A facile access to the synthesis of functionalised unsymmetrical biaryls from 2*H*-pyran-2-ones through carbanion induced C–C bond formation †

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A convenient synthesis of highly functionalised biaryls **3** and **6** has been delineated through carbanion induced C–C bond formation from 6-aryl-3-cyano-4-substituted-2*H*-pyran-2-ones (**1**, **4**) and acetone. Extension of this reaction, using aromatic ketones led to (4,6-diarylpyran-2-ylidene)acetonitrile (**7**) in lieu of the anticipated 2,4-diaryl-6-methylthiobenzonitrile (**8**). The structure of 2-methyl-6-methylthio-4-(3,4-methylenedioxyphenyl)benzonitrile (**3f**) was ascertained by single crystal X-ray diffraction analysis and displayed a variety of weak interactions, responsible for the stability and packing of the molecule in the crystalline state.

Introduction

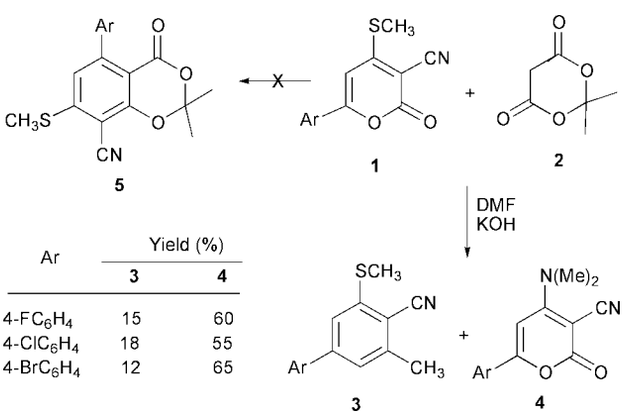
The biaryl system serves as a central building block in numerous natural products of biological significance. Besides diverse therapeutic potential, these compounds display interesting properties as chiral reagents[1] and crown ethers,[2] as chiral host molecules for inclusion compounds,[3] as chiral phases for chromatography[4] and as chiral liquid crystals.[5]

Symmetrical biaryls have been synthesized earlier by coupling of two aromatic moieties in the presence of different coupling reagents.[6–14] A highly versatile procedure, commonly used in natural product synthesis, is based on palladium catalysed cross coupling of electrophilic (R–X) species and arylboronic acid.[15] Unsymmetrical biaryls have been synthesized from 2*H*-pyran-2-one either by Diels–Alder reactions[16] or by ring transformation from Grignard reagents.[17] Unsymmetrical biaryls have been also obtained[18] through dihydrooxazole-mediated coupling reactions.

Results and discussion

We report here an alternative efficient and convenient synthesis of unsymmetrical biaryls from 6-aryl-3-cyano-4-substituted-2*H*-pyran-2-ones (**1**, **4**) obtained from the reaction of ethyl 2-cyano-3,3-dimethylthioacrylate and an aromatic ketone[19] using acetone as a source of carbanion, generated *in situ* or as a reagent. This reaction is of high synthetic significance in terms of (1) versatility and compatibility, (2) mild reaction conditions, (3) use of cost effective reagents, (4) easy work-up, and (5) no use of catalyst. The only limitation of this reaction is that aromatic ketones do not follow the same course of reaction to yield **8**, as enolization is favoured followed by cyclization to form (4,6-diarylpyran-2-ylidene)acetonitrile (**7**).

The synthesis of biaryls is based on the carbanion induced ring transformation of 6-aryl-3-cyano-4-substituted-2*H*-pyran-2-one (**1**, **4**) with acetone. Pyran-2-ones (**1** and **4**) may be considered to be a cyclic methylthioketene hemiacetal (**1**) and a cyclic ketene hemiaminal (**4**) with three electrophilic centres C-2, C-4 and C-6 in which C-6 is highly vulnerable to nucleophilic attack due to extended conjugation and the presence of an electron withdrawing substituent at position 3 of the pyran ring. Reaction of **1** with the anion obtained from 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) failed to provide the anticipated product, 5-aryl-8-cyano-2,2-dimethyl-7-methylthio-4*H*-1,3-benzodioxin-4-one (**5**). The products isolated were assigned as 4-aryl-2-methyl-6-methylthiobenzonitrile (**3**) and 6-aryl-3-cyano-4-dimethylamino-2*H*-pyran-2-one (**4**). The genesis for compounds **3** and **4** is based on the reaction of **1** with acetone and dimethylamine formed *in situ* from Meldrum's acid and DMF respectively from the reaction mixture (Scheme 1).



Ar	Yield (%)	
	3	**4**
4-FC_6H_4	15	60
4-ClC_6H_4	18	55
4-BrC_6H_4	12	65

Scheme 1

Under similar reaction conditions no product analogous to **4** was obtained in the absence of Meldrum's acid while in the reaction without DMF neither compound **3** nor **4** was isolated. These observations confirmed that DMF plays an important role in the generation of acetone and dimethylamine *in situ* from the reaction mixture. A change of solvent from DMF to DMSO also failed to yield ring transformed product **3**.

