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Oxidation and ring cleavage reactions of 3-benzhydrylchromones. Generation of triarylmethine cations from methylidenechroman-4-ones and benzopyrano[4,3-*c*]pyrazoles

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Abstract—The oxidation of 3-[bis-(diaryl)methyl]chromones **2** with *p*-chloranil affords novel acetals, 3-[bis-(diaryl)methylene]-2-methoxychroman-4-ones, **4** through interception of a pyrylium type intermediate. Oxidation of 3-(2-hydroxyphenyl)-4-[bis-(diaryl)methyl]pyrazoles **8**, derived from **2** and hydrazines, gave 4,4-diarylbenzopyrano[4,3-*c*]pyrazoles **15**. The electronic absorption spectra of **4** and **15** upon protonation are comparable with those of triarylmethine cationic dyes.

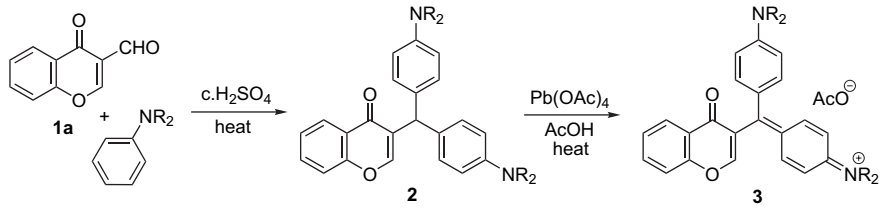
1. Introduction

Chromone-3-carboxaldehyde (4-oxo-4*H*[1]benzopyran-3-carboxaldehyde) **1a** displays a rich and varied chemistry.[1] It can be readily converted into a broad range of heterocyclic systems, e.g., xanthones[2] and pyranobenzopyranones[3] by cycloaddition strategies,[2] pyrazolopyrimidines,[4] benzopyranopyridopyrimidines,[5] pyrimidopyrimidines,[6] benzopyranobenz-thiazepines, -oxazepines and -diazepines,[7] furobenzopyranones[8] and *o*-hydroxyphenyl substituted azoles[9] and pyrimidines[9,10] through condensation with a variety of bis-nucleophiles. Harnish has investigated the addition of tertiary aromatic amines to the formyl group of **1a** and obtained the diarylmethyl analogues **2**, which were subsequently oxidised with $Pb(OAc)_4$ in AcOH to the triarylmethine dyes **3** (Scheme 1).[11]

We were interested in exploring some chemistry of **2**, particularly their reaction with bis-nucleophiles and their oxidation with *p*-chloranil. The addition of bis-nucleophiles to chromone and substituted chromones that do not have an electron withdrawing substituent at C-3 has been shown to be critically dependant upon the reaction conditions.[12] This feature is conveniently illustrated by the addition of hydroxylamine to chromone, which under anhydrous conditions affords the simple oxime, whereas using aqueous ethanol results in pyran ring cleavage to afford a mixture of isomeric (*o*-hydroxyphenyl)isoxazoles.[13]

2. Discussion

Chromone-3-carboxaldehyde **1a** was efficiently obtained (74%) in a single step from *o*-hydroxyacetophenone by



Scheme 1.

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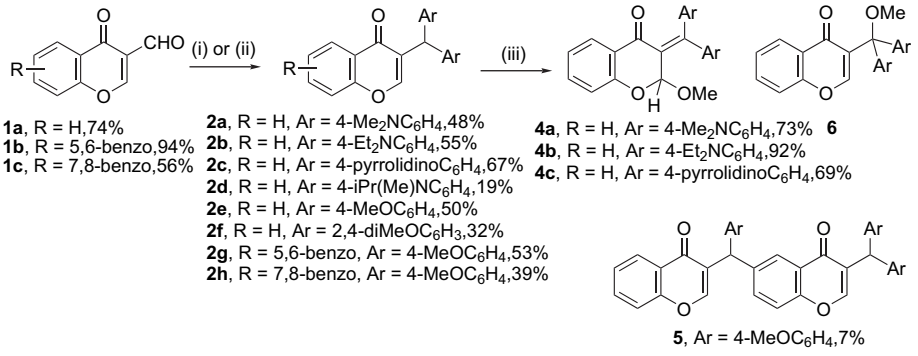
a double Vilsmeier formylation reaction.[11] The benzologues **1b** and **1c** were similarly obtained in 94 and 56% yield from 1-acetyl-2-hydroxynaphthalene and 2-acetyl-1-hydroxynaphthalene, respectively. The acid-catalysed condensation of **1a** with a range of tertiary aromatic amines gave the 3-[bis-(4-aminophenyl)methyl]chromones (benzhydrylchromones) **2a–d** in moderate yield. The aminoaryl groups of **2a–d** are equivalent affording signals in their ^{1}H NMR spectra at ~δ 6.6 and δ 7.0 due to the aromatic protons *ortho* and *meta* to the amino function, respectively. The low field signal at ca. δ 8.2 is assigned to 5-H as a consequence of its *peri* relationship with the C=O group and the methine proton resonates at ~δ 5.6. 2-H appears as a doublet ($J \approx 1.0$ Hz) at ~δ 7.4, shifted upfield relative to 2-H (δ 7.88) in chromone[14] as a consequence of shielding by the diarylmethine unit. Our attempts to obtain 3-[bis-(4-methoxyphenyl)methyl]chromone **2e** using this methodology were unsuccessful. Similar attempts to obtain **2e** by treatment of **1a** in anisole with a catalytic amount of TFA failed.[15] However, **2e** was accessed in 50% yield by heating **1a** in dichloromethane containing 2.1 equiv of anisole and 6 equiv of $BF_3 \cdot OEt_2$ for 20 h with purification effected by column chromatography and recrystallisation from EtOAc and hexane. The ^{1}H NMR spectrum of **2e** displayed the expected singlet at δ 5.7 and the equivalent methoxy groups resonated at δ 3.8. A second component was isolated from the reaction mixture, which displayed two methine signals (δ 5.54 and δ 5.92) and two overlapping signals for 5-H, *peri* to a chromone type C=O function, at δ 8.14. The presence of three 4-methoxyphenyl units was confirmed by the two signals at δ 3.73 (6H) and δ 3.74 (3H). Furthermore, two chromone C=O units were present as indicated by signals at δ 176.6 and δ 176.7 in the ^{13}C NMR spectrum. These data and a molecular ion (electrospray, M+H$^+$) m/z=637.2217 Da suggest the bis-adduct, structure **5** (7%). Chromones have been reported to undergo S_EAr at the 6-position[16] particularly in the absence of electron donating groups in the pyranone and it is probable that **5** is formed by interception of a carbocationic intermediate, derived from **1a** and 1 mol of anisole, by the substituted chromone **2e**. Compound **2f** (32%) was similarly obtained from **1a** and 1,3-dimethoxybenzene though the reaction time was somewhat shorter (7 h) than that of **2e**.

The benzologues **2g** (53%), **h** (39%) were obtained using a similar protocol to that employed for **2e**. The ^{1}H NMR spectra of **2g** and **2h** displayed a singlet at ~δ 5.7 assigned to the methine protons. Of greater significance is the chemical shift of 10-H in **2g**, which appears at δ 10.1 and the corresponding proton (5-H) in **2h**, which resonates at δ 8.4; a feature, which enables these isomers to be readily distinguished.

