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Synthetic and mass spectral fragmentation studies on trisubstituted 2*H*-pyran-2-ones and comparative EIMS behaviour of biologically active 3,5-disubstituted pyrazoles and isoxazoles

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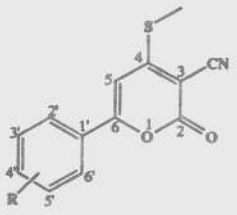
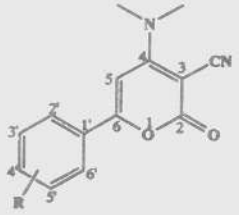
Eight 3-cyano-4-thiomethyl-6-aryl-2*H*-pyran-2-ones **1-8** and three 3-cyano-4-(*N,N*-dimethyl)amino-6-aryl-2*H*-pyran-2-ones **9-11** have been synthesised and their detailed mass fragmentation pattern alongwith the X-ray crystal structure of a novel pyrone **5** have been studied. In addition, a comparative EIMS behaviour of 3,5-disubstituted pyrazoles **16-23** and isoxazoles **12-15** is reported. The pyrazole derivative **23** has been found to possess strong anti-invasive activity against human breast carcinoma cells.

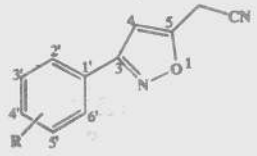
3-Cyano-4-thiomethyl-6-aryl-2*H*-pyran-2-ones are well-known starting materials for the synthesis of a variety of heterocyclic compounds[1,2]. We are engaged in a research programme involving synthesis of pyrazolyl- and isoxazolyl-coumarins and their analogs for structure-activity relationship studies as potential biologically active compounds. During the course of synthesis of the starting pyrones **1-8**, we obtained minor side products in three cases, which were characterized as the corresponding 3-cyano-4-(*N,N*-dimethylamino)-6-aryl-2*H*-pyran-2-ones **9-11**. As the detailed mass spectral fragmentation pattern of the compounds **1-11** has not been reported earlier, we herein report the unusual behaviour of these compounds under electron impact. We have also carried out the comparative EIMS studies on the fragmentation pattern of the isoxazoles **12-15** and the pyrazoles **16-23**, synthesised from the pyrones **1-8**. The pyrazole **23** has shown strong anti-invasive activity against human breast carcinoma cells. The molecular structure of **5** has been confirmed by an X-ray crystallographic investigation.



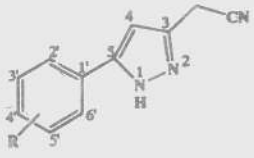
1 R=H
2 R=4'-F
3 R=4'-Cl
4 R=4'-Br
5 R=3'-Br
6 R=4'-OCH_3
7 R=3'-OCH_3
8 R=4'-CH_3



9 R=H
10 R=3'-Br
11 R=4'-CH_3



12 R=H
13 R=4'-Cl
14 R=4'-OCH_3
15 R=4'-CH_3



16 R=H
17 R=4'-F
18 R=4'-Cl
19 R=4'-Br
20 R=3'-Br
21 R=4'-OCH_3
22 R=3'-OCH_3
23 R=4'-CH_3

Results and Discussion

The compounds **1-8** were synthesised by the method reported earlier[1,2]. During the synthesis of **1, 5** and **8**, we have isolated in each case a side product, characterized as **9,10** and **11**, respectively. The spectral data of these compounds alongwith the X-ray crystal structure of **5** (Figure 1) are being reported here (*cf.* Experimental).

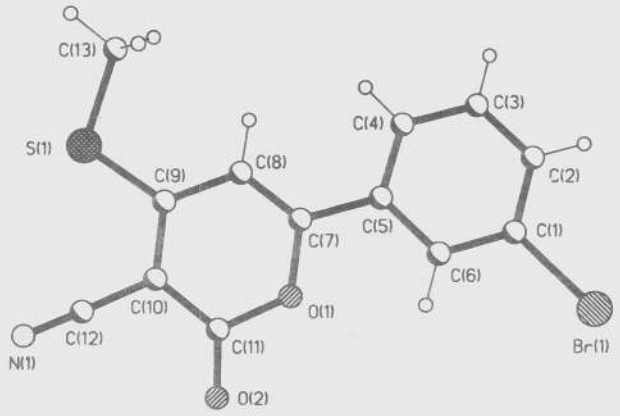


Figure 1—Molecular structure of 5 showing the numbering scheme of the non-hydrogen atoms. The hydrogen atoms are represented by small circles

