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# Chalcone dimerisation and a mass spectral conflict

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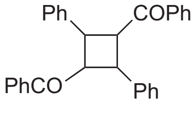
The reaction of a trimethoxychalcone with acetic anhydride and sulfuric acid gives a deep red triarylindenopyrylium cation (as its hydrogen sulfate salt) the structure of which is established by X-ray crystallography and $^{1}$H NMR spectroscopy.

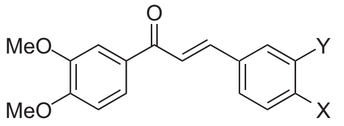
**Keywords:** chalcones, dimerisation, pyrylium salt, X-ray crystal structure

By reacting the simple chalcone 1,3-diphenylpropenone with acetic anhydride and sulfuric acid H. Wieland[1] obtained the colourless tetrasubstituted cyclobutane **1**. The attempted preparation[2] of comparable compounds from chalcones such as **2–4** carrying methoxy substituents was unsuccessful, however, deep red products being formed instead. These were unaffected by aerial oxygen but decomposed when subjected to chromatography giving rise to mixtures of ill-defined yellow products. In only one case, that of the trimethoxychalcone **4** ($C_{18}H_{18}O_4$), was a homogeneous deep red product obtained which was amenable to purification by crystallisation; we have now determined its structure.

The establishment of the molecular formula of the red compound proved to be unexpectedly difficult. The mass spectrum obtained using electron impact (EI) ionisation showed a molecular ion with *m/z* 592 having the formula $C_{36}H_{32}O_8$ *i.e.* ($2 \times C_{18}H_{18}O_4 - 4H$). In contrast, both electrospray (ES) and fast atom bombardment (FAB) mass spectral measurements gave a molecular ion with *m/z* 577 corresponding to the formula $(C_{36}H_{33}O_7)^+$ *i.e.* $(2 \times C_{18}H_{18}O_4 - H_2O - H)^+$. The situation was further complicated by the elemental analysis which showed that sulfur was present and provided yet another formulation, $C_{36}H_{34}O_{11}$ S,$^{1}/_{2}H_2O$. The proton NMR signals of the compound indicated that 33 of the protons were linked to carbon.



**1**



**2**; X = Y = H
**3**; X = Y = OMe
**4**; X = OMe, Y = H

By carrying out an X-ray crystal structure determination we have established that the red product is the pyrylium salt **5;** the structural detail for the organic component is shown in Fig. 1. The geometrical parameters are those expected for such a conjugated system. Thus the tricyclic indenopyrylium nucleus is close to planar (root-mean-square deviation from the best plane for C1–C7/C9–C12/O1 = 0.044 Å), with the sp$^3$ hybrid atom C8 significantly displaced from the best plane by 0.096 (8) Å. C8 is chiral; in the arbitrarily chosen asymmetric molecule it has the *R* configuration, but crystal symmetry generates a 50: 50 *R*/*S* racemic mixture. The C1–C2 bond length of 1.435 (9) Å indicates that there is significant conjugation between the six-membered C1–O1 and C2–C7 rings as would be expected, the one being electron-deficient and the other electron-rich. A notable feature is the differing degrees of twisting of the pendant aryl rings with respect to the tricyclic core of the molecule (Fig. 1), C13–C18 being almost coplanar, C19–C24 close to perpendicular, and C25–C30 intermediate between the two. A number of C–H...O interactions (Table 1) may be involved in consolidating the crystal packing. All the O atoms involved in these links except O2 are parts of hydrogen sulfate moieties. A probable π...π stacking interaction involving the C25–C30 rings of adjacent molecules is also present (Table 1).

