Benzopyrones. Part VIII.[1] Mono- and Di-tetrazol-5-ylchromones. The Infrared Cyano-absorption of Some 4-Oxochromencarbonitriles

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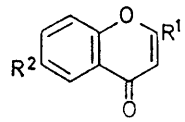
Some chromones containing a nitrile group at C-2, C-6, or C-8, or at both C-2 and C-6, have been synthesized. I.r. absorption by a nitrile group at C-6 or C-8 is of normal intensity, but that of such a group at C-2 is over 100 times less intense, and is not visible at the concentrations commonly used. Reasons for this behaviour are suggested and the difference in absorption was used to identify the mononitrile obtained by successive amidification and dehydration of diethyl 4-oxochromen-2,6-dicarboxylate. Ethyl 7-ethoxycarbonylmethoxy-4-oxochromen-2-carboxylate also gave a mononitrile; the structure of the latter was proved by the synthesis of both possible products; neither of the nitrile groups of 7-cyanomethoxy-4-oxochromen-2-carbonitrile absorbs appreciably in the CN stretching region. Most of the 4-oxochromencarbonitriles were converted into the corresponding mono- and di-tetrazoles, some of which show a high level of activity as antiallergic agents. 4-Methyl-3-(tetrazol-5-yl)-coumarin is inactive.

SOME 2-(tetrazol-5-yl)chromones have been shown to possess a high degree of antiallergic activity.[1] We now describe the synthesis of analogues of these compounds in which the tetrazole ring is attached at C-6, C-8, or, through a $-CH_2 \cdot O-$ linkage, to C-7. In addition, chromones containing two tetrazolyl groups have been synthesized. 2-Methyl-4-oxochromen-6-carbonitrile (4) was synthesized by two routes (Scheme 1). For one of these, 3-acetyl-4-hydroxybenzonitrile was required; a new synthesis gives this compound in good yield from the commercially available 4-hydroxybenzonitrile by a Fries reaction on 4-cyanophenyl acetate. The cyanoketone was condensed with the appropriate ester to give the 6-carbonitrile (4) and ethyl 6-cyano-4-oxochromen-2-carboxylate (10). Less conveniently, the latter compound was prepared from ethyl 6-bromo-4-oxochromen-2-carboxylate. Wheeler's method [2] of preparing flavone

[1] Part VII, G. P. Ellis and D. Shaw, submitted for publication in *J. Medicin. Chem.*

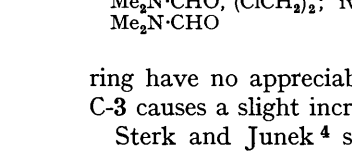
[2] T. S. Wheeler, *Org. Synth.*, 1963, Coll. Vol. IV, p. 478.

was adapted and modified for the synthesis of 2-phenyl-4-oxochromen-6-carbonitrile (6) from 3-acetyl-4-hydroxybenzonitrile.

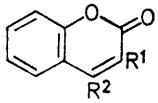


(1) R^1 = Me, R^2 = CO_2Et
(2) R^1 = Me, R^2 = CO_2H
(3) R^1 = Me, R^2 = $CO{\cdot}NH_2$
(4) R^1 = Me, R^2 = CN
(5) R^1 = Me, R^2 = CHN_4 [a]
(6) R^1 = Ph, R^2 = CN
(7) R^1 = Ph, R^2 = CHN_4
(8) R^1 = R^2 = CO_2Et
(9) R^1 = R^2 = CO_2H
(10) R^1 = CO_2Et, R^2 = CN
(11) R^1 = CO_2H, R^2 = CN
(12) R^1 = CO_2Et, R^2 = CHN_4
(13) R^1 = CO_2H, R^2 = CHN_4
(14) R^1 = $CO{\cdot}NH_2$, R^2 = CO_2Et
(15) R^1 = R^2 = $CO{\cdot}NH_2$
(16) R^1 = $CO{\cdot}NH_2$, R^2 = CN
(17) R^1 = CN, R^2 = CO_2Et
(18) R^1 = R^2 = CN
(19) R^1 = CHN_4, R^2 = CO_2Et
(20) R^1 = CHN_4, R^2 = CO_2H
(21) R^1 = R^2 = CHN_4
(22) R^1 = CN, R^2 = H