The structure of both the compounds (**3**, **4**) was also ascertained by their independent synthesis from the reaction of **1** with acetone and dimethylamine. The formation of **3** is presumed to occur through attack of the carbanion generated from acetone *in situ* at C-6 in **1** with ring opening, followed by decarboxylation and recyclization involving carbonyl and methylene groups. A plausible mechanism for the reaction is

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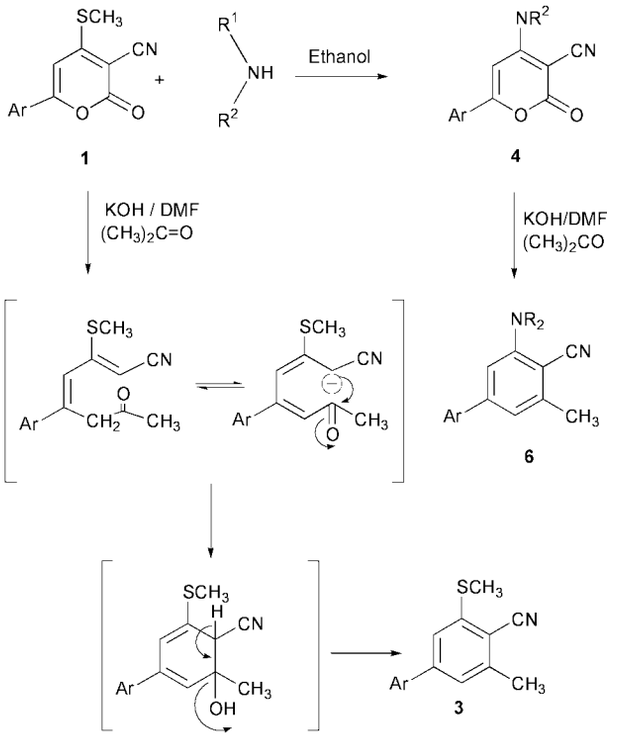


1,3, 4,6	Ar	NR^2	Yield (%) 3	4	6
a	4-FC_6H_4	$(CH_3)_2N$	65	70	-
b	4-ClC_6H_4	$(CH_3)_2N$	68	73	62.8
c	4-BrC_6H_4	$(CH_3)_2N$	58	70	-
d	4-$NO_2C_6H_4$	$(CH_3)_2N$	69	70	-
e	3,4-$Cl_2C_6H_3$	$(CH_3)_2N$	62	75	50
f	3,4-$CH_2O_2C_6H_3$	$(CH_3)_2N$	68	69.7	-
g	4-FC_6H_4	4-methylpiperidino	-	70	62
h	4-ClC_6H_4	4-methylpiperidino	-	70	48.9

Scheme 2

depicted in Scheme 2. The scope of this reaction was further explored by subjecting 6-aryl-3-cyano-4-substituted-2*H*-pyran-2-one (**4**) to ring transformation reactions from acetone analogously. The product isolated in moderate yield from this reaction was spectroscopically characterized as 4-aryl-2-methyl-6-substituted-benzonitrile (**6**).

This reaction provided conclusive evidence that the SCH_3 substituent at position 4 in **1** is not essential for the ring transformation reactions. However the reaction of lactone **1** with aromatic ketones did not follow the same course of reaction, and failed to yield the anticipated 1,3-teraryl (**8**) as it favours enolization followed by cyclization. In this reaction the anion generated from the aromatic ketone attacks at the C-6 position in **1** with ring opening followed by decarboxylation, enolization and cyclization with elimination of methanethiol to yield (4,6-diarylpyran-2-ylidene)acetonitrile (**7**). The configuration of the isolated geometrical isomer **7** was ascertained by an NOE experiment. Irradiation of vinylic proton at δ 6.45 showed enhancement in the signal intensity of the H-3 proton by 25% without any change in signal intensity of the H-5 proton, which unambiguously confirmed the *Z* configuration of the isolated product **7** (Scheme 3). The 6-aryl substituent in **1** plays a pivotal role in the ring transformation reactions by either increasing or maintaining the electrophilicity of the C-6 carbon of the pyran ring but reduction in the electropositive character of C-6 by the presence of an alkyl substituent, did not yield desired compound. Thus the reaction of 3-cyano-6-methyl-4-methylthio-2*H*-pyran-2-ones with acetone failed to yield a compound analogous to **3** but led to recovery of starting material.