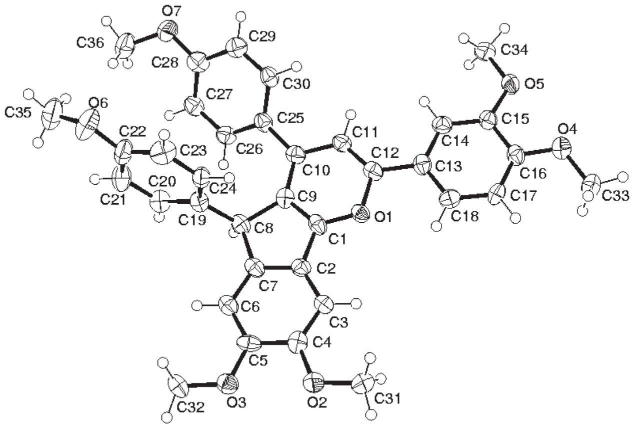


**Fig. 1** The organic component of 5 (50% displacement ellipsoids and arbitrary spheres for the H atoms). Selected geometrical data (Å, °): C1–O1 1.323 (7), C1–C2 1.435 (9), C7–C8 1.524 (9), C8–C9 1.550 (9), C12–O1 1.380 (7), C9–C10 1.407 (9), C8–C19 1.515 (9), C10–C25 1.473 (9), C12–C13 1.476 (9), C7–C8–C9 101.1 (5), C7–C2–C1–C9 0.2 (8), C8–C9–C1–O1 180.0 (6). Dihedral angles (°) for the pendant aryl rings with respect to the best plane for the C1–C7/C9–C12/O1 grouping: C13–C18 3.8 (3), C19–C24 78.97 (15), C25–C30 37.66 (16). Displacements (Å) of the methyl C atoms from the best planes of the aromatic rings carrying the methoxy groups concerned: C31 0.198 (10), C32 0.174 (9), C33 –0.293 (12), C34 –0.140 (12), C35 –0.417 (14), C36 0.462 (13).

The above formulation provides an explanation for the colour of the compound because triarylpyrylium salts are known[3] to be red. It may be significant that many of the canonical formulae which can be drawn for the pyrylium ion present in **5** contain quinonoid structures. The golden fluorescence shown

**Table 1** Weak intermolecular interactions in **5**

| | | | |
|---|---|---|---|
| C3–H3...O11$^{\text{i}}$ | 2.56 | 3.509 (8) | 179 |
| C8–H8...O11$^{\text{ii}}$ | 2.35 | 3.255 (9) | 150 |
| C11–H11...O8$^{\text{iii}}$ | 2.49 | 3.342 (8) | 150 |
| C14–H14...O8$^{\text{iii}}$ | 2.58 | 3.434 (8) | 149 |
| C17–H17...O9$^{\text{i}}$ | 2.54 | 3.404 (8) | 151 |
| C18–H18...O11$^{\text{i}}$ | 2.43 | 3.292 (9) | 150 |
| C24–H24...O2$^{\text{iv}}$ | 2.32 | 3.200 (8) | 154 |
| C30–H30...O8$^{\text{iii}}$ | 2.42 | 3.326 (8) | 160 |
| $\pi1\ldots\pi1^{\text{v}}$ | 3.833 (4) | 0.0 | |

For the C–H...O bonds, the three values refer to the H...O and C...O distances (Å) and C–H...O angle (º), respectively. For the π...π stacking, the two values refer to the *Cg*...*Cg* separation (Å) and the dihedral angle between ring planes (º) where π1 is the centroid (*Cg*) of atoms C25–C30. Symmetry codes: (i) 3/2–*x*, 1/2 + *y*, *z*; (ii) 2–*x*, 1/2 + *y*, *z*–1/2; (iii) 1–*x*, 1/2 + *y*, *z*–1/2; (iv) *x*–1/2, *y*, 1/2–*z*; (v) 1–*x*, 1–*y*, 1–*z*.

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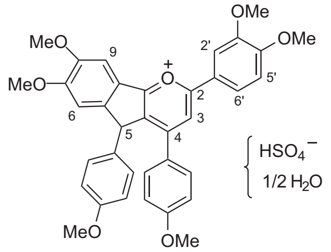
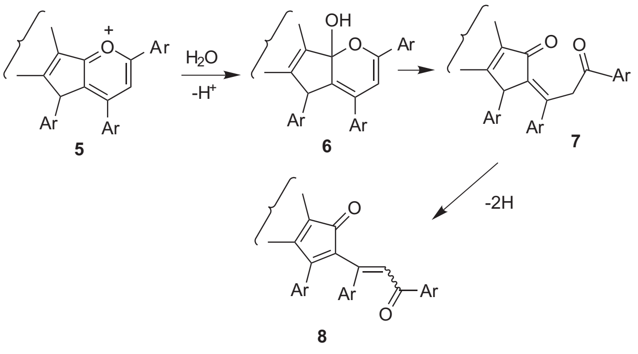