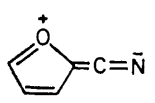
(23) R^1 = R^2 = CO_2Et
(24) R^1 = R^2 = CO_2H
(25) R^1 = CO_2Et, R^2 = CN
(26) R^1 = CO_2Et, R^2 = CHN_4
(27) R^1 = $CO{\cdot}NH_2$, R^2 = CO_2Et
(28) R^1 = $CO{\cdot}NH_2$, R^2 = CN
(29) R^1 = CN, R^2 = CO_2Et
(30) R^1 = R^2 = CN
(31) R^1 = CHN_4, R^2 = CO_2Et
(32) R^1 = CHN_4, R^2 = CO_2H
(33) R^1 = R^2 = CHN_4



(34) R = CN
(35) R = CHN_4



(36) R^1 = CO_2Et, R^2 = H
(37) R^1 = $CO{\cdot}NH_2$, R^2 = H
(38) R^1 = CN, R^2 = H
(39) R^1 = CN, R^2 = Me
(40) R^1 = CHN_4, R^2 = Me



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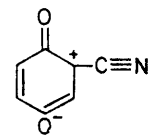

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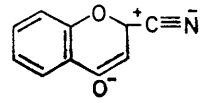
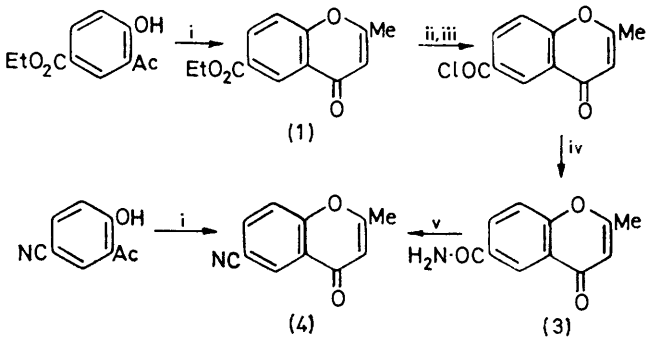


(43)

[a] Tetrazol-5-yl.

Chromones which contain a nitrile group attached to the benzene ring absorb normally in the i.r. region, that is they show a medium-strength absorption at about 2230—2245 cm^{-1} (C≡N stretch). In contrast, 4-oxochromen-2-carbonitrile [1] shows virtually no absorption in the 2300—2200 cm^{-1} range. A wide variation in the intensity of i.r. absorption by a cyano-group has been reported; [3] nitriles containing an α-hydroxy- or α-ether group,[4] for example methoxyacetonitrile, absorb weakly. On the other hand, furan-2-carbonitrile [5] shows the normal absorption at 2250 cm^{-1}. Examination of 4-oxochromen-2-carbonitrile (22) in a solvent which allowed a high concentration to be achieved showed the presence of a sharp absorption at 2235 cm^{-1}; for instance, measurement of an 0·8M-solution in dimethylformamide gave a value of about five for the apparent extinction coefficient [6] (ε_a). With dimethyl sulphoxide [4] as solvent and an almost saturated solution (0·4M), ε_a was again about five [*cf.* 105 for methoxyacetonitrile (in dimethyl sulphoxide) [4] and 110 for furan-2-carbonitrile (in chloroform) [5]]. Substituents in the benzene



SCHEME 1 Reagents: i, $MeCO_2Et$–Na, H^+; ii, H_3O^+; iii, $SOCl_2$, $Me_2N{\cdot}CHO$, $(ClCH_2)_2$; iv, NH_3; v, 4-$MeC_6H_4{\cdot}SO_2Cl$, pyridine, $Me_2N{\cdot}CHO$

ring have no appreciable effect but a methyl group at C-3 causes a slight increase in the CN band intensity.