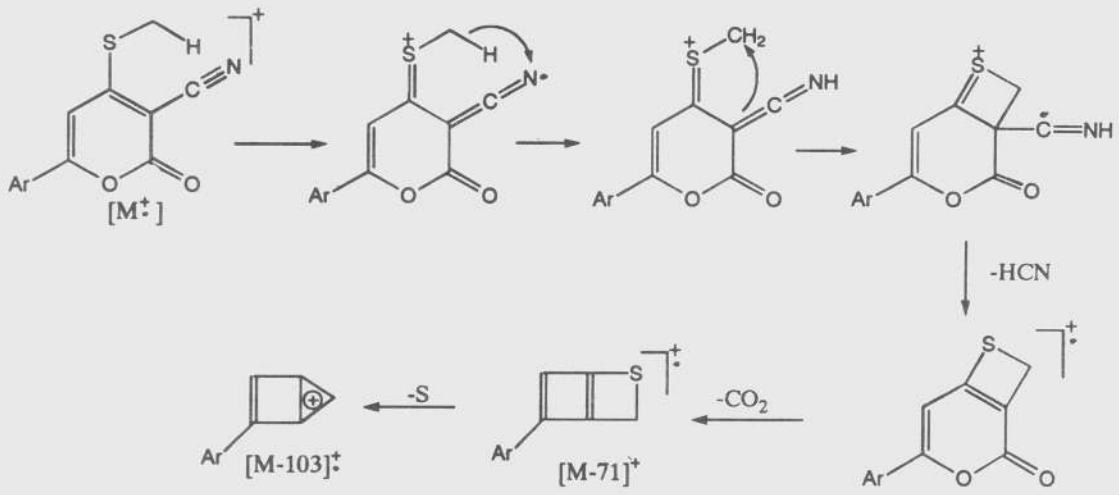
We have synthesised 3,5-disubstituted isoxazoles **12-15** and pyrazoles **16-23** *via* an efficient method using the pyrones **1-8** as the starting materials involving modification of the literature procedures[2-5] for the preparation of these compounds. The compounds **5,7,10,12,14,20** and **22** are new compounds and have been synthesised by us for the first time.

Compounds **1-8** behaved quite unusually towards EIMS in the sense that they invariably showed peaks at *m/z* $(M-71)^+$ and $(M-103)^+$. These peaks seem to be the result of a complex rearrangement, presumably by a mechanism involving the McLafferty type migration of a proton from -S-CH_3 to the nitrile function with simultaneous loss of HCN and CO_2 (Scheme I) producing a fragment which accounts for $(M-71)^+$ peak. This fragment subsequently loses sulphur forming a fragment accounting for the peak at *m/z* $(M-103)^+$. Apart from these peaks, other important peaks are easily accountable and are in agreement with the mass spectra of a similar compound 4-methoxy-6-methyl-2-pyrone reported earlier[6]. The molecular ions lose the aryl radical giving rise to a peak at *m/z* 166; this fragment undergoes rearrangement and loses C_2O_2, when a fragment ion at *m/z* 110 is formed (Scheme II). 2-Pyrones are also known to lose CO and so do our compounds giving rise to peaks at *m/z* $(M-28)^+$; the peaks due to loss of CH_3 radical at *m/z* $(M-15)^+$, and peaks for $ArCO^+$ and Ar^+ moities are also quite expected, and observed in our compounds (Scheme II). The detailed MS data and respective relative intensities of different prominent peaks in compounds **1-8** are given in Table I.