**5**



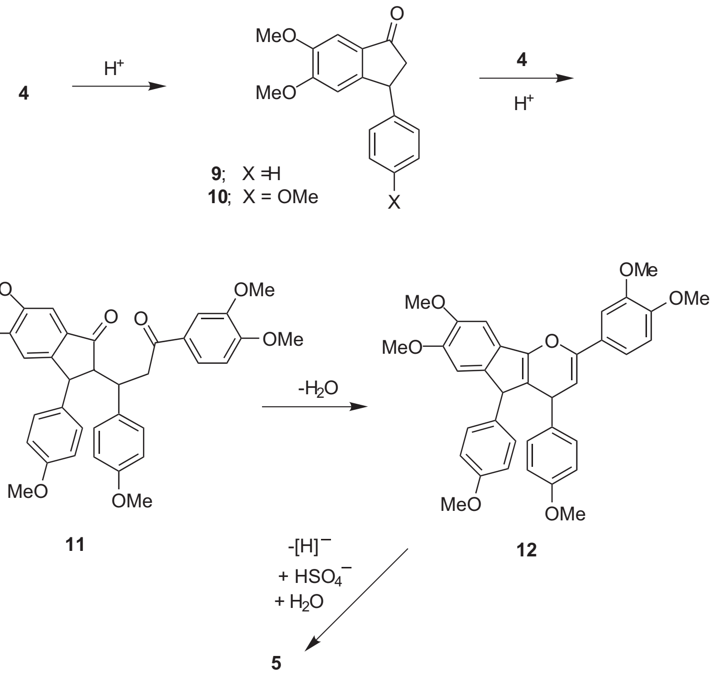
**Scheme 1**

by the compound on exposure to UV light (λ = 254 nm) is also a characteristic feature of such pyrylium salts.[4] The conflicting molecular formulae indicated by the different MS procedures can also be accounted for. Under the relatively mild conditions used in the ES and FAB procedures the indenopyrylium ion from **5** remains intact and provides the observed ion *m/z* 577. EI MS, however, requires the sample to be volatilised by heating and we suggest that during this process the electron-deficient pyrylium grouping of **5** undergoes nucleophilic attack by the water present as shown in Scheme 1. The initial product, the hemiketal **6**, tautomerises to give the dione **7** which in turn loses two hydrogen atoms, *e.g.* by disproportionation, to form the more stable, fully conjugated molecule **8** ($C_{36}H_{32}O_8$); this then provides the observed molecular ion *m/z* 592.

Turning now to the NMR signals of compound **5**, those for the protons of the two 4-methoxyphenyl substituents are typical of such *p*-substituted benzene derivatives. Although strictly they have AA′BB′ spin systems the signals bear a strong resemblance to those of simple AB systems and for comparison purposes may be considered as such. Thus the 4-methoxyphenyl group attached to the C-5 saturated carbon atom shows signals at δ 6.62 and 6.85 which differ by 0.23 ppm and are similar to those[5] of 4-methoxytoluene at δ 6.80 amd 7.08 which differ by a similar amount (0.28 ppm). In contrast, the 4-methoxyphenyl group attached to the electron-withdrawing pyrylium group at C-4 gives rise to signals at δ 6.92 and 7.79 which differ by a much larger amount (0.87 ppm) and are comparable with those shown by 4-methoxyacetophenone[6] at δ 6.93 and 7.94, the difference here being 1.01 ppm.

The NMR spectrum of **5** includes signals for four methine protons which appear not to be coupled. We attribute the singlet at δ 5.66 to H-5 because the shift is close to that calculated (δ 5.40)[7] for such a triarylmethane proton. The signals at δ 6.89 and 7.52 are similar to those at δ 6.66 and 7.36 found for the C-4 and C-7 protons of the dimethoxyindanone **9** and we assign the former to H-6 and H-9 respectively. The signal at δ 8.02 shows the down-field shift typical[8] of a β-proton attached to a pyrylium system and we assign this to H-3. Finally the characteristic couplings of the aromatic protons confirm the presence of the 3,4-dimethoxyphenyl group at C-2.