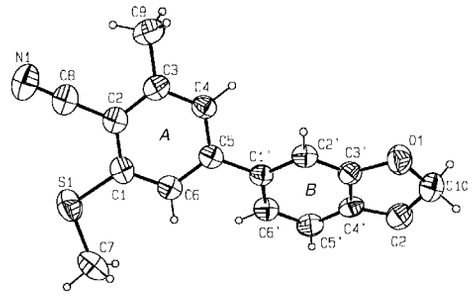
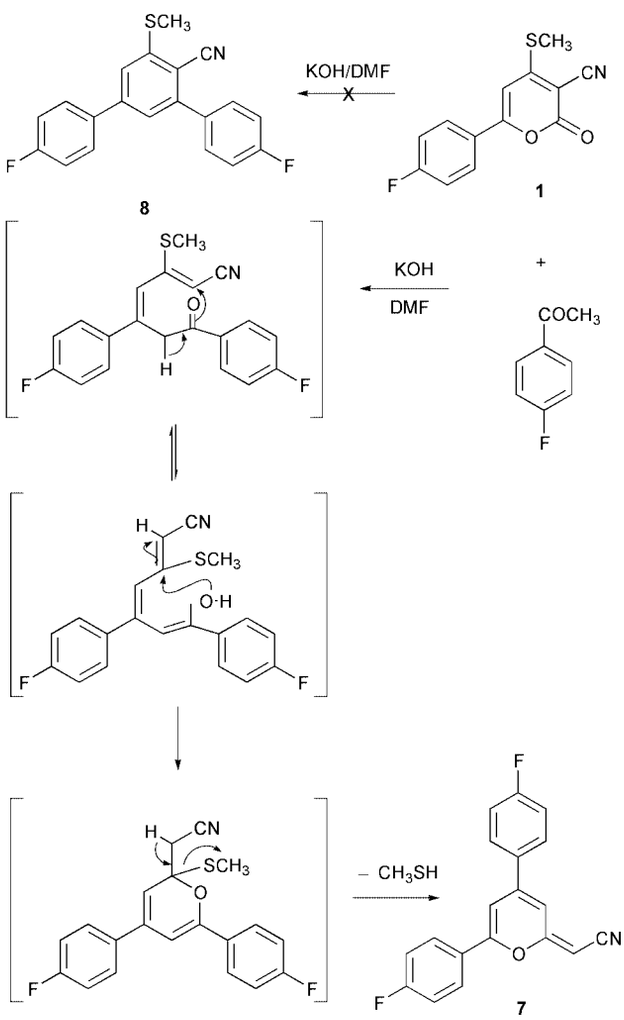


Fig. 1 Crystal structure of compound **3f**.



Scheme 3

The structure of one of the biaryls (**3f**) was further confirmed by single crystal X-ray diffraction analysis. The crystal structure of **3f** (Fig. 1) showed that ring *A* is twisted with respect to ring *B* by an angle of 30.7°.

The crystal packing revealed some interesting aspects of weak, intermolecular non-covalent interactions. Weak hydrogen bonds of the nature of C–H···O, C–H···N and uncommon C–H···S interactions are present. The importance of such interactions is currently being recognised in the stability of nucleic acids,[20] protein structures, molecular recognition processes, crystal engineering[21] and supramolecular design. The important hydrogen bonding parameters are shown in Table 1.

The observed C–H···A (A = N, O and S) geometrical parameters compare well with the literature values. There are only a few previous reports of C–H···S interactions.[22]

The four molecules in the unit cell (Fig. 2) show intermolecular aromatic π–π interactions (APPI). The molecules

Table 1 Intermolecular distances and angles for C–H · · · A interactions in **3f**

H-bond	H · · · A/Å	C · · · A/Å	C–H · · · A/°
C9–H9C · · · N1(X, 1 − Y, −1/2 + Z)	2.880	3.817	165.5
C5′–H5′ · · · N1(−1/2 + X, −1/2 + Y, −1 + Z)	2.804	3.702	162.5
C7–H7A · · · O1(1/2 + X, −1/2 + Y, 1 + Z)	2.638	3.591	171.6
C4–H4 · · · S1(−1/2 + X, 1/2 − Y, −1/2 + Z)	3.191	3.882	132.7
C6–H6 · · · S1(X, − Y, −1/2 + Z)	3.289	4.131	151.7

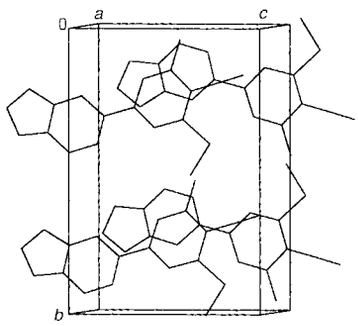


Fig. 2 Crystal packing of compound **3f**.

are stacked in pairs (along the *a*-axis), each with a symmetry-translated molecule at an equivalent position. Phenyl rings (*A*) and (*B*) overlap in an offset geometry. This is in accordance with Hunter's electrostatic model[23–26] of APPI. The stacked rings are separated by an average interplanar distance of 3.5 Å, while the centre-to-centre distance measures 4.16 Å. The stacked rings are almost parallel (angle between the planes ~7.6°) but are rotated almost by ~31° about the stacking axis. This, thus presents an interesting example of the contribution of these weak interactions towards the stability and packing of the molecule **3f** in the crystalline state.