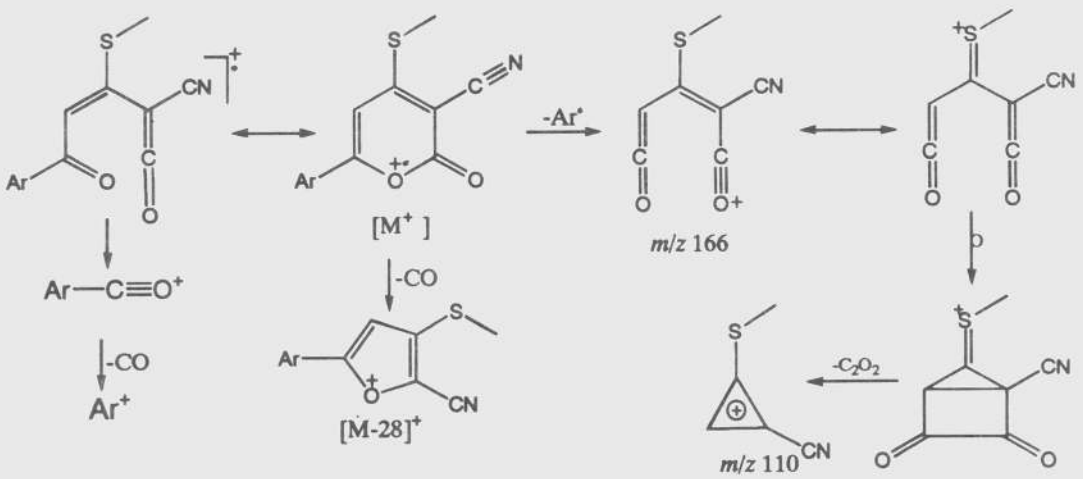
Compounds **9-11** behaved similarly to EIMS as did compounds **1-8**. They showed a characteristic but unusual peak at *m/z* $(M-71)^+$, formation of which can be accounted through the pathway exactly similar to that of 3-cyano-4-thiomethyl-6-aryl-2*H*-pyran-2-ones **1-8** as depicted in Scheme I. Remaining peaks are consistent with the pattern reported earlier[5,6] and the ones exhibited by compounds **1-8** (Schemes I and II). The mass spectrometric data and the relative intensities of peaks observed in compounds **9-11** are given in Table II.

The molecular ion peak appeared as a strong peak in isoxazoles **12-15** and as the base peak in pyrazoles **16-23**. This indicated the immense stability of these heterocyclic systems. The base peak in isozaxoles at *m/z* $(M-40)^+$ was due to a fragment obtained by the loss of -CH_2CN radical (Scheme III). The peak due to the loss of CN group at *m/z* $(M-26)^+$ was observed in pyrazoles (Scheme IV; Table IV), but not in isoxazoles. The peak at *m/z* $(M-55)^+$ in the mass spectra of pyrazoles is accounted *via* a rearrangement pathway through the formation of a six-membered diazine ring accompanied by loss of N_2H radical (Scheme IV). Such a rearrangement and loss are known to occur in similar systems[8]. Peaks for $(M-40)^+$, $(M-79)^+$ and Ar^+ fragments in case of compounds **21** and **22** are not observed because a different pathway of fragmentation is prevalent here. The molecular ion first loses CH_3 radical from the methoxy group in the benzenoid ring giving rise to a peak at *m/z* $(M-15)^+$, followed by loss of CO accounting for a peak at *m/z* $(M-43)^+$. The detailed fragmentation mechanisms of isoxazoles and pyrazoles are shown in Schemes III and IV, respectively and their MS data are given in Tables III and IV, respectively. The molecular structure of **5**, as determined by an X-ray investigation is illustrated in Figure I; all crystallographic data, bond lengths and angles (Tables V-VII) are unexceptional.

The fragmentation pathways depicted in this paper could find utility in the identification of new analogs of these compounds. The aryl lactones **1-8** show quite identical features in their EI mass spectra which bear two unusual peaks, which may be used as diagnostic peaks for such types of compounds. Though the isoxazoles and pyrazoles



Scheme I—EIMS rearrangement-fragmentation mechanism of compounds **1-8**



Scheme II—EIMS fragmentation pathways of compounds **1-8**

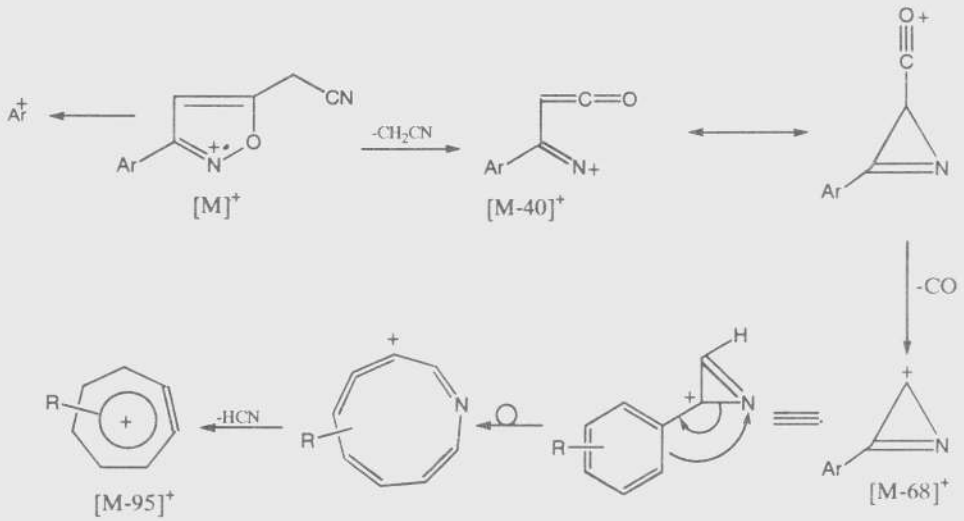
Table I—Major ions (with relative intensities in parentheses) in EIMS of compounds **1-8** (values in m/z)

