and dried over dry sodium sulphate. Crude mixture was purified by silica-gel column chromatography using 8% ethyl acetate in hexane as an eluent:

3-(1-(Cyano(phenyl)methyl)-3,4-dihydronaphthalen-2-yl)-3-(piperidin-1-yl)acrylonitrile 9a. Yield: 35%, 0.50 R_f (20% ethylacetate–hexane), orange solid; mp: 135–137 °C; IR (KBr): 2925, 2853, 2192 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.50–1.84 (m, 6H, $-CH_2-$), 2.50–2.62 (m, 2H, $-CH_2-$), 2.70–2.81 (m, 1H, $-CH_2-$), 2.82–2.91 (m, 1H, $-CH_2-$), 3.20–3.32 (m, 4H, $-CH_2-$), 4.13 (s, 1H, –CH–), 5.41 (s, 1H, –CH–), 6.97 (t, $J = 7.96$ Hz, 1H, ArH), 7.05–7.20 (m, 3H, ArH), 7.21–7.26 (m, 1H, ArH), 7.30–7.40 (m, 2H, ArH), 7.58 (d, $J = 7.5$ Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 27.9, 28.9, 29.6, 36.9, 63.6, 118.7, 121.4, 125.8, 126.2, 127.0, 127.7, 128.1, 128.8, 129.0, 129.9, 130.4, 132.8, 136.9, 137.0, 164.8; HRMS (ESI) calculated for $C_{26}H_{25}N_3$, 380.2121 (MH^+); found for *m*/*z*, 380.2118.

3-(1-(Cyano(phenyl)methyl)-6-methoxy-3,4-dihydronaphthalen-2-yl)-3-(piperidin-1-yl)acrylonitrile 9b. Yield: 30%, 0.41 R_f (20% ethylacetate–hexane), orange solid; mp: 141–143 °C; IR (KBr): 2925, 2853, 2192 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.40–1.80 (m, 6H, $-CH_2-$), 2.45–2.58 (m, 2H, $-CH_2-$), 2.67–2.85 (m, 2H, $-CH_2-$), 3.12–3.30 (m, 4H, $-CH_2-$), 3.71 (s, 3H, $-O-CH_3$), 4.11 (s, 1H, –CH–), 5.37 (s, 1H, –CH–), 6.45–6.52 (dd, $J = 2.4$ Hz, 1H, ArH), 6.68 (d, $J = 2.4$ Hz, 1H, ArH), 7.08 (d, $J = 8.5$ Hz, 1H, ArH) 7.20–7.27 (m, 1H, ArH), 7.30–7.38 (m, 2H, ArH), 7.57 (d, $J = 7.93$ Hz, 2H, ArH); ^{13}C NMR (100 MH, $CDCl_3$): δ 23.8, 28.3, 28.8, 36.9, 51.1, 63.6, 110.8, 113.9, 118.8, 121.6, 122.8, 126.9, 127.2, 127.7, 128.8, 129.0, 129.9, 129.9, 132.9, 134.1, 139.0, 159.1, 165.0; HRMS (ESI) calculated for $C_{27}H_{27}N_3O$, 410.2227 (MH^+); found for *m*/*z*, 410.2222.

General procedure for the synthesis of 2-amino-5-aryl-4-*sec* amino-benzo[*h*]quinoline-6-carbonitrile (11a–11d)

A mixture of 6-aryl-2-oxo-4-*sec* amino-2*H*-pyran-3-carbonitriles (0.5 mmol), 2-cynomethyl-benzonitrile (0.5 mmol; 142.0 mg) and $NaNH_2$ (1.0 mmol; 78.0 mg) in dry DMF (5.0 mL) was stirred at 100 °C for 35–50 h. After completion of reaction, mixture was poured onto crushed ice followed by neutralization with 10% HCl. The obtained solid material was filtered, washed with water, dried and purified by silica gel column chromatography using hexane : ethyl acetate (7 : 3) as eluent. Compound **11a** and **11b** is reported earlier.[18]

2-Amino-5-(2-fluoro-phenyl)-4-piperidin-1-yl-benzo[*h*]quinoline-6-carbonitrile 11c. Yield: 60%; 0.21 R_f (30% ethylacetate–hexane), grey solid, mp: 187–189 °C; IR (KBr): 3399, 2938, 2208 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.31–0.46 (m, 1H, $-CH_2-$), 0.80–1.06 (m, 2H, $-CH_2-$), 1.13–1.27 (m, 1H, $-CH_2-$), 1.33–1.50 (m, 2H, $-CH_2-$), 2.12–2.27 (m, 1H, $-CH_2-$), 2.45–2.57 (m, 1H, $-CH_2-$), 2.73–2.85 (m, 1H, $-CH_2-$), 2.95–3.06 (m, 1H, $-CH_2-$), 4.91 (s, 2H, $-NH_2$), 6.35 (s, 1H, ArH), 7.07–7.15 (m, 1H, ArH), 7.25–7.30 (m, 1H, ArH), 7.36–7.45 (m, 1H, ArH), 7.55–7.62 (m, 1H, ArH), 7.63–7.75 (m, 2H, ArH), 8.23 (d, $J = 7.9$ Hz, 1H, ArH), 9.12–9.14 (dd, $J = 1.83$ Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.3, 24.4, 24.7, 52.2, 54.6, 99.8, 106.7, 113.7, 114.9 (d, $J_{C-F} = 22.0$ Hz), 118.1, 123.4, 125.2, 127.2, 127.4, 129.2, 129.8 (d, $J_{C-F} = 8.6$ Hz), 130.3, 131.4, 131.7, 131.8, 138.4, 150.1, 158.9, 160.3 (d, $J_{C-F} = 247.2$ Hz), 162.0; HRMS (ESI) calculated for $C_{25}H_{21}FN_4$, 397.1823 (MH^+); found for *m*/*z*, 397.1822.

2-Amino-4-(4-benzylpiperazin-1-yl)-5-(4-methoxyphenyl)benzo[*h*]quinoline-6-carbonitrile 11d. Yield: 74%; 0.20 R_f (30%

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ethylacetate–hexane), yellow solid, mp: 216–218 °C; IR (KBr): 3352, 2928, 2195 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.00–2.33 (m, 4H, $-CH_2-$), 2.80–3.15 (m, 4H, $-CH_2-$), 3.40 (s, 2H, $-CH_2-$), 3.84 (s, 3H, $-OCH_3$), 5.09 (s, 2H, $-NH_2$), 6.93 (d, J = 8.0 Hz, 2H, ArH), 7.15–7.35 (m, 7H, ArH), 7.48–7.58 (m, 2H, ArH), 7.64–7.72 (m, 1H, ArH), 7.82 (d, J = 8.8 Hz, 1H, ArH), 8.20 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 62.5, 67.6, 99.7, 112.5, 113.3, 118.1, 120.9, 121.1, 121.8, 126.1, 126.3, 127.3, 128.2, 129.0, 129.3, 129.6, 130.2, 133.7, 136.8, 144.7, 145.6, 159.7, 159.8; HRMS (ESI) calculated for $C_{32}H_{29}N_5O$, 500.2445 (MH^+); found for m/z, 500.2446.

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One-pot and step-wise synthesis of thieno[3,2-*c*]pyridin-4-ones†

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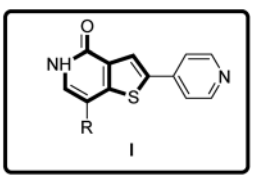
Both one pot and step wise synthesis of methyl 3,5-diaminothieno[3,2-*c*]pyridin-4-one-2-carboxylates **6** have been delineated by the reaction of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles **3**, methyl mercaptoacetate and hydrazine hydrate. During the stepwise synthesis, functionalized thieno[3,2-*c*]pyran-4-ones **4** were isolated and treated with hydrazine hydrate to afford the desired products. Analogously, condensation–cyclisation of **5** with hydrazine hydrate delivered identical products, thieno[3,2-*c*]pyridin-4-ones **6**, in excellent yields. The structure of isolated product **6** was ascertained by spectroscopic and single crystal X-ray diffraction analyses.

Introduction

Fusion of thiophene with different sites of a pyridinone ring can result in numerous possible isomers of thienopyridinones, including thieno[2,3-*b*]-, thieno[3,2-*b*]-, thieno[2,3-*c*]-, thieno[3,2-*c*]- and thieno[3,4-*b*]pyridinones, *etc.* They are known for their diverse pharmacological activities, as inhibitors of glycogen synthase kinase-3β (GSK-3β), which play a role in glycogen metabolism, and for regulating diverse cell functions (Fig. 1, compound **I**).[1] The AMP-activated protein kinase (AMPK), which is known as a sensor and regulator for energy metabolism in the body,[2] and some other thienopyridines also acts as checkpoint-1 kinase (Chk-1) activators working to repair damaged DNA.[3] A literature survey revealed that various *N*-substituted thienopyridinones act against Gram negative bacteria. 2-Chloro-7-ethyl-4-oxo-4,7-dihydro-thieno[2,3-*b*]pyridine-5-carboxylic acid[4] and many more derivatives act as antibacterials[5] and DNA gyrase inhibitors prevent the growth of MCF-7 breast tumor and A549 lung cancer cells.[6] Thieno[3,4-*c*]pyridin-4(5*H*)-ones are reported as poly(ADP-ribose)polymerase (PARP) inhibitors, and are implicated in the repair of damaged DNA and potentiate chemotherapy of cancer.[7] The isomeric thieno[2,3-*b*]pyridinones are reported as antagonists of *N*-methyl-D-aspartate (NMDA), a contributor to excitatory neurotransmission[8] and synaptic plasticity,[9] as well as neurodegenerative disorders and neurological bipolar disorders[10] like stroke, epilepsy, Parkinson's disease, Huntington's chorea, Alzheimer's disease and HIV dementia. However, an extensive literature survey revealed that the chemistry and therapeutic importance of isomeric thieno[3,2-*c*]pyridin-4-ones have not been extensively explored.



I

Fig. 1 Biologically active fused thienopyridinones (I–IV).

The synthesis of isomeric 7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-ones and 7-hydroxy-6-phenylthieno[3,2-*b*]pyridin-5(4*H*)-ones[11] require appropriately substituted aminothiophenes[12] as key precursors. However, this methodology is limited to the introduction of an aryl functional group in the pyridine ring. Furthermore, the 3-aminothiophen-2-carboxylate precursors are difficult to access with different substituents at position 5. Rodinovskaya *et al.* have developed a one pot approach for the synthesis of tricyclic 4-hydroxy-7-methoxypyridino[2,3-*d*]thieno[3,2-*b*]pyridin-2(1*H*)-one.[13] Another compound, 7-hydroxy-4*H*-thieno-[3,2-*b*]pyridin-5-one was synthesized by the reaction of ethyl-3-aminothiophene-2-carboxylate and diethyl malonate.[14] Lee and co-worker have developed an excellent method for the synthesis of 4-alkyl- and 2-aryl-6-diazo-4*H*-thieno[3,2-*b*]pyridin-5,7-diones by the reaction of 3-(3-alkyl and aryl-amino-5-arylthieno-2-yl)-2-diazo-3-oxopropanoates and TMSOTf in presence of Et_3N in CH_2Cl_2.[15] In addition, a one pot synthesis of functionalized 7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-ones from the corresponding β-substituted β-chloropropenonitrile was also performed.[16]

Herein, we are providing a novel approach for the synthesis of functionalized *N*-aminothieno[3,2-*c*]pyridin-5-ones **6** by the

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† Electronic supplementary information (ESI) available: All the proton and ^{13}C NMR spectra are given. CCDC 1484442. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6ra17315b

reaction of pyranothiophenes with hydrazine hydrate under solvent free conditions.

Results and discussion

We previously reported a synthesis of tetrasubstituted thiophene[18] **5** by coupling methyl 3,3-dimethylthio-2-cyanoacrylate **1** and aryl methyl ketone **2** in the presence of powdered KOH in DMSO; subsequent product of the above mentioned reactants yielded **3**,[17] which was coupled with methyl mercaptoacetate in the presence of triethylamine, and the resultant lactone **4** was further subjected to methanolysis, as shown in Scheme 1.

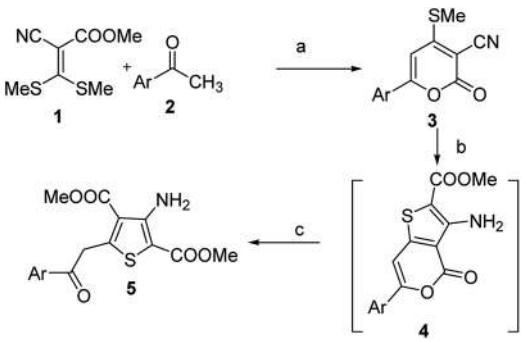
We envisaged an efficient and economical synthesis of *N*-aminothieno[3,2-*c*]pyridin-4-ones **6** from thieno[3,2-*c*]pyran-4-ones **4**, which can be prepared from **3**. In order to optimize the reaction conditions, the model substrate methyl 3-amino-4-oxo-6-(*p*-tolyl)-4*H*-thieno[3,2-*c*]pyran-2-carboxylate **4d** was generated *in situ* by the reaction of 4-(methylthio)-2-oxo-6-(*p*-tolyl)-2*H*-pyran-3-carbonitrile **3d** and methyl mercaptoacetate, which on addition of hydrazine hydrate, delivered *N*-aminothieno[3,2-*c*]pyridin-4-one **6d**.

We performed the reaction in various solvents, like methanol, DMF and DMSO, and found that if we perform the reaction using DMF at 80 °C, it provides a better yield of the desired product (entry 2, Table 1). However, if the same reaction is carried out in THF for 24 h at room temperature, only a trace amount of the desired product was observed on TLC, possibly due to the low dielectric constant of the solvent (entry 4, Table 1). Further, attempts to improve the yield were made by the addition of KOH, $NaNH_2$ and NaH bases in conjunction with Et_3N in aprotic solvents, such as DMF and DMSO, under analogous reaction conditions.

Additional base did not improve the yield of thieno[3,2-*c*]pyridin-4-one **6d**, which ranged between 40% and 50% (entry 5–8, Table 1).

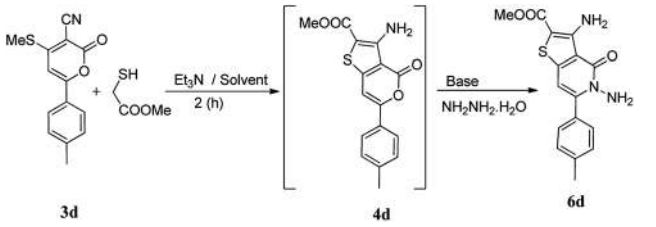
From the optimization study, we have concluded that triethylamine in DMF (entry 2, Table 1) is the best reaction condition for the formation of **6**.

Generality of the protocol was tested for the synthesis of various derivatives of *N*-aminothieno[3,2-*c*]pyridin-4-ones **6**. The yields of various isolated thieno[3,2-*c*]pyridin-4-ones from different reactions are reported in Table 2. Two step synthesis were also performed in which **6** was obtained in good yields from isolated thieno[3,2-*c*]pyran-4-one **4** by reaction with hydrazine hydrate at 80 °C in DMF.