Experimental

General

Mps were determined in an open capillary with a Büchi-530 melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker WM (400 MHz) spectrometer using TMS as reference. IR spectra were obtained in KBr discs on a Perkin-Elmer Ac-1 spectrophotometer. EI mass spectra were obtained at 70 eV using a JEOL JMS-D 300 spectrometer. Elemental analyses (C,H,N) were carried out on a Carlo Erba-1108 elemental analyser. TLC was performed on 7 × 3 cm thin layer analytical plates (SRL).

Precursors **1** and **4** were synthesized according to standard procedures.[19] The structure of the product **3f** was assigned by single crystal X-ray diffraction.

Synthesis of 4-aryl-2-methyl-6-methylthiobenzonitrile (3) and 6-aryl-3-cyano-4-dimethylamino-2*H*-pyran-2-one (4)

General procedure A. A mixture of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-one (**1**, 1 mmol) and 2,2-dimethyl-1,3-dioxane-4,6-dione (**2**, 1 mmol) in dry DMF (12 ml) containing powdered KOH (0.22 g, 4 mmol) was stirred under an atmosphere of nitrogen at ambient temperature for 30 h. After completion of the reaction, the mixture was poured into ice–water and acidified with 10% HCl. The precipitate obtained was collected and purified on a silica gel column using hexane as eluent.

The two products isolated from the column were characterized as 4-aryl-2-methyl-6-methylthiobenzonitrile (**3**) and 6-aryl-3-cyano-4-dimethylamino-2*H*-pyran-2-one (**4**).

Both compounds **3** and **4** were further independently synthesized.

General procedure B. A mixture of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-one (**1**, 10 mmol), acetone (15 mmol) and potassium hydroxide (15 mmol) in dry DMF was stirred at room temperature under a nitrogen blanket for 30 h. The reaction mixture was poured into ice–water with vigorous stirring for half an hour, and thereafter acidified with 10% HCl. The precipitate obtained was filtered, washed with water and purified on a silica gel column using chloroform–hexane (1 : 1) as eluent.

The yields of the isolated products prepared by following procedure B are given below.

4-(4-Fluorophenyl)-2-methyl-6-methylthiobenzonitrile (3a). Yield: 65%; mp: 106 °C; ν_{max}/cm^{-1} 2212 (CN); *m*/*z* (EI) 257 (M$^+$, 27%), 256 (100), 241 (3.5), 240 (9.6), 224 (34.1), 208 (15.6), 182 (12.2); δ_H (200 MHz, $CDCl_3$) 2.59 (s, 3H, CH_3), 2.60 (s, 3H, SCH_3), 7.23 (s, 1H, ArH), 7.25 (s, 1H, ArH), 7.26–7.28 (m, 2H, ArH), 7.52–7.57 (m, 2H, ArH) (Found: C, 69.80; H, 4.92; N, 5.63. $C_{15}H_{12}FNS$ requires: C, 70.01; H, 4.70; N, 5.44%).

4-(4-Chlorophenyl)-2-methyl-6-methylthiobenzonitrile (3b). Yield: 68%; mp: 85 °C; ν_{max}/cm^{-1} 2210 (CN); *m*/*z* (EI) 273 (M$^+$, 21.3%), 272 (39.7), 269 (34.3), 239 (11.7), 189 (11.1); δ_H (300 MHz, $CDCl_3$) 2.59 (s, 3H, CH_3), 2.60 (s, 3H, SCH_3), 7.23 (s, 1H, ArH), 7.26 (d, 2H, J = 7.8 Hz, ArH), 7.27 (s, 1H, ArH), 7.45 (d, 2H, J = 7.8 Hz, ArH) (Found: C, 65.80; H, 4.42; N, 5.33. $C_{15}H_{12}ClNS$ requires: C, 65.79; H, 4.71; N, 5.11%).

4-(4-Bromophenyl)-2-methyl-6-methylthiobenzonitrile (3c). Yield: 58%; mp: 132 °C; ν_{max}/cm^{-1} 2210 (CN); *m*/*z* (EI) 318 (M$^+$, 88.4%), 317 (100), 303 (4.5), 301 (3.4), 286 (19.3), 284 (16.9), 237 (5.3), 222 (16.2), 190 (52.0); δ_H (300 MHz, $CDCl_3$) 2.59 (s, 3H, CH_3), 2.60 (s, 3H, SCH_3), 7.23 (s, 1H, ArH), 7.26 (s, 1H, ArH), 7.43 (d, 2H, J = 8.4 Hz, ArH), 7.6 (d, 2H, J = 8.4 Hz, ArH) (Found: C, 56.48; H, 4.15; N, 4.58. $C_{15}H_{12}BrNS$ requires: C, 56.60; H, 3.80; N, 4.40%).