Compd	M^+	$(M-15)^+$	$(M-28)^+$	$(M-71)^+$	$(M-103)^+$	$ArCO^+$	$(M-Ar)^+$	Ar^+	$(M-ArCO-CO)^+$
1	243(79)	228(11)	215(88)	172(27)	140(17)	105(88)	166(7)	77(100)	110(13)
2	261(72)	246(9)	233(72)	190(32)	158(16)	123(100)	166(5)	95(83)	110(10)
3	277/279 (89/30)	262/264 (9/3)	249/251 (66/22)	206/208 (15/5)	174/176 (6/2)	139/141 (100/33)	166(19)	111/113 (57/19)	110 (9)
4	321/323 (99/100)	306/308 (7/7)	293/295 (63/64)	250/252 (9/10)	218/220 (6/6)	183/185 (60/61)	166 (14)	155/157 (42/43)	110 (13)
5*	321/323 (45/45)	306/308 (4/4)	293/295 (25/25)	250/252 (3/3)	218/220 (3/3)	183/185 (22/22)	166 (9)	155/157 (15/15)	110 (4)
6	273 (100)	258 (6)	245 (56)	202 (9)	170 (9)	135 (60)	166 (5)	107 (22)	110 (4)
7	273 (100)	258 (4)	245 (65)	202 (15)	170 (10)	135 (81)	166 (2)	107 (6)	110 (7)
8	257 (100)	242 (8)	229 (61)	186 (10)	154 (7)	119 (60)	166 (3)	91 (37)	110 (3)

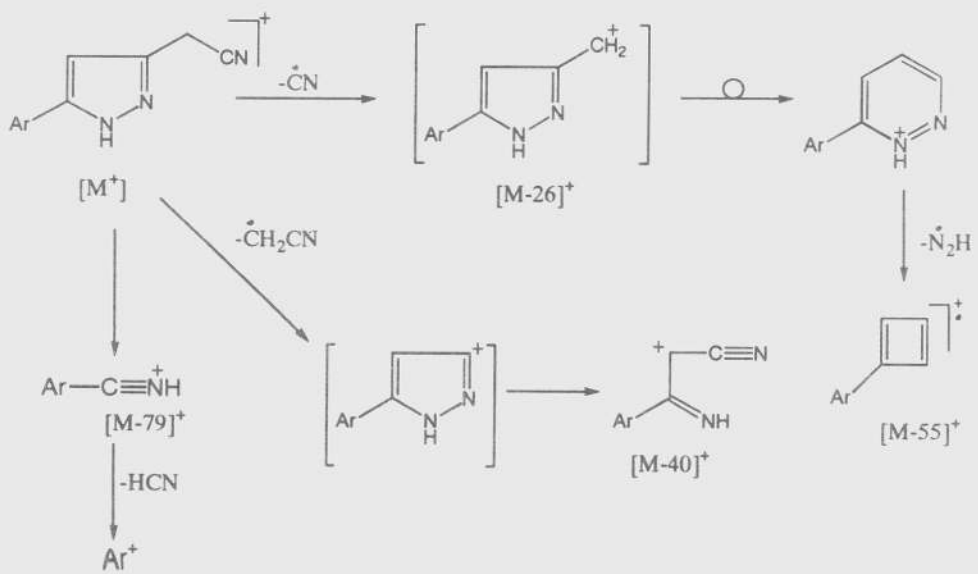
*Base peak in the mass spectrum of this compound appeared at *m/z* 18

Table II—Major ions (with relative intensities in parentheses) in EIMS of compounds **9-11** (values in m/z)

