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(±)-(4-Oxo-4*H*-chromen-2-yl)-(phenyl)methyl acetate

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The title compound, $C_{18}H_{14}O_4$, forms a supramolecular structure *via* π–π stacking and weak C—H···O and C—H···π interactions. The benzopyran moiety is almost planar. The benzene ring of the phenylmethyl acetate substituent is nearly perpendicular to the fused benzene and pyran rings and also to the methyl acetate group.

Comment

Chromone and coumarin derivatives exhibit a wide spectrum of biological activity, including spasmolytic, anti-arrhythmic, cardiothonic, antiviral, anticancer and alkylating properties (Gabor, 1988; Valenti *et al.*, 1993, 1998). In general, alkylating agents are the first class of cytostatics used for therapy (Zon, 1982). Under *in vivo* conditions, these agents alkylate the nucleophilic centres of nucleobases and amino acids, resulting in either cleavage or crosslinking of double-stranded DNA molecules or proteins. Such cleavage causes damage to DNA, while covalent crosslinks prevent the unwinding of nucleic acids, which is functionally important in replication and transcription processes (Lindermann & Harbers, 1980).

In the multistep reaction of α-bromoketone (I) with trimethyl phosphite, we obtained two products of the Perkov- and Arbuzov-type (Budzisz *et al.*, 2002). The compound cyclizes to form a mixture of diastereoisomers which, subsequently, either lose dimethyl phosphate to give the Wittig-type (March, 1992) product, (III), or undergo 1,2-*trans*-elimination of water on a chromatography column to give the 3-phosphonochromone derivative (II).

The alkylating properties of the test derivatives can be determined by an *in vitro* Preussmann test (Preussmann *et al.*, 1969). This test permits the estimation of the direct ability of the compound to alkylate the model target molecule, 4-(4-nitrobenzyl)pyridine, and it provides a useful indication of alkylation potential for nucleophilic centres of amino acids and nucleobases. However, due to its simplicity, the Preussmann test does not allow the determination of the mode of DNA alkylation. The title compound, (III), possesses very high (+++) alkylating activity (Budzisz *et al.*, 2002). Against this background, and in order to obtain detailed information about the molecular structure of the title compound in the solid state, an X-ray structure investigation was carried out and the results are presented here.

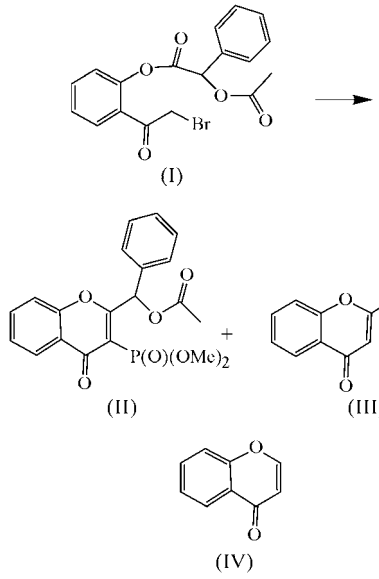

Fig. 1 shows a perspective view of the molecule of (III) with the atom-numbering scheme, and selected bond distances and angles are given in Table 1. Most of the bond lengths and angles are comparable with expected values (Allen *et al.*, 1987). The molecule of (III) consists of two condensed rings, namely a benzene and a pyran ring. The phenylmethyl acetate group is attached in position 2. The two fused rings are almost coplanar; the dihedral angle between the best planes of rings *A* (atoms C5–C10) and *B* (atoms O1/C2–C4/C10/C9) is 3.61 (5)°. The best plane of ring *B* is nearly planar; the deviations of atoms O1, C2, C3, C4, C10 and C9 from the weighted least-squares plane are −0.023, 0.029, 0.017, −0.045,