2-Methyl-6-methylthio-4-(4-nitrophenyl)benzonitrile (3d). Yield: 69%; mp: 193 °C; ν_{max}/cm^{-1} 2206 (CN); *m*/*z* (EI) 284 (M$^+$, 44.2%), 283 (100), 254 (14.6), 237 (42.3), 222 (17.5), 208 (20.1), 205 (22.2); δ_H (300 MHz, $CDCl_3$) 2.62 (s, 3H, CH_3), 2.63 (s, 3H, SCH_3), 7.29 (s, 1H, ArH), 7.36 (s, 1H, ArH), 7.72 (d, 2H, J = 9.3 Hz, ArH), 8.72 (d, 2H, J = 9.3 Hz, ArH) (Found: C, 63.52; H, 4.38; N, 10.21. $C_{15}H_{12}N_2O_2S$ requires: C, 63.36; H, 4.26; N, 9.89%).

4-(3,4-Dichlorophenyl)-2-methyl-6-methylthiobenzonitrile (3e). Yield: 62%; mp: 100 °C; ν_{max}/cm^{-1} 2208 (CN); *m*/*z* (EI) 308 (M$^+$, 2.2%), 307 (5.4), 279 (3.3), 200 (57.5), 187 (37.2), 185 (100); δ_H (300 MHz, $CDCl_3$) 2.57 (s, 3H, CH_3), 2.58 (s, 3H, SCH_3), 7.2 (d, 1H, J = 8.4 Hz, ArH), 7.27 (s, 1H, ArH), 7.28 (s, 1H, ArH), 7.84 (d, 1H, J = 8.1 Hz, ArH), 7.92 (s, 1H, ArH) (Found: C, 58.32; H, 4.86; N, 4.72. $C_{15}H_{11}Cl_2NS$ requires: C, 58.45; H, 4.58; N, 4.54%).

2-Methyl-4-(3,4-methylenedioxyphenyl)-6-methylthiobenzonitrile (3f). Yield: 68%; mp: 142 °C; ν_{max}/cm^{-1} 2216 (CN); *m*/*z* (EI) 283 (M$^+$, 100%), 281 (19.3), 253 (30.6), 250 (19.1), 210 (3.8); δ_H (300 MHz, $CDCl_3$) 2.54 (s, 3H, CH_3), 2.57 (s, 3H, SCH_3), 6.01 (s, 2H, CH), 6.88 (d, 1H, J = 8.4 Hz, ArH), 7.03 (d,

1H, J = 8.6 Hz, ArH), 7.04 (s, 1H, ArH), 7.17 (s, 1H, ArH), 7.20 (s, 1H, ArH) (Found: C, 68.12; H, 4.83; N, 5.23. $C_{16}H_{13}NO_2S$ requires: C, 67.82; H, 4.62; N, 4.94%).

6-Aryl-3-cyano-4-dimethylamino-2*H*-pyran-2-one (4a–f)

A mixture of 3-cyano-6-aryl-4-methylthio-2*H*-pyran-2-one (**1**, 0.26 g, 1 mmol), dimethylamine hydrochloride (0.12 g, 1.5 mmol) and potassium carbonate (0.21 g, 1.5 mmol) in acetone was refluxed for 6 h. The solvent was removed under reduced pressure and the residue was treated with water to remove the inorganic material. The product thus obtained was crystallized from methanol.

3-Cyano-4-dimethylamino-6-(4-fluorophenyl)-2*H*-pyran-2-one (4a). Yield: 0.18 g (70%); mp: 230 °C; ν_{max}/cm^{-1} 1683 (CO), 2206 (CN); *m*/*z* (EI) 258 (M^+, 82%), 243 (25), 214 (20), δ_H (300 MHz, $CDCl_3$) 3.45 (s, 6H, $(CH_3)_2N$), 6.36 (s, 1H, CH), 7.13–7.19 (m, 2H, ArH), 7.82–7.85 (m, 2H, ArH) (Found: C, 65.32; H, 4.51; N, 10.76. $C_{14}H_{11}FN_2O_2$ requires: C, 65.11; H, 4.26; N, 10.85%).

6-(4-Chlorophenyl)-3-cyano-4-dimethylamino-2*H*-pyran-2-one (4b). Yield: 0.20 g (73%); mp: 256 °C; ν_{max}/cm^{-1} 1683 (CO), 2202 (CN); *m*/*z* (EI) 276 (19.4), 274 (M^+, 56.7%), 246 (14.3), 183 (11.2), 163 (13.3), 139 (100), 111 (48); δ_H (300 MHz, $CDCl_3$) 3.46 (s, 6H, $(CH_3)_2N$), 6.40 (s, 1H, CH), 7.45 (d, 2H, J = 8.7 Hz, ArH), 7.75 (d, 2H, J = 8.7 Hz, ArH) (Found: C, 61.38; H, 4.32; N, 10.42. $C_{14}H_{11}ClN_2O_2$ requires: C, 61.26; H, 4.00; N, 10.19%).