Compd	M^+	$(M-28)^+$	$(M-71)^+$	$(M-Ar)^+$	$(M-ArCO)^+$	$(M-ArCO-CO)^+$	$ArCO^+$	Ar^+
9	240 (47)	212 (15)	169 (8)	163 (7)	135 (4)	107 (13)	105 (100)	77 (85)
10	318/320 (99/100)	290/292 (19/19)	247/249 (5/5)	163 (31)	135 (11)	107 (16)	183/185 (80/80)	155/157 (28/28)
11	254 (69)	226 (15)	183 (10)	163 (7)	135 (3)	107 (8)	119 (100)	91 (45)



Scheme III—EIMS fragmentation mechanism of compounds **12-15**



Scheme IV—EIMS fragmentation mechanism of compounds **16-23**

Table III—Major ions (with relative intensities in parentheses) in EIMS of compounds **12-15** (values in m/z)

Compd	M^+	$(M-40)^+$	$(M-68)^+$	$(M-95)^+$	Ar^+
12	184 (46)	144 (100)	116 (14)	89 (6)	77 (38)
13	218/220 (50/17)	178/180 (100/33)	150/152 (28/9)	123/125 (7/2)	111/113 (1)
14	214 (82)	174 (100)	146 (63)	119 (5)	—
15	198 (55)	158 (100)	130 (19)	103 (3)	91 (21)

Table IV—Major ions (with relative intensities in parentheses) in EIMS of compounds **16-23** (values in m/z)

Compd	M^+	$(M-26)^+$	$(M-40)^+$	$(M-55)^+$	$(M-79)^+$	Ar^+
16	183 (100)	157 (12)	143 (13)	128 (34)	104 (12)	77 (29)
17	201 (100)	175 (3)	161 (5)	146 (10)	122 (4)	95 (4)
18	217/219 (100/33)	191/193 (4/1)	177/179 (6/2)	162/164 (11/4)	138/140 (4/1)	111/113 (5/2)
19	261/263 (100/100)	235/237 (4/4)	221/223 (6/6)	206/208 (9/9)	182/184 (4/4)	155/157 (16/16)
20	261/263 (100/100)	235/237 (2/2)	221/223 (2/2)	206/208 (2/2)	182/184 (3/3)	155/157 (10/10)
21	213 (100)	187 (2)	—	158 (2)	—	—
22	213 (100)	187 (2)	—	158 (2)	—	—
23	197 (100)	171 (3)	157 (4)	142 (4)	118 (2)	91 (3)

Table V—Crystal data and structure refinement for **5**

Molecular formular	$C_{13}H_8BrNO_2S$		
Formula weight	322.17		
Temperature	220 (2) K		
Wavelength	0.71073 Å		
Crystal system	Monoclinic		
Space group	C2/c		
Unit cell dimensions	a = 36.59 (3) Å	α = 90°	
	b = 4.719 (4) Å	β = 93.89 (7)°	
	c = 14.368 (12) Å	γ = 90°	
Volume	2475 (4) $Å^3$		
Z	8		
Density (calculated)	1.729 Mg/m^3		
Absorption coefficient	3.482 mm^{-1}		
F (000)	1280		
Crystal size	0.64 × 0.12 × 0.09 mm		
θ range for data collection	2.23 to 23.05°		
Index ranges	$0 \le h \le 40$, $0 \le k \le 5$, $-15 \le l \le 15$		
Reflections collected	1748		
Independent reflections	1717 [R(int) = 0.2384]		
Absorption correction	None		
Refinement method	Full-matrix least-squares on F^2		
Data/restraints/parameters	1714/0/164		
Goodness-of-fit on F^2	1.048		
Final R indices [I>2 sigma (I)]	R1 = 0.0746, wR2 = 0.1885		
R indices (all data)	R1 = 0.0951, wR2 = 0.2190		
Largest diff. peak and hole	2.144 and −1.223 $e.A^{-3}$		

reported in this investigation are skeletonwise similar, but there is marked difference in their mass spectra; fragmentation of isoxazoles is simple and easily accountable while that of pyrazoles proceeds *via* a rearrangement. The pyrazoles and isoxazoles reported in this paper are being used by us in the synthesis of some novel heterocyclic compounds, i.e. pyrazolyl/isoxazolyl styrenes, coumarins, chromanones and triazoles for structure-activity relationship studies.