The formation of the red compound **5** would seem to follow the sequence outlined in Scheme 2. The first step, the sulfuric acid-catalysed cyclisation of the chalcone **4**, would give the arylindanone **10**; related reactions using polyphosphoric acid are known to occur readily.[9] The conjugate addition of the indanone **10** to another molecule of the chalcone **4** would provide the 1,5-diketone **11** which after enolisation and cyclisation produces the pyran **12**. Subsequent removal of hydride ion[10,11] by the protonated chalcone **4** or by the acetylium ion, and the addition of hydrogen sulfate ion and water would give the pyrylium salt **5**.



**Scheme 2**

## Experimental

*General*

IR spectra were measured for potassium bromide discs and UV-visible spectra were obtained for methanolic solutions. $^1$H NMR spectra were measured at 250 or 400 MHz for solutions in deuterochloroform using respectively $Me_4Si$ and residual $CHCl_3$ (7.25 ppm) as internal standards. Electron impact MS were obtained at 70eV.

*Reaction of 1-(3,4-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-enone* **4** *with acetic anhydride and sulfuric acid***:** A solution of the trimethoxychalcone **4**[12] (2 g, 6.71 mmol) in acetic anhydride (50 ml) and concentrated sulfuric acid (1.0 ml) was kept at 20 °C in the dark for 21 days and the resulting crystalline material was collected. The filtrate was added to hot (75 °C) water and kept for 21 days while more crystals separated. The combined solids were washed successively with water and a little chloroform to remove yellow contaminants and crystallised from methanol- chloroform (1: 6) to give 7,8-dimethoxy-2-(3,4-dimethoxyphenyl)-4,5-bis(4-methoxyphenyl)indeno[1,2-*b*] pyrylium hydrogen sulfate hemihydrate **5** (0.53 g, 0.79 mmol, 23.5%) as fine red needles m.p. 244 °C (decomp.) [Found: C, 63.17; H, 5.06; S, 5.02%; M$^+$ (by ES MS), 577.3. $C_{36}H_{34}O_{11}S$, $^1/_2H_2O$ requires C, 63.24; H, 5.16; S, 4.68%. $C_{36}H_{33}O_7^+$ requires *M*, 577.22]; $\nu_{max}$/cm$^{-1}$ 1588 and 1488 (aromatic C =C) and 1226 (aryl ether C-O); $\lambda_{max}$/nm 245.2infl (log ε 5.09), 264.8 (5.06), 295.2infl (4.84), 345.2infl (4.66), 424.5 (5.03) and 505.7 (5.10); $\delta_H$ (400 MHz) 3.68 and 3.84 (each 3H, s, 2 × $CH_3OAr$), 3.93. 3.98, 4.01 and 4.06 (each 3H, s, 2 × $(CH_3O)_2Ar$), 5.66 (1 H, s, H-5), 6.62 and 6.85 (each 2H, d, *J* = 8.8 Hz, AA′BB′ spin system of 4-methoxyphenyl group at C-5), 6.89 (1H, s, H-6), 6.92 and 7.79 (each 2H, d, *J* = 8.8 Hz, AA′BB′ spin system of 4-methoxyphenyl group at C-4), 7.11 (1H, d, *J* = 8.4 Hz, H-5′), 7.52 (1H, s, H-9), 7.68 (1H, d, *J* = 2.0 Hz, H-2′), 7.96 (1H, dd, *J* = 2.0 and 8.4 Hz, H-6′) and 8.02 (1H, s, H-3).

The EI mass spectrum showed a molecular ion with M$^+$, 592.2100 ($C_{36}H_{32}O_8$ requires *M*, 592.2096); *m/z* 592 (73%, M), 427 [37, M-$(MeO)_2C_6H_3CO$] and 165 [100%, $(MeO)_2C_6H_3CO$]. The molecular ion of sulfur dioxide (*m/z* 64, 82%) was also present.