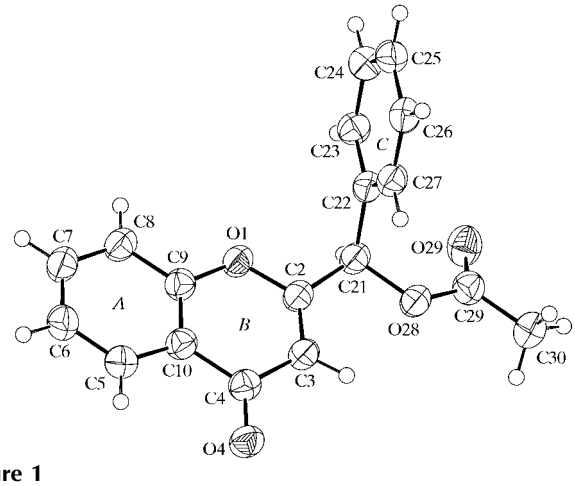

Figure 1
A view of the molecule of (III), with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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0.030 and 0.014 Å, respectively, and this is typical for 255 structures with the benzopyran moiety found in the Cambridge Structural Database (CSD, Version 5.25, November 2003; Allen, 2002). The planarity of the benzopyran moiety confirms the aromatic character of this system. Neverthertheless, a lengthening of the C4—C10 and C4—C3 bonds is observed, to 1.469 (2) and 1.443 (2) Å, respectively, and the C3—C4—C10 valence bond angle decreases to 114.4 (1)°. In contrast, the shortest bond length and the largest angle are observed for atom C2, *viz*. 1.339 (2) Å and 123.6 (1)°, respectively. The C10—C9—C8 and C9—C10—C5 angles are 121.9 (1) and 118.0 (1)°, respectively. Similar variations in the geometric parameters of the pyran ring in the benzopyran system have been reported previously (Rybarczyk-Pirek & Nawrot-Modranka, 2004; Thinagar *et al.*, 2003). It is worth mentioning that a search of the CSD for structures containing the benzopyran fragment, (IV), revealed similar geometric parameters for 255 fragments. Mean values for the geometric parameters of the above analyzed fragment are: C4—C10 = 1.45 (2), C4—C3 = 1.44 (2) and C2—C3 = 1.35 (2) Å; C10—C4—C3 = 115 (2), C3—C2—O1 = 122 (2), C8—C9—C10 = 122 (2) and C5—C10—C9 = 117 (2)°.

Benzene ring *C* (atoms C22–C27) of (III) is almost perpendicular to both the benzopyran moiety and the methyl acetate group. The dihedral angle between ring *C* and rings *A* and *B* is 86.49 (2)°, and the O1—C2—C21—C22 and C3—C2—C21—C22 torsion angles are 63.5 (2) and −116.7 (2)°, respectively, showing a +synclinal (+*sc*) orientation of ring *C* with respect to the benzopyran system. The C22—C21—O28—C29 torsion angle of −76.2 (2)° confirms that it is perpendicular to the methyl acetate group. The structural parameters for the above-mentioned group are consistent with those of 14 similar structures found in the CSD that have a methyl acetate group.

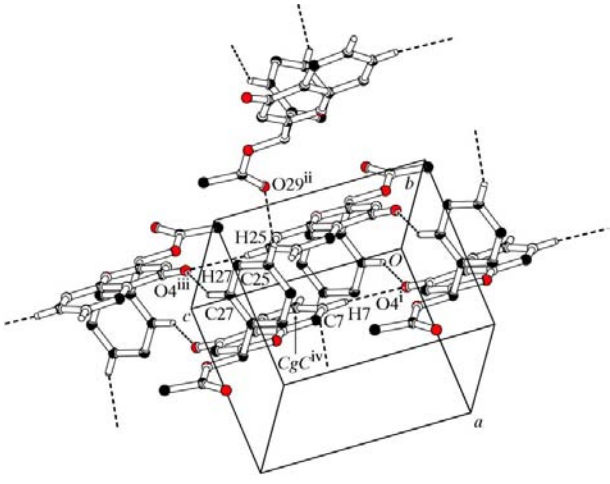

Figure 2
Part of the molecular packing of (III), showing the C—H···O and C—H···π interactions [symmetry codes: (i) $x, y, z-1$; (ii) $x-1, \frac{1}{2}-y, z-\frac{1}{2}$; (iii) $-x, -y, 2-z$; (iv) $-x, -y, 1-z$]. All H atoms, apart from H7, H25, H26 and H6, have been omitted for clarity. *CgC* is the centroid of ring C (atoms C22–C27).