6-(4-Bromophenyl)-3-cyano-4-dimethylamino-2*H*-pyran-2-one (4c). Yield: 0.22 g (70%); mp: 263 °C; ν_{max}/cm^{-1} 1683 (CO), 2203 (CN); *m*/*z* (EI) 319 (M^+, 75.0%), 304 (15.5), 293 (16.0), 291 (17.2), 186 (77.2), 184 (100); δ_H (300 MHz, $CDCl_3$) 3.46 (s, 6H, $(CH_3)_2N$), 6.41 (s, 1H, CH), 7.62 (d, 2H, J = 8.7 Hz, ArH), 7.68 (d, 2H, J = 8.7 Hz, ArH) (Found: C, 52.53; H, 3.56; N, 9.12. $C_{14}H_{11}BrN_2O_2$ requires: C, 52.68; H, 3.47; N, 8.78%).

3-Cyano-4-dimethylamino-6-(4-nitrophenyl)-2*H*-pyran-2-one (4d). Yield: 0.2 g (70%); mp: 234 °C; ν_{max}/cm^{-1} 1687 (CO), 2206 (CN); *m*/*z* (EI) 285 (M^+, 38.7%), 150 (70); δ_H (300 MHz, $CDCl_3$) 3.45 (s, 6H, $(CH_3)_2N$), 6.36 (s, 1H, CH), 7.28 (d, 2H, J = 8.5 Hz, ArH), 7.74 (d, 2H, J = 8.5 Hz, ArH) (Found: C, 59.21; H, 4.15; N, 14.85. $C_{14}H_{11}N_3O_4$ requires: C, 58.94; H, 3.89; N, 14.72%).

3-Cyano-6-(3,4-dichlorophenyl)-4-dimethylamino-2*H*-pyran-2-one (4e). Yield: 0.23 g (75%); mp: 240–242 °C; ν_{max}/cm^{-1} 1678 (CO), 2208 (CN); *m*/*z* (EI) 309 (M^+, 18.7%), 281 (16.4), 199 (55.7), 184 (100), 172 (59.8); δ_H (300 MHz, $CDCl_3$) 3.49 (s, 6H, $(CH_3)_2N$), 6.42 (s, 1H, CH), 7.55 (d, 1H, J = 8.4 Hz, ArH), 7.65 (d, 1H, J = 8.4 Hz, ArH), 7.92 (s, 1H, ArH) (Found: C, 54.62; H, 3.52; N, 8.98. $C_{14}H_{10}Cl_2N_2O_2$ requires: C, 54.39; H, 3.26; N, 9.06%).

3-Cyano-4-dimethylamino-6-(3,4-methylenedioxyphenyl)-2*H*-pyran-2-one (4f). Yield: 0.2 g (69.7%); mp: >280 °C; ν_{max}/cm^{-1} 1685 (CO), 2203 (CN); *m*/*z* (EI) 284 (M^+, 84%); δ_H (300 MHz, $CDCl_3$) 3.42 (s, 6H, $(CH_3)_2N$), 6.08 (s, 2H, CH), 6.31 (s, 1H, CH), 6.89 (d, 1H, J = 8.6 Hz, ArH), 7.19 (s, 1H, ArH), 7.23 (d, 1H, J = 8.8 Hz, ArH) (Found: C, 63.25; H, 4.38; N, 9.56. $C_{15}H_{12}N_2O_4$ requires: C, 63.37; H, 4.26; N, 9.86%).

3-Cyano-6-(4-fluorophenyl)-4-(4-methylpiperidino)-2*H*-pyran-2-one (4g). Yield: 0.22 g (70.5%); mp: >280 °C; ν_{max}/cm^{-1} 1685 (CO), 2203 (CN); *m*/*z* (EI) 312 (M^+, 68.4%), 298 (18.0), 268 (19.5); δ_H (300 MHz, $CDCl_3$) 1.03 (d, 3H, J = 6.5 Hz, CH_3), 1.32–1.44 (m, 1H, CH), 1.75–1.81 (m, 2H, CH_2), 1.83–1.92 (m, 2H, CH_2), 3.22–3.27 (m, 2H, NCH_2), 4.39 (t, 2H, J = 7.8 Hz, NCH_2), 6.4 (s, 1H, CH), 7.13–7.20 (m, 2H, ArH), 7.79–7.84 (m, 2H, ArH) (Found: C, 68.93; H, 5.16; N, 8.73. $C_{18}H_{17}FN_2O_2$ requires: C, 69.22; H, 5.48; N, 8.97%).