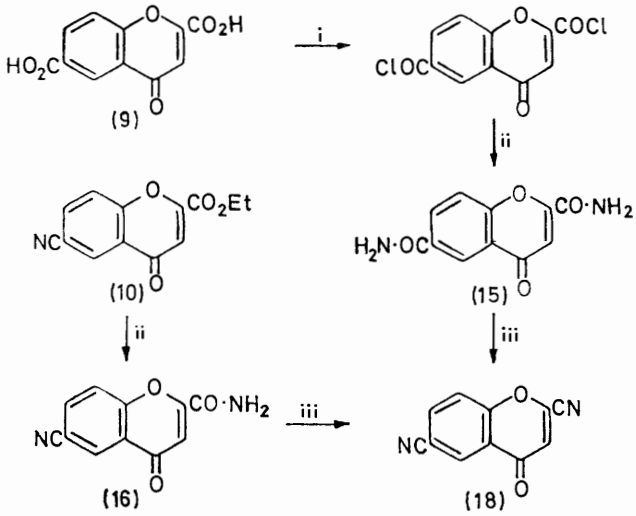
Sterk and Junek [4] suggest that association between the oxygen atom and nitrile group of methoxyacetonitrile lowers the absorption intensity of the CN vibration. They ascribe the normal absorption of furan-2-carbonitrile to ' blocking of the electronic conjugation of the oxygen '.

The difference between furan-2-carbonitrile and chromen-2-carbonitrile (22) may be expressed in terms of the possible resonance forms of the two molecules. Whilst the contribution of structures such as (41) to the furan-2-carbonitrile molecule permits a change of dipole and thus gives rise to i.r. absorption, the corresponding resonance form cannot be written for the nitrile (22). The low intensity of the CN absorption of cyano-quinones has been attributed [7] to resonance forms such as (42); a similar explanation may apply to the 4-oxochromen-2-carbonitriles: structures such as (43) would suppress the contribution of the dipolar form, $-\overset{+}{C}=\overset{-}{N}$. Chromones are known [8] to be electron-deficient at C-2. Normal absorption by 2-oxochromen-3-carbonitriles (38) and (39) at 2230 cm^{-1} is consistent with this interpretation.

The pronounced difference in i.r. absorption between the 2- and the 6- or 8-carbonitriles provides a convenient method of deciding whether or not a nitrile group is at C-2. This method was applied in the identification of the product obtained by amidification and subsequent dehydration of diethyl 4-oxochromen-2,6-dicarboxylate (8), which was prepared from ethyl 3-acetyl-4-hydroxybenzoate. The absence of absorption

[3] L. J. Bellamy, ' Advances in Infra-red Group Frequencies,' Methuen, London, 1968, p. 72.
[4] H. Sterk and H. Junek, *Monatsh.*, 1968, **99**, 810.
[5] A. R. Katritzky and J. M. Lagowski, *J. Chem. Soc.*, 1959, 657.
[6] A. R. Katritzky, *J. Chem. Soc.*, 1958, 4162.
[7] M. F. Ansell, B. W. Nash, and D. A. Wilson, *J. Chem. Soc.*, 1963, 3028.
[8] V. A. Zagorevskii, S. M. Glozman, and S. M. Kluyev, *Chem. Heterocyclic Compounds*, 1967, **3**, 478.

in the 2300—2200 cm^{-1} region showed that the cyano-ester formed was ethyl 2-cyano-4-oxochromen-6-carboxylate (17). The reaction of the diester (8) with ammonia at 0° is thus specific to the 2-carboxylic ester group. The inertness of the 6-carboxylic ester group under these conditions was confirmed by the recovery of ethyl 2-methyl-4-oxochromen-6-carboxylate (1) after similar treatment. 4-Oxochromen-2,6-dicarbonitrile (18) is best synthesized from ethyl 6-cyano-4-oxochromen-2-carboxylate (10), although it is possible to obtain it from the diamide (15), prepared from the diacyl chloride (Scheme 2).