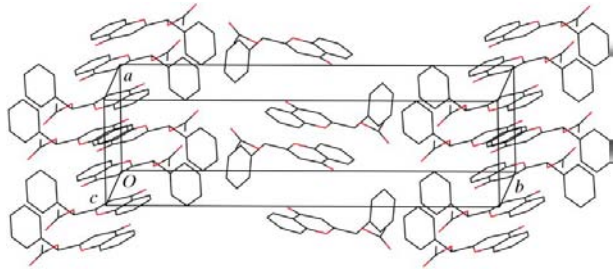

Figure 3
A crystal packing diagram for (III), showing the intermolecular π–π stacking between benzopyran rings.

In compound (III), the supramolecular aggregation is stabilized by a combination of π–π stacking interactions and weak C—H···O and C—H···π interactions (Figs. 2 and 3, and Table 2). Aromatic π–π stacking interactions are formed between rings *A* and *B*. The distances between the ring centroids, $CgA\cdots CgA^{v}$ and $CgB\cdots CgB^{vi}$, are 3.682 (1) and 4.228 (1) Å, respectively [*CgA* is the centroid of ring *A* and *CgB* is the centroid of ring *B*; symmetry codes: (v) $-x, -y, 1-z$; (vi) $1-x, -y, 2-z$]. The perpendicular distances are 3.298 (1) and 3.290 (1) Å for rings *A* and *B*, respectively.

An analysis of the hydrogen bonding in (III) shows many non-conventional C—H···O and C—H···π interactions. Atom C7 is involved in a weak C—H···O intermolecular interaction with atom O4($x, y, z-1$), so generating a $C(7)$ chain motif (Bernstein *et al.*, 1995). Atom O4($-x, -y, 2-z$) is also an acceptor for a weak C4—H4···O4 interaction, which produces an $R_2^2(16)$ motif centred at (0, 0, 1). Atom C25 acts as a donor in an intermolecular interaction [graph set $C(9)$] with atom O29($x-1, \frac{1}{2}-y, z-\frac{1}{2}$). Weak Csp^3—H···π_{arene} interactions, for instance, C6—H6···CgC^{v} [*CgC* is the centroid of ring *C*], complete the range of intermolecular interactions.

Experimental

Acetate (I) (10 mmol) was melted in a flask and trimethyl phosphite (12 mmol) was added dropwise at 383–388 K. After heating for 30 min, excess phosphite was removed by distillation and the resulting yellow oil was applied to a silica-gel column, which was then eluted with a chloroform–acetone mixture (5:1 *v*/*v*). The product was purified by crystallization from acetone (yield 9%). Absorption (diethyl ether): R_F = 0.86; IR (KBr, ν, cm^{-1}): 1764.1, 1658.8 (C═O), 1620 (C═C), 1034 (C—O—C); ^{1}H NMR ($CDCl_3$, p.p.m.): 2.22 (*s*, 3H, CH_3), 6.48 (*s*, 1H, CH), 6.62 (*s*, 1H, CH), 7.42–7.58 (*m*, 9H, aromatic); ^{13}C NMR (75.5 MHz, $CDCl_3$, p.p.m.): 20.54 (–C–CH_3), 74.43 (CH), 76.59 (CH), 123.98, 128.08, 131.16, 146.22, 170.39 (C═O), 189.82 (C═O); EIMS, *m*/*z* (%): 295 (100, $M^+ + 1$), 245 (16).