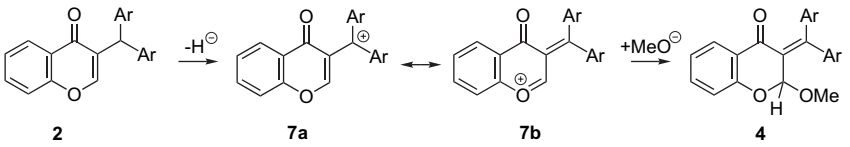
There are few reports pertaining to the use of *p*-chloranil for the oxidation of triarylmethanes to triarylmethanols.[17] Refluxing a methanolic solution of **2a** containing a slight excess of *p*-chloranil for ca. 4 h and treatment of the cooled reaction mixture with NaOMe to remove the tetrachlorohydroquinone by-product gave a new orange-red compound. The ^{1}H NMR spectrum of this product was not in agreement with the expected methoxytriarylmethane **6** (Ar=4-$Me_2NC_6H_4$), the precursor of dyes **3**, since the dimethylaminophenyl groups are non-equivalent to the NMe_2 groups resonating at δ 2.98 and δ 3.04. Interestingly, the ^{1}H NMR spectrum of this product also contained a singlet at δ 3.43 (3H) and a singlet at δ 5.56 (1H). Furthermore, the furthest downfield signal appeared at δ 7.95, which suggests that the relationship between the C=O group and 5-H has changed. Examination of the literature reveals that the chemical shift of 5-H is extremely sensitive to the level of oxidation of the benzopyranone unit. Typically, 5-H in chromones (4-oxo-4*H*[1]benzopyrans) resonates at ca. δ 8.2, whereas in the reduced analogues, the chromanones (2,3-dihydro-4-oxo-4*H*[1]benzopyrans), 5-H usually appears at ca. δ 7.9.[18] Furthermore, the singlet at δ 5.56 is in a region typically associated with the methine proton of an acetal unit.[19] With this information in hand, we proposed that this compound is the acetal **4a**. The treatment of **2b**, **c** under identical conditions afforded the corresponding acetals **4b**, **c**, respectively, with similar spectroscopic properties to **4a** (Scheme 2).

Our attempts to oxidise **2e**, **f** and **g** with *p*-chloranil failed and instead starting material was recovered. The use of triphenylcarbenium fluoroborate in anhydrous CH_2Cl_2 at room temperature[20] was also investigated for the oxidation step but again unchanged starting material was recovered. Presumably, the oxidation fails as a consequence of the less efficient resonance stabilisation of the cation **7a** (Scheme 3) by the methoxyphenyl groups compared with the *N*,*N*-dialkylaminophenyl units of **2a–c**.

The formation of **4** is thought to proceed by initial hydride abstraction by the *p*-chloranil to generate the carbocation



Scheme 2. Reagents and conditions: (i) aq H_2SO_4, *N*,*N*-dialkylaminobenzene, 110 °C; (ii) (di)methoxybenzene, $BF_3 \cdot OEt_2$, CH_2Cl_2, reflux; (iii) *p*-chloranil, methanol, reflux then NaOMe, rt.



Scheme 3.

7a that is efficiently resonance stabilised, not only by the adjacent aminophenyl groups, but also by the oxygen atom of the pyran ring. This latter resonance stabilisation may be likened to a pyrylium type cation **7b**. Nucleophilic addition of pyrylium salts to C-2 is well established[21] and in this instance interception of the less hindered oxonium ion by methoxide affords **4** (Scheme 3).

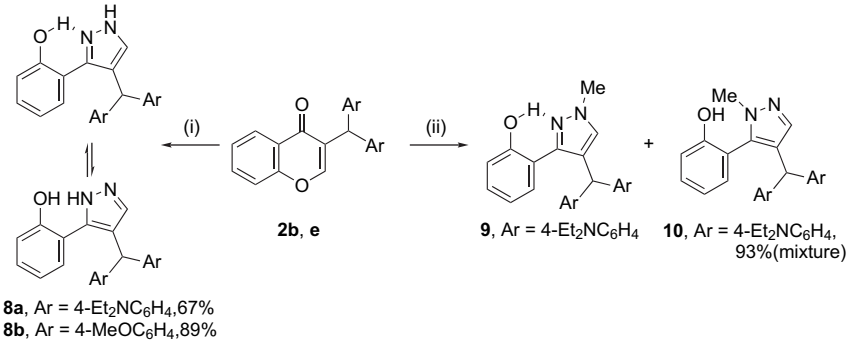
Treatment of **2b**, **e** with hydrazine hydrate in refluxing ethanol gave the *o*-hydroxyphenyl pyrazoles **8a** and **8b** in 67 and 89% yield, respectively (Scheme 4). Their formation is readily explained by the conjugate addition of hydrazine to the enone unit of **2** followed by enol–keto tautomerism to regenerate the benzylic C═O group; a 5-*exo-trig* ring closure completes the sequence to the pyrazole. Despite the possibility of annular prototropy of the pyrazole ring,[22] the ^{1}H NMR spectrum of **8a** was well resolved with only the OH (δ 11.0) and NH (δ 10.0) signals exhibiting broadening. The pyrazole ring proton (5-H) appeared as a singlet at ~δ 7.1.

The ^{1}H NMR spectrum of the product of the reaction between **2b** and methylhydrazine was more complex and indicated that two isomeric pyrazoles **9** and **10** had been formed. The ratio of the two isomers was determined as 2:3 based upon comparison of the integrals for the *N*-methyl signals at δ 3.62 (major) and δ 3.84 and the methine signals at δ 4.85 (major) and δ 5.40. Interestingly, simple (2-hydroxyaryl)pyrazoles obtained from α-hydroxymethylene–acetophenones and hydrazines have been evaluated as UV absorbers with an energy quenching proton transfer process similar to that of 2′-hydroxybenzophenones and hydroxyphenylbenzotriazoles;[23] the new hydroxyphenylpyrazoles **8**, **9** and **10** may offer similar photophysical properties.