SCHEME 2 Reagents: i, $SOCl_2$, $Me_2N{\cdot}CHO$, $(ClCH_2)_2$; ii, NH_3; iii, $PhSO_2Cl$, pyridine, $Me_2N{\cdot}CHO$

In order to determine whether the same selectivity was shown in the amidification of a compound containing both an aliphatic and a C-2 ester group, ethyl 7-ethoxycarbonylmethoxy-4-oxochromen-2-carboxylate (23) was synthesized from ethyl 7-hydroxy-4-oxochromen-2-carboxylate and ethyl bromoacetate. Amidification of the diester (23) gave a mono-amide, which was dehydrated to give a mono-nitrile (A) which did not absorb in the CN stretching region. I.r. spectroscopy does not enable us to distinguish between the two possible products (25) and (29) since aryloxyacetonitriles, like their alkoxy-homologues, would not be expected to absorb appreciably. We therefore synthesized ethyl 7-cyanomethoxy-4-oxochromen-2-carboxylate (25) by an unequivocal route from the 7-hydroxy-ester and chloroacetonitrile. M.p. and mixed m.p. determinations of (A) with compound (25) showed that the materials were different; the former must therefore be the isomer (29). The chemical shifts of the C-3 proton of the two isomers (25) and (29) fall within the limits given [1] for 2-carboxylic esters and 2-carbonitriles. Thus, the ester group attached to C-2 is amidified in preference to an aliphatic and to a benzenoid ester function. A similar conversion of ethyl 2-oxochromen-3-carboxylate into the 3-carboxamide (at 0° rather than 90° as previously reported [9]) demonstrated that the ester group was more reactive than the lactone function.

7-Cyanomethoxy-4-oxochromen-2-carbonitrile (30) was synthesized from the 2-carboxylic ester (25) *via* the amide, and is a rare example [10] of a dinitrile which does not absorb in the CN stretching region.

The tetrazoles listed in the Table were prepared from the nitriles by the previously described method; [1,11] some of these are covered by a patent application; [12] the carboxylic acids were obtained [1] from the esters. The compounds in the Table were screened for anti-allergic and central nervous stimulant and depressant activity by the usual tests.[1] The tetrazoles (13), (19), (20), (21), (31), and (32) showed antiallergic activity comparable with or greater than that of disodium cromoglycate in the passive cutaneous anaphylaxis test. Comparison with the other tetrazolylchromones (which were less active) suggest that either a carboxy- or tetrazolyl group at C-2 may be essential for a high level of antiallergic activity. The tetrazolylcoumarin (40) was inactive in this test, but, like the amide nitrile (16), showed the same level of activity as aspirin in the phenylquinone writhing test.

EXPERIMENTAL

M.p.s were determined with a Reichert hot-stage apparatus. Low values for the nitrogen content of a few tetrazoles were obtained although the combustion time was increased as recommended by the manufacturer of the instrument (Hewlett–Packard). U.v. spectra were determined for solutions in methanol with a Unicam SP 700A spectrophotometer. I.r. data were obtained for potassium bromide discs (unless otherwise stated) with Perkin-Elmer model 521 and 237 spectrophotometers. N.m.r. spectra were determined with Perkin-Elmer R10 (60 MHz) and R14 (100 MHz) instruments. Chemical shifts are expressed in p.p.m. from internal tetramethylsilane.

The following compounds were prepared by published methods: 3-acetyl-4-hydroxybenzoic acid,[13] ethyl 3-acetyl-4-hydroxybenzoate,[13] ethyl 7-hydroxy-4-oxochromen-2-carboxylate,[14] ethyl 2-oxochromen-3-carboxylate (36),[15] and 4-methyl-2-oxochromen-3-carbonitrile (39).[16]

3-Acetyl-4-hydroxybenzonitrile.—An intimate mixture of 4-cyanophenyl acetate [17] (30 g, 0·183 mol) and anhydrous aluminium chloride (74·3 g, 0·0558 mol) was heated on an oil-bath at 180—185° for 3 h. The cooled mixture was finely powdered and decomposed with ice–water (500 g) and concentrated hydrochloric acid (75 ml) to give 3-acetyl-4-hydroxybenzonitrile (17·4 g, 58%), m.p. 100—101°