3-Cyano-6-(4-chlorophenyl)-4-(4-methylpiperidino)-2*H*-pyran-2-one (4h). Yield: 0.23 g (70%); mp: >280 °C; ν_{max}/cm^{-1} 1685 (CO), 2203 (CN); *m*/*z* (EI) 328 (M^+, 76.5%), 311 (12.2), 299 (18.3), 286 (34.5); δ_H (300 MHz, $CDCl_3$) 1.03 (d, 3H, J = 6.3 Hz, CH_3), 1.31–1.45 (m, 1H, CH), 1.76–1.81 (m, 2H, CH_2), 1.82–1.93 (m, 2H, CH_2), 3.22–3.31 (m, 2H, NCH_2), 4.39 (t, 2H, J = 7.8 Hz, NCH_2), 6.43 (s, 1H, CH), 7.45 (d, 2H, J = 8.7 Hz, ArH), 7.74 (d, 2H, J = 8.7 Hz, ArH) (Found: C, 65.56; H, 4.98; N, 8.23. $C_{18}H_{17}ClN_2O_2$ requires: C, 65.75; H, 5.21; N, 8.52%).

4-(4-Chlorophenyl)-2-dimethylamino-6-methylbenzonitrile (6b)

Compound **6b** was prepared by stirring a mixture of 6-(4-chlorophenyl)-3-cyano-4-dimethylamino-2*H*-pyran-2-one (**4b**, 0.275 g, 1 mmol), dry acetone (0.5 mL, 7 mmol) and powdered KOH (0.084 g, 1.5 mmol) in dry DMF (10 ml) at ambient temperature under a nitrogen blanket for 35 h. The reaction mixture was poured onto ice, stirred for 1 h and thereafter acidified with 10% HCl. The precipitate thus obtained was filtered and the crude product was purified on a silica gel column. Yield: 0.17 g (62.8%); mp: 110 °C; ν_{max}/cm^{-1} 2208 (CN); *m*/*z* (EI) 270 (M^+, 100%), 269 (88.2), 255 (24.1), 227 (7.7), 190 (17.0), 165 (15.8), 149 (40.5); δ_H (300 MHz, $CDCl_3$) 2.59 (s, 3H, CH_3), 3.15 (s, 6H, $(CH_3)_2N$), 7.12 (s, 1H, ArH), 7.32 (s, 1H, ArH), 7.44 (d, 2H, J = 9 Hz, ArH), 7.52 (d, 2H, J = 9 Hz, ArH) (Found: C, 71.21; H, 5.32; N, 10.56. $C_{16}H_{15}ClN_2$ requires: C, 70.97; H, 5.58; N, 10.35%).

4-(3,4-Dichlorophenyl)-2-dimethylamino-6-methylbenzonitrile (6e)

Compound **6e** was obtained from the reaction of 3-cyano-6-(3,4-dichlorophenyl)-4-dimethylamino-2*H*-pyran-2-one (**4e**, 0.31 g, 1 mmol), acetone (0.5 ml) and powdered KOH (0.084 g, 1.5 mmol) in dry DMF and isolated as described in the preceding experiment. Yield: 0.15 g (50%); mp: 100 °C; ν_{max}/cm^{-1} 2208 (CN); *m*/*z* (EI) 305 (M^+, 58.5%), 304 (100), 291 (8.8), 290 (8.2), 190 (14.0), 159 (10.7); δ_H (300 MHz, $CDCl_3$) 2.56 (s, 3H, CH_3), 3.09 (s, 6H, $(CH_3)_2N$), 6.94 (s, 2H, ArH), 7.40 (d, 1H, J = 9 Hz, ArH), 7.53 (d, 1H, J = 8.4 Hz, ArH), 7.64 (s, 1H, ArH) (Found: C, 62.68; H, 4.38; N, 8.95. $C_{16}H_{14}Cl_2N_2$ requires: C, 62.96; H, 4.62; N, 9.18%).

4-(4-Fluorophenyl)-2-(4-methylpiperidino)-6-methylbenzonitrile (6g)

Compound **6g** was prepared by the reaction of 3-cyano-6-(4-fluorophenyl)-4-(4-methylpiperidino)-2*H*-pyran-2-one (**4g**, 0.31 g, 1 mmol), acetone (0.5 ml) and powdered KOH (0.084 g, 1.5 mmol) in dry DMF and isolated as described in the preceding experiment. Yield: 0.16 g (52%); mp: 115 °C; ν_{max}/cm^{-1} 2206 (CN); *m*/*z* (EI) 308 (M^+, 100%), 307 (93.5), 292 (20.2), 265 (18.9), 238 (26.3); δ_H (300 MHz, $CDCl_3$) 0.96 (d, 3H, J = 6 Hz, CH_3), 1.12–1.14 (m, 1H, CH), 1.50–1.55 (m, 4H, CH_2), 2.52 (s, 3H, CH_3), 2.83 (t, 2H, J = 9 Hz, NCH_2), 3.60 (t, 2H, J = 9 Hz, NCH_2), 6.99 (s, 1H, ArH), 7.01 (s, 1H, ArH), 7.10–7.16 (m, 2H, ArH), 7.50–7.54 (m, 2H, ArH) (Found: C, 77.58; H, 6.49; N, 8.86. $C_{20}H_{21}FN_2$ requires: C, 77.89; H, 6.86; N, 9.08%).