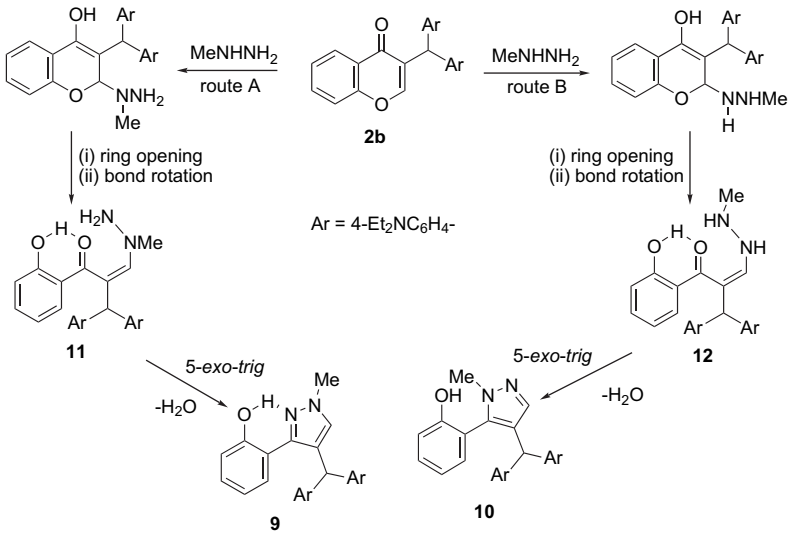
The formation of these isomeric methyl pyrazoles may be conveniently rationalised by considering the differing nucleophilicities of the hydrazine N atoms. In route A (Scheme 5) N-1 of methylhydrazine attacks C-2 of **2b**. Regeneration of the C-2–C-3 double bond with elimination of phenoxide results in **11**, which contains a stabilising intramolecular H-bond, after rotation of the *o*-hydroxyphenyl function. Dehydrative ring closure affords pyrazole **9**. In route B attack by N-2 initiates the sequence to afford, after ring-opening and bond rotation, enaminone **12** that affords pyrazole **10** on cyclisation.

The pyrazole **8a** was readily oxidised with *p*-chloranil using the procedure for the oxidation of **2**. The ^{1}H NMR spectrum of the product displayed a single set of signals for the NEt_2 functions suggesting their equivalence, a feature, which precludes the diazafulvene **13**. Additionally, 3-H resonates at δ 7.25, a chemical shift typical to some simple 4,4-dialkyl substituted benzo- and benzothio-pyrano[4,3-*c*]pyrazoles.[24] The possibility that the oxidation product was the hydroxyphenylpyrazole **14** was eliminated by the addition of D_2O since only one exchangeable signal was noted, whereas **14** has three such protons. The structure of the product was thus proposed as the benzopyrano[4,3-*c*]pyrazole **15**. Further evidence for this benzopyranopyrazole accrued from the ^{13}C NMR spectrum, which displayed a signal at δ 84.4 (4-C), which is in the typical range for *gem* diaryl substituted carbon atom in benzo- and naphtho-pyrans (Scheme 6).[25]

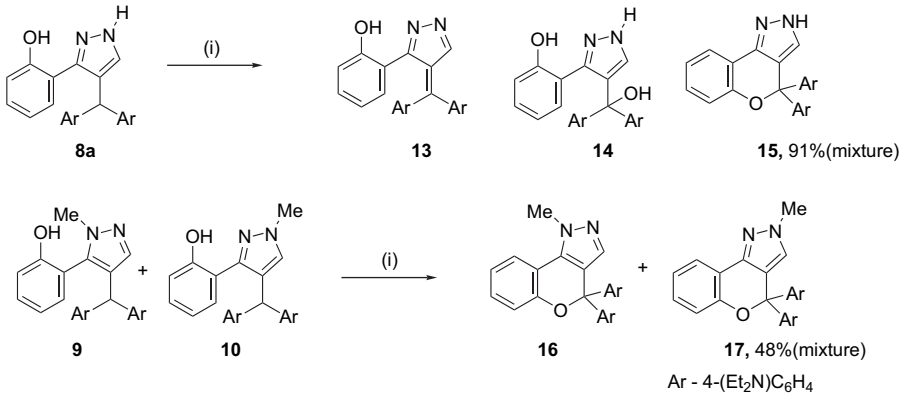
The structure of **15** was firmly established as the benzopyranopyrazole by X-ray crystallography (Fig. 1).[26] Interestingly, **15** exists as a hydrogen bonded dimer composed of two crystallographically different units in the solid state. The bond lengths and angles of the pyrazole ring of **15** compare favourably with those of pyrazole itself.[27] The length of the N1–C3 (1.338 Å) and C2–C4 (1.375 Å) bonds (crystallographic numbering) is suggestive for double bond character and confirms the location of the H atom on N2 (N2–H, 0.88 Å). The most significant difference between the independent units of the dimer is a twist of one of the *N*-ethyl groups. The O1–C1 bond (1.486 Å) of the pyran ring is longer than the typical O–C ether bond (1.42 Å)[28] and compares favourably with the O–C bond (ca. 1.46 Å) of diaryl substituted naphthopyrans.[29]



Scheme 4. Reagents and conditions: (i) $NH_2NH_2{\cdot}H_2O$, EtOH, reflux; (ii) $MeNHNH_2$, EtOH, reflux.



Scheme 5.



Scheme 6. Reagents and conditions: (i) *p*-chloranil, methanol, reflux, then NaOMe, rt.

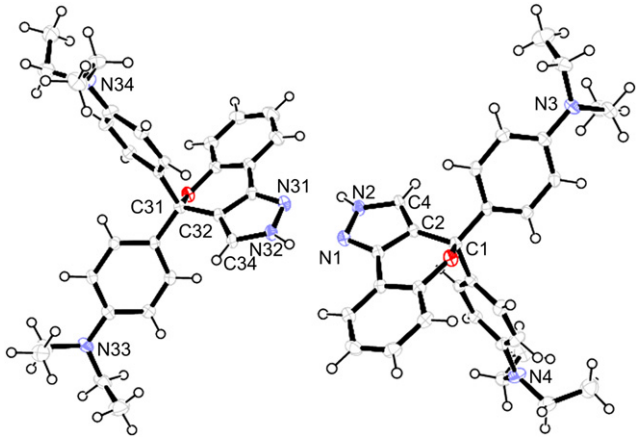
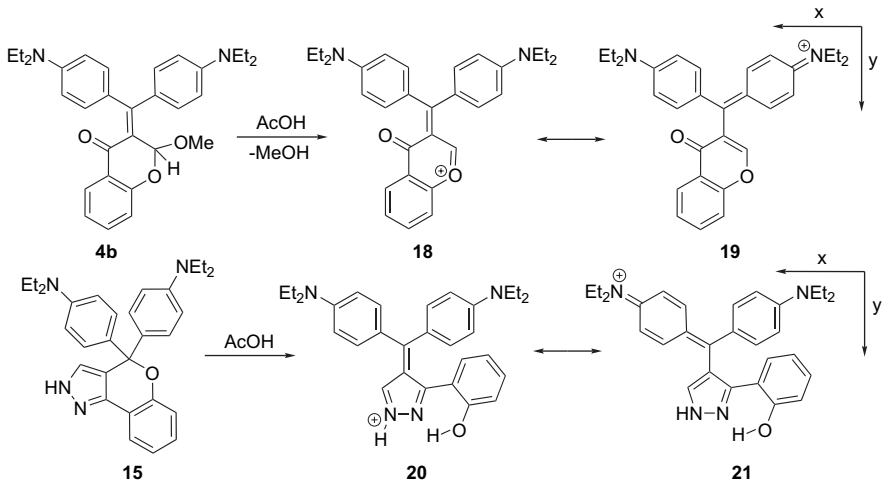


Figure 1. X-ray crystallographic structure of benzopyranopyrazole **15**.