Scheme 1 Reagent and conditions (a) KOH, DMSO, rt (b) $SHCH_2$-COOMe, Et_3N, 80 °C (c) DMF, NaOMe, rt.

Table 1 Optimization of reaction conditions[a]



Entry	Additional base	Solvent	Temp (°C)	Time (h)	Yield (%)
1	—	CH_3OH	80	10	30
2	**—**	**DMF**	**80**	**3**	**80**
3	—	DMSO	80	3	75
4[b]	—	THF	rt[d]	30	Trace
5[c]	KOH	DMF	90	4	50
6[c]	$NaNH_2$	DMF	90	4	40
7[c]	NaH	DMF	90	5	45
8[c]	NaH	DMSO	90	5	45

[a] Reactions were carried out by stirring **3d** (0.5 mmol), methyl thioglycolate (0.75 mmol), Et_3N (1.0 mmol) for 2 h and then hydrazine hydrate (0.75 mmol) was added at a different temperature. [b] Reactions were carried out at room temperature for 5 h upto intermediate stage, followed by addition of hydrazine hydrate. [c] Furthermore, Et_3N, other bases were added while adding hydrazine and reaction was carried out for given time at mentioned temperature. [d] Room temperature was ranging between 30 °C and 35 °C.

A chemical research, always has an environmental concern.[19] Thus, call for a clean procedure, which avoids the use of harmful organic solvent, is inevitable. In anticipation of this, we examined the reaction of methyl 6-aryl-3,5-diaminothieno[3,2-*c*]pyridin-4-one-2-carboxylate **4** and hydrazine hydrate under solvent free conditions, and surprisingly, were afforded the desired products in good yields. The required precursor **4** can be synthesized using L-proline[19] as a catalyst and overall synthesis can be made environmentally friendly. When the yield of the desired product is compared in solvent and under solvent free conditions, in most cases the latter gives the best result (Table 3). Apart from the work-up, the solvent free reactions are easier to perform.

A plausible mechanism for the reaction is depicted in Scheme 2. Possibly, the reaction is initiated by attack of hydrazine at the C2 position of pyranothiophene, followed by ring opening to afford intermediate **A**. Involvement of the amide nitrogen in cyclization, followed by loss of water leads to the product *N*-aminothieno[3,2-*c*]pyridin-4-one **6**. The structure of the isolated product was confirmed on the basis of spectroscopic as well as single crystal X-ray diffraction (see ESI†) analyses of methyl 3,5-diamino-6-(2-methoxyphenyl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate **6c**.‡

‡ Crystal data for **6c** (CCDC 1484442): $C_{16}H_{15}N_3O_4S$, FW = 345.37, monoclinic, *P*21/*c*, bond precision: C–C = 0.0032 Å, wavelength = 0.71073 Å, cell: a = 11.6062(6), b = 18.6702(6), c = 7.5550(3), α = 90°, β = 107.089(5), γ = 90°, T = 293 K, V = 1564.82(12), Z = 4, Mu (mm^{-1}) = 0.234, R_1 [$I > 2\sigma(I)$] = 0.0467, wR_2 = 0.1195, R_1 [all data] = 0.0592, wR_2 = 0.1267.

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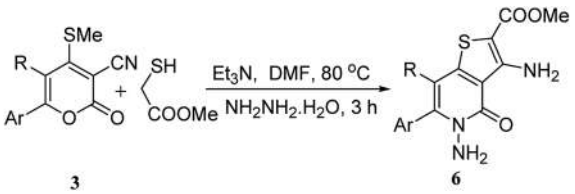
Table 2 One pot synthesis of various *N*-aminothieno[3,2-*c*]pyridin-4-ones **6**[a]

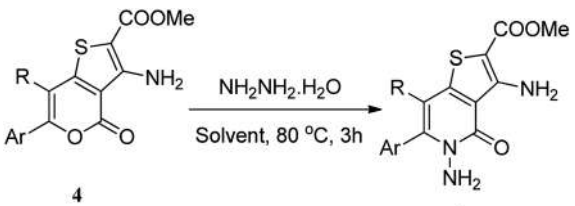


3 6

6	Ar	R	Yield[b]%
a	C_6H_5	H	68
b	*p*-$OCH_3 \cdot C_6H_4$	H	70
c	*o*-$OCH_3 \cdot C_6H_4$	H	73
d	*p*-$CH_3 \cdot C_6H_4$	H	75
e	*p*-$Cl \cdot C_6H_4$	H	68
f	*P*-$F \cdot C_6H_4$	H	72
g	*P*-$Br \cdot C_6H_4$	H	76
h	2-Naphthyl	H	70
i	1-Naphthyl	H	74
j	2-Theinyl	H	68
k	2-Furyl	H	55
l	C_6H_5	C_6H_5	60

[a] All reactions were carried out by stirring **3** (0.5 mmol), methyl thioglycolate (0.75 mmol) and Et_3N (1.0 mmol) at 80 °C in DMF (4.0 mL) followed by the addition of hydrazine hydrate (0.75 mmol) after consumption of **3**. [b] Yields are reported after purification through column chromatography.

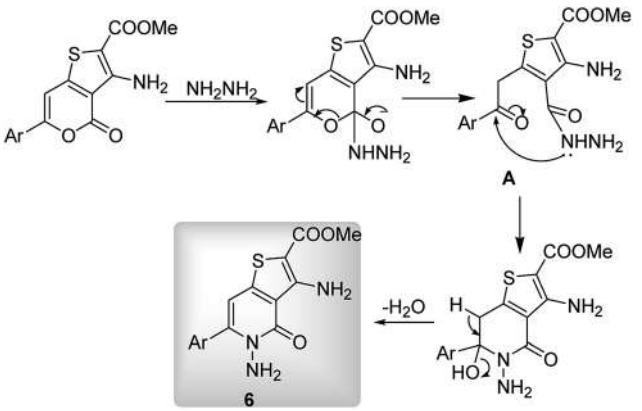
Table 3 Synthesis of methyl 6-aryl-3,5-diaminothieno[3,2-*c*]pyridin-4-one-2-carboxylates (**6**)



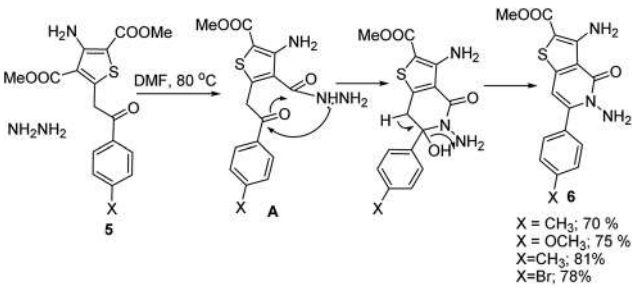
4 6

6	Ar	R	Yield[a,c]% (in DMF)	Yield[b,c]% (solvent free)
a	C_6H_5	H	77	65
b	*p*-$OCH_3 \cdot C_6H_4$	H	77	84
c	*o*-$OCH_3 \cdot C_6H_4$	H	72	80
d	*p*-$CH_3 \cdot C_6H_4$	H	74	80
e	*p*-$Cl \cdot C_6H_4$	H	82	81
f	*P*-$F \cdot C_6H_4$	H	82	85
g	*P*-$Br \cdot C_6H_4$	H	79	76
h	2-Naphthyl	H	78	81
i	1-Naphthyl	H	70	76
j	2-Theinyl	H	73	80
k	2-Furyl	H	60	72
l	C_6H_5	C_6H_5	70	77

[a] All reactions were carried out by stirring **4** (0.5 mmol) and hydrazine hydrate (0.75 mmol) at 80 °C in DMF (4 mL) as solvent. [b] Reaction was carried out by stirring **4** (0.5 mmol) and hydrazine hydrate (1 mL) at 80 °C. [c] Yields are reported after purification through column chromatography.



Scheme 2 A plausible mechanism for the formation of *N*-aminothieno[3,2-*c*]pyridin-4-ones **6**.



Scheme 3 Synthesis of *N*-aminothieno[3,2-*c*]pyridin-4-ones **6** from tetrasubstituted thiophenes **5**.

To further enhance the scope of starting material, we used tetrasubstituted thiophene[18a] (Scheme 3) as a precursor and performed the reaction with hydrazine hydrate in DMF at 80 °C. Usual work-up and purification afforded *N*-aminothieno[3,2-*c*]pyridin-4-ones **6** in good yield. Therefore, another protocol was developed for the preparation of *N*-aminothieno[3,2-*c*]pyridin-5-ones **6** from suitably functionalized tetrasubstituted thiophenes by condensation–cyclization with hydrazine hydrate.

Attempts were made to transform methyl 3-amino-10,11-dihydrothieno[3,2-*c*]chromene-4-one-2-carboxylate to methyl 3,5-diamino-10,11-dihydrothieno[3,2-*c*]benzo[*h*]quinilin-4-one-2-carboxylate, obtained[19] from the reaction of 4-methylthio-2*H*-benzo[*h*]chromene-2-one-3-carbonitrile and methyl mercaptoacetate using Et_3N as a base in DMF at 80 °C, but failed and starting material was recovered. The failure of this reaction was possibly due to steric crowding present at position C10b.

The structure of one of the compounds (**6c**) was confirmed by single crystal X-ray (please see ESI†).

Conclusion

In conclusion, we developed both a one pot and a step wise approach for the synthesis of methyl 3,5-diaminothieno[3,2-*c*]pyridin-4-one-2-carboxylates **6** by the reaction of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles **3**, methyl mercaptoacetate and hydrazine hydrate. During the stepwise synthesis,

functionalized thieno[3,2-*c*]pyran-4-one **4** was isolated and treated with hydrazine hydrate to afford the desired product. Analogously, condensation–cyclisation of tetrasubstituted thiophenes **5** with hydrazine hydrate delivered identical products, thieno[3,2-*c*]pyridin-4-ones **6** in excellent yields. The structure of the isolated product **6** was ascertained by spectroscopic and single crystal X-ray diffraction analyses. This procedure is simple, efficient and economical. It does not require any metal catalyst.

Experimental

General remarks

Relevant reagents and solvents were obtained commercially and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz and 100 MHz NMR spectrometers, respectively. $CDCl_3$ and DMSO-d_6 were used as solvents for NMR. Chemical shift (δ) is reported in ppm, considering $CDCl_3$ δ 7.24 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR, and DMSO δ 2.49 and 3.33 ppm for ^{1}H NMR and δ 39.51 ppm ^{13}C NMR as an internal standard. Signal patterns are indicated as s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), and br s (broad singlet). Coupling constants (J) are in hertz (Hz). Infrared (IR) spectra were recorded on AX-1 spectrophotometer and reported as wave number (cm^{-1}). HRMS was recorded on Agilent G6530AA (LC-HRMS-Q-TOF) mass spectrometer.

Intensity data for **6c** were collected at 298(2) K on a OXFORD CrysAlis diffractometer system equipped with graphite monochromated Mo Kα radiation $\lambda = 0.71073$ Å. The final unit cell determination, scaling of the data, and corrections for Lorentz and polarization effects were performed with CrysAlis RED.[20] The structures were solved by direct methods (SHELXS-97)[21] and refined by a full-matrix least squares procedure based on F^2.[22] All the calculations were carried out using WinGX system Ver-1.64.[23]

General procedure for the synthesis of methyl 6-aryl-3,5-diaminothieno[3,2-*c*]pyridin-4-one-2-carboxylate

Method A. A mixture of 4-(methylthio)-2-oxo-6-aryl-2*H*-pyran-3-carbonitriles[17] (0.5 mmol) and methyl thioglycolate (0.75 mmol) in 4.0 mL DMF in presence of triethylamine (1.0 mmol) was stirred for 2 h at 80 °C. Complete formation of intermediate (3-amino-2-carbmethoxy-6-aryl-4*H*-thieno[3,2-*c*]pyran-2-one) was monitored by TLC. Thereafter, hydrazine hydrate (0.75 mmol) was added to the reaction mixture and further stirred for 3 h. Formation of the desired product was monitored on TLC. The reaction mixture was poured onto crushed ice with vigorous stirring. Obtained precipitate was filtered, dried and purified over silica-gel column chromatography using 30% ethyl acetate in hexane as an eluent.

Method B. First, we have synthesized 3-amino-2-carbethoxy-6-aryl-4*H*-thieno[3,2-*c*]pyran-2-one (**4**) according to the previously reported procedure.[18] Then, a mixture of thienopyranone (0.5 mmol) and hydrazine hydrate (0.75 mmol) in DMF were stirred at 80 °C for 2–3 h. Formation of the desired product was monitored by TLC. The reaction mixture was poured onto crushed ice with vigorous stirring. Obtained precipitate was filtered, dried and purified over silica-gel column chromatography using 30% ethyl acetate in hexane as an eluent.

In another approach, we stirred compound **4** in hydrazine hydrate (1.0 mL) for 3 h at 80 °C. After completion and usual work-up of the reaction we isolated the desired product. The product was further purified by silica-gel column chromatography using 30% ethyl acetate in hexane as an eluent.

Method C. Compound **6** was also synthesized by stirring **5** (0.5 mmol) and hydrazine hydrate (0.75 mmol) in DMF at 80 °C for 2 h. The reaction mixture was poured onto crushed ice with vigorous stirring. Obtained precipitate was filtered, dried and purified over silica-gel column chromatography using 30% ethyl acetate in hexane as an eluent.

Methyl 3,5-diamino-4-oxo-6-phenyl-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6a)

Yield: 68% (107 mg); yellow solid; mp: 198–200 °C; IR (KBr): 3464, 3345, 1680 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.75 (s, 3H, OCH_3), 5.59 (s, 2H, NH_2), 6.80 (s, 1H, CH), 7.44–7.45 (m, 3H, ArH), 7.58–7.60 (m, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.1, 93.2, 102.6, 116.2, 127.7, 128.8, 129.3, 134.3, 147.8, 148.4, 152.0, 158.8, 163.8; HRMS (*m*/*z*, ESI) calculated for $C_{15}H_{13}N_3O_3S$, (M + H^+) 316.0750; found 316.0765.

Methyl 3,5-diamino-6-(4-methoxyphenyl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6b)

Yield: 70% (120 mg); yellow solid; mp: 217–218 °C; IR (KBr): 3470, 3350, 1673 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.72 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 5.58 (s, 2H, NH_2), 6.74 (s, 1H, CH), 6.97 (d, J = 9.16 Hz, 2H, ArH), 7.53 (d, J = 9.16 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.1, 55.3, 102.4, 113.2, 115.8, 126.5, 127.8, 130.9, 147.7, 148.5, 152.1, 158.9, 159.8, 163.9; HRMS (*m*/*z*, ESI) calculated for $C_{16}H_{15}N_3O_4S$, (M + H^+) 346.0856; found 346.0866.

Methyl 3,5-diamino-6-(2-methoxyphenyl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6c)

Yield: 73% (126 mg); yellow solid; mp: 187–188 °C; IR (KBr): 3467, 3348, 1673 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.72 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 5.45 (s, 2H, NH_2), 6.70 (s, 1H, CH), 7.00 (t, J = 7.25 Hz, 1H, ArH), 7.08 (d, J = 8.39 Hz, 1H, ArH), 7.26 (d, J = 6.87 Hz, 1H, ArH), 7.43 (t, J = 7.01 Hz, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.2, 55.6, 102.9, 110.8, 116.3, 120.2, 123.7, 129.8, 130.9, 145.7, 148.3, 152.1, 156.7, 158.3, 163.9; HRMS (*m*/*z*, ESI) calculated for $C_{16}H_{15}N_3O_4S$, (M + H^+) 346.0856; found 346.0869.