Crystal data

$C_{18}H_{14}O_4$
M_r = 294.29
Monoclinic, $P2_1/c$
a = 6.8750 (6) Å
b = 25.3741 (17) Å
c = 8.3964 (8) Å
β = 96.303 (8)°
V = 1455.9 (2) Å^3
Z = 4
D_x = 1.343 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 15 217 reflections
θ = 1.6–26.2°
μ = 0.10 mm^{-1}
T = 193 (2) K
Block, colourless
0.50 × 0.24 × 0.20 mm

Data collection

Stoe IPDS-II diffractometer	$R_{int} = 0.087$
φ scans	$\theta_{max} = 26.2^\circ$
15 217 measured reflections	$h = -8 \rightarrow 8$
2926 independent reflections	$k = -30 \rightarrow 31$
2206 reflections with $I > 2\sigma(I)$	$l = -10 \rightarrow 10$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0763P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.042$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.118$	$\Delta\rho_{max} = 0.19$ e Å^{-3}
$S = 1.00$	$\Delta\rho_{min} = -0.18$ e Å^{-3}
2926 reflections	Extinction correction: *SHELXL*97 (Sheldrick, 1997)
202 parameters	Extinction coefficient: 0.059 (7)
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

O1—C2	1.3586 (16)	C9—C8	1.3938 (19)
O1—C9	1.3784 (16)	C22—C23	1.3869 (19)
O28—C29	1.3579 (18)	C22—C21	1.5181 (19)
O28—C21	1.4472 (16)	C26—C25	1.392 (2)
C2—C3	1.3391 (19)	C8—C7	1.376 (2)
C2—C21	1.5030 (19)	C23—C24	1.387 (2)
O4—C4	1.2348 (17)	O29—C29	1.2012 (19)
C27—C26	1.384 (2)	C5—C6	1.374 (2)
C27—C22	1.392 (2)	C5—C10	1.402 (2)
C4—C3	1.443 (2)	C25—C24	1.383 (2)
C4—C10	1.4690 (19)	C7—C6	1.395 (2)
C9—C10	1.391 (2)	C29—C30	1.488 (2)
C2—O1—C9	118.46 (11)	O1—C9—C8	116.33 (12)
C29—O28—C21	115.84 (11)	O28—C21—C2	105.32 (11)
C3—C2—O1	123.64 (13)	O28—C21—C22	110.55 (11)
O1—C2—C21	109.28 (11)	O29—C29—O28	122.58 (13)
O4—C4—C3	123.30 (12)	O29—C29—C30	126.59 (14)
O4—C4—C10	122.28 (13)	O28—C29—C30	110.81 (14)
O1—C9—C10	121.79 (12)		

Table 2
Hydrogen-bonding and short-contact geometry (Å, °).

CgC is the centroid of ring *C* (atoms C22–C27).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C7—H7···O4^{i}	0.93	2.45	3.364 (1)	169
C25—H25···O29^{ii}	0.93	2.48	3.353 (1)	156
C27—H27···O4^{iii}	0.93	2.51	3.286 (1)	141
C6—H6···*CgC*^{iv}	0.93	2.73	3.615 (1)	160

Symmetry codes: (i) $x, y, z-1$; (ii) $x-1, \frac{1}{2}-y, z-\frac{1}{2}$; (iii) $-x, -y, 2-z$; (iv) $-x, -y, 1-z$.

All H atoms were positioned geometrically and refined with a riding model; for phenyl H atoms, C—H = 0.93 Å and U_{iso}(H) = $1.2U_{eq}$(C), and for methyl H atoms, C—H = 0.96 Å and U_{iso}(H) = $1.5U_{eq}$(C). The H atoms of the C30 methyl group showed orientational disorder and were modelled with alternative positions of 20 (2)% occupancy.

Data collection: *Win-EXPOSE* in *X-AREA* (Stoe & Cie, 2000); cell refinement: *Win-CELL* in *X-AREA*; data reduction: *Win-INTEGRATE* in *X-AREA*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 1998); software used to prepare material for publication: *PARST*97 (Nardelli, 1996).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1758). Services for accessing these data are described at the back of the journal.

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