Experimental Section

General. Mass spectra were recorded on an MS-50 mass spectrometer using direct insertion probe at 70 eV. The source temperature was 300°C and the probe temperature was 150-175°C for

Table VI—Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **5**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor

	x	y	z	U(eq)
Br	2294(1)	−56(2)	1637(1)	42(1)
S(1)	390(1)	−12170(4)	−354(1)	36(1)
O(1)	1304(1)	−8108(11)	1430(3)	29(1)
O(2)	1181(2)	−10805(13)	2630(4)	42(2)
N(1)	430(3)	−15371(15)	1896(6)	52(2)
C(1)	1991(2)	−1858(15)	688(5)	29(2)
C(2)	2017(2)	−1153(18)	−238(6)	37(2)
C(3)	1789(2)	−2408(18)	−903(6)	39(2)
C(4)	1538(2)	−4386(17)	−667(6)	34(2)
C(5)	1515(2)	−5185(13)	249(5)	23(2)
C(6)	1749(2)	−3894(16)	939(5)	29(2)
C(7)	1251(2)	−7341(15)	511(5)	25(2)
C(8)	981(2)	−8486(15)	−41(5)	27(2)
C(9)	746(2)	−10614(14)	301(5)	26(2)
C(10)	814(2)	−11458(15)	1218(5)	26(2)
C(11)	1099(2)	−10266(14)	1820(5)	27(2)
C(12)	602(2)	−13661(17)	1605(6)	34(2)
C(13)	336(3)	−10059(16)	−1389(6)	41(2)

Table VII—Selected bond lengths (Å) and angles [deg.] for **5**

Bond lengths	
Br-C(1)	1.898(8)
S(1)-C(9)	1.720(8)
S(1)-C(13)	1.789(8)
O(1)-C(7)	1.370(8)
O(1)-C(11)	1.403(9)
O(2)-C(11)	1.208(9)
N(1)-C(12)	1.121(11)
Bond angles	
C(9)-S(1)-C(13)	104.7(4)
C(7)-O(1)-C(11)	122.1(6)
C(6)-C(1)-Br	118.7(6)
O(2)-C(11)-O(1)	115.7(7)
N(1)-C(12)-C(10)	178.7(9)

compounds **1-8**, 200°C for **9-11**, 80°C for **12-15** and 100°C for **16-23** and the data obtained are given in Tables I-IV.

Melting points were determined in a sulphuric acid-bath and are uncorrected. IR spectra were recorded (KBr pellet or film) on a Perkin-Elmer 1720 FT-IR spectrophotometer and UV spectra on a Beckmann UV spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-250 spectrometer at 250 and 62.5 MHz, respectively.

General procedure for the preparation of 3-cyano-4-thiomethyl-6-aryl-2*H*-pyran-2-ones 1-8. Ethyl 2-cyano-3,3-bis(thiomethyl)propenoate[1] (4.34 g, 0.02 mole) was dissolved in DMF (40 mL), and KOH (2.24 g, 0.04 mole) added to it. The solution was stirred for 10 min. The corresponding acetophenone (0.02 mole) was added and air sucked from RB flask using a septum and syringe. The contents were stirred for 6 hr at 28-30°C. The reddish-brown coloured supernatant was poured on to crushed ice (200 g) and the contents were stirred for 4 hr when a yellow solid precipitated out. It was filtered, dried and purified by column chromatography, followed by crystallization from acetone.

General procedure for the preparation of [3-arylisoxazol-5-yl]acetonitriles 12-15. 6-Aryl-4-thiomethyl-2-oxo-2*H*-pyran-3-carbonitrile (6 m moles) was dissolved in pyridine (15 mL) at 70-80°C, hydroxylamine hydrochloride (7 m moles) added to it and the reacton mixture stirred for 40-48 hr at 70-80°C; the earlier procedure involved refluxing conditions. Pyridine was distilled off under reduced pressure and the residue taken up in ethyl acetate, washed with water, dil HCl and dried over Na_2SO_4. The gummy mass, thus obtained on removal of ethyl acetate was subjected to column chromatography over silica gel. The compounds were eluted by ethyl acetate-pet. ether (10-15% v/v) and were obtained in higher yields as compared to those reported earlier (35-45%, literature yields 20-30%).

General procedure for the preparation of [5-arylpyrazol-3-yl]acetonitriles 16-23. 6-Aryl-4-thiomethyl-2-oxo-2*H*-pyran-3-carbonitrile (6 m moles) was dissolved in methanol (30 mL), hydrazine hydrate (15 m moles) added to it and the contents were refluxed for 1-2 hr. The reaction mixture was concentrated under reduced pressure and poured over crushed ice (200 g). The contents were stirred vigorously when a brownish-yellow solid precipitated out. It was filtered, washed with water, dried and column chromatographed over silica gel. Using ethyl acetate-petroleum ether (10-20% v/v) as eluent, a white solid was obtained which was crystallized from acetone.