Methyl 3,5-diamino-4-oxo-6-(*p*-tolyl)-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6d)

Yield: 75% (123 mg); yellow solid; mp: 198–200 °C; IR (KBr): 3469, 3349, 1675 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.35 (s, 3H, CH_3), 3.74 (s, 3H, OCH_3), 5.60 (s, 2H, NH_2), 6.77 (s, 1H, CH), 7.25 (d, J = 7.63 Hz, 2H, ArH), 7.48 (d, J = 8.39 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.9, 51.1, 102.5, 116.0, 128.3,

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129.3, 131.5, 138.6, 147.9, 148.4, 152.1, 158.8, 163.9; HRMS (*m*/*z*, ESI) calculated for $C_{16}H_{15}N_3O_3S$, (M + H^+) 330.0907; found 330.0907.

Methyl 3,5-diamino-6-(4-chlorophenyl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6e)

Yield: 68% (118 mg); yellow solid; mp: 228–229 °C; IR (KBr): 3469, 3350, 1678 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.75 (s, 3H, OCH_3), 5.58 (s, 2H, NH_2), 6.83 (s, 1H, CH), 7.52 (d, J = 9.16 Hz, 2H, ArH), 7.61 (d, J = 8.39 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.2, 102.84, 116.4, 127.8, 131.3, 133.2, 133.8, 146.8, 148.4, 152.07, 158.9, 163.8; HRMS (*m*/*z*, ESI) calculated for $C_{15}H_{12}ClN_3O_3S$, (M + H^+) 350.0361; found 350.0360.

Methyl 3,5-diamino-6-(4-fluorophenyl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6f)

Yield: 72% (120 mg); yellow solid; mp: 190–192 °C; IR (KBr): 3462, 3343, 1675, 1508 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.72 (s, 3H, OCH_3), 5.56 (s, 2H, NH_2), 6.78 (s, 1H, CH), 7.01 (br s, 2H, NH_2), 7.26 (t, J = 8.77 Hz, 2H, ArH), 7.60–7.64 (m, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.2, 102.8, 114.7 (d, J = 22.04 Hz), 116.3, 129.9, 130.8, 131.8, (d, J = 8.63 Hz), 147.0, 148.4, 152.0, 158.9, 162.4, (d, J = 246.33 Hz), 163.91; HRMS (*m*/*z*, ESI) calculated for $C_{15}H_{12}FN_3O_3S$, (M + H^+) 334.0656; found 334.0674.

Methyl 3,5-diamino-6-(4-bromophenyl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6g)

Yield: 76% (149 mg); yellow solid; mp: 207–209 °C; IR (KBr): 3461, 3351, 1674 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.72 (s, 3H, OCH_3), 5.50 (s, 2H, NH_2), 6.79 (s, 1H, CH), 7.51 (d, J = 8.39 Hz, 2H, ArH), 7.62 (d, J = 8.39 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.2, 102.7, 116.4, 122.5, 124.6, 129.9, 130.7, 137.5, 133.6, 146.8, 148.4, 152.0, 158.9, 163.8; HRMS (*m*/*z*, ESI) calculated for $C_{15}H_{12}BrN_3O_3S$, (M + H^+) 393.9856; found 393.9853.

Methyl 3,5-diamino-6-(naphthalen-2-yl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6h)

Yield: 70% (128 mg); yellow solid; mp: 194–196 °C; IR (KBr): 3468, 3350, 1675 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.75 (s, 3H, OCH_3), 5.66 (s, 2H, NH_2), 6.93 (s, 1H, CH), 7.37 (br s, 2H, NH_2) 7.54–7.60 (m, 2H, ArH), 7.74–7.77 (m, 1H, ArH) 7.93–7.98 (m, 3H, ArH), 8.11 (s, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.2, 93.3, 103.0, 116.3, 126.5, 126.6, 127.0, 127.3, 127.5, 128.2, 132.1, 132.3, 132.7, 147.9, 148.5, 152.1, 158.9, 163.9; HRMS (*m*/*z*, ESI) calculated for $C_{19}H_{15}N_3O_3S$, (M + H^+) 366.0907; found 366.0899.

Methyl 3,5-diamino-6-(naphthalen-1-yl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6i)

Yield: 74% (125 mg); yellow solid; mp: 218–220 °C; IR (KBr): 3465, 3350, 1676 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.85 (s, 3H, OCH_3), 4.91 (br s, 2H, NH_2), 6.61 (s, 1H, CH), 7.06 (br s, 2H, NH_2), 7.46–7.57 (m, 5H, ArH), 7.92 (d, J = 7.63 Hz, 1H, ArH), 7.97 (d, J = 8.39 Hz, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.3, 104.0, 117.3, 124.3, 125.1, 126.4, 126.8, 127.4, 128.7, 130.0, 131.2, 131.6, 133.1, 145.3, 148.9, 152.6, 158.7, 164.8; HRMS (*m*/*z*, ESI) calculated for $C_{19}H_{15}N_3O_3S$, (M + H^+) 366.0907; found 366.0928.

Methyl 3,5-diamino-4-oxo-6-(thiophen-2-yl)-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6j)

Yield: 68% (109 mg); yellow solid; mp: 209–210 °C; IR (KBr): 3466, 3349, 1673 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.74 (s, 3H, OCH_3), 5.84 (s, 2H, NH_2),7.00 (br s, 2H, NH_2), 7.16 (t, J = 3.81 Hz, 1H, ArH), 7.30 (s, 1H, CH), 7.79 (d, J = 5.34 Hz, 1H, ArH), 7.88 (d, J = 3.81 Hz, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.1, 99.9, 115.2, 126.7, 130.2, 131.9, 133.7, 141.8, 148.7, 152.0, 159.0, 163.8; HRMS (*m*/*z*, ESI) calculated for $C_{13}H_{11}N_3O_3S_2$, (M + H^+) 322.0315; found 322.0315.

Methyl 3,5-diamino-6-(furan-2-yl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6k)

Yield: 55% (83 mg); asparagus solid; mp: 248–249 °C; IR (KBr): 3472, 3353, 1675 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.74 (s, 3H, OCH_3), 5.92 (s, 2H, NH_2), 6.71–6.72 (m, 1H, ArH), 7.01 (br s, 2H, NH_2), 7.24 (s, 1H, ArH), 7.56 (d, J = 3.05 Hz, 1H, ArH), 7.92 (s, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.1, 98.7, 112.6, 115.2, 116.8, 137.0, 145.0, 148.2, 151.9, 158.5, 163.8; HRMS (*m*/*z*, ESI) calculated for $C_{13}H_{11}N_3O_4S$, (M + H^+) 306.0543; found 306.0538.

Methyl 3,5-diamino-4-oxo-6,7-diphenyl-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxylate (6l)

Yield: 60% (mg); pale yellow solid; mp: 256–258 °C; IR (KBr): 3468, 3348, 1677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H, OCH_3), 5.02 (br s, 2H, NH_2), 7.08–7.27 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.2, 116.7, 127.8, 128.0, 128.3, 128.8, 130.0, 132.4, 135.0, 142.9, 151.6, 157.9, 164.8; HRMS (*m*/*z*, ESI) calculated for $C_{21}H_{17}N_3O_3S$, (M + H^+) 392.1063; found 392.1063.

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ASIAN JOURNAL OF ORGANIC CHEMISTRY Communication

Chemoselective Cyclization

A Base-Mediated 6-*exo*-trig versus 6-*exo*-dig Carbocyclization Strategy for the Synthesis of Functionalized Biaryl Compounds

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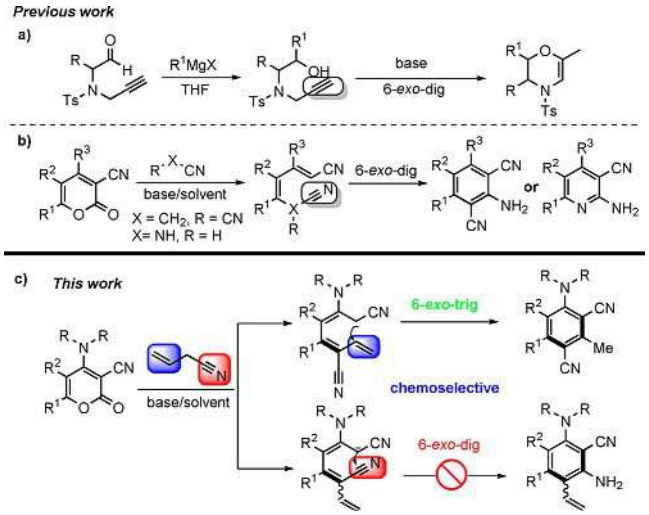
Dedicated to Dr. Vishnu Ji Ram on his 75th birthday.

Abstract: A base-mediated carbocyclization study has been performed between two allowed Baldwin cyclization modes (6-*exo*-trig and 6-*exo*-dig) and it was found that 6-*exo*-trig cyclization was preferred over 6-*exo*-dig. Allyl cyanide was found to be suitable and efficient pronucleophile for this investigation and two sp^2–sp^2 transition-metal-free C–C bond formations took place in a single operation to yield two differently functionalized biaryl compounds.

Carbocyclizations of alkenes and alkynes are extremely important and useful processes for the construction of carbocycles and heterocycles, as these skeletons are frequently encountered in nature.[1] According to the CRC dictionary of natural products,[2] 90% of chemically individual molecules discovered in nature contain either a carbocyclic or a heterocyclic subunit.[3] The success of a new synthetic strategy often depends on the ability to make these key cyclic structural units precisely and efficiently. In 1976, Baldwin developed a classification system for the possible cyclization patterns and suggested a set of general stereoelectronic guidelines to define the favorable modes of ring closure.[4] Over the years, these rules have been successfully applied in a wide variety of cyclization reactions, with and without metal catalysts, to construct carbocycles and heterocycles.[1,5]

Apart from well-established metal-catalyzed cyclization strategies[1,5] metal-free intramolecular cyclization has attracted the attention of researchers in recent years.[6] Very recently, Wang et al. reported a base-promoted *exo*-mode cyclization of alkynyl alcohols (Scheme 1 a).[7] Meanwhile, Ram and co-workers have shown an intramolecular carbocyclization reaction of malononitrile and cyanamide with functionalized 2*H*-pyran-2-ones in the presence of a base to synthesize biaryls and heterobiaryls (Scheme 1 b).[8] In these ring-transformation reactions, cyclization occurs through a 6-*exo*-dig manner on a -CN group, which was the only possible mode of cyclization. In another approach, Liu et al. described a base-catalyzed cycloisomerization through an intramolecular cyclization of 5-cyano-pentyne derivatives in a 5-*endo*-dig fashion.[9] Recently, Smith et al. reported a base-catalyzed 6-*endo*-trig interconversion of diastereomeric indolines in the presence of certain quaternary ammonium catalysts.[10] While designing the cyclization strategy for the formation of *exo*- and *endo*-selective products, achieving regioselectivity continued to be the main focus; however, chemoselectivity remained an untouched issue over the years.[11] In view of these reports, we wanted to know if there were two different allowed cyclization modes present in the same molecule, and then the outcome of the reaction. In this regard, we report herein a tandem transition-metal-free chemoselective carbocyclization strategy for the synthesis of highly functionalized biaryls.



Scheme 1. Base-mediated cyclization strategies for the synthesis of carbocycles and heterocycles.

2*H*-Pyran-2-ones have been extensively explored in recent years for their diverse applications in organic synthesis.[12] As versatile intermediates, 2*H*-pyran-2-ones can readily accept nucleophilic additions or undergo pericyclic reactions. During our

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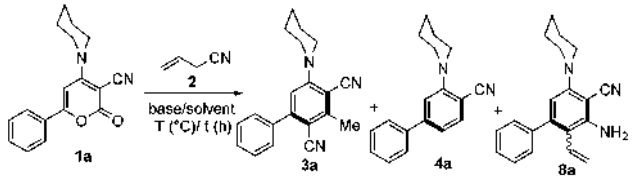
ongoing investigations on the ring transformation of 2*H*-pyran-2-ones for the synthesis of various aromatic as well as heteroaromatic scaffolds,[12,13] we envisioned that 2*H*-pyran-2-ones could react with allyl cyanide[14] and undergo two possible modes of cyclization: 6-*exo*-trig and 6-*exo*-dig. Therefore, they can serve as excellent starting materials for this investigation, in the presence of a suitable base (Scheme 1, entry iii).

We commenced our study by using 2-oxo-6-phenyl-4-(piperidin-1-yl)-2*H*-pyran-3-carbonitrile (**1a**) and allyl cyanide (**2**) as model substrates in the presence of KOH and DMF at room temperature. Unfortunately, we did not observe any reaction (Table 1, entry 1). To achieve the desired result, different bases

Table 1. Reaction optimizations.[a]

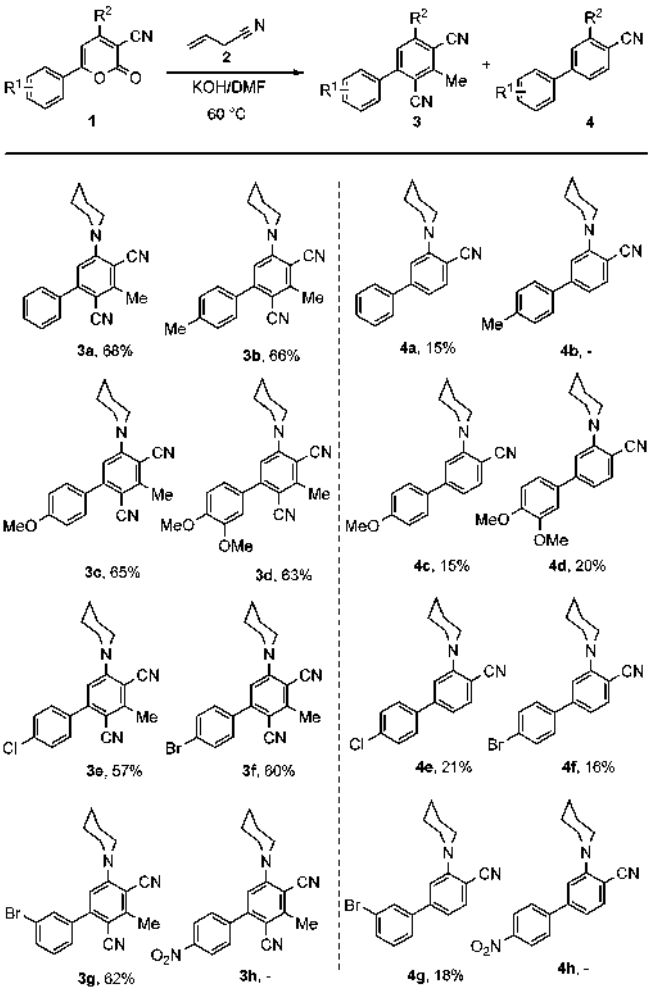


Entry	Base	Solvent	*T* [°C]	*t* [h]	Yield [%][b]		
					3a	**4a**	**8a**
1	KOH	DMF	RT	10	–	–	–
2	NaOH	DMF	RT	10	–	–	–
3	K_2CO_3	DMF	RT	10	–	–	–
4	KOH	DMF	60	6	68	15	–
5	KOH	DMSO	60	6	40	–	–
6	KOH	NMP	60	6	15	–	–
7	KOH	THF	60	10	20	–	–
8	NaOH	DMF	60	6	24	10	–
9	Cs_2CO_3	DMF	60	6	45	12	–
10	KOH	DMF	100	6	46	18	–
11[c]	KOH	DMF	100	0.25	52	20	–
12	*n*BuLi	THF	−78	2	Complex mixture		

[a] The reaction was conducted with 2-oxo-6-phenyl-4-(piperidin-1-yl)-2*H*-pyran-3-carbonitrile **1a** (0.5 mmol), allyl cyanide **2** (0.6 mmol), base (0.75 mmol) using various solvents (5.0 mL). [b] Yield of isolated product. [c] Under microwave at 100 °C for 15 minutes.

and solvents were screened, but they were not suitable at room temperature. Gratifyingly, when the same reaction was performed at 60 °C using KOH/DMF, it underwent 6-*exo*-trig cyclization to furnish **3a** as the major product (68%) and **4a** as the minor product (15%). To access selective 6-*exo*-trig cyclized product **3a**, other solvents such as THF, DMSO, NMP and different bases were used under different reaction conditions such as conventional heating and microwave irradiation. They were not found effective and were unable to yield 6-*exo*-trig cyclization with complete selectivity (Table 1). However DMSO, NMP and THF gave 6-*exo*-trig product **3a** in low yields in the presence of KOH.