Similarly, oxidation of the mixture of N-Me pyrazoles **9** and **10** gave a mixture of benzopyranopyrazoles **16** and **17** (48%). The isomer ratio was calculated as 2:3, again established by comparison of the relative intensities of the *N*-methyl signals at δ 3.92 (minor) and 4.16 (major). Attempts to oxidise the pyrazole **8b** with either *p*-chloranil or triphenylcarbenium fluoroborate failed. The formation of pyrazoles **15**, **16** and **17** involves the trapping of the carbocationic intermediate that results from the abstraction of hydride ion by *p*-chloranil from the diarylmethine moiety by the pendant 2-hydroxyphenyl unit. This intramolecular pyran ring forming protocol constitutes a new route to the fused benzopyranopyrazole ring system; previous approaches rely upon the construction of the pyrazole ring by condensation of a hydrazine derivative with a suitably functionalised benzopyranone.[30] Interestingly, the colour forming properties of 4,4-diarylbenzopyranopyrazoles have been previously reported; however, these compounds were obtained by an alternative procedure involving the $POCl_3$ promoted condensation of Michler's ketone and a substituted 5-(2-hydroxyphenyl)pyrazole.[31]

The electronic absorption spectra of **4** and pyrazoles **15**, **16** and **17** were investigated, since protonation of these compounds generates an intensely coloured cationic species (Scheme 7). Dissolution of **4a–c** and pyrazoles **15** and mixture **16**, **17** in acetic acid resulted in the instantaneous development of an intense green colour. The visible spectra of these compounds (ca. 2×10^{-5} mol dm^{-3} in 98% aqueous acetic acid) are displayed in Figures 2 and 3. The visible spectra of cations **18/19** developed from **4** show two distinct absorption bands; a weak short wavelength band at 428 nm



Scheme 7.

and a significantly more intense band at ca. 640 nm. The spectra of the pyrazoles also display two bands with the short wavelength band appearing at ca. 453 nm and the long wavelength band at ca. 630 nm. The molar extinction coefficients for the long wavelength bands of **18/19** are comparable with those of triarylmethine dyes[32] and are in the range

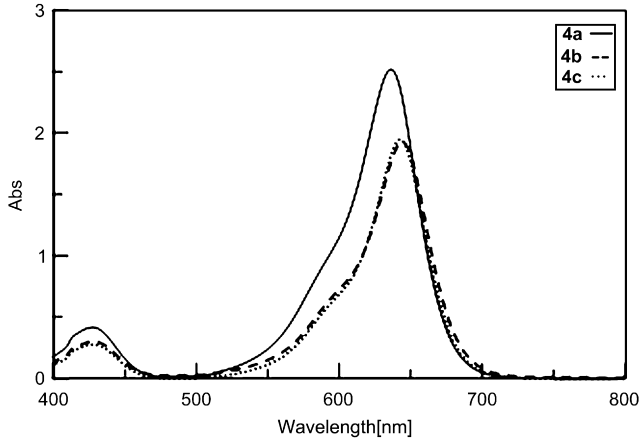


Figure 2. Visible spectra of benzopyranones **4** in acetic acid.

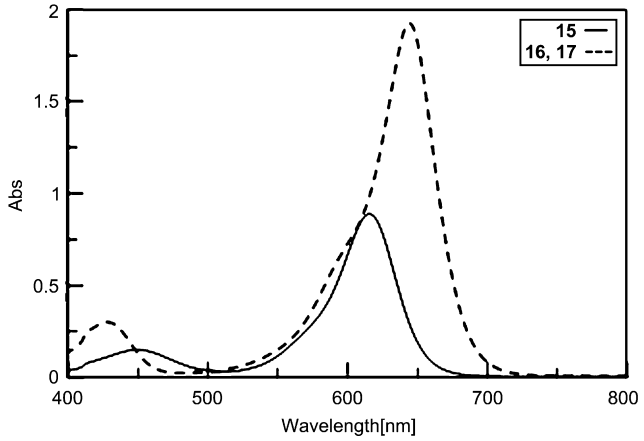


Figure 3. Visible spectra of benzopyranopyrazoles **15** and mixture **16**, **17** in acetic acid.

80–110,000 $mol^{-1}\,dm^3\,cm^{-1}$ (Table 1), whereas those for the cations **20/21** developed from the pyrazoles are lower.

The evolution of the absorption bands is comparable with those of triarylmethine dyes where the long wavelength absorption (x) band may be considered to arise from electronic transitions associated with the cyanine type resonance structures **19** and **21** (N-donor, N-acceptor), whereas the short wavelength (y) band results from electronic transitions associated to resonance structures **18** and **20** (Scheme 7).[33]

We were interested in further exploring the structure of the cationic species that result from protonation of **4b** and **15** by NMR spectroscopy using CD_3CO_2D as the solvent. In the ^1H NMR spectrum of **4b** recorded in CD_3CO_2D the terminal NEt_2 groups are now equivalent and resonate at δ 1.36 (t, J=6.8 Hz, CH_3) and δ 3.76 (q, J=6.8 Hz, NCH_2); the latter group shifted downfield by ca. 0.4 ppm on protonation. Interestingly, the signal for the MeOD unit, derived from the elimination of methanol from **4b** upon deuteration, appears at δ 3.46 as a singlet presumably, as a consequence of rapid deuterium exchange. 2-H now resonates at δ 8.34, significantly deshielded compared with non-protonated **4b** (δ 5.57), and appears further downfield of the chemical shift range normally associated with 2-H of chromones (ca. δ 7.8) but not as far downfield as 2-H in benzopyrylium salts (ca. δ 9.6).[18] The ^{13}C NMR spectrum of **4b** in CD_3CO_2D shows a singlet at δ 13.1 and δ 46.9 accounting for equivalent NEt_2 groups. The low field signal at δ 177.1 is assigned to a chromone-like C=O group [chromone δ C=O 176.9 ($CDCl_3$)[18]] and resonates further upfield of the chromanone-like C=O group in non-protonated **4b**. These NMR data are suggestive of a cationic dye structure in which form **19** predominates.

Table 1. Spectroscopic data for compounds **4**, **15**, **16** and **17** in acetic acid

No.	Wavelength (nm)	$\varepsilon\times10^4$ ($mol^{-1}\,dm^3\,cm^{-1}$)
4a	428, 636	11.0
4b	428, 642	8.1
4c	428, 644	9.4
15	450, 616	3.6
16, **17**	456, 644	6.5

The ^{1}H NMR spectrum of **15** recorded in CD_3CO_2D at 20 °C was less informative as a consequence of incomplete ring-opening of the pyran ring as indicated by the presence of two signals (ratio 1:2) for the methyl groups of the terminal NEt_2 units at δ 1.13 and δ 1.29 (minor, ring-opened form). A similar ratio was observed for the pyrazole ring protons, which appeared at δ 7.56 (major, ring-closed form) and at δ 7.84 (minor, ring-opened form). The ^{1}H NMR spectrum of a solution of **15** equilibrated at 75 °C for 1 h showed significant broadening of the aromatic signals but did however results in complete conversion to the ring-opened form as indicated by the absence of a signal at δ 1.13. This shift in the equilibrium between the ring-closed and -opened forms on warming confirms that the diaryl substituted pyranopyrazole system offers potential as a thermochromic material.

