Acta Crystallographica Section E
Structure Reports
Online
ISSN 1600-5368

(*E*)-3-{[(Dimethoxythiophosphoryl)methylhydrazono]methyl}-4*H*-1-benzopyran-4-one, a new chromone derivative substituted with phosphorohydrazide at position 3

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Received 28 April 2004
Accepted 4 May 2004
Online 15 May 2004

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.006 Å
R factor = 0.047
wR factor = 0.127
Data-to-parameter ratio = 12.0

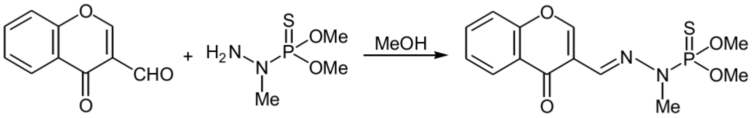
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The molecule of the title compound, $C_{13}H_{15}N_2O_4PS$, consists of a benzopyran moiety substituted with a phosphorohydrazone group in position 3. There are two planar groups, *viz*. benzopyran and methylhydrazone, which are slightly twisted with respect to each other. Owing to the tetrahedral hybridization of the P atom, two methoxy groups are arranged out of the planes. There are intermolecular C—H···O contacts in the crystal structure.

Comment

Compounds involving the benzopyran moiety are analogues of chromone and coumarin, which are natural biologically active compounds. They are known to exhibit diverse pharmacological properties (Gabor, 1988). On the other hand, phosphoramides and phosphorohydrazides have been found to exhibit anticancer activity (Arnold *et al.*, 1961, Quin, 2000; Holland & Frei, 2000) by alkylation of nucleophilic centres of nucleobases and amino-acids. The combination of phosphorohydrazide and heterocyclic moieties in one molecule gives the possibility of obtaining novel compounds with interesting properties.

For the above reasons, many chromone derivatives with a phosphoryl substituent have been synthesized (Nawrot-Modranka & Kostka, 1995; Nawrot-Modranka, 1995). They attracted our attention due to their alkylation properties *in vitro* in the Preussmann test with 4-(4-nitrobenzyl)pyridine (NBP) (Preussmann *et al.*, 1969), and the expected antitumour activity *in vivo* by analogy with other chromones (Valenti *et al.*, 1996; Rajski & Williams, 1998). The possible application in cancer chemotherapy makes knowledge of their molecular structure of great importance. Against this background and in order to obtain detailed information about the molecular structure, in continuation of our previous research (Rybarczyk *et al.*, 1999; Rybarczyk-Pirek *et al.*, 2003; Rybarczyk-Pirek, Grabowski & Nawrot-Modranka, 2002; Rybarczyk-Pirek, Grabowski, Małecka & Nawrot-Modranka, 2002), the crystal structure of the title compound, (I), has been determined by X-ray diffraction methods.



(I)

The molecule of the title compound consists of two condensed rings, forming a benzopyran moiety, substituted in position 3 with a thiophosphorylmethylhydrazide group. The geometry of the benzopyran ring system confirms its aromatic

DOI: 10.1107/S1600536804010943

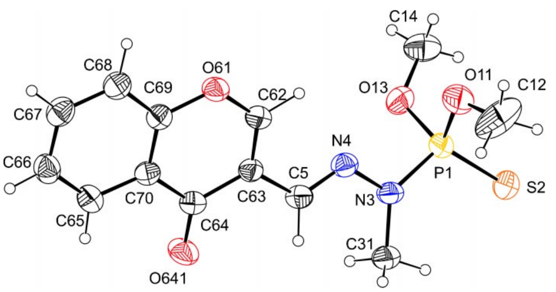


Figure 1
A view of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level. H atoms are shown as small spheres of arbitrary radii.

character. The maximum deviation from the least-squares plane (Nardelli, 1996) is observed for atom C67 [0.014 (5) Å]. Atom C64 is engaged in a formal double C═O bond which results in an elongation of the C—C bonds to 1.462 (6) Å and a decrease of the valence angle to 114.2 (4)° for this atom. In contrast, the shortest bond length and the largest angle are observed for atom C62, *viz*. 1.330 (5) Å and 125.1 (4)°, respectively. Such variations of geometric parameters in the benzopyran system have been reported also for other compounds (Thinagar *et al.*, 2003; Wallet & Gaydou, 1992; Adams *et al.*, 1991). These distances can be compared with the typical aromatic bond length of 1.384 (13) Å (Allen *et al.*, 1987). The dihedral angle between the least-squares planes of the condensed rings forming the benzopyran system is 2.2 (1)°.