On the basis of the studies carried out by our group, we found that KOH/DMF was the most suitable combination to furnish the synthesis of biaryl **3a**, and structurally interesting **4a** was also observed as the minor product. Encouraged by the result above, we ventured to study other functionalized 2*H*-pyran-2-ones to assess the generality of the protocol. All 2*H*-pyran-2-ones **1a–g** reacted very well to generate the desired products through 6-*exo*-trig cyclization. Using this protocol, different unsymmetrical highly substituted biphenyls **3a–g** were synthesized in good yields along with **4a–g** as the minor products (Scheme 2). In general, carbocyclization occurred very smoothly for substituted 2*H*-pyran-2-ones to yield highly functionalized biaryls, but in the case of strong electron-withdrawing groups such as 4-NO_2-C_6H_4 (**3h/4h**), no product was obtained.



Scheme 2. Synthesis of biaryls **3** and **4**. Reactions were performed at 60 °C for 6 h by stirring **1** (0.5 mmol), **2** (0.6 mmol) and KOH (0.75 mmol) in DMF (5.0 mL). Yields of isolated products are reported.

To explore the scope of this carbocyclization strategy, we next examined this protocol for the synthesis of substrates bearing heteroarenes such as thiophene and furan (Scheme 3). The substrates **5a–c** smoothly transformed into the heterobiaryls **6a–c** in good yields and **7a–c** were obtained as minor products. To further gauge the efficacy of the present protocol, bridged biphenyls,[15] which are ubiquitous structural motifs in a wide range of natural products and functional molecules, were synthesized. For this purpose, substituted 5,6-dihydro-2*H*-benzo[*h*]chromen-2-ones **5d** and **5e** were treated with allyl cy-

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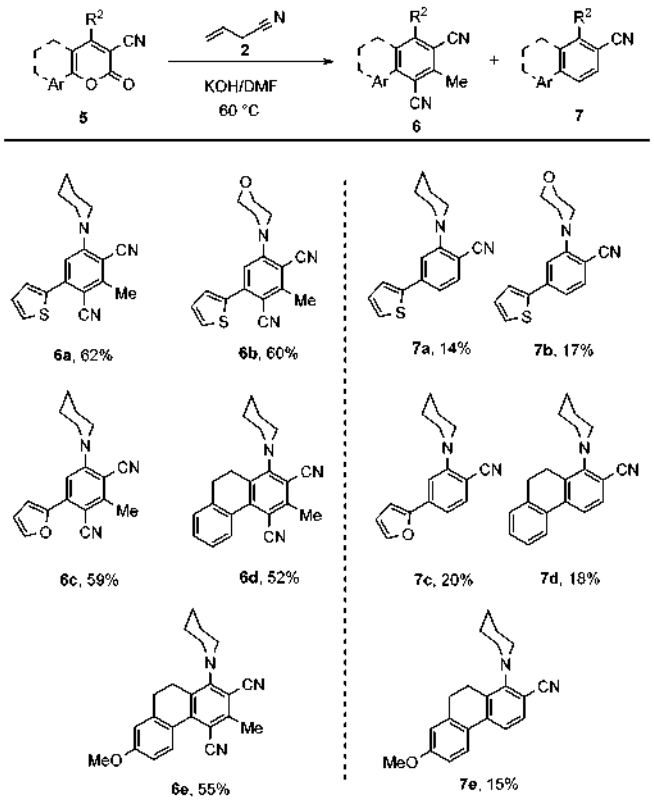


Scheme 3. Synthesis of heteroaromatic and bridged biaryl compounds **6** and **7**. Reactions were performed at 60 °C for 6 h by stirring **5** (0.5 mmol), **2** (0.6 mmol) and KOH (0.75 mmol) in DMF (5.0 mL). Yields of isolated products are reported.

anide **2** under similar reaction conditions. To our delight, structurally more complex **5d** and **5e** also cleanly cyclized to furnish 3-methyl-1-(piperidin-1-yl)-9,10-dihydrophenanthrene-2,4-dicarbonitriles **6d/e** in good yields along with 1-(piperidin-1-yl)-9,10-dihydrophenanthrene-2-carbonitriles **7d/e** as minor products (Scheme 3). It is noteworthy that both of the synthesized biaryl nuclei are interesting and useful precursors for generating molecular libraries and functional materials.[16,17] The structure of **3c** was confirmed by single crystal X-ray crystallography (Figure 1).[18]

To get some mechanistic insight into the reaction, we performed some control experiments, and it is noteworthy that in the absence of KOH the reaction did not occur (Scheme 4a), thereby indicating that the reaction did not proceed via a [4+2] cycloaddition, which could be another possible way to yield the desired product. This result also confirms that the first step is generation of carbanion **2a/2b** from allyl cyanide in the

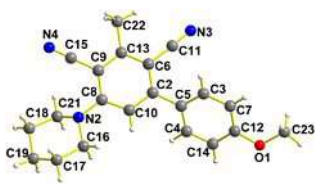
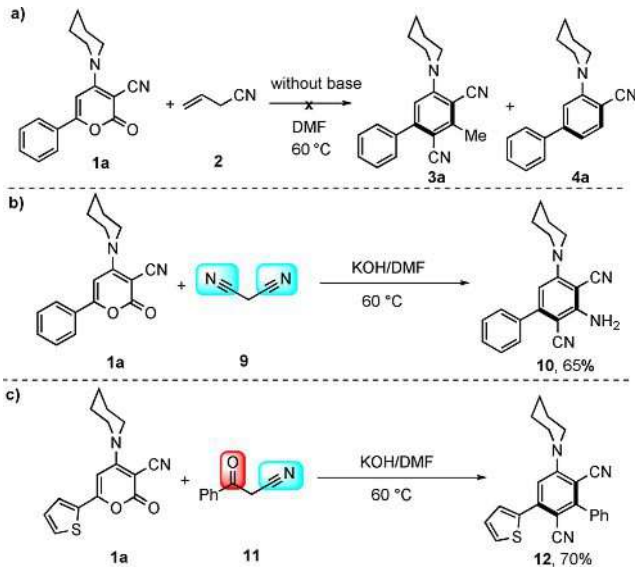


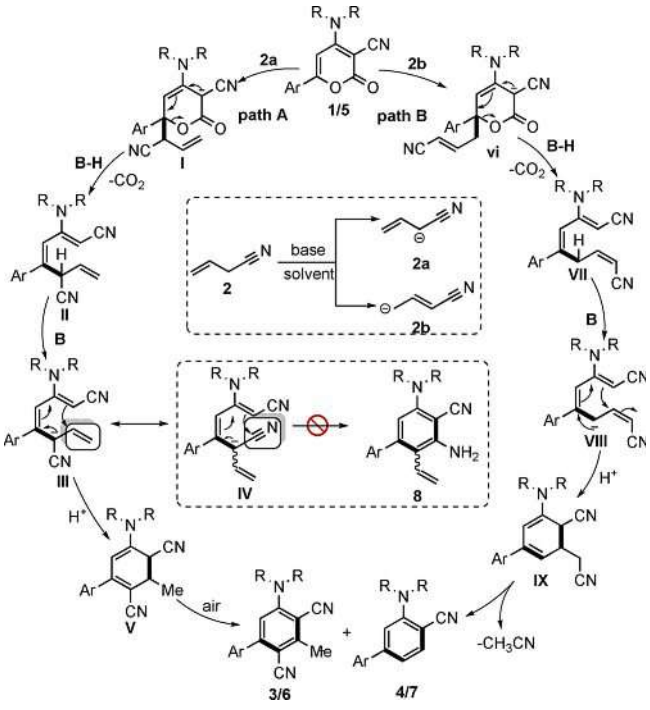
Figure 1. Perspective view of the molecular structure of **3c**.



Scheme 4. Control experiments for mechanistic studies of carbocyclization.

presence of base. Under newly developed conditions, the reaction of **1a** and malononitrile **9** was also performed to synthesize 6-*exo*-dig cyclized product 3-amino-5-(piperidin-1-yl)-[1,1′-biphenyl]-2,4-dicarbonitrile (**10**) (Scheme 4b). This supports involvement of the cyano group (6-*exo*-dig) in the carbocyclization process if no other possible mode of cyclization is present.

Based on these experiments, two plausible reaction pathways were proposed (Scheme 5). Two carbanions **2a** and **2b** can be generated from allyl cyanide **2**, which can trigger the reaction in two different directions to yield **3/6** and **4/7**. In the



Scheme 5. Proposed mechanistic approach for the synthesis of biaryl compounds.

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first case (path A) α-allyl carbanion **2a** attacks at the C6/10b position of 2*H*-pyran-2-ones and forms **I** via 1,6-conjugate addition, which can further undergo decarboxylation and protonation to yield **II**. This intermediate **II** can undergo deprotonation in the presence of base to provide two conformers **III** and **IV**, which serve as key intermediates for the chemoselectivity when forming biaryl compounds **3/6** or **8**. In this case, chemoselective carbocyclization involves the vinyl group through a 6-*exo*-trig cyclization, which generates intermediate **V**. To support this result and to further check the applicability of the developed hypothesis, we investigated another nucleophile 2-benzoylacetonitrile (**11**), which can undergo two cyclization modes: 6-*exo*-trig involving the carbonyl group and 6-*exo*-dig involving the cyano group. In this reaction, only one product was observed via 6-*exo*-trig cyclization involving the carbonyl group (Scheme 4c). In the next step, **V** furnishes major products **3/6** via in situ aromatization. Mechanistically, *6-exo*-dig cyclization would also be possible with the nitrile group of allyl cyanide (intermediate **IV**) to afford the product **8**, but not observed during the reaction.

In the other case (path B), reaction proceeds via generation of a γ-allyl carbanion, which react at the most electrophilic center to provide intermediate **VI**, which further undergoes decarboxylation to produce acyclic intermediate **VII**. In the next step, **VII** converts into **VIII** via deprotonation. In the key step **VIII** undergoes 6-*exo*-trig carbocyclization to yield **IX**, which undergoes aromatization via loss of acetonitrile to yield minor products **4/7**.

To explain the specific selectivity towards cyclization for involvement of only 6-*exo*-trig over the 6-*exo*-dig mode of cyclization, we proposed that probably both conformers **III** and **IV** are available during the reaction, but the best possible angle for anionic attack has been obtained for 6-*exo*-trig and is favored. If we compare the electrophilicity of the vinyl and nitrile groups, the vinyl group should not be involved in the cyclization over the nitrile group. Involvement of an sp^2 carbon over an sp^3 carbon also indicates that the angle of nucleophilic attack is more important than the electrophilicity of the reacting center involved.

In summary, an efficient metal-free base-mediated chemoselective carbocyclization strategy has been developed for the synthesis of highly functionalized biaryls. The main focus of this study was identifying chemoselectivity between 6-*exo-trig* and 6-*exo-dig* cyclization modes. It was found that if two allowed Baldwin cyclization modes (6-*exo*-trig and 6-*exo*-dig) are available within the same molecule, the 6-*exo*-trig cyclization will be favored over the 6-*exo*-dig cyclization in the presence of base. This hypothesis was further supported by control experiments, where use of 2-benzoylacetonitrile as a nucleophile afforded the *6-exo*-trig cyclization preferentially. Further extension of this work regarding selectivity is in progress.

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Conflict of interest

The authors declare no conflict of interest.

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शोध, समीक्षण, सृजन एवं संचार का

मुक्तांचल

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आदिवासी अस्मिता बोध का संकट और हिंदी उपन्यास

डॉ. उमेश कुमार पाण्डेय

भारत एक विशाल देश है। सन् 2011 की जनगणना के अनुसार हमारे देश की जनसंख्या 1.21 अरब है, जो कि चीन के बाद विश्व में सर्वाधिक है। अपनी समृद्ध सांस्कृतिक विरासत तथा विविधताओं के कारण भारत की सभ्यता संसार की एक प्राचीन सभ्यता है। भारतीय सामाजिक व्यवस्था में जनजातियों का बहुत महत्त्वपूर्ण स्थान है। ''भारत में जनजातियों की आबादी अफ्रीका के बाद दुनिया में सर्वाधिक है।''[1] ऐसा विश्वास किया जाता है कि ये लोग भारतीय प्रायद्वीप के मूल निवासी हैं। मूल निवासी होने के कारण ही इन्हें सामान्यतया 'आदिवासी' कहा जाता है। ''हमारे देश में करीब 550 जनजातियाँ हैं।''[2] सन् 2011 की जनगणना के अनुसार इनकी जनसंख्या 10.42 करोड़ है, जो कि देश की कुल जनसंख्या का 8.6 प्रतिशत है।

''भारत की जनजातीय जनसंख्या व्यापक रूप से बिखरी हुई है लेकिन कुछ क्षेत्रों में उनकी आबादी काफी घनी है। जनजातीय जनसंख्या का लगभग 85 प्रतिशत भाग 'मध्य भारत' में रहता है जो कि पश्चिम में गुजरात तथा राजस्थान से लेकर पूर्व में पश्चिम बंगाल और उड़ीसा तक फैला हुआ है और जिसके हृदय-स्थल (मध्य भाग) में मध्य प्रदेश, झारखण्ड, छत्तीसगढ़, महाराष्ट्र तथा तेलंगाना और सीमान्ध्र के कुछ भाग स्थित हैं। जनजातीय जनसंख्या के शेष 15 प्रतिशत में से 11 प्रतिशत से अधिक पूर्वोत्तर राज्यों में और बाकी के 3 प्रतिशत से थोड़े-से अधिक शेष भारत में रहते हैं। यदि हम राज्य की जनसंख्या में जनजातियों के हिस्से पर दृष्टिपात करें तो पाएँगे कि पूर्वोत्तर राज्यों में इनकी आबादी सबसे घनी है।''[3] मिजोरम देश का ऐसा राज्य है जहाँ की लगभग 95 प्रतिशत आबादी जनजातीय है। वहीं दूसरी ओर मध्य प्रदेश में 1.53 करोड़ जनजातीय लोग रहते हैं और संख्या के लिहाज से यह राज्य देश में शीर्ष पर हैं।