3. Experimental

3.1. General

Melting points were determined in capillary tubes and are uncorrected. Visible spectra were recorded for solutions in spectroscopic grade glacial acetic acid (98% aq) in 10 mm quartz cells at 20 °C using an Analytik Jena Specord S100 diode array spectrophotometer. Infrared spectra were recorded on a Perkin–Elmer Spectrum Spotlight infrared spectrophotometer. NMR spectra were recorded on a Bruker Avance 400 MHz instrument for solutions in $CDCl_3$. The formyl benzo-(naphtho)-pyrans **1a**, **1b** and **1c** were obtained according to the method described by Harnish.[11]

3.2. General method for the preparation of 3-[bis-(4-aminophenyl)methyl]benzopyranones

A solution of concentrated sulfuric acid (5 mL) and water (4 mL) was added to a stirred mixture of 3-formyl-4*H*[1]benzopyran-4-one (8.7 g, 50 mmol) and an aromatic tertiary amine (100 mmol). The mixture was maintained at 110 °C for 8 h and then upon cooling to ca. 60 °C was diluted with aqueous NaOAc solution [($NaOAc \cdot 3H_2O$ (30 g, 220 mmol), water (150 mL)]. The resulting suspension was extracted with CH_2Cl_2 (6×50 mL) and the combined extracts were washed with water (2×50 mL). Removal of the dried (anhydrous Na_2SO_4) solvent gave the crude adduct, which was recrystallised from EtOAc/hexane.

3.2.1. 3-[Bis-(4-dimethylaminophenyl)methyl]-4*H*[1]-benzopyran-4-one (2a). Pale green microcrystals (9.6 g, 48%); mp 169–171 °C; ν_{max} 1646, 1611 cm^{-1}; δ_H 2.91 (12H, s, $(NMe_2)_2$), 5.60 (1H, s, methine), 6.67 (4H, m, Ar-H), 7.06 (4H, m, Ar-H), 7.35 (1H, m, 6-H), 7.39 (1H, dd, *J*=8.2, 0.9 Hz, 8-H), 7.43 (1H, d, *J*=1.2 Hz, 2-H), 7.62 (1H, m, 7-H), 8.20 (1H, dd, *J*=8.1, 1.2 Hz, 5-H) (found: C, 78.1; H, 6.6; N, 6.9. $C_{26}H_{26}N_2O_2$ requires C, 78.4; H, 6.5; N, 7.0%).

3.2.2. 3-[Bis-(4-diethylaminophenyl)methyl]-4*H*[1]benzopyran-4-one (2b). Bright yellow microcrystals (12.5 g, 55%); mp 132–134 °C [lit. mp 131–131.5 °C[11]]; ν_{max} 1650, 1611 cm^{-1}; δ_H 1.13 (12H, t, *J*=7.2 Hz, $(N(CH_2CH_3)_2)_2$), 3.30 (8H, q, *J*=7.2 Hz, $(N(CH_2CH_3)_2)_2$), 5.57 (1H, s, methine), 6.60 (4H, m, Ar-H), 7.02 (4H, m, Ar-H), 7.35 (1H, m, 6-H), 7.40 (1H, dd, *J*=8.1, 1.0 Hz, 8-H), 7.47 (1H, d, *J*=0.9 Hz, 2-H), 7.61 (1H, m, 7-H), 8.20 (1H, dd, *J*=8.0, 1.3 Hz, 5-H); δ_C 13.1, 44.8, 45.4, 112.3, 118.4, 124.5, 125.1, 126.7, 129.3, 129.6, 130.2, 133.6, 146.8, 155.6, 156.7, 177.4.

3.2.3. 3-[Bis-(4-pyrrolidinophenyl)methyl]-4*H*[1]benzopyran-4-one (2c). Off-white microcrystals (15.1 g, 67%); mp 178–180 °C; ν_{max} 1642, 1612 cm^{-1}; δ_H 1.97 (8H, m, $((CH_2)_2)_2$), 3.25 (8H, m, $(N(CH_2)_2)_2$), 5.59 (1H, s, methine), 6.49 (4H, m, Ar-H), 7.04 (4H, m, Ar-H), 7.34 (1H, m, 6-H), 7.39 (1H, dd, *J*=8.2, 1.1 Hz, 8-H), 7.43 (1H, d, *J*=0.8 Hz, 2-H), 7.61 (1H, m, 7-H), 8.20 (1H, dd, *J*=8.1, 1.6 Hz, 5-H) (found: C, 79.6; H, 6.6; N, 6.2. $C_{30}H_{30}N_2O_2$ requires C, 80.0; H, 6.7; N, 6.2%).

3.2.4. 3-{Bis-[4-(*N*-isopropyl-*N*-methylamino)phenyl]-methyl}-4*H*[1]benzopyran-4-one (2d). Pale yellow microcrystals (4.3 g, 19%); mp 161–163 °C; ν_{max} 1649, 1611 cm^{-1}; δ_H 1.13 (12H, d, *J*=6.6 Hz, $(CH(CH_3)_2)_2$), 2.69 (6H, s, $(NMe)_2$), 4.04 (2H, sept, *J*=6.6 Hz, $(CH(CH_3)_2)_2$), 5.59 (1H, s, methine), 6.70 (4H, m, Ar-H), 7.03 (4H, m, Ar-H), 7.35 (1H, m, 6-H), 7.41 (1H, dd, *J*=8.0, 0.9 Hz, 8-H), 7.44 (1H, d, *J*=1.0 Hz, 2-H), 7.63 (1H, m, 7-H), 8.20 (1H, dd, *J*=8.0, 1.6 Hz, 5-H) (found: C, 79.0; H, 7.6; N, 6.2. $C_{30}H_{34}N_2O_2$ requires C, 79.3; H, 7.5; N, 6.2%).

3.3. General method for the preparation of [bis-(methoxyphenyl)methyl]benzopyranones

$BF_3 \cdot OEt_2$ (21.8 mL, 172 mmol) was added in a single portion to a stirred solution of the formylbenzo- or -naphthopyran (29 mmol) and the methoxybenzene (60 mmol) in dry CH_2Cl_2 (70 mL) at room temperature. The solution was heated to reflux and followed by TLC. On completion of the reaction the cooled mixture was poured into water (400 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL) and then the combined CH_2Cl_2 extracts were washed with water (2×50 mL), dried (anhyd Na_2SO_4) and evaporated to afford the crude product. The crude product was eluted from silica with 30% EtOAc in hexane to afford the title compounds, which were further purified by recrystallisation from EtOAc and hexane.