The methylhydrazone group (atoms C5, N4, N3 and C31) is planar. Including H atoms, the local symmetry of this moiety is C_s. The methylhydrazone is twisted around the C5—C63 bond with respect to the benzopyran system, with a dihedral angle between the least-squares planes of 16.2 (2)°. Such an arrangement of both groups reduces the possibility of resonance between them.

The P1═S2 bond lies slightly above the methylhydrazone plane; the distances are 0.207 (2) Å for P1 and 0.107 (2) Å for S2. The normal to the methylhydrazone plane forms an angle of 87.0 (2)° with the P1═S2 bond. Thus, the group of atoms C5/N4/N3/C31/P1/S2 can be regarded as almost planar. Such a planar arrangement provides π-conjugation along the C5—N4—N3—P1 chain and induces a planar geometry around the atom N3; this is confirmed by the P1—N3 bond length [1.643 (3) Å], which is much closer to the standard $\text{P—N}_{\text{planar}}$ distance of 1.65 (2) Å than the $\text{P—N}_{\text{pyramidal}}$ distance of 1.68 (1) Å (Allen *et al.*, 1987).

The geometry around the four-coordinate P atom indicates a slight deformation of the tetrahedron towards a trigonal pyramid, typical for such derivatives with one double bond. The bond angles in the P environment range from 97.7 (2) to 117.8 (1)°.

Significant differences in bond length are observed for the methoxy groups, indicating that they are not chemically equivalent. In addition, comparatively large displacement parameters of atom C12 may indicate some disorder of the O11/C12 group.

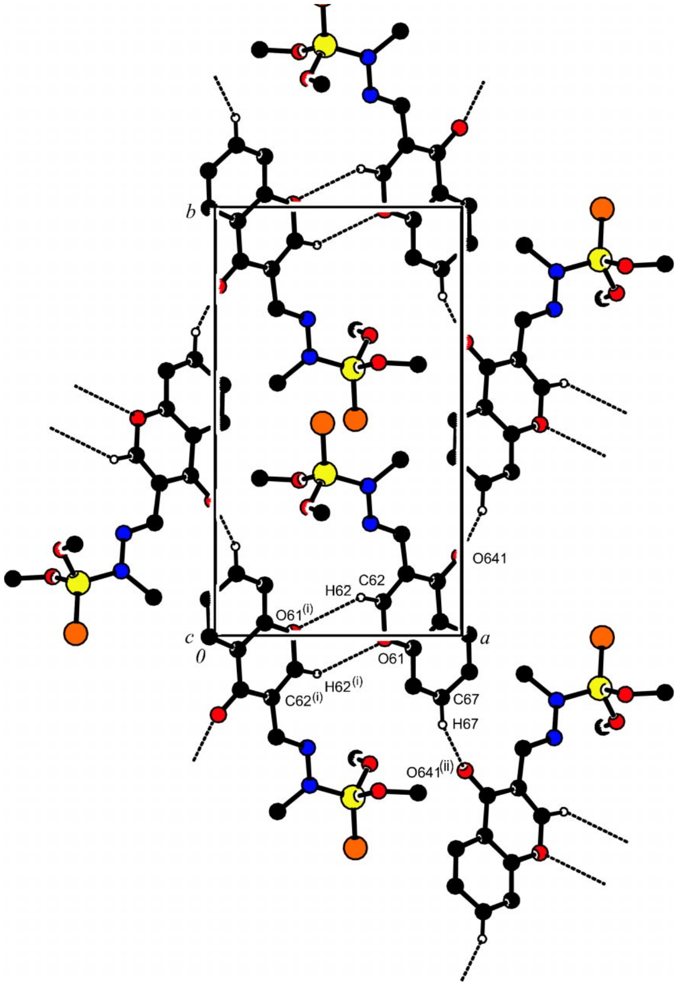


Figure 2
The crystal packing, viewed along the *c* axis, with intermolecular C—H···O contacts indicated by dashed lines. Symmetry codes as in Table 2.

The overall molecular geometry most resembles the molecular geometry of (*E*)-3-{[(diphenoxyphosphoryl)methylhydrazono]methyl}-4*H*-1-benzopyran-4-one, (II) (Rybarczyk-Pirek, Grabowski & Nawrot-Modranka, 2002), a compound in which the only differences are the substituents on P. There are two phenoxy instead of methoxy groups and oxygen instead of sulfur in (II). There are no differences in bond distances and angles greater then 0.012 Å and 4°, respectively, in similar molecular fragments of both compounds. The only exceptions are the N4—C5—C63—C62 and N4—C5—C63—C64 torsion angles which describe the twist of the molecule around the C5—C63 bond.