शताब्दियों से आदिवासी समाज अपने अस्तित्व की लड़ाई लड़ रहा है। औपनिवेशिक युग में शोषकों की एक पूरी फौज ने उनका सामाजिक-आर्थिक शोषण किया और तत्कालीन सरकार ने उनके अलगाव की नीति जारी रखी। देश की स्वतंत्रता के बाद हालांकि तमाम सरकारों ने उन्हें मुख्यधारा में लाने के प्रयास किये हैं, लेकिन इसके बावजूद अभी भी वे शोषण, घुटन और अलगाव से पीड़ित हैं और अपने अस्तित्व के लिए संघर्ष कर रहे हैं।

बाजारीकरण और भूमंडलीकरण के वर्तमान युग में आदिवासियों के समक्ष अपनी कला, संस्कृति, सामाजिक व्यवस्था, रीति-रिवाज और परंपराओं को बचाने का बहुत बड़ा संकट खड़ा

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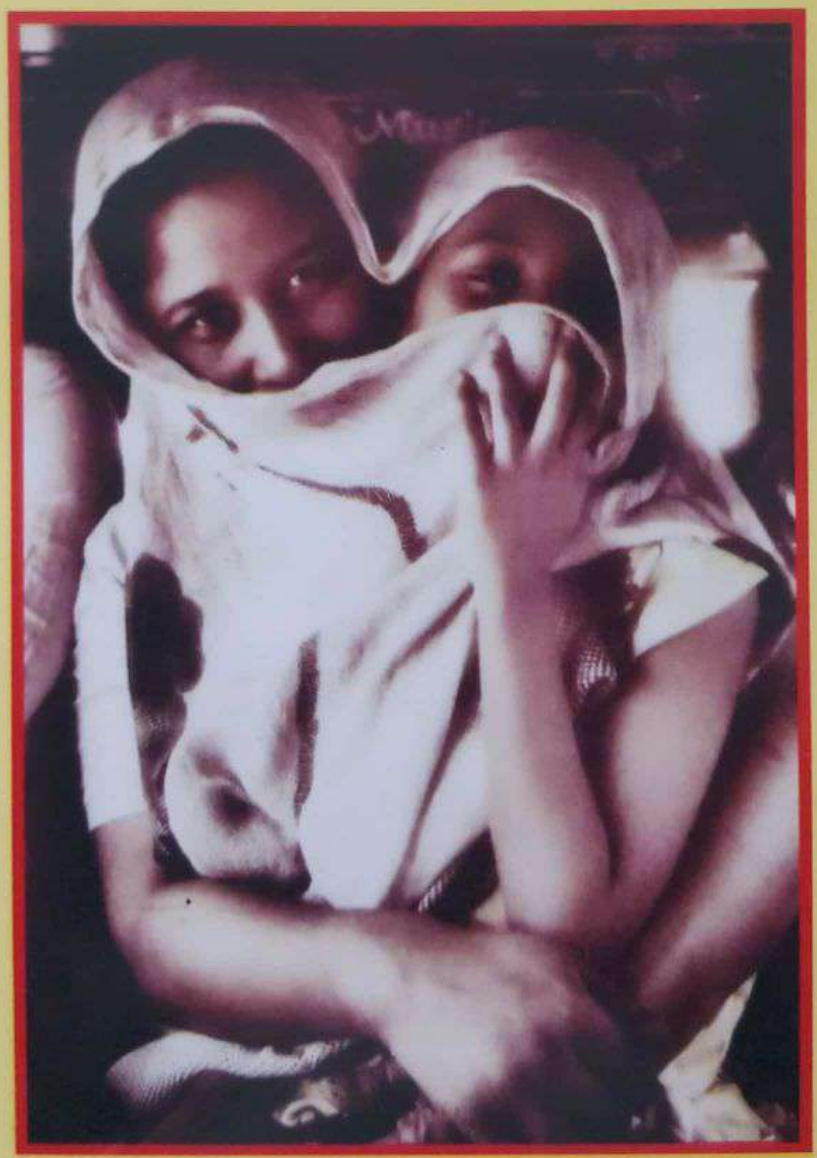

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श्रीश मिश्र / प्रीतपाल सिंह

विषय–सूची

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संघर्ष, सृजन एवं सांस्कृतिक बोध की वैचारिकी

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त्रैमासिक शोध-पत्रिका

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यात्रा वृतांत

तपोभूमि चित्रकूट

D.J - 9 Jun 96

परबस हो हृदय यादों के झरोखों से उलझ कर प्राकृतिक मनोरमता के विशाल गह्वर में कूद पड़ता है। इस तीर्थस्थल से बिछुड़ने पर इस नश्वर संसार में ये क्षणिक जीवन निः सत्व एवं निरीह लगता है। यहां मन्दाकिनी नदी का कल-कल प्रवाह व उन्मुक्त रूप से बिहरण करते हुए लतखों का झुंड कल्पना को भी यथार्कता के रूप में परिलक्षित होने में भी सानी नहीं रखता है यहीं वहां की मानवीय अनुक्रियाएं जीवन को सरस व निर्मल बना देती हैं। संध्या के समय पक्षियों का स्वछंद गगन में बिहरण व श्रद्धालुओं को पर्वत परिक्रमण, ऐसा लगता है मानों वास्तविक स्वर्ग यह तपोभूमि ही है। चांदनी रात्रि में चंद्रमा का पर्यास्वनी नदी में नर्तन कम हृदयग्राही नहीं लगता है। पेड़ों की नैसर्गिक सुषमा कम चित्ताकर्षक नहीं । पहाड़ी से अनवरत अविरल प्रवाहित होते झरने मानों अपने अतीत को प्रखर कर अतीत के गौरव को नवीन वेश पहना रहे हों।

सतना से 78 कि.मी. दूर स्थित यह पवित्र स्थल जहां श्रृष्टि निर्माता ब्रह्माजी, पालनहार विष्णु जी एवं त्रिनेत्रधारी भगवान शिव का बालावतार माना जाता है, जीवन का वास्तविक सुख यहीं सुलभ होता है।

मैं जब प्रथम बार गया था तब आषाढ़ का महीना था। मन्दाकिनी नदी ने विकराल रूप धारण किया था। उसका उफान देखते ही बनता था। पर्वत का दृश्य मनमोहक एवं रमणीय था। पर्वतों के ऊपर उगे हुए वृक्ष व्योम की ओर इस प्रकार टकटकी लगाये थे, मानों ये व्योम को इस वैभवशाली तीर्थ को भ्रमण करने का न्यौता दे रहे हों। हनुमान धारा एवं पंचमुखी हनुमान धारा में श्रद्धालुओं का तांता लगा रहता है। मानसून की सनसनाहट से पौधे मस्ती में झूमते दिखाई देते हैं। चारों दिशाओं में प्रफुल्लित कुसुम दृष्टिगोचर हो रहे होते हैं। शरद ऋतु में मां जाह्नवी का सलिल ठीक उसी प्रकार स्वच्छ एवं निर्मल हो जाता, जिस प्रकार सज्जन पुरुषों का हृदय पवित्र एवं पावन रहता है।

सती अनुसुइया आश्रम जो कि 5 कि.मी. दूर चित्रकूट क्षेत्र में अवस्थित है की निराली छटा अत्यंत मनमोहक लगती है। किंवदन्ती है कि मां त्रिपथगा (चित्रकूट) की [illegible] जिस गुप्त [illegible] का उद्भव उसी स्थल से हुआ था। घने जंगलों से सुशोभित यह आश्रम मां अनुसुइया के त्याग एवं तपोबल की गाथा गाता है। पतिव्रता नारियों के लिए उनका अविरल शिष्ट सभ्यता के लिए एक अद्भुत मिशाल है। आदर्शों के प्रति निष्ठा ही मां का एकमात्र ध्येय था। और आश्रम से कुछ ही दूर है यह स्फटिक शिला जहां मां जाह्नवी में थोड़ा सा ही चना विसर्जित करने से हजारों मछलियों का झुण्ड इसे प्राप्त करने की लिप्सा में होड़ सा लगा देता है व अनायास ही दाता का हृदय गदगद हो उठता है।

द्वितीय बार जब मैं गया था तब कार्तिक की मनुहार थी। शीत ऋतु का प्रारंभ मात्र ही था। शीत ऋतु में कुहरे से ढका यह नगर ऐसा प्रतीत होता है मानों कहीं समाहित हो गया हो। कार्तिक में दीपावली के सुअवसर पर जन सैलाब देखते ही बनता है। दीपमलिकाओं का संध्याकाल में मां त्रिपथगा में विसर्जन, ऐसा प्रतीत होता है मानों मां त्रिपथगा ने ज्ञान का विसर्जन कर दिया हो। "संसार के समस्त मानव चाहे वे पापी हों या क्रोड़ी सज्जन हों या दुर्जन सब अपने कृत्य कर्मों को भुलाकर परबस ही इसकी ओर खिंचे होने का मार्ग अपनाते हैं।" दीपावली के शुभ अवसर पर चित्रकूट की पवित्र भूमि तिल-तिल पर श्रद्धालुओं से गंसी रहती है।

राममुहान जहां पर विराजित है चित्रकूट के सबसे प्रमुख देवता जो कि आदिकाल से आज तक लोगों को उनके कर्मों के हिसाब से आशीर्वाद वितरित करते हैं। परम पिता कामता स्वामी जी के दर्शन के लिए लाखों लोग आते हैं व मोक्ष प्राप्त करते है।

अन्तिम बार मैं ग्रीष्म ऋतु में वैसाख के महीनें में गया था, हवा के प्रखर प्रवाह में मां त्रिपथगा का जल हिलोरे ले रहा था। उसे देखकर तो ऐसा लगता था मानों मां ने संसार के सम्पूर्ण वैभव को स्वयं अंगीकृत कर लिया हो। गुप्त गोदावरी की आंख मिचौनी कम हृदयग्राही नहीं लगती। उसे अन्दर बनी हुई गुफाएं उत्कृष्ट नमूनों का उत्कृष्ट उदाहरण है। यहां की गुफाओं में चमत्कार सा परिलक्षित होता है यहां गुफा के अन्दर ग्रीष्म में शीतलता एवं शीत में ग्रीष्मता का अनुभव होता है।

चित्रकूट भारत की पवित्र भूमि का एक अभिन्न अंग है। यहां जीवन मूल्य की यथार्कता परबस ही परिलक्षित होती है। चित्रकूट से लौटने पर मेरा मन पागल सा हो गया ठीक उसी प्रकार जिस प्रकार ममतामयी मां एक क्षण अपने पुत्र को न देखकर पागल हो उठती है। जिस प्रकार सूर्य व उसकी ऊष्णता को पृथक नहीं किया जा सकता ठीक उसी प्रकार मेरा मन चित्रकूट से अभिन्न नहीं है। आज भी चित्रकूट की यादें तटवित भावनाओं को ताजा कर देती हैं।

International Research

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स्मृतियों में भारतीय न्याय पद्धति

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सारांश

स्मृतियाँ सनातन संस्कृति का सनातन उपहार हैं। ये पृथ्वी पर मानव जन्म के पश्चात उसके जीवन की प्रकृति के साथ समरसता स्थापित करने के लिए मानव समाज की अति मूल्यवान निधि हैं। पाश्चात्य इतिहासकारों ने राजनीतिक दर्शन व चिन्तन का स्रोत यूरोप में ढूँढने का प्रयास किया है, लेकिन वास्तविकता तो यह है कि प्राचीन भारत में राजनीतिक व विधिक चिन्तन की एक स्वस्थ व दीर्घ परम्परा दिखाई देती है। स्मृतियाँ प्राचीन भारतीय राज्य व्यवस्था व न्याय व्यवस्था का मुख्य स्रोत रही हैं। भारतीय स्मृतियों में निहित शाश्वत मूल्य आज भी प्रासंगिक है। प्रस्तुत प्रपत्र में स्मृतियों में वर्णित भारतीय न्याय पद्धति का वर्णन किया गया है।

कुंजी शब्द– दण्डपारूष्य, स्तेय, अप्रच्छन्न, वाक्पारूष्य।

भारतवर्ष एक धर्म प्रधान देश है। भारतीय धर्म का मूलाधर वेद हैं। प्राचीन भारतीय साहित्य में स्मृतियों का स्थान वेदों के बाद आता है। वेद विधि के मूल स्रोत भी माने गए है तथा स्मृतियों के विधि–विधान उन्हीं पर आधारित हैं। स्मृति के बारे में कहा गया है "स्मर्यत इति स्मृति" अर्थात् ऐसे ग्रन्थ जो ऋषियों द्वारा स्मृति के आधार पर लिखे गए हैं, स्मृतियाँ कहलाएँ है।[1] स्मृतियों का आधार मूलरूप से वह रीति (Custom) लोकाचार (Convention) तथा सम्प्रदाय (Tradition) बना जिसे समाज ने दीर्घकाल से आत्मसात् कर रखा था। इन्हें 'समयाधारिक धर्म' कहा जा सकता है। आपस्तम्ब धर्मसूत्र के टीकाकार हरदत्त ने इसे 'पौरुषेयीव्यवस्था' माना है।[2]

विधि के दूसरे स्रोत स्मृति शब्द को कुछ विद्वानों ने स्मरण से जोड़ा है। गौतम धर्मसूत्र में प्रयुक्त 'स्मृतिशील'[3] तथा मनु द्वारा प्रयुक्त इसी शब्दयुग्म[4] में अल्टेकर प्रभृति विद्वानों ने स्मृति का अर्थ स्मरण (Memory) माना है। गौतम, वशिष्ठ और बोधायन ने स्मृति को वेद के जानने वालों का स्मरण बताया है। यह मान्यता है कि स्मृतियाँ वेदों के लुप्त पाठों पर आधारित हैं अर्थात् स्मृतियाँ ऋषियों द्वारा स्मरण रखे गये वेदों के पाठों के आशय को अन्तर्विष्ठ करती हैं। 'स्मृति' शब्द का दूसरा अभिप्राय 'धर्मशास्त्र' माना गया है।[5] अल्टेकर की यह धारणा है कि रीति, लोकाचार तथा सम्प्रदाय व्यवहार पहले शिष्टों की स्मृति में थे जिन्हें बाद में लिपिबद्ध किया गया और उपचार से इन ग्रंथों को ही स्मृति–ग्रंथ की संज्ञा दी गयी।[6] पी.एन. सेन का भी मानना यही है कि स्मृतिकार धर्मों के साक्षात् द्रष्टा नहीं हैं बल्कि ऋषियों की स्मृति के ही आधार पर इनकी रचनाएँ हैं। मनु ने भी स्मृति का अर्थ **'वेदज्ञों का स्मरण'** माना और उसका उपयोग धर्मशास्त्र के अर्थ में किया है।[7]