3.3.1. 3-[Bis-(4-methoxyphenyl)methyl]-4*H*[1]benzopyran-4-one (2e) and 6-[(4-methoxyphenyl)-(4-oxo-4*H*[1]benzopyran-3-yl)methyl]-3-bis(4-methoxyphenyl)-methyl-4*H*[1]benzopyran-4-one (5). Elution from silica gave two fractions. Fraction 1: 3-[bis-(4-methoxyphenyl)-methyl]-4*H*[1]benzopyran-4-one (**2e**) from anisole and (**1a**) as off-white microcrystals (5.4 g, 50%); mp 98–101 °C; ν_{max} 1636, 1608, 1509, 1242, 759 cm^{-1}; δ_H 3.77 (6H, s, $(OMe)_2$), 5.67 (1H, s, methine), 6.82 (4H, m, Ar-H), 7.11 (4H, m, Ar-H), 7.39 (3H, m, 6-H, 8-H, 2-H), 7.64 (1H, m, 7-H), 8.19 (1H, dd, *J*=8.1, 1.5 Hz, 5-H) (found: C, 77.4; H, 5.3; [M+H$^+$] 373.1429. $C_{24}H_{20}O_4$ requires C, 77.4; H, 5.4%; [M+H$^+$] 373.1434). Fraction 2: 6[(4-methoxyphenyl)-(4-oxo-4*H*[1]benzopyran-3-yl)methyl]-3-bis(4-methoxyphenyl)methyl-4*H*[1]benzopyran-4-one (**5**) as off-white microcrystals (1.29 g, 7%); mp 170–174 °C; ν_{max} 1635, 1608, 1464, 1242, 755 cm^{-1}; δ_H 3.73 (6H, s, $(OMe)_2$), 3.74 (3H, s, OMe), 5.54 (1H, s, methine), 5.92 (1H, d, *J*=4.8 Hz, methine), 6.74 (5H, m, Ar-H), 6.81 (1H,

dd, J=8.4, 2.8 Hz, Ar-H), 6.99 (5H, m, Ar-H), 7.29 (2H, m, Ar-H), 7.35 (4H, m, Ar-H), 7.63 (2H, m, Ar-H), 8.14 (2H, m, 5-H); δ_C 40.0, 45.3, 45.4, 55.1, 55.2, 55.6, 110.7, 113.7, 113.8, 117.9, 118.0, 123.9, 124.7, 124.8, 126.1, 127.4, 128.4, 129.7 (6), 129.7 (9), 129.8 (4), 130.3, 133.1, 133.2, 133.3 (6), 133.4, 154.1, 154.5, 155.0, 155.1, 155.6, 156.1, 156.2, 156.3, 158.0 (6), 158.1, 176.6, 176.7 (found: C, 77.2; H, 5.1; [M+H$^+$] 637.2217. $C_{41}H_{32}O_7$ requires C, 77.3; H, 5.1%; [M+H$^+$] 637.2226).

3.3.2. 3-[Bis-(2,4-dimethoxyphenyl)methyl]-4*H*[1]benzopyran-4-one (2f). Obtained from 1,3-dimethoxybenzene and **1a** as pale yellow microcrystals (4.0 g, 32%); mp 178–181 °C; ν_{max} 1638, 1610, 1584, 1463, 1137, 1033, 753 cm^{-1}; δ_H 3.74 (6H, s, $(OMe)_2$), 3.79 (6H, s, $(OMe)_2$), 6.15 (1H, s, methine), 6.35 (2H, dd, J=8.4, 2.4 Hz, Ar-H), 6.47 (2H, d, J=2.4 Hz, Ar-H), 6.81 (2H, d, J=8.4 Hz, Ar-H), 7.29 (1H, d J=1.1 Hz, 2-H), 7.34 (1H, m, 6-H), 7.40 (1H, dd, J=8.0, 1.9 Hz, 8-H), 7.61 (1H, m, 7-H), 8.20 (1H, dd, J=8.0, 1.7 Hz, 5-H) (found: C, 72.2; H, 5.6. $C_{26}H_{24}O_6$ requires C, 72.2; H, 5.6%).

3.3.3. 2-[Bis-(4-methoxyphenyl)methyl]-1*H*-naphtho[2,1-*b*]pyran-1-one (2g). Obtained from anisole and **1b** as cream microcrystals (6.5 g, 53%); mp 138–140 °C; ν_{max} 1639, 1610, 1596, 1438, 1237 cm^{-1}; δ_H 3.77 (6H, s, $(OMe)_2$), 5.78 (1H, s, methine), 6.84 (4H, m, Ar-H), 7.14 (4H, m, Ar-H), 7.42 (1H, d, J=1.1 Hz, 2-H), 7.46 (1H, d, J=9.2 Hz, Ar-H), 7.59 (1H, m, Ar-H), 7.68 (1H, m, Ar-H), 7.88 (1H, dd, J=8.9, 1.8 Hz, Ar-H), 8.08 (1H, d, J=8.7 Hz, Ar-H), 10.10 (1H, dd, J=8.8, 2.2 Hz, 10-H) (found: C, 79.6; H, 5.2. $C_{28}H_{22}O_4$ requires C, 79.6; H, 5.2%).

3.3.4. 3-[Bis-(4-methoxyphenyl)methyl]-4*H*-naphtho[1,2-*b*]pyran-4-one (2h). Obtained from anisole and **1c** as a pale brown glass (4.8 g, 39%); ν_{max} 1639, 1608, 1239, 1029 cm^{-1}; δ_H 3.78 (6H, s, $(OMe)_2$), 5.74 (1H, s, methine), 6.85 (4H, m, Ar-H), 7.14 (4H, m, Ar-H), 7.58 (1H, d, J=1.2 Hz, 2-H), 7.65 (3H, m, Ar-H), 7.91 (1H, d, J=8.8 Hz, Ar-H), 8.14 (1H, d, J=8.9 Hz, Ar-H), 8.40 (1H, d, J=8.7 Hz, 5-H) (found: C, 79.3; H, 5.2. $C_{28}H_{22}O_4$ requires C, 79.6; H, 5.2%).

3.4. General method for the oxidation of 3-[bis(4-aminophenyl)methyl]benzopyranones and hydroxyphenylpyrazoles

p-Chloranil (1.1 g, 4.5 mmol) was added in a single portion to a stirred suspension of the 3-[bis(4-aminophenyl)methyl]-benzopyranone or hydroxyphenylpyrazole (4.0 mmol) in anhydrous methanol (50 mL). The mixture was refluxed until no starting material remained by TLC examination (ca. 4 h). Sodium methoxide [from sodium (0.46 g, 20 mmol) and anhydrous methanol (40 mL)] was added to the cold solution and the resulting precipitate was collected by vacuum filtration, washed well with cold methanol (3×20 mL) and air dried. Analytically pure material was obtained by recrystallisation from EtOAc/hexane.

3.4.1. 3-[Bis-(4-dimethylaminophenyl)methylene]-2,3-dihydro-2-methoxy-4*H*[1]benzopyran-4-one (4a). Obtained from **2a** as orange-red crystals (1.3 g, 73%); mp 180–182 °C; ν_{max} 1655, 1603 cm^{-1}; δ_H 2.98 (6H, s, NMe_2), 3.04 (6H, s, NMe_2), 3.43 (3H, s, 2-OMe), 5.56 (1H, s, 2-H), 6.58 (2H, m, Ar-H), 6.67 (2H, m, Ar-H), 7.07 (4H, m, 6-H, 8-H, Ar-H), 7.19 (2H, br m, Ar-H), 7.46 (1H, m, 7-H), 7.95 (1H, dd, J=7.8, 1.9 Hz, 5-H) (found: C, 75.5; H, 6.4; N, 6.4; [M+H$^+$] 429.2176. $C_{27}H_{28}N_2O_3$ requires C, 75.7; H, 6.5; N, 6.5%; [M+H$^+$] 429.2173).