*5,6-Dimethoxy-3-phenylindan-1-one* **9.** This[9] had $\delta_H$ (250 MHz) 2.65 (1 H, dd, $^2J$ = 19.0 Hz, $^3J$ = 3.4 Hz, H-2a), 3.24 (1H, dd, $^2J$ = 19.0 Hz, $^3J$ = 7.7 Hz, H-2b), 3.86 and 3.96 (each 3H, s, ArOMe), 4.51 (1H, dd, $^3J$ = 3.4 and 7.7 Hz, H-3), 6.66 (1H, s, H-4), 7.12-7.34 (5H, m, ArH of Ph) and 7.36 (1H, s, H-7).

*Crystal structure analysis*

Intensity data for a bright red needle (0.18 × 0.04 × 0.03 mm) of **5** were collected using a Nonius Kappa CCD diffractometer (graphite monochromated MoKα radiation, $\lambda$ = 0.71073 Å, *T* = 120 K) with the aid of the COLLECT[13] program to a maximum 2θ value of 52°. The orthorhombic cell parameters of *a* = 10.0575 (5) Å, *b* = 22.2736 (10) Å and *c* = 29.5124 (16) Å [*V* = 6611.3 (6) Å$^3$] were refined against 115094 full or partial reflection positions measured in the 2θ range 5.8–52.0°. The merging of symmetry- equivalent and multiply measured data resulted in 6264 independent reflections ($R_{int}$ = 0.117) from the 44510 measured. The structure of **5** was solved by direct methods in space group *Pbca* (No. 61) using SHELXS-97,[14] which located most of the non-hydrogen atoms. The other non-H atoms were located in difference maps during the full-matrix nonlinear least squares refinement on $|F^2|$, carried out with SHELXL-97.[14] All the H atoms of the organic component were placed in idealised positions [d(C–H) = 0.93–0.97 Å] and refined as riding on their carrier atoms with the constraint $U_{iso}$(H) = 1.2$U_{eq}$(carrier) or 1.5$U_{eq}$(methyl carrier) applied. The S and O atoms of the hydrogen sulfate group were well defined in a difference map, but refinement consistently led to one of the S–O vertices being unreasonably long at 1.58 Å. A difference-map feature presumably corresponding to the postulated water molecule of crystallisation was clearly visible in the vicinity of the sulfate ion (Fig. 2) and was modelled as such. The refinement was practically insensitive to the site occupation factor of this species and essentially identical residuals resulted for full occupancy and the 50% occupancy suggested by the analytical and thermal data. A free refinement of the site occupancy of O12 slowly converged to about 0.93. There are no obvious structural reasons (*e.g.* close contacts) indicating the need for partial occupancy of the water molecule in this structure. The H atoms associated with the hydrogen sulfate and water species were not located although there may well be O–H…O hydrogen bonds between the water molecule and the hydrogen sulfate ion. Final *R*(*F*) and *wR*($F^2$) values of 0.133 and 0.253 resulted. The minimum (–0.49 eÅ$^{-3}$) and maximum (1.21 eÅ$^{-3}$) residual electron density values are both in the vicinity of O12. The diffraction quality was relatively poor which may well correlate with the high value of $R_{Int}$, and the high refinement *R* factors. However, the atomic connectivity revealed for the organic component of **5** is unambiguous.

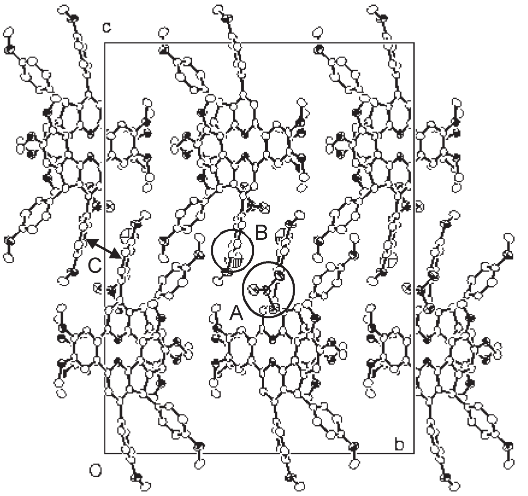


**Fig. 2** Unit cell packing for **5** (H atoms omitted for clarity). The three capital letters indicate respectively the positions of a hydrogen sulfate ion (A), a water molecule (B), and a π…π interaction (C).

Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-275115. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: + 44–(0)1223–336033 or e-mail: deposit@ccdc.cam.ac.uk].

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