However, (I) and (II) pack differently, most probably due to different intermolecular interactions. There are relatively short intermolecular C—H···O contacts in (I) (Table 2), which stabilize the crystal packing (Fig. 2).

Experimental

The title compound, (I), was obtained by the reaction of equimolar amounts of 4-oxo-4*H*-benzopyran-3-carbaldehyde (0.41 g) and N^1-dimethoxyphosphonate-N^1-methylhydrazide (0.40 g) in dry methanol (see reaction scheme). After refluxing for 2 h and cooling, the product was precipitated from the reaction solution. Recrystallization from methanol finally gave 0.5 g of the title compound (m.p. 400–402 K). ^{1}H NMR (CDCl$_3$, δ): 3.32 [*d*, 3H, N-CH$_3$, *J*(PN-CH$_3$) = 9.6 Hz], 3.77 [*d*, 3H, O-CH$_3$, *J*(PO-CH$_3$) = 13.8 Hz], 7.28–8.32 (*m*, 5H, aromatic, CH=N), 8.52 (*s*, 1H, CH). ^{31}P NMR (CDCl$_3$, δ): 74.91. Crystals for X-ray analysis were obtained by recrystallization from methanol. Because the compound showed a tendency to form twinned crystals, a thin plate for X-ray measurement had to be cut.

Crystal data

$C_{13}H_{15}N_2O_4PS$
M_r = 326.30
Monoclinic, $P2_1/c$
a = 8.5760 (9) Å
b = 14.9072 (9) Å
c = 12.0912 (5) Å
β = 92.146 (7)°
V = 1544.7 (2) Å^3
Z = 4
D_x = 1.403 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 20 reflections
θ = 20.1–28.6°
μ = 3.00 mm^{-1}
T = 293 (2) K
Plate, colorless
0.20 × 0.20 × 0.05 mm

Data collection

Rigaku AFC-5*S* diffractometer
ω scans
Absorption correction: analytical (de Meulenaer & Tompa, 1965)
$T_{\min}$ = 0.530, $T_{\max}$ = 0.725
2930 measured reflections
2751 independent reflections
1105 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.025
$\theta_{\max}$ = 68.5°
$h = -2 \rightarrow 10$
$k = -1 \rightarrow 17$
$l = -14 \rightarrow 14$
3 standard reflections every 150 reflections intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.127
S = 1.01
2751 reflections
230 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = [\exp\{4.2(\sin\theta/\lambda)^2\}]/[\sigma^2(F_o^2) + (0.0533P)^2]$ where $P = 0.33F_o^2 + 0.67F_c^2$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max}$ = 0.62 e Å^{-3}
$\Delta\rho_{\min}$ = −0.25 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0009 (2)

Table 1
Selected geometric parameters (Å, °).

P1—O11	1.543 (3)	C5—C63	1.467 (5)
P1—O13	1.613 (3)	O61—C62	1.349 (5)
P1—N3	1.643 (3)	O61—C69	1.383 (5)
P1—S2	1.911 (2)	C62—C63	1.330 (5)
O11—C12	1.435 (5)	C63—C64	1.462 (5)
O13—C14	1.381 (5)	C64—O641	1.231 (5)
N3—N4	1.389 (4)	C64—C70	1.462 (6)
N3—C31	1.456 (6)	C69—C70	1.384 (5)
N4—C5	1.272 (5)		
O11—P1—O13	97.7 (2)	N4—C5—C63	121.1 (4)
O11—P1—N3	108.6 (2)	C62—O61—C69	118.1 (3)
O13—P1—N3	102.1 (2)	C63—C62—O61	125.1 (4)
O11—P1—S2	117.9 (2)	C62—C63—C64	120.5 (4)
O13—P1—S2	115.0 (2)	C62—C63—C5	121.5 (4)
N3—P1—S2	113.5 (1)	C64—C63—C5	118.0 (4)
C12—O11—P1	119.0 (3)	O641—C64—C70	122.7 (4)
C14—O13—P1	123.0 (3)	O641—C64—C63	123.1 (4)
N4—N3—C31	120.5 (4)	C70—C64—C63	114.2 (4)
N4—N3—P1	114.0 (3)	O61—C69—C70	121.5 (4)
C31—N3—P1	125.0 (3)	C69—C70—C64	120.5 (4)
C5—N4—N3	118.7 (4)		
O11—P1—N3—N4	43.7 (3)	N3—N4—C5—C63	177.9 (4)
O13—P1—N3—N4	−58.8 (3)	N4—C5—C63—C62	−15.8 (7)
S2—P1—N3—N4	176.8 (2)	N4—C5—C63—C64	163.2 (4)
S2—P1—N3—C31	−11.6 (5)	C5—C63—C64—O641	0.5 (6)
P1—N3—N4—C5	172.1 (3)		