4-(4-Chlorophenyl)-2-(4-methylpiperidino)-6-methylbenzonitrile (6h)

Compound **6h** was prepared by the reaction of 3-cyano-6-(4-chlorophenyl)-4-(4-methylpiperidino)-2*H*-pyran-2-one (**4h**, 0.32 g, 1 mmol), acetone (0.5 ml) and powdered KOH (0.084 g, 1.5 mmol) in dry DMF and isolated as described in the preceding experiment. Yield: 0.18 g (55.6%); mp: 110 °C; ν_{max}/cm^{-1} 2200 (CN); *m*/*z* (EI) 324 (M^+, 48.9%), 323 (100), 322 (82.4), 308 (23.3); δ_H (200 MHz, $CDCl_3$) 1.01 (d, 3H, J = 6 Hz, CH_3), 1.47–

1.56 (m, 1H, CH), 1.68–1.70 (m, 4H, CH_2), 2.55 (s, 3H, CH_3), 2.81 (t, 2H, $J = 9$ Hz, NCH_2), 3.44 (t, 2H, $J = 9$ Hz, NCH_2), 6.96 (s, 1H, ArH), 7.01 (s, 1H, ArH), 7.49 (d, 2H, $J = 8.8$ Hz, ArH), 7.51 (d, 2H, $J = 8.8$ Hz, ArH) (Found: C, 73.56; H, 6.33; N, 8.28. $C_{20}H_{21}ClN_2$ requires: C, 73.95; H, 6.51; N, 8.62%).

[4,6-Bis(4-fluorophenyl)-2*H*-pyran-2-ylidene]acetonitrile (7)

A mixture of **1a** (0.26 g, 1 mmol), 4-fluoroacetophenone (0.74 g, 1 mmol) and powdered KOH (0.12 g, 2 mmol) in anhydrous DMF (8 ml) was stirred at ambient temperature for 20 h. The reaction mixture was poured into ice–water and acidified with 10% HCl. The precipitate obtained was purified on silica gel column using $CHCl_3$–hexane (1 : 1) as eluent. Yield: 0.1 g (30%); mp: 149 °C; ν_{max}/cm^{-1} 2200 (CN); *m*/*z* (EI) 307 (M^+, 22%), 306 (100), 280 (41); δ_H (300 MHz, $CDCl_3$) 6.45 (s, 1H, CH), 6.90 (s, 1H, ArH), 7.30 (s, 1H, ArH), 7.52 (d, 2H, $J = 8$ Hz, ArH), 7.58 (d, 2H, $J = 8.1$ Hz, ArH), 7.72 (d, 2H, $J = 8.0$ Hz, ArH) 7.86 (d, 2H, $J = 8.2$ Hz, ArH) (Found: C, 74.35; H, 3.46; N, 4.25. $C_{19}H_{11}F_2NO$ requires: C, 74.26; H, 3.6; N, 4.56%).

Crystal data for 3f

$C_{16}H_{13}NO_2S$, monoclinic, space group *Cc*, $a = 11.283(1)$ Å, $b = 13.226(1)$ Å, $c = 9.239(1)$ Å, $\beta = 98.35(1)°$, $V = 1364.1(2)$ Å^3, $Z = 4$, Mo-Kα, $\lambda = 0.71073$ Å, $\mu = 0.24$ mm^{-1}, $D_c = 1.380$ g cm^{-3}. X-Ray data were collected on an Enraf-Nonius CAD4 diffractometer (graphite monochromator, $T = 293(2)$ K, $\theta = 25°$). The structure was solved by direct methods using SHELXS86[27] and refined anisotropically on non-H atoms by full-matrix least-squares method on F^2 using SHELXL93[28] (1272 reflections and 183 parameters). All H-atoms were placed in geometrically idealised positions and refined using the riding model. Convergence was reached [$(\Delta/\sigma)_{max} = 0.000$] at $R = 0.0383$ for 1228 reflections with $I > 2\sigma(I)$ [$wR_2 = 0.1107$, $S = 0.767$]. The final difference Fourier map showed no significant peaks ($\Delta\rho_{max,min} = 0.17, -0.31$ e Å^{-3}).

CCDC reference number 207/482. See http://www.rsc.org/suppdata/p1/b0/b005572g/ for crystallographic files in .cif format.

The ORTEP[29] and view of the crystal packing (PLUTO[29]) diagrams of **3f** are shown in Fig. 1 and Fig. 2 respectively.

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