[9] A. Lèspagnol, J. Mercier, and P. Giraud, *Ann. pharm. franç.*, 1964, **22**, 131.
[10] R. E. Kitson and N. E. Griffith, *Analyt. Chem.*, 1952, **24**, 334.
[11] W. G. Finnegan, R. A. Henry, and R. Lofquist, *J. Amer. Chem. Soc.*, 1958, **80**, 3908.
[12] B.P. Appl. 5533/1970.
[13] D. N. Shah and N. M. Shah, *J. Indian Chem. Soc.*, 1949, **26**, 235.
[14] G. Barker and G. P. Ellis, *J. Chem. Soc.* (*C*), 1970, 2609.
[15] E. C. Horning, M. G. Horning, and D. A. Dimmig, *Org. Synth.*, 1960, Coll. Vol. III, p. 165.
[16] C. H. Schroeder and K. P. Link, *J. Amer. Chem. Soc.*, 1953, **75**, 1886.
[17] F. D. Chattaway, *J. Chem. Soc.*, 1931, 2495.

(lit.,[18] 103°) (from aqueous ethanol) (Found: C, 67·0; H, 4·4; N, 8·4. Calc. for $C_9H_7NO_2$: C, 67·1; H, 4·4; N, 8·7%), $\nu_{max.}$ 2215 cm^{-1} (C≡N); $\lambda_{max.}$ 228 (log ε 4·59), 245sh (3·99), 251 (4·01), 258 (3·86), 283 (3·34), and 323 (3·49) nm; δ ($CDCl_3$) 12·74 (1H, s, OH), 8·13 (1H, d, *J* 2 Hz, 2-H), 7·74 (1H, q, *J* 9 and 2 Hz, 6-H), 7·09 (1H, d, *J* 9 Hz, 5-H), and 2·70 (3H, s, Ac).

Esters.—(*a*) The esters (8) and (10) were prepared from the appropriate 2-hydroxyacetophenones.[19]

(*b*) *Ethyl 2-methyl-4-oxochromen-6-carboxylate* (1) was prepared from ethyl 3-acetyl-4-hydroxybenzoate by Baker's method.[20]

(*c*) Ethyl 7-hydroxy-4-oxochromen-2-carboxylate (25·5 g), ethyl bromoacetate (17·5 g), and potassium carbonate (10 g) in anhydrous acetone (100 ml) were heated under reflux for 8 h. The solvent was removed by distillation and the remaining solid was washed with water to give *ethyl 7-ethoxycarbonylmethoxy-4-oxochromen-2-carboxylate* (23) (22·6 g, 65%), m.p. 113—114°; $\nu_{max.}$ 1746, 1730, and 1650 cm^{-1} (C=O). The 7-hydroxy-ester was similarly treated with chloroacetonitrile to give *ethyl 7-cyanomethoxy-4-oxochromen-2-carboxylate* (25), m.p. 131—132°, $\nu_{max.}$ 1738 and 1650 cm^{-1} (C=O).

Amides.—(*a*) The amides (14), (16), (27), (28), and (37) were prepared [1] from the appropriate esters by treatment in ethanol with gaseous ammonia at 0° for 20 min.

(b) *2-Methyl-4-oxochromen-6-carboxamide* (3) *and 4-oxochromen-2,6-dicarboxamide* (15) were synthesized *via* the acyl chlorides.[1]

Nitriles.—(*a*) The nitriles (4), (17), (18), (29), (30), and (38) were prepared by the method previously described.[1]

(*b*) *2-Methyl-4-oxochromen-6-carbonitrile* (4) was also obtained by Baker's method [2] from 3-acetyl-4-hydroxybenzonitrile.

(*c*) *2-Phenyl-4-oxochromen-6-carbonitrile* (6) was prepared in three stages [2] from 3-acetyl-4-hydroxybenzonitrile. In the second stage, however, heating the reaction mixture on a water-bath at 60—65° 2 h was necessary for rearrangement of the *O*-benzoyl compound to 2-benzoyl-5′-cyano-2′-hydroxyacetophenone.