Table 2
Intermolecular C—H···O contacts (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C62—H62···O61$^{\rm i}$	1.04 (5)	2.69 (5)	3.316 (5)	119 (3)
C67—H67···O641$^{\rm ii}$	0.98 (5)	2.59 (4)	3.417 (6)	142 (4)

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

Methoxy H atoms were positioned geometrically, with C—H = 0.96 Å, and refined using a rigid body model, with U(H) = 1.2$U_{\rm eq}$(C). The other H atoms were refined freely.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1989); cell refinement: *MSC/AFC Software Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1989); program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 1998); software used to prepare material for publication: *SHELXL*97, *PARST*97 (Nardelli, 1996) and WinGX (Farrugia, 1999).

This work was financially supported by the Polish State Committee for Scientific Research (KBN No. 4T09A 09925). Financial support for JNM from the Medical University of Łódź (grant No. 502-13-850) is gratefully acknowledged.

References

Adams, H., Bailey, N. A., Giles, P. R. & Marson, C. M. (1991). *Acta Cryst.* C**47**, 1332–1334.

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–19.

Arnold, H., Bourseaux, F. & Brock, N. (1961). *Arzneim. Forsch.*, **11**, 143–158.

Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.

Gabor, M. (1988). *The Pharmacology of Benzopyran Derivatives and Related Compounds*. Budapest: Akadèmiai Kiádo.

Holland, J.F. & Frei, E. (2000). *Cancer Medicine* e.5. Hamilton, London: B.C. Decker Inc.

Meulenaer, J. de & Tompa, H. (1965). *Acta Cryst.* **19**, 1014–1018.

Molecular Structure Corporation (1989). *MSC/AFC Diffractometer Control Software* and *TEXSAN*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Nardelli, M. (1996). *J. Appl. Cryst.* **29**, 296–300.

Nawrot-Modranka, J. (1995). *Pol. J. Chem.* **69**, 1250–1256.

Nawrot-Modranka, J. & Kostka, K. (1995). *Pol. J. Chem.* **69**, 1148–1155.

Preussmann, R., Schneider, H. & Epple, F. (1969). *Arzneim. Forsch.* **19**, 1059–1073.

Quin, L. D. (2000). *A Guide to Organophosphorus Chemistry*. New York: John Wiley and Sons Inc.

Rajski, S. R. & Williams, R. M. (1998). *Chem. Rev.* **98**, 2723–2795.

Rybarczyk, A. J., Olszak, T. A., Małecka, M. & Nawrot-Modranka, J. (1999). *Acta Cryst.* C**55**, 1313–1315.

Rybarczyk-Pirek, A. J., Grabowski, S. J., Małecka, M. & Nawrot-Modranka, J. (2002). *J. Phys. Chem.* **106**, 11956–11962.

Rybarczyk-Pirek, A. J., Grabowski, S. J. & Nawrot-Modranka, J. (2002). *Acta Cryst.* C**58**, o405–o406.

Rybarczyk-Pirek, A. J., Grabowski, S. J. & Nawrot-Modranka, J. (2003). *J. Phys. Chem.* **107**, 9232–9239.

Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Spek, A. L. (1998). *PLATON*. University of Utrecht, The Netherlands.

Thinagar, S., Velmurugan, D., Shanmuga Sundara Raj, S., Fun, H.-K., Gupta, S. C., Merazig, H. & Bouaciada, S. (2003). *Acta Cryst.* C**59**, o181–o183.

Valenti, P., Fabbri, G., Rampa, A., Bisi, A., Gobbi, S., Da Re, P., Carrara, M., Sgevano, A. & Cima, L. (1996). *Anti-Cancer Drug Des.* **11**, 243–252.

Wallet, I. C. & Gaydou, E. M. (1992). *Acta Cryst.* C**48**, 86–88.