स्मृतियों की संख्या अत्यंत अधिक है। इसका कारण यह है कि समाज की गतिशीलता, नयी संस्कृतियों का प्रवेश तथा परिस्थितियों की बाध्यता के कारण प्रचलित प्रथाओं का विरोध सम्भव नहीं था और वे श्रुतियों की व्याख्याओं की सीमा में नहीं आते थे। ऐसे में समाज के सचेतक विद्वान विभिन्न–व्याख्याओं तथा तर्कों द्वारा, बदलते परिवेश के अनुसार, अपनी रचनाओं में तत्कालीन समस्याओं के समाधान तथा प्रचलित प्रथाओं के माप–दण्ड के अनुसार स्मृतियों की रचनाएँ करने में प्रयत्नशील हुए। फलतः इनकी संख्या बहुत अधिक हो गयी क्योंकि उन दिनों न तो कापीराइट कानून थे, न उन्हें यश की लिप्सा थी और न तो उनको आर्थिक लाभ ही था।[8] उनका प्रयत्न समाज में एकता तथा समरसता की स्थापना करने तथा श्रुतिगत–नियमों की अपरिहार्यता तथा मर्यादा की रक्षा करने के लिए ही था।

प्राचीन भारतीय ग्रंथों में मनुस्मृति का स्थान प्रमुख है। इसमें प्रतिपादित विचार लम्बे ऐतिहासिक काल व परम्परा का प्रतिनिधित्व करते है। मनुस्मृति मानव–धर्मसूत्र का स्मृति ग्रंथ के रूप में परिवर्तित एवं सम्भवतः परिवर्धित रूप है। राजा के कर्तव्यों की व्याख्या करते हुए प्राचीन भारतीय न्याय–प्रशासन पर यह महत्वपूर्ण प्रकाश डालती है। मनुस्मृति में उपलब्ध सामग्री का सम्बंध मानव समाज से है। वर्णों की उत्पत्ति, उनके अधिकार, व कर्तव्य, आश्रम–व्यवस्था, विवाह संस्कार, राज्य कर्मचारी एवं पति–पत्नी के अधिकार व कर्तव्य, दीवानी, फौजदारी से सम्बंधित कानून, धार्मिक एवं सामाजिक अपराध तथा प्रायश्चित, उत्तराधिकार के नियम आदि का उल्लेख कर मनुस्मृति प्राचीन भारतीय न्याय प्रशासन के विविध पहलुओं पर प्रकाश डालती है।

स्मृतियों में विधि के लिए 'व्यवहार' का प्रयोग किया गया है। मनु के अनुसार इसका अर्थ है– झगड़ा या वाद।[9] सर्वप्रथम मनुस्मृति में 18 विषयों अथवा व्यवहार पदों के नाम गिनाएँ गए है। वे इस प्रकार हैं– ऋणादान, निक्षेप, अस्वामिविक्रय, सम्भूयसमुत्थान, दत्तस्यानपाकर्म, वेतनादान, संविदव्यतिक्रम, क्रयविक्रयानुशय स्वामिपालविवाद, सीमाविवाद, वाक्यारूष्य, दण्डपारुष्य, स्तेय, साहस, स्त्रीपुंधर्म, विभाग,

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अर्चना गुप्ता*

विवेकानन्द अध्यात्म के क्षेत्र में एक अविस्मरणीय नाम है जिनके सम्बंध में स्वयं उनके गुरु श्री रामकृष्ण परमहंस कहा करते थे कि वे सागर के बीच महासागर हैं। स्वामी विवकानन्द एक महान देशभक्त, चिंतक, आध्यात्मिक नेता, मानवता प्रेमी तथा जीवात्माओं को जागृत करने वाले महान संत थे। रामकृष्ण परमहंस की शिक्षा के प्रचार तथा विकास का मुख्य श्रेय स्वामी विवेकानन्द को है। विवेकानन्द भारतीय गगन मंडल में एक ऐसे सितारे की भांति हैं जो सदैव जगमगाते रहेंगे।

स्वामी विवेकानन्द ने भारत भूमि पर विकसित सर्वश्रेष्ठ दर्शन वेदान्त का अनूठे ढंग से देश व विदेश में प्रतिपादित किया। इनका दर्शन व राष्ट्रवाद नव– वेदांत के नाम से जाना जाता है। उन्होंने 19वीं सदी के अंतिम और 20वीं सदी के शुरूआती वर्षों के दौरान बंगाल तथा भारत के अन्य हिस्सों में सांस्कृतिक पुनरुत्थान में महत्वपूर्ण भूमिका निभाई। उनके व्याख्यान तथा लेख महात्मा गांधी, जवाहरलाल नेहरू, नेता जी सुभाष चन्द्र बोस, सी. राजगोपालाचारी जैसे आजादी से पूर्व के बहुत से राजनीतिक नेताओं के लिए प्रेरणास्रोत बने। इन सभी ने स्वामीजी के विचारों के प्रति कृतज्ञता प्रकट की है।

स्वामी जी का कहना था कि गरीबों की उपेक्षा और उनका शोषण भारत के पतन और पिछड़ेपन का मुख्य कारण है। वह उन पहले आध्यात्मिक नेताओं में से थे, जिन्होंने जनसामान्य के समर्थन में आवाज उठाई। उन्होंने देश में गरीबों की दुर्दशा के बारे में राष्ट्रीय जागरूकता पैदा करने की कोशिश की। उनके इस उद्घोष ने सैकड़ों युवाओं के मन में समाज सेवा को जीवन पद्धति के रूप में अपनाने के लिए प्रेरित किया था कि, **'जब तक लाखों लोग भूख और अज्ञानता में रह रहे हैं, तब तक मैं हर उस व्यक्ति को देशद्रोही मानता हूं जिसने उनके पैसे से शिक्षा प्राप्त करने के बावजूद उन पर थोड़ा भी ध्यान नहीं दिया।'** देश की दासता और निर्धनता का चित्रण करते हुए स्वामी विवेकानन्द ने कहा था: **"अब भारतराजनैतिक शक्ति नहीं, आज वह दासता में बंधी हुई एक जाति है। अपने ही प्रशासन में भारतीयों की कोई आवाज नहीं है, उनका कोई स्थान नहीं है– वे केवल 30 करोड़ गुलाम हैं और कुछ नहीं।"**

स्वामी जी देश की अवनति के प्रति केवल अश्रुपात करने वाले व्यक्ति नहीं थे, उनके अन्तःकरण में देश का उत्थान करने की प्रबल इच्छा आन्दोलित हो रही थी। उन्होंने भारतवासियों में गर्वीन प्राण का संचार करने वाला उद्बोधन करते हुए कहा था– **"ये भारत क्या दूसरों की हाँ में हाँ मिलाकर दूसरों की नकल कर परमुखापेक्षी होकर इन दासों की सी दुर्बलता, इस घृणित, जघन्य, निष्ठुरता से तुम वीरभोग्या स्वाधीनता प्राप्त करोगे? ऐ भारत तुम मत भूलना कि तुम्हारी स्त्रियों का आदर्श सीता, सावित्री, दमयन्ती हैं; मत भूलना कि तुम्हारे उपास्य सर्वत्यागी उमानाथ शंकर हैं; मत भूलना कि तुम्हारा समाज उस विराट महामाया की छायामात्र है, मत भूलना कि नीच, अज्ञानी, दरिद्र, चमार और मेहतर तुम्हारा रक्त और तुम्हारे भाई हैं। ऐ वीर! साहस का आश्रय लो। गर्व से बोलो कि मैं भारतवासी हूँ और प्रत्येक भारतवासी मेरा भाई है। बोलो कि अज्ञानी भारतवासी, दरिद्र भारतवासी, ब्राह्मण भारतवासी, चाण्डाल भारतवासी, सब मेरे भाई हैं। भाई, बोलो कि भारत की मिट्टी मेरा स्वर्ग है। भारत के कल्याण में मेरा कल्याण है, और रात–दिन कहते रहो कि –हे गौरीनाथ! हे जगदम्बे! मुझे मनुश्यत्व दो; माँ, मेरी दुर्बलता और कापुरुषता दूर कर दो, मुझे मनुष्य बना दो।"**

उस समय में जबकि भारत उदासीनता आलस्य और निराशा के घोर वातावरण में डूबा हुआ था, स्वामी जी के विचारों ने भारतवासियों में निर्भीकता और कर्मठता का संचार किया। स्वामी जी ने भारतवासियों को जहाँ स्वाधीनता की प्राप्ति की आशा बंधाई वहीं उन्हें त्यागपूर्ण वृत्ति धारण करने की शिक्षा दी, सामाजिक व राष्ट्रीय एकता और सार्वजनिक कल्याण की प्राप्ति पर बल दिया और विदेशी शासकों के आतंक से उत्पन्न होने वाली कापुरुषता का परित्याग करने का आह्वान किया। भारत के राजनैतिक पुनर्जागरण के सन्दर्भ में ये समस्त विचार महत्वपूर्ण स्थान रखते हैं।

विवेकानन्द भारत के उस युग में आते हैं जब भारत आत्महीनता से ग्रस्त था। विवेकानन्द के सामने सबसे अहम प्रश्न यह था कि भारतवासियों में कैसे उर्जा भक्ति का संचार किया जाए। वस्तुतः, विवेकानन्द उस अन्धी शताब्दी में पैदा होते हैं, जिसमें व्यक्ति अपने अस्तित्व को भूल बैठा था। अन्धी शताब्दी को जो व्यक्ति ज्योतित करता है वह ज्योति पुरुष कहा जाता है।

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(अनुचित साधन-प्रयोग के प्रकरण का अरोपण - पत्र)

पंजीकृत/स्पीड पोस्ट

गोपनीय

प्रेषक

प्राचीन भारतीय ग्राम अदालतों की प्रासंगि

अर्चना

ग्राम अदालतें प्राचीन भारतीय न्याय व्यवस्था का आधार रही हैं। प्राची में बड़े–बड़े मुकदमों का निपटारा गाँव की पंचायतों द्वारा ही कर दिया जाता थ स्तर पर न्यायिक इकाइयाँ पंचायतों एवं महापंचायतों के रूप में सक्रिय थीं। रहने वाले व्यक्तियों को न्याय पाने के लिए नगरों की तरफ भागना नहीं पड़ता न ही आज की तरह इसके लिए भारी खर्च उठाने पड़ते थे। 'न्याय आपके द परिकल्पना प्राचीन भारतीय न्याय व्यवस्था में निहित थी। वर्तमान समय में न्याय व्यवस्था की स्थिति डांवाडोल है। न्यायालयों पर लंबित मुकदमों का बोझ जा रहा है और परिणाम स्वरूप न्याय मिलने में अनावश्यक रूप से विलंब की विकराल होती जा रही है। ऐसी स्थिति में ग्राम अदालतों की प्रासंगिकता स्पष्ट है। वर्तमान न्याय प्रणाली में त्वरितता लाने एवं न्याय को लोगों के द्वार तक के लिए ग्राम अदालतों की स्थापना अत्यंत आवश्यक है।

ग्राम अदालतों की पृष्ठभूमि–

अति प्राचीन काल से आधुनिक युग तक ग्राम भारतीय सभ्यता का आध शासन–व्यवस्था की धुरी रहे हैं। 'ग्राम' शब्द ऋग्वेद में भी आया है। वैदिक ग्रामों की समृद्धि के लिए बहुत बार प्रार्थना की गयी है। वैदिक काल छोटे–छोटे होते थे, इस कारण ग्रामों का महत्व और भी बढ़ गया था। वेदों में अधिकारी को 'ग्रामणी' कहा गया है।[1] वैदिक काल में ग्रामणी का महत्वपूर्ण स्थ वह न्यायिक व्यवस्था में स्थानीय इकाई का प्रधान था। उसका पद चुना हुआ अपराधविधि में उसे अधिक अधिकार थे। ग्रामणी ब्राह्मण नहीं होता था। कौ 'ग्रामवृद्धों' के हाथ में न्यायिक अधिकार दिया था।[2]

ग्राम न्यायालयों का अस्तित्व वैदिक काल में भी था और वे प्रथागत कानूनों को प्रशासित करते थे। धर्म–शास्त्रों व नीति–शास्त्रों में स्थानीय न्यायालयों का उल्लेख है–

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मनुस्मृति में न्याय एवं दण्ड

अर्चना गुप्ता*

सारांश

प्राचीन भारतीय ग्रंथों में मनुस्मृति का स्थान प्रमुख है। इसमें प्रतिपादित विचार लम्बे ऐतिहासिक काल व परम्परा का प्रतिनिधित्व करते हैं। मनुस्मृति मानव–धर्मसूत्र का स्मृति ग्रंथ के रूप में परिवर्तित एवं सम्भवतः परिवर्धित रूप है। राजा के कर्तव्यों की व्याख्या करते हुए प्राचीन भारतीय न्याय–प्रशासन पर यह महत्वपूर्ण प्रकाश डालती है। मनुस्मृति में उपलब्ध सामग्री का सम्बंध मानव समाज से है। वर्णों की उत्पत्ति, उनके अधिकार व कर्तव्य, आश्रम–व्यवस्था, विवाह संस्कार, राज्य कर्मचारी एवं पति–पत्नी के अधिकार व कर्तव्य, दीवानी, फौजदारी से सम्बंधित कानून, धार्मिक एवं सामाजिक अपराध तथा प्रायश्चित, उत्तराधिकार के नियम आदि का उल्लेख कर मनुस्मृति प्राचीन भारतीय न्याय प्रशासन के विविध पहलुओं पर प्रकाश डालती है।

कुंजी शब्द– न्यायिक–सक्रियता, पूर्वाग्रहता, प्राड्विवाक।

स्मृतियों में विधि के लिए 'व्यवहार' का प्रयोग किया गया है। मनु के अनुसार इसका अर्थ है– झगड़ा या वाद।[1] सर्वप्रथम मनुस्मृति में 18 विषयों अथवा व्यवहार पदों के नाम गिनाएँ गए है। वे इस प्रकार हैं– ऋणादान, निक्षेप, अस्वामिविक्रय, सम्भूयसमुत्थान, दत्तस्यानपाकर्म, वेतनादान, संविद्व्यतिक्रम, क्रयविक्रयानुशय स्वामिपालविवाद, सीमाविवाद, वाक्यारूष्य, दण्डपारुष्य, स्तेय, साहस, स्त्रीपुत्रधर्म, विभाग, धूतसमाह्वय।[2] मनुस्मृति में व्यवहार सम्बंधी विस्तृत विवरण अध्याय 8 व अध्याय 9 में दिया गया है। यद्यपि याज्ञवल्क्य व नारद स्मृतियों की तरह इसमें व्यवहार प्रक्रिया का अधिक विस्तार नहीं दिखाई देता है लेकिन न्याय व्यवस्था पर मनु का विवरण बहुत रोचक और व्यवस्थित तरीके से दिया गया है।