(*d*) Compounds (10) and (34) were prepared from the corresponding bromo-compounds as illustrated for ethyl 8-cyano-6-methyl-4-oxochromen-2-carboxylate. A stirred mixture of ethyl 8-bromo-6-methyl-4-oxochromen-2-carboxylate [1] (15·5 g), copper(I) cyanide (8·1 g), and *N*-methylpyrrolidone (40 ml) was refluxed for 6 h. The resulting

Chromone and coumarin derivatives

Compound	M.p. (°C)	Yield (%)	Solv.[a]	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N
(1)	102—103	84	A	67·2	5·3		$C_{13}H_{12}O_4$	67·2	5·2	
(2)	263—264[b]	49	B	64·4	4·0		$C_{11}H_8O_4$	64·7	3·9	
(3)	305—306[b]	80	C	64·6	4·5	6·5	$C_{11}H_9NO_3$	65·0	4·5	6·9
(4)	161—162	58	A	71·4	3·6	7·5	$C_{11}H_7NO_2$	71·3	3·4	7·6
(5)	298—299[b]	84	B	57·6	3·3	24·0	$C_{11}H_8N_4O_2$	57·9	3·5	24·5
(6)	172—173	45	B	77·8	3·4	5·6	$C_{16}H_9NO_2$	78·1	3·6	5·6
(7)	306—307[b]	69	B	66·0	3·4	18·8	$C_{16}H_{10}N_4O_2$	66·2	3·5	19·3
(8)	126—127	65	A	62·1	4·9		$C_{15}H_{14}O_6$	62·1	4·9	
(9)	312—314[b]	96	B	56·7	2·6		$C_{11}H_6O_6$	56·4	2·6	
(10)	190—191	82	A	64·4	3·7	5·4	$C_{13}H_9NO_4$	64·2	3·7	5·8
(11)	268—269[b]	90	B	61·0	2·7	6·4	$C_{11}H_5NO_4$	61·4	2·3	6·5
(12)	266—268[b]	59	B	54·5	3·3	19·1	$C_{13}H_{10}N_4O_4$	54·5	3·5	19·6
(13)	307—308[b]	96	B	51·2	2·6	21·1	$C_{11}H_6N_4O_2$	51·2	2·3	21·7
(14)	306—308[b]	93	C	59·7	4·2	5·2	$C_{13}H_{11}NO_5$	59·8	4·2	5·4
(15)	>350[b]	94	C	56·7	3·8	11·8	$C_{11}H_8N_2O_4$	56·9	3·5	12·1
(16)	332—334[b]	97	C	61·4	3·1	13·3	$C_{11}H_6N_2O_3$	61·7	2·8	13·1
(17)	161—162	93	A	64·0	3·7	5·7	$C_{13}H_9NO_4$	64·2	3·7	5·8
(18)	245—246	86	B	67·3	1·8	13·9	$C_{11}H_4N_2O_2$	67·4	2·1	14·3
(19)	233—234[b]	65	B	54·3	3·5	19·1	$C_{13}H_{10}N_4O_4$	54·5	3·5	19·6
(20)	293—294[b]	91	B	50·8	2·5	21·2	$C_{11}H_6N_4O_2$	51·2	2·3	21·7
(21)	>330[b]	56	C	46·6	2·3	39·2	$C_{11}H_6N_8O_2$	46·8	2·1	39·7
(23)	113—114	77	A	59·9	5·0		$C_{16}H_{16}O_7$	60·0	5·0	
(24)	300—301[b]	93	B	54·6	3·3		$C_{12}H_8O_7$	54·6	3·1	
(25)	131—132	65	A	61·2	4·0	4·9	$C_{14}H_{11}NO_5$	61·5	4·1	5·1
(26)	194—195[b]	68	B	52·9	4·0	17·5	$C_{14}H_{12}N_4O_5$	53·2	3·8	17·7
(27)	270—271[b]	86	C	57·6	4·7	4·6	$C_{14}H_{13}NO_6$	57·7	4·5	4·8
(28)	301—305[b]	96	C	59·0	3·3	11·6	$C_{11}H_8N_2O_4$	59·0	3·3	11·5
(29)	127—128	72	A	61·6	4·1	4·8	$C_{14}H_{11}NO_5$	61·5	4·1	5·1
(30)	135—136	86	A	63·8	2·6	12·2	$C_{12}H_6N_2O_3$	63·7	2·7	12·4
(31)	237—238[b]	73	B	52·8	4·0	17·2	$C_{14}H_{12}N_4O_5$	53·2	3·8	17·7
(32)	291—292[b]	88	B	49·6	3·0	19·1	$C_{12}H_8N_4O_5$	50·0	2·8	19·4
(33)	265—266[b]	67	C	45·7	2·7	35·0	$C_{12}H_8N_8O_3$	46·1	2·6	35·9
(34)	192—193	52	B	65·0	4·1	5·3	$C_{14}H_{11}NO_2$	65·4	4·3	5·4
(35)	264—265[b]	73	B	56·2	4·1	18·5	$C_{14}H_{12}N_4O_4$	56·0	4·0	18·7
(36)	91—92[c]	90	A							
(37)	264—265[d]	95	C	63·8	3·7	7·3	$C_{10}H_7NO_3$	63·5	3·7	7·4
(38)	183—184[e]	84	B	70·1	2·9	8·1	$C_{10}H_5NO_2$	70·2	2·9	8·2
(39)	190—191[f]	62	A							
(40)	214—215[b]	45	B	57·8	3·4	24·3	$C_{11}H_8N_4O_2$	57·9	3·5	24·6