3-Cyano- 4 -thiomethyl- 6 -(3-bromophenyl)-2*H*-pyran-2-one 5. Yellow shiny needles from acetone, yield 60%, m.p. 233-35°; UV(MeOH): λ_{max} 209, 239, 251, 323 and 362 nm; IR (KBr): 2250, 1720, 1600, 1560, 1495, 1420, 1340, 1220, 1190, 1180 and 1060 cm^{-1}; ^1H NMR (DMSO-d_6): δ2.85 (3H, s, S-CH_3), 7.30 (1H, s, H-5), 7.54 (1H, m, H-5'), 7.81 (1H, m, H-6'), 8.00 (1H, m, H-4') and 8.25 (1H, s, H-2'); ^{13}C NMR (DMSO-d_6): δ 14.36 (–SCH_3), 89.85(C-3), 100.43(C-5),

113.90(*C*≡N), 122.44(C-3'), 125.88(C-6'), 129.26(C-2'), 131.24(C-5'), 132.02(C-1'), 135.10(C-4'), 156.80(C-6), 159.04(C-4) and 171.50(*C*=O).

3-Cyano- 4 -thiomethyl- 6 -(3-methoxyphenyl-2*H*-pyran-2-one 7. Yellow shiny needles from ethyl acetate, yield 57%, m.p. 190°; UV(MeOH): λ_{max} 215, 251, 321 and 368 nm; IR(KBr): 2280, 1720, 1580, 1490, 1435, 1325, 1300, 1275, 1245, 1200, 1160 and 1035 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.73 (3H, s, S-CH_3), 3.88 (3H, s, OCH_3), 6.73 (1H, s, H-5), 7.12(1H, m, H-5'), 7.41 (1H, s, H-2') and 7.43 (2H, m, H-4' and H-6'); ^{13}C NMR (DMSO-d_6): δ 14.70 (S*C*H_3), 55.53 (O*C*H_3), 98.24(C-3), 111.92(C-2' and C-5), 113.22(*C*≡N), 118.54(C-4'), 118.92(C-6'), 130.28(C-5'), 131.02(C-1'), 160.14(C-3' and C-6), 161.78(C-4) and 169.83(*C*=O).

3-Cyano- 4 -(N, N-dimethylamino)-6-(3-bromophenyl)-2*H*-pyran-2-one 10. Reddish-yellow shiny needles from acetone, yield 5%, m.p. 263-65°; UV(MeOH): λ_{max} 232, 245 and 305 nm; IR(KBr): 2240, 1690, 1640, 1570, 1470, 1415, 1360, 1260, 1240, 1210, 1180, 1140 and 1070 cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.41 (6H, s, $N(CH_3)_2$), 7.00 (1H, s, H-5), 7.50 (1H, m, H-5'), 7.75 (1H, m, H-6'), 7.92 (1H, m, H-4') and 8.18 (1H, m, H-2'); ^{13}C NMR (DMSO-d_6): δ 42.51[$N(CH_3)_2$], 96.21(C-3 and C-5), 117.97(*C*≡N), 122.34(C-3'), 125.22(C-6'), 128.68(C-2'), 131.11(C-5'), 132.82(C-1'), 134.25(C-4'), 156.79(C-6), 159.99(C-4) and 161.60(*C*=O).

5-Cyanomethyl-3-phenylisoxazole 12. White shiny needles from chloroform, yield 39%, m.p. 83-84°; UV (MeOH): λ_{max} 205 and 240 nm; IR(KBr): 2920, 2900, 2260, 1620, 1595, 1480, 1420 and 1395 cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.50 (2H, s, CH_2CN), 7.08 (1H, s, H-4), 7.52 (3H, m, H-3', H-4' and H-5') and 7.89 (2H, m, H-2' and H-6'): ^{13}C NMR (DMSO-d_6): δ 15.80 (*C*H_2CN), 101.55 (C-4), 115.70 (*C*≡N), 126.60(C-3' and C-5'), 127.95(C-1'), 129.08 (C-2' and C-6'), 130.39 (C-4'), 162.34 (C-5) and 163.18 (C-3).