मनुस्मृति में राजा के न्यायिक अधिकार के सम्बंध में पर्याप्त विचार सामग्री उपलब्ध है। राज्य में न्याय की समुचित व्यवस्था उसके प्रगति का द्योतक है प्रजा के स्वत्व की रक्षा करने वाले विधान संस्कृति के मापदण्ड होते हैं। मनुस्मृति के महत्व का एक कारण उसकी न्याय तथा विधि सम्बन्धी प्रगतिशील विचारधारा है।[3] मनु राजतंत्र का समर्थन करते है। चूँकि राजतंत्र शक्ति विभाजन सिद्धांत के प्रतिकूल है, अतः राजा के अन्य अधिकारों के साथ उसके पास न्यायिक अधिकार भी रहते है। राजा इस शक्ति के कारण न्याय का स्रोत है।[4] राजा के पास विधि निर्माण का अधिकार नहीं है। विधि की व्याख्य का कार्य धर्मशास्त्रों अथवा विद्वान मनीषियों के अधिकार क्षेत्र में है। फलतः राजा निर्मित विधि के माध्यम से ही न्याय करता है। परन्तु राजा, जो अदण्ड्य है, वह दण्डित न हो जाए, जो दण्ड्य हो वह मुक्त न हो जाए, इसका ध्यान रखता है।[5] इस प्रकार की यदि घटना हो जाए जो राजा के साथ मंत्री, पुरोहित अर्थात न्यायिक प्रशासन उत्तरदायी होता है और दण्ड स्वरूप प्रायश्चित करता है।[6] इसके साथ यदि राजा न्यायालय में समय पर उपस्थित न हो अथवा कार्यवाही के संचालन में किसी प्रकार की अवमानना करता है तो वह अपराधी समझा जाता है। उसकी सामान्य अवमानना से न्याय के अन्य कर्मचारियों में प्रमाद का विस्तार सम्भव है।[7] राज्य के विरूद्ध क्रांतियों न्याय व्यवस्था में सम्पूर्ण कार्यवाही के संचालन का अधिकार राजा को प्राप्त है। मनुस्मृति में 'सक्रिय–न्यायपालिका' एवं 'न्यायिक–सक्रियता' का रूप पाया जाता है।[8]

मनुस्मृति में न्यायिक प्रशासन सम्बन्धी उल्लेख से स्पष्ट है कि विभिन्न प्रकार के न्यायालयों को संगठित करने का राजा कोई विशेष प्रयास नहीं करता। इस सम्बन्ध में याज्ञवल्क्यस्मृति कुछ अधिक प्रगतिशील है। मनु ने प्रशासकीय अधिकारियों को न्याय कार्य का अधिकार सौंपा है। वे राजा द्वारा नियुक्त कर्मचारी है। प्रशासनिक अधिकारियों में सबसे नीचे की ईकाई का अधिकारी ग्रामिक है। ग्रामिक के अधिकारों में न्यायिक अधिकार भी सम्मिलित है। इसकी क्षेत्र तथा सीमा एक ग्राम तक संकुचित है। यदि ग्राम अधिकारी व्यवहारों को निश्चित करने में असमर्थता का अनुभव करता है, तब दश ग्राम के अधिपति के पास भेजा जाता है। इस प्रक्रिया में सहस्राधिपति तक निर्णय करने के लिए जाया जा सकता है। परन्तु ग्रमिक, विंशी, विंशती, शती, सहस्रपति आदि सभी राजा द्वारा नियुक्त अधिकारी हैं।[9] मनुस्मृति में यह स्पष्ट नहीं है कि ग्राम पदाधिकारी किस प्रकार के विषयों को अपने अधिकार क्षेत्र के अन्तर्गत रखते हैं। मनुस्मृति केवल ग्राम दोषों का उल्लेख करती है। यद्यपि ग्राम दोषों में सभी प्रकार के दोष आ जाते हैं। ऋण दान, सीमा विवाद, स्वामिपाल–विवाद आदि से लेकर सभी इसके अन्तर्गत हैं। निष्कर्ष यह है कि इन प्रशासकीय पदाधिकारियों को ग्राम की शांति एवं व्यवस्था बनाये रखने के हेतु सभी प्रकार के विषयों को ग्रहण का अधिकार है, जिनसे

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प्राचीन भारत में न्यायालयों का संगठन

*अर्चना गुप्ता**

न्यायालय न्यायिक प्रशासन के अंग हैं। उनके संगठन एवं विकास के माध्यम से न्यायपालिका का स्वरूप सामने आता है। प्राचीन भारत में न्यायालयों का विकास समाज की न्यायिक एवं सामाजिक संस्थाओं से होता है। ऐसी संस्थाएं न्याय के साथ नीति एवं विधान संचालन करती थीं। वैदिक काल की न्यायिक संस्थाओं में परिषद, सभा आदि केवल न्यायालय का कार्य नहीं करती थीं अपितु वे सामाजिक एवं राजनीतिक संस्थाओं के भी रूप में थीं। राजशक्ति के विकास के साथ राजसभा के उदय होने पर उसने इन संस्थाओं का प्रभाव था। फलतः राजसभा राजा की इच्छा पर न्याय करने वाली न हो सकी। प्राचीन भारतीय शासन व्यवस्था में केन्द्रीय शासन के विकसित होने पर भी स्थानीय न्यायिक शक्तियों का महत्व कम नहीं हुआ। केन्द्र के साथ प्रशासन की दृष्टि से उनका सम्बंध जोड़ा गया लेकिन उनकी स्वतंत्रता नहीं समाप्त की गयी। वर्गीय न्यायालयों की स्वतंत्रता की सुरक्षा की गयी। उत्तरवर्ती काल के न्यायालयों के जो नियम स्वीकार किये गये उनमें विधि–सम्प्रभुता के कार्यान्वयन का ही प्रयास किया गया। राजा एवं न्यायाधीश भी उन नियमों की सीमा में ही बँधे रहे। इन तथ्यों के स्पष्टीकरण के लिए वैदिक काल से स्मृतिकाल तक की न्यायिक संस्थाओं का अध्ययन करना आवश्यक हो जाता है।[1]

ग्रामणी

वैदिक काल में ग्रामणी का महत्वपूर्ण स्थान था। प्राचीन ग्राम–संगठन, न्यूनाधिक रूप में एक नैसर्गिक विकास का प्रतिफल था न कि किसी केन्द्रिय शासन की उपज। जिस क्षेत्र में लोग सामूहिक रूप से निवास करते थे, उसे जनपद कहा जाता था। कुलों के समूह को 'गोत्र' कहते थे तथा गोत्रों के समूह का नाम 'गोष्ठी' था। कई गोष्ठियों के समूह से एक ग्राम बनता था जिसका प्रधान 'ग्रामणी' कहा जाता था। ग्रामणी का उल्लेख मनु ने भी किया है, जिसे सामग्री के रूप में अनुमोदित राशि मिलती थी। मनु तथा कौटिल्य ने 'ग्रामणी' की जगह 'ग्रामिक' शब्द का प्रयोग किया किया है। ग्रामणी न्यायिक प्रशासन में स्थानीय इकाई का प्रधान था। उसका पद चुना हुआ था और अपराध विधि में उसे अधिक अधिकार प्राप्त थे। वेदों के 'ग्रामवादिन' को मैकडॉनल और कीथ ग्राम सभा का अध्यक्ष मानते हैं।[2]

परिषद

वैदिक उदाहरणों से परिषद की एतिहासिक परम्परा पर प्रकाश पड़ता है। धर्मसूत्रों और उनके बाद परिषद का वैधानिक रूप स्पष्ट होता है। ऋग्वेद से अर्थशास्त्र तक परिषद की परम्परा के अध्ययन से उसमें न्यायपालिका सम्बंधी तथ्यों का स्पष्टीकरण होता है।[3] परिषद में राजा की उपस्थिति का उल्लेख ब्राह्मण ग्रंथो में मिलता है। उपनिषदों एवं गृहसूत्रों के समय सामाजिक परिवर्तनों का प्रभाव परिषद पर भी पड़ा। वैदिक इण्डेक्स के लेखकों का मानना है कि 'परिषद' ऐसी समिति थी जो केवल दार्शनिक विषयों पर अपना मत तथा निर्णय देती थी किन्तु परवर्ती साहित्य से यह अभिव्यक्त होता है कि धार्मिक विषयों के निर्णय के अतिरिक्त यह न्यायाधीशों के साथ सभ्यों के रूप में मत व्यक्त करती थी तथा प्रधानमंत्री या सामान्य मंत्री के सहयोगी के रूप में भी अपना मत व्यक्त करती थी।[4]

उपनिषद् काल के पश्चात् सूत्रकाल तक परिषद का स्वरूप दार्शनिक से हटकर विधि–व्याख्याता के रूप में विकसित हो गया। उसके गठन तथा सदस्यता आदि के विषय में नियम निर्धारित किये गये। गौतम के अनुसार उसमें दस सदस्यों का होना अनिवार्य है, जिसमें

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  धीरेन्द्र नाथ चाबे, शोध छात्र, हिन्दी विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी
- भारतीय नाट्य मण्डप की प्रासंगिकता — 217-219
  पूजा मिश्रा, सहायक आचार्य, (तदर्थ) संस्कृत, माता सुंदरी महिला महाविद्यालय, दिल्ली विश्वविद्यालय, दिल्ली
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  अमरनाथ सिंह, दर्शन एवं धर्म विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी
- श्री अरविन्द-साहित्य में राष्ट्रवादी चिन्तन — 222-225
  अश्वनी कुमार, शोध छात्र, दर्शन एवं धर्म विज्ञान, काशी हिन्दू विश्वविद्यालय, वाराणसी।
- नागार्जुन : एक दृष्टि — 226-228
  सत्यवीर, शोध छात्र, हिन्दी विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी-221005
- महाकाव्यों में वर्णित न्याय एवं दण्ड व्यवस्था — 229-233
  अर्चना गुप्ता, शोध छात्रा, राजनीति विज्ञान विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी।
- प्राचीन भारत में शिल्प व उद्योग — 234-239
  डॉ. अवनीश कुमार सिंह, प्राचीन भारतीय इतिहास, संस्कृति एवं पुरातत्व विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी।
- शान्तिपर्व एवं अनुशासनपर्व में वर्णित कराधान : एक अध्ययन — 240-246
  डॉ. मीनाक्षी सिंह, एसोसिएट प्रोफेसर, प्रा.भा.इ. एवं सं. तथा पुरातत्व विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी
  शानु आनन्द, शोध छात्र प्रा.भा.इ. एवं सं. तथा पुरातत्व विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी
  पंकज कुमार, शोध छात्र प्रा.भा.इ. एवं सं. तथा पुरातत्व विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी
  श्रवण कुमार यादव, शोध छात्र प्रा.भा.इ. एवं सं. तथा पुरातत्व विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी
- भवभूति साहित्य में चित्रकला — 247-250
  डॉ. राहुल, असिस्टेन्ट प्रोफेसर, संस्कृत विभाग, पी.जी. कॉलेज गाजीपुर, गाजीपुर, उ.प्र.
- संगीत शिक्षण परम्परा का सैद्धान्तिक अध्ययन एवं क्रमिक विकास — 251-253
  मनीष कुमार वर्मा, शोध छात्र, गायन विभाग, संगीत एवं मंच कला संकाय, काशी हिन्दू विश्वविद्यालय, वाराणसी
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प्राचीन भारतीय विधि की व्यावहारिकता का विश्लेषणात्मक अध्ययन

अर्चना गुप्ता

प्राचीन भारतीय न्यायविदों ने न्याय को धर्म का ही एक भाग माना है, जिसका प्रारम्भिक स्वरूप धर्मसूत्रों एवं स्मृतियों में पाया जाता है, जो दूसरे अर्थों में मानव–आचार संहिता है। धर्मशास्त्रकारों के अनुसार प्राचीन भारतीय न्याय के मूल स्रोत वेद (श्रुति), स्मृति, धर्मशास्त्रग्रंथ, सदाचार एवं परिषद् हैं। पुराण, न्याय मीमांसा पर की गई टीकाएँ भी प्राचीन भारतीय न्याय–प्रशासन पर प्रकाश डालती हैं और विधि की व्यवहारिकता को सिद्ध करती हैं।

वेदों में विधि के स्रोत निहित हैं। प्राचीन भारतीय न्याय प्रशासन ऋत से प्रारम्भ होता है। वैदिक काल में विधि ऋत के रूप में ही थी।[1] उसकी शक्ति सर्वोच्च थी तथा उसी के आधार पर समाज को संगठित करने का प्रयास किया गया। मानव कल्याण के सभी पदार्थ ऋत में निहित रहते हैं और ऋत द्वारा ही उनका मानव कल्याण के हित में विनियोग होता है।[2]

स्मृतियों के अध्ययन से यह स्पष्ट हो जाता है कि प्राचीन भारतीय विधि काल्पनिक नहीं थी बल्कि व्यवहार में प्रचलित थी। स्मृतियों में विधि के लिए 'व्यवहार' शब्द का प्रयोग किया गया है। मनु के अनुसार इसका अर्थ है– झगड़ा या वाद।[3] सर्वप्रथम मनुस्मृति में 18 विषयों अथवा व्यवहार पदों के नाम गिनाएँ गए हैं। वे इस प्रकार हैं– ऋणादान, निक्षेप, अस्वामिविक्रय, सम्भूयसमुत्थान, दत्तस्यानपाकर्म, वेतनादान, संविद्व्यतिक्रम, क्रयविक्रयानुशय, स्वामिपालविवाद, सीमाविवाद, वाक्पारुष्य, दण्डपारुष्य, स्तेय, साहस, स्त्रीपुंधर्म, विभाग, धूतसमाह्वय।[4] मनुस्मृति में व्यवहार सम्बंधी विस्तृत विवरण अध्याय 8 व अध्याय 9 में दिया गया है। न्याय व्यवस्था पर मनु का विवरण बहुत रोचक और व्यवस्थित तरीके से दिया गया है। मनु विश्व के सर्वप्रथम विधि–प्रणेता के रूप में सर्वमान्य हैं। इतना ही नहीं इस स्मृति का प्रसार सुदूर पूर्वी द्वीपों में भी था। बर्मा का 'धम्मथट' मनुस्मृति पर ही केन्द्रित है।

मनु ने अपराध 5 प्रकार के माने हैं, यथा– वाक्पारुष्य, दण्डपारुष्य, स्तेय, स्त्री संग्रहण तथा अन्य दण्ड। अपशब्दों के प्रयोग अथवा मन में क्षोभ उत्पन्न करने वाले शब्दों को वाक्पारुष्य कहा गया है। किसी को हाथ, पैर, मुद्रा, डण्डा, कीचड़ आदि से पीड़ा पहुँचाना दण्डपारुष्य है। स्तेय का तात्पर्य चोरी से है। मनु ने चोरी के दो रूप बताए हैं प्रच्छन्न और अप्रच्छन्न चोरी अर्थात् सामने व पीठ पीछे छिपकर चोरी करने वाले। मनु का यह भी कहना है कि चोर की चोरी सिद्ध होने पर ही चोर को मृत्युदण्ड दिया जाए अन्यथा नहीं। चोर को आश्रय देने वाले को भी वध योग्य माना गया है।[5]

मनुस्मृति के अध्याय 8 के श्लोक संख्या 352 से 387 में परस्त्री व्यभिचार करने वालों के सन्दर्भ में चर्चा करते हुए राजा को यह अधिकार दिया है कि वह ऐसे लोगों का अंग–भंग करके देश से निकाल दे।[6] मनु ने अन्य अपराधों में रिश्वत लेना, यातायात में किसी को चोट मारना और उसका मर जाना, वैद्य की असावधानी से मृत्यु आदि होना, असत्य गवाही देना आदि अनगिनत अपराध गिनाए हैं। सभी के लिए दण्ड की व्यवस्था भी तदनुसार ही बताई है।