3.4.2. 3-[Bis-(4-diethylaminophenyl)methylene]-2,3-dihydro-2-methoxy-4*H*[1]benzopyran-4-one (4b). Obtained from **2b** as lustrous red crystals (1.8 g, 92%); mp 209–211 °C; ν_{max} 1651, 1602 cm^{-1}; δ_H 1.16 (6H, t, J=6.8 Hz, $N(CH_2CH_3)_2$), 1.21 (6H, t, J=6.8 Hz, $N(CH_2CH_3)_2$), 3.35 (8H, m, $(N(CH_2CH_3)_2)_2$), 3.44 (3H, s, 2-OMe), 5.57 (1H, s, 2-H), 6.51 (2H, m, Ar-H), 6.62 (2H, m, Ar-H), 7.01 (4H, m, 6-H, 8-H, Ar-H), 7.17 (2H, br m, Ar-H), 7.45 (1H, m, 7-H), 7.96 (1H, dd, J=7.9, 1.8 Hz, 5-H); δ_C 12.6, 12.7, 44.2, 44.3, 55.2, 104.8, 110.1, 117.7, 121.5, 123.1, 123.9, 127.0, 127.3, 127.5, 133.0, 133.2, 134.6, 138.1, 148.7, 148.9, 155.9, 158.6, 183.3; δ_H (CD_3CO_2D) 1.36 (12H, t, J=6.8 Hz, $N(CH_2CH_3)_2$), 3.46 (3H, s, OMe), 3.76 (8H, m, $(N(CH_2CH_3)_2)_2$), 7.06 (4H, m, Ar-H), 7.64 (1H, m, 6-H), 7.75 (1H, d, J=8.4 Hz, 8-H), 7.96 (1H, m, 7-H), 8.29 (1H, dd, J=8.0, 1.9 Hz, 5-H), 8.37 (1H, s, 2-H); δ_C (CD_3CO_2D) 13.1, 46.9, 49.8, 114.8, 119.7, 125.7, 127.5, 127.8, 128.1, 136.5, 141.2, 156.7, 157.4, 162.8, 165.9, 170.8, 177.1; (found: C, 76.8; H, 7.5; N, 5.6; [M+H$^+$] 485.2799. $C_{31}H_{36}N_2O_3$ requires C, 76.9; H, 7.4; N, 5.8%; [M+H$^+$] 485.2799).

3.4.3. 3-[Bis-(4-pyrrolidinophenyl)methylene]-2,3-dihydro-2-methoxy-4*H*[1]benzopyran-4-one (4c). Obtained from **2c** as red microcrystals (1.3 g, 69%); mp 215–218 °C; ν_{max} 1659, 1604 cm^{-1}; δ_H 1.97 (4H, m, $(CH_2)_2$), 2.04 (4H, m, $(CH_2)_2$), 3.31 (8H, m, $(N(CH_2)_2)_2$), 3.42 (3H, s, 2-OMe), 5.56 (1H, s, 2-H), 6.41 (2H, m, Ar-H), 6.52 (2H, m, Ar-H), 7.01 (4H, m, 6-H, 8-H, Ar-H), 7.19 (2H, br m, Ar-H), 7.45 (1H, m, 7-H), 7.95 (1H, dd, J=7.8, 1.6 Hz, 5-H) (found: C, 77.4; H, 6.6; N, 5.5; [M+H$^+$] 481.2478. $C_{31}H_{32}N_2O_3$ requires C, 77.3; H, 6.7; N, 5.8%; [M+H$^+$] 481.2468).

3.4.4. 4,4-Bis-(4-diethylaminophenyl)-1*H*,4*H*[1]benzopyrano[4,3-*c*]pyrazole (15). Obtained from **8a** as green blocks (1.7 g, 91%); mp 179–181 °C; ν_{max} 3220, 2969, 1603, 1516, 1462, 1189, 1143 cm^{-1}; δ_H 1.12 (12H, t, J=7.0 Hz, $(N(CH_2CH_3)_2)_2$), 3.30 (8H, q, J=7.0 Hz, $(N(CH_2CH_3)_2)_2$), 6.55 (4H, m, Ar-H), 6.91 (1H, m, 8-H), 7.05 (1H, d, J=8.0 Hz, 6-H), 7.15 (5H, m, Ar-H), 7.25 (1H, s, 3-H), 7.63 (1H, d, J=7.9 Hz, 9-H), 9.41 (1H, br s, NH); δ_C 12.6, 44.2, 84.4, 104.5, 110.6, 118.4, 120.6, 121.2, 122.0, 129.0, 129.4, 130.9, 147.1, 153.7; δ_H (CD_3CO_2D, 75 °C) 1.29 (12H, t, J=6.8 Hz, $(N(CH_2CH_3)_2)_2$), 3.64 (8H, q, J=6.8 Hz, $(N(CH_2CH_3)_2)_2$), 6.73 (1H, br s, Ar-H), 6.82 (4H, br m, Ar-H), 7.11 (2H, br s, Ar-H), 7.53 (4H, m, Ar-H), 7.83 (1H, br s, pyrazole-H) (found: C, 77.2; H, 7.3; N, 11.7; [M+H$^+$] 467.2808. $C_{30}H_{34}N_4O$ requires C, 77.3; H, 7.3; N, 12.0%; [M+H$^+$] 467.2805).

3.4.5. 4,4-Bis-(4-diethylaminophenyl)-1-methyl-1*H*,4*H*[1]benzopyrano[3,4-*d*]pyrazole (16) and 4,4-bis-(4-diethylaminophenyl)-2-methyl-2*H*,4*H*[1]benzopyrano[4,3-*c*]pyrazole (17). Obtained from mixture **9**, **10** as pale green microcrystals (0.9 g, 48%); mp 69–70 °C; ν_{max} 3647, 3389, 2966, 1605, 1514, 1239, 1150 cm^{-1}; δ_H 1.12

(24H, t, J=7.1 Hz, ($N(CH_2CH_3)_2)_2$), 3.30 (16H, q, J=7.1 Hz, ($N(CH_2CH_3)_2)_2$), 3.92 (3H, s, NMe minor), 4.16 (3H, s, NMe major), 6.54 (8H, m, Ar-H), 6.90 (2H, m, Ar-H), 7.02 (2H, m, Ar-H), 7.09–7.20 (12H, m, Ar-H, pyrazole-H), 7.48 (1H, dd, J=7.8, 1.4 Hz, 9-H major), 7.67 (1H, dd, J=7.7, 1.4 Hz, 9-H minor); δ_C 12.6, 39.1, 39.3, 44.2, 83.8, 84.9, 110.5, 110.6, 116.4, 118.3, 118.6, 118.9, 121.0, 121.2, 121.7, 121.8, 121.9, 128.0, 128.9, 129.1, 129.3, 130.6, 131.2, 133.2, 135.6, 143.6, 147.0, 147.1, 153.4, 153.7 (found: C, 77.1; H, 7.5; N, 11.6; [M+H$^+$] 481.2961. $C_{31}H_{36}N_4O$ requires C, 77.5; H, 7.5; N, 11.7%; [M+H$^+$] 481.2962).