[a] Solvent for recrystallization: A = aqueous EtOH, B = EtOH, C = Me_2N·CHO–EtOH. [b] Decomposed at m.p. [c] Ref. 15; m.p. 91—93°. [d] Ref. 9; m.p. 266°. [e] Ref. 21; m.p. 184—185°. [f] Ref. 16; m.p. 191—192°.

[18] P. L. Cheng, P. Fournari, and J. Tirouflet, *Bull. Soc. chim. France*, 1963, 2248.

[19] V. A. Zagorevskii, D. A. Zykov, and E. K. Orlova, *J. Gen. Chem.* (*U.S.S.R.*), 1960, **30**, 3850.

[20] W. Baker, *J. Chem. Soc.*, 1933, 1385.

[21] W. Baker and C. S. Howes, *J. Chem. Soc.*, 1953, 119.

dark brown mixture was poured into a solution of hydrated iron(III) chloride (20 g) in concentrated hydrochloric acid (5 ml) and water (50 ml) and heated on a water-bath at 60—70° for 20 min. The hot solution was filtered to remove the dark insoluble inorganic matter and then cooled. Separation of the two layers was not possible since the interface was obscured by the dark colour. The mixture was therefore extracted with chloroform (3 × 100 ml) and the extracts were washed with dilute hydrochloric acid and water before drying (Na_2SO_4). Distillation of the chloroform gave *ethyl 8-cyano-6-methyl-4-oxochromen-2-carboxylate* (34) (6·7 g), m.p. 192—193°.

Tetrazoles.—The tetrazoles (5), (7), (12), (21), (26), (31), (33), (35), and (40) were prepared by the method of Finnegan, Henry, and Lofquist.[11]

Carboxylic Acids.—The acids (2), (9), (11), (13), (20), (24), and (32) were obtained by hydrolysis of the corresponding esters with a mixture of acetic and hydrochloric acids.[1]

Determination of the Apparent Extinction Coefficient (ε_a) *for the* CN *Stretching Absorption.*—The percentage absorption was measured for solutions of the nitrile in dimethylformamide or dimethyl sulphoxide at various concentrations in 1 mm cells The ε_a value was calculated [6] from $\varepsilon_a = (1/cl) \log I_0/I$, ere c = concentration (mol l^{-1}) and l = path length of cell (cm).

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