मनुस्मृति में न्याय तथा विधि सम्बन्धी प्रगतिशील विचारधारा है। मनुस्मृति में राजा प्रारम्भिक एवं अंतिम न्यायालय है। सर्वोच्च न्यायालय के रूप में राजा दण्ड देने का अन्तिम अधिकारी है। राजा की भूमिका आधुनिक सुप्रीम कोर्ट जैसा ही है।[7] इस प्रकार न्याय व्यवस्था की सम्पूर्ण

(33)

भारत में न्यायिक सक्रियता व जनहितवाद

अर्चना गुप्ता*

सारां''।

व्यक्ति एवं समाज के सहअस्तित्व के लिए निर्धारित नियम एवम् सिद्धांत ही विधि है। मनुष्य की स्वाभाविक स्वार्थपरता एवम् उच्श्रृंखलता को नियंत्रि कर सामाजिक विघटन की प्रक्रिया को रोकने के लिए न्याय एवं न्याय–प्रशासन की आवश्यकता होती है। नई परिस्थितियों से साम्य एवं गतिशीलता स्थापित कर विकास का मार्ग प्रशस्त करने में भी न्याय–प्रशासन की महत्वपूर्ण भूमिका रही है। इस तरह समाज के विभिन्न घटकों में सामंजस्य स्थापित करने के लिए कानून व्यवस्था परमावश्यक है। न्याय प्रशासन का मुख्य उद्देश्य सत्य को प्रस्तुत करना तथा समाज को निर्धारित नियमों से बाँधकर रखना है। मनुष्य के लिए निर्धारित आचार संहिता का पालन सामाजिक संवृद्धि के लिए आवश्यक है। न्याय–प्रशासन समाज द्वारा स्वीकृत आचार संहित को बनाये रखने का एक सशक्त प्रयास है।
पिछले दो दशकों में भारत की न्याय व्यवस्था के स्वरूप में क्रांतिकारी परिवर्तन आया है। इन दशकों में न्यायपालिका का आकार, प्रक्रिया, व्यवहार, क्षेत्राधिकार और विशेष रूप से उसका लक्ष्य ही बदल गया है। वर्तमान में न्यायपालिका का लक्ष्य व्यक्तिगत न्याय के साथ सामाजिक न्याय की स्थापना करना हो गया है। आज न्यायपालिका केवल न्याय प्रदान करने का ही कार्य नहीं कर रही है वरन् एक प्रशासक, सुधारक, अनुसंधानकर्ता और नीति–निर्धारक की भूमिका भी अदा कर रही है।

पिछले दो दशकों में भारत की न्याय व्यवस्था के स्वरूप में क्रांतिकारी परिवर्तन आया है। इन दशकों में न्यायपालिका का आकार, प्रक्रिया, व्यवहार, क्षेत्राधिकार और विशेष रूप से उसका लक्ष्य ही बदल गया है। वर्तमान में न्यायपालिका का लक्ष्य व्यक्तिगत न्याय के साथ सामाजिक न्याय की स्थापना करना हो गया है। आज न्यायपालिका केवल न्याय प्रदान करने का ही कार्य नहीं कर रही है वरन् एक प्रशासक, सुधारक, अनुसंधानकर्ता और नीति–निर्धारक की

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दालता की भागीदारी। चूँकि इस सम्मेलन का कांग्रेस ने बहिष्कार किया था, इसलिए यह किसी निर्णय पर पहुँचे बिना ही समाप्त हो गया।

डा0 अंबेडकर ने साप्ताहिक हरिजन के लिए यह कहते हुये संदेश देने से इन्कार कर दिया कि जाति–व्यवस्था को नष्ट किया बिना अछूतों का उद्धार संभव नहीं है, जैसा कि किसान आंदोलन के मामले में हुआ था, गाँधीवादी हरिजन कार्य भी, अधिक रूप से नीचे से अधिक संभावनापूर्ण दबावों पर वर्चस्व स्थापित करने का प्रयास किया था। तमिलनाडु में ई0वी0 रामास्वामी नायकर का आत्मसम्मान आंदोलन चौथे दशक के आरंभ में तेजी से फैला इसके ब्राह्मणवादी विरोधी लोकवादी शैली विकसित कर ली जो 1932 में सोवियत संघ से लौटकर नायकर ने कोयम्बटूर में स्टालिन हाल का निर्माण करवाया और बुजुर्ग कम्युनिस्ट नेता सिंगारवेलु चेटियार के नास्तिकवादी एवं समाजवादी लेखन के लिए अपनी पत्रिका कुडी आरासू के द्वार खोल दिये।

डा0 अंबेडकर संवैधानिक एवं कानूनी कदमों के अंग थे। आजादी से पहले के मतभेदों के बावजूद कांग्रेस ने उन्हें संविधान की मसविदा (प्रारूप) समिति का अध्यक्ष बनाया और वे नेहरू की कैबिनेट में कानून मंत्री थे। लेकिन बाद में मतभेद पैदा हो गए उन्होंने सरकार छोड़ दी और अखिल भारतीय अनुसूचित जाति महासंघ का निर्माण किया। इस संगठन ने चुनाव भी लड़े लेकिन आरक्षित सीटों में यह अधिकतर कांग्रेस से हार गयी। 1956 में उन्होंने फिर से धर्मान्तरण की नीति अपना ली और इसे जरूरी बताया। यह जल्द ही बौद्ध धर्म स्वीकार कर लिया गया। दलित राजनीति का दुसरा काल 1960 से 1980 तक का है दलित आंदोलन ब्राह्मणवाद और पूँजीवाद के लिए घातक था, दीक्षा समारोह घातक नहीं था कम से कम इस घटना से हम उन परिस्थितियों को समझ सकते है जिनसे दलित आंदोलन को गुजरना पड़ा।

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भारत में गठबंधन की राजनीति : लोकतंत्र के बदलते आयाम

अर्चना गुप्ता

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"मिलीजुली सरकारों के गठन और जीवन तथा कार्यकरण के लिए जिस प्रतिभा और संस्कृति की आवश्यकता होती है, भारत की लोकतांत्रिक राजनीति में अभी तक वस्तुतः उसका अभाव रहा है। अस्थायी मिलीजुली, सरकारों या अल्पमत सरकारों के क्रम ने राज्य के संकट में योगदान किया है, क्योंकि राज्य सरकार के साथ गुंथा हुआ है।"[1]

भारत अपनी स्वतंत्रता के लगभग 65 वर्ष पूरे कर चुका है। इन 65 वर्षों में भारतीय राजनीति और शासन व्यवस्था में कुछ ऐसे आमूल परिवर्तन हुए हैं, जिनकी कल्पना भी नहीं की जा सकती थी। विशेषकर 1967 के बाद से भारतीय राजनीति में कुछ नये मोड़ आये, जैसे देश में एकदलीय प्रभुत्व का अन्त, केन्द्र तथा राज्यों में मिश्रित सरकारों की स्थापना, संविधान में बड़ी संख्या में मूलभूत संशोधन, संसद और न्यायपालिका के बीच सर्वोच्चता की समस्या, क्षेत्रीय राजनीतिक दलों का सशक्त रूप में विकास आदि ऐसी घटनाएँ हैं, जिन्होंने भारतीय राजनीति और शासन के मूलस्वरूप को बहुत अधिक प्रभावित किया है। भारत में गठबंधन की राजनीति की शुरूआत 1967 के चतुर्थ आम चुनाव के बाद से हुई। इस चुनाव में कांग्रेस दल के राजनीतिक एकाधिकार का अन्त हो गया। इस चुनाव में केन्द्र में यद्यपि कांग्रेस दल को ही बहुमत प्राप्त हुआ, लेकिन इसे प्राप्त स्थानों में भारी कमी आयी। 1967 में जिन 16 राज्यों में विधानसभा के चुनाव हुए उनमें से आठ राज्यों में कांग्रेस सहित कोई भी राजनीतिक दल पूर्ण बहुमत पाने में असफल रहा। इस प्रकार देश के सांविधानिक इतिहास में पहली बार आठ राज्यों में मिश्रित मंत्रिमण्डल का निर्माण हुआ। वास्तविकता यह है कि मिली जुली सरकार का पूरा अनुभव 1967–71 के बीच ही हुआ। इन चार वर्षों में 32 राज्य सरकारों का निर्माण और अन्त हुआ।[2]

साधारणतया मिश्रित मंत्रिमण्डल का गठन उन देशों में होता है जहाँ अनेक छोटे–छोटे दल हों और कोई ऐसा प्रभावशाली राजनीतिक दल न हो जो, सदन में स्पष्ट बहुमत पा सके। ऑग के अनुसार, "मिलीजुली सरकार एक ऐसे सहयोग प्रबन्ध का नाम है, जिसमें विभिन्न राजनीतिक दलों के सदस्य सरकार के गठन या मंत्रिमण्डल के निर्माण के लिए एक हो जाते हैं।" मिलीजुली सरकार राजनीतिक समुदायों तथा शक्तियों का गठजोड़ है जो अस्थायी और कुछ विशिष्ट प्रयोजनों के लिए होता है। राजनीतिक दलों का यह मिलन

[illegible] की ऐतिहासिकता की है। वैदिक काल में राजा, राजशक्ति, सामाजिक संगठन एवं न्यायिक संगठनों का [illegible] मिलता है, किन्तु राज्य नामक संस्था का उल्लेख नहीं है। सभा, समिति जैसे संगठनों, [illegible] आदि से स्पष्ट है कि वैदिक काल के मध्य राजशक्ति का उदय हो चुका था। इतना अवश्य है कि राजशक्ति का स्रोत एवं केन्द्र सामाजिक संगठन थे। उत्तर वैदिक काल में राजशक्ति का स्पष्ट विकास होता है। [illegible] राज्य के अनेक अंगों आदि का उल्लेख मिलने लगता है। [illegible] पर राज्य नामक संस्था का गठन होता है। वस्तुतः परवर्ती युग अर्थात् अर्थशास्त्र, मनुस्मृति आदि [illegible] में राज्य के सभी घटकों, उनके परस्पर सम्बन्ध आदि स्पष्ट रूप से मिल जाता है।

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भारतीय राजनीति में न्याय का प्राचीन व वर्तमान स्वरूप

अर्चना गुप्ता

न्याय का सम्बन्ध मानव संस्कृति के साथ अनन्य रूप से जुड़ा हुआ है। मानव जैसे-जैसे युगों के साथ अपने को जोड़ते हुए विकास करता गया, वह लगभग उसी क्रम में असभ्य से सभ्य भी होता गया। वस्तुतः प्राचीन भारत में अस्तित्व में रही न्याय की परम्परा उतनी ही पुरानी है जितनी की मानवता। भारत की समृद्ध एवं उन्नत न्याय परम्परा की नींव प्राचीन काल में ही पड़ी।

न्याय का प्राचीन स्वरूप-

भारतीय विधि विश्व की प्राचीनतम जीवित योजना है। प्राचीन भारतीय विधि का मूल स्रोत श्रुत है। न्याय के प्राचीन स्वरूप का वर्णन निम्न बिन्दुओं के अन्तर्गत किया जा सकता है-

1. न्याय व्यवस्था धर्म से सम्बद्ध -

प्राचीन भारतीय न्याय व्यवस्था धर्म से आबद्ध थी। 'धर्म' समस्त भारतीय शास्त्रीय चिंतन में [illegible] रहा है। भारतीय संस्कृति में 'धर्म' का तात्पर्य कर्मकाण्डों से नहीं है बल्कि धर्म सदाचार व कर्तव्यों के पालन में निहित है इस रूप में जिसका जो भी कर्तव्य है, उसका निष्ठापूर्वक पालन ही उसके लिए धर्म कहा जा सकता है। समाज में न्याय की स्थापना तभी हो सकती है जब प्रत्येक व्यक्ति अपने निर्धारित कर्तव्यों का निष्ठापूर्वक पालन करें। न्याय में ही धर्म का तत्व निहित है, जब दण्ड द्वारा अशुभ का परिहार किया जाता है तब भी धर्म की स्थापना ही लक्ष्य होता है। वस्तुतः न्याय की अवधारणा धर्म की स्थापना को ही लक्ष्य करके विकसित की गयी है। प्राचीन भारत में न्यायालयों के लिए 'धर्माधिकरण' तथा 'धर्म सभा' जैसे शब्द प्रयुक्त होते थे, व न्यायाधीश को 'धर्माधिकारी' कहा जाता था। न्यायाधीश के आसन को 'धर्मासन' कहा जाता था। इन तथ्यों से ध्वनित होता है कि धर्म व न्याय एक दूसरे में समाहित थे।

2. न्यायाधीशों की नियुक्ति योग्यता के आधार पर-

न्यायाधीश के गुणों का वर्णन बहुधा मिलता है। आपस्तम्बधर्मसूत्र के अनुसार न्यायाधीशों में विद्या, कुलीन वंशोत्पत्ति, वृद्धावस्था, चातुर्य तथा धर्म के प्रति सावधानी होनी चाहिए। नारद के अनुसार न्यायाधीश को अठारहों सम्पत्ति-विवाद सम्बन्धी कानूनों में, उनके 8000 उपभेदों, आन्वीक्षिकी वेद एवं स्मृतियों में पारंगत होना चाहिए। जिस प्रकार वैद्य शल्य चिकित्सा में पारंगत होने के कारण शल्य-प्रयोग से शरीर में घुसे लोहे के टुकड़े को निकाल देता है, उसी प्रकार कुशल न्यायाधीश को पेचीदे मामले में से धोखे की बातें अलग निकाल देनी चाहिए। कौटिल्य ने अमात्यों की नियुक्ति के लिए धर्म, अर्थ, काम एवं भय के अवसरों में प्रलोभन आदि से परीक्षा लेने की सम्मति दी है, किन्तु मंत्रियों के लिए सत्यता (ईमानदारी) एवं विश्वासपात्रता की जाँच सभी प्रकार की परीक्षाओं के सम्मिलित रूप में आवश्यक मानी है। इस प्रकार की जाँच प्रणाली को उपधा कहते हैं। नीतिवाक्यामृत ने 'उपधा' की परिभाषा की है। कई प्रकार के उपायों से (गुप्तचरों द्वारा) धर्म, अर्थ, काम एवं भय के अवसरों में मनुष्यों का परीक्षण ही उपधा है।

3. न्यायिक कार्यों में पारदर्शिता व निष्पक्षता-

निष्पक्ष न्याय करना एवं अपराधी को दण्ड देना राजा के प्रमुख कार्यों में था। राजा न्याय का स्रोत माना जाता था। कौटिल्य ने लिखा है कि दिन के दूसरे भाग में राजा को पौर-जानपदों (नागरवासियों एवं ग्रामवासियों) के झगड़ों को निपटाना चाहिए। मनु ने भी लिखा है कि लोगों के झगड़ों को निपटाने की इच्छा से राजा को ब्राह्मणों एवं मंत्रियों के साथ सभा (न्याय-भवन) में प्रवेश करना चाहिए और प्रति दिन