3.5. General method for the preparation of hydroxyphenylpyrazoles

The hydrazine (19.8 mmol) was added in a single portion to a solution of the 3-[bis(aryl)methyl]benzopyranone (6.6 mmol) in anhydrous ethanol (40 mL). The mixture was refluxed until no benzopyranone remained by TLC examination (ca. 6 h). The cooled mixture was diluted with water (250 mL) and extracted with EtOAc (4×50 mL). The combined EtOAc extracts were washed with water (3×50 mL), dried (anhyd Na_2SO_4) and evaporated to afford a dark green gum, which was recrystallised from EtOAc and hexane.

3.5.1. 4-[Bis-(4-diethylaminophenyl)methyl]-3-(2-hydroxyphenyl)-1*H*-pyrazole (8a). Obtained from **2b** and hydrazine hydrate as pale green microcrystals (2.1 g, 67%); mp 155–158 °C; ν_{max} 3378, 1613, 1570, 1229 cm^{-1}; δ_H 1.13 (12H, t, J=7.2 Hz, ($N(CH_2CH_3)_2)_2$), 3.29 (8H, q, J=7.2 Hz, ($N(CH_2CH_3)_2)_2$), 5.43 (1H, s, methine), 6.59 (4H, m, Ar-H), 6.74 (1H, m, Ar-H), 6.97 (4H, m, Ar-H), 7.01 (1H, dd, J=8.0, 1.6 Hz, Ar-H), 7.10 (1H, s, 5-H), 7.15 (1H, m, Ar-H), 7.44 (1H, dd, J=7.9, 1.5 Hz, Ar-H), 10.02 (1H, br s, NH), 11.06 (1H, br s, OH) (found: C, 76.7; H, 7.8; N, 11.7. $C_{30}H_{36}N_4O$ requires C, 76.9; H, 7.7; N, 12.0%).

3.5.2. 4-[Bis-(4-methoxyphenyl)methyl]-3-(2-hydroxyphenyl)-1*H*-pyrazole (8b). Obtained from **2e** and hydrazine hydrate as a pale brown viscous oil (2.3 g, 89%), which decomposed on attempted purification by vacuum distillation; ν_{max} 3279, 1606, 1582, 1232, 749 cm^{-1}; δ_H 3.76 (6H, s, $(OMe)_2$), 5.55 (1H, s, methine), 6.68 (1H, m, Ar-H), 6.80 (4H, m, Ar-H), 7.01 (6H, m, Ar-H, 5-H), 7.12 (1H, m, Ar-H), 7.31 (1H, dd, J=8.3, 1.4 Hz, Ar-H), 10.18 (1H, br s, NH), 11.09 (1H, br s, OH).

3.5.3. 4-[Bis-(4-diethylaminophenyl)methyl]-3-(2-hydroxyphenyl)-1-methyl-1*H*-pyrazole (minor isomer) (9) and 4-[bis-(4-diethylaminophenyl)methyl]-5-(2-hydroxyphenyl)-1-methyl-1*H*-pyrazole (major isomer) (10). Obtained from **2b** and methylhydrazine as pale green microcrystals (3.0 g, 93%); mp (mixture) 161–166 °C; ν_{max} 3290, 1609, 1514, 1263 cm^{-1}; δ_H 0.90 (12H, t, J=7.0 Hz, ($N(CH_2CH_3)_2)_2$ minor), 1.01 (12H, t, J=7.0 Hz, ($N(CH_2CH_3)_2)_2$ major), 3.20 (8H, q, J=7.0 Hz, ($N(CH_2CH_3)_2)_2$ minor), 3.25 (8H, q, J=7.0 Hz, ($N(CH_2CH_3)_2)_2$ major), 3.62 (3H, s, NMe major), 3.84 (3H, s, NMe minor), 4.85 (1H, s, methine major), 5.40 (1H, s, methine minor), 6.60 (8H, m, Ar-H major and minor), 6.74 (1H, s, Ar-H minor), 6.89–7.02 (13H, m, Ar-H major and minor, 5-H minor), 7.14 (1H, m, Ar-H minor), 7.31 (1H, m, Ar-H major), 7.40 (1H, dd, J=8.3, 1.9 Hz, Ar-H minor), 7.44 (1H, s, 3-H major), 8.51 (1H, br s, OH major) 11.10 (1H, s, OH minor) (found: C, 76.8; H, 8.0; N, 11.4. $C_{31}H_{38}N_4O$ requires C, 77.2; H, 7.9; N, 11.6%).

4. Conclusion

The oxidation of 3-[bis-(diaryl)methyl]chromones **2** with *p*-chloranil provides novel acetals, 3-[bis-(diaryl)methylene]-2-methoxychroman-4-ones, **4** through interception of a pyrylium type intermediate. Treatment of **4** with acid unmasks the acetal and generates an intensely coloured cationic dye. Condensation of **2** with hydrazines affords 3-(2-hydroxyphenyl)-4-[bis-(diaryl)methyl]pyrazoles **8**, **9** and **10**. Oxidation of these (2-hydroxyphenyl)pyrazoles affords 4,4-diarylbenzopyrano[4,3-*c*]pyrazoles **15**, **16** and **17** via interception of a diarylmethine cation; a process, which constitutes a new route to benzopyranopyrazoles. The electronic absorption spectra of **15**, **16** and **17** in acid solution are comparable with those of triphenylmethine cationic dyes.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.08.090.

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26. A suitable crystal of **5** was selected and data collected on a Bruker Nonius KappaCCD Area Detector at the window of a Bruker Nonius FR591 rotating anode (λMo Kα=0.71073 Å) driven by COLLECT (Hooft, R.; Nonius, B. V. *Collect: Data collection software*; 1998) and DENZO (Otwinowski, Z.; Minor, W. Methods in Enzymology. *Macromolecular Crystallography, part A*; Carter, C. W., Jr., Sweet, R. M., Eds.; Academic: London, 1997; Vol. 276, pp 307–326) software at 120 K; The structures were determined in SHELXS-97 (Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467–473) and refined using SHELXL-97 (Sheldrick, G. M. University of Göttingen: Göttingen, Germany, 1997). All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were included in idealised positions with thermal parameters riding on those of the parent atom. Crystallographic data: dark green block, size=0.26×0.22×0.14 mm^3, $C_{30}H_{34}N_4O$; Mr=466.61, T=120(2) K; triclinic, space group P-1, a=10.4914(2) Å, b=15.7502(4) Å, c=16.4434(4) Å; α=100.1210(10)°, β=107.7300(10)°, γ=98.1710(10)°; V=2491.73(10) Å^3, Z=4; $\rho_{(calcd)}$=1.244 Mg m^{-3}; μ=0.077 mm^{-1}, reflections collected=49741, independent reflections=11402 [R_{int}=0.0485], final R indices [$I>2\sigma(I)$], R_1=0.0719, wR_2=0.1643; R indices (all data), R_1=0.0954, wR_2=0.1745. Crystallographic data (excluding structural factors) for the structure in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 296390. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
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