5-Cyanomethyl- 3 -(4-methoxyphenyl)isoxazole 14. White shiny needles from chloroform, yield 40%, m.p. 103-104°; UV (MeOH): λ_{max} 216, 258 and 263 nm; IR(KBr): 3000, 2900, 2300, 1620, 1580, 1540, 1460, 1440, 1380, 1300 and 1260 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.85 (3H, s, OCH_3), 3.92 (2H, s, –CH_2CN), 6.60 (1H, s, H-4), 6.97 (2H, d, *J*=9Hz, H-3' and H-5') and 7.71 (2H, d, *J*=9Hz, H-2' and H-6'): ^{13}C NMR ($CDCl_3$): δ 16.69 (*C*H_2CN), 55.36 (O*C*H_3), 101.59 (C-4), 113.21 (*C*≡N), 114.45 (C-3' and C-5'), 122.62 (C-1'), 128.25 (C-2' and C-6'), 161.12 (C-4' and C-5) and 165.31 (C-3).

3-Cyanomethyl-5-(3-bromophenyl)pyrazole 20. White shiny needles from acetone, yield 40%, m.p. 142-144°; UV (MeOH): λ_{max} 240, 246, 258, 269 and 279 nm; IR(KBr): 3200, 2900, 2260, 1580, 1560, 1490, 1415, 1270, 1175 and 1010 cm^{-1}; ^1H NMR (acetone-d_6): δ 4.11 (2H, s, CH_2CN), 6.89 (1H, s, H-4), 7.51 (1H, m, H-5'), 7.64 (1H, m, H-6'), 7.90 (1H, m, H-4'), 8.11 (1H, s, H-2') and 12.63 (1H, brs, NH); ^{13}C NMR (acetone-d_6): δ 16.67 (*C*H_2CN), 102.51 (C-4), 117.42 (*C*≡N), 122.78 (C-3'), 124.45 (C-2' and C-4'), 128.28 (C-5') and 131.08 (C-1' and C-6').

3-Cyanomethyl- 5 -(3-methoxyphenyl)pyrazole 22. White shiny needles from acetone, yield 52%, m.p. 151°; UV (MeOH): λ_{max} 206, 240, 246, 270 and 289 nm; IR(KBr): 3200, 3000, 2300, 1600, 1580, 1420, 1290, 1220, 1185 and 1160 cm^{-1}; ^1H NMR (acetone-d_6): δ 3.97 (3H, s, OCH_3), 4.07 (2H, s, CH_2CN), 6.81 (1H, s, H-4), 7.05 (1H, s, H-2') and 7.48 (3H, m, H-4', H-5' and H-6'); ^{13}C NMR (acetone-d_6): δ 16.45 (*C*H_2CN), 55.01 (O*C*H_3), 102.01 (C-4), 110.85 (C-4'), 114.31 (C-2' and *C*≡N), 117.01 (C-1'), 117.90 (C-5'), 130.29 (C-6') and 160.57 (C-3', C-3 and C-5).

X-Ray Crystallography. All measurements were made using a Siemens P3R3 four-circle diffractometer equipped with an Oxford Cryosystems Cryostream Cooler (version 2.4). Graphite monochromated Mo-Kα radiation (λ=0.71073 Å) was used to collect the intensity data in the ω-2θ mode. Unit cell parameters and orientation matrices were obtained by least-squares refinement of the setting angles of 15 high angle reflections.

The crystallographic programme system was SHELXTL PLUS[9] and SHELXL-93[10]; the refinement programme used was atomic scattering factors taken from International Tables for Crystallography[11]. The structure was solved by direct methods and refined using full-matrix least-squares on F^2. All non-hydrogen atoms were inserted using a riding model and given isotropic thermal parameters equal to 1.2 (or 1.5 for methyl

groups) times the equivalent isotropic displacement parameter of the atom to which the H atom is attached.

The weighting scheme was of the form $w^{-1} = [\sigma^2(F_o)^2 + (0.1566)^2]$ where $P = [\max.(F_o^2,0) + 2F_c^2]/3$. The R factors are defined as $R1=\Sigma||F_o|-|F_c||/\Sigma|F_o|$ and $wR2=[\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$.

A summary of the crystal data and refinement details for compound **5** are given in Table V; atomic coordinates and selected bond lengths and angles are given in Tables VI and VII. Additional material, available from the Cambridge Crystallographic Data Centre includes a full list of bond lengths and angles, thermal parameters and hydrogen coordinates.

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