

The influence of sulfur substituents on the molecular geometry and packing of thio derivatives of *N*-methylphenobarbital

Alicja Janik,^{a*} Andrzej Olech,^a Anna Stasiewicz-Urban^b
and Katarzyna Stadnicka^a

^aFaculty of Chemistry, Jagiellonian University, Ingardena 3, 30-060 Krakow, Poland, and ^bFaculty of Pharmacy, Medical College, Jagiellonian University, Medyczna 9, 30-688 Krakow, Poland
Correspondence e-mail: janik@chemia.uj.edu.pl

Received 13 November 2008

Accepted 17 December 2008

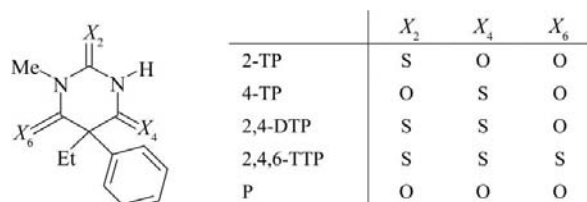
Online 14 January 2009

The room-temperature crystal structures of four new thio derivatives of *N*-methylphenobarbital [systematic name: 5-ethyl-1-methyl-5-phenylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione], C₁₃H₁₄N₂O₃, are compared with the structure of the parent compound. The sulfur substituents in *N*-methyl-2-thiophenobarbital [5-ethyl-1-methyl-5-phenyl-2-thioxo-1,2-dihydropyrimidine-4,6(3*H*,5*H*)-dione], C₁₃H₁₄N₂O₂S, *N*-methyl-4-thiophenobarbital [5-ethyl-1-methyl-5-phenyl-4-thioxo-3,4-dihydropyrimidine-2,6(1*H*,5*H*)-dione], C₁₃H₁₄N₂O₂S, and *N*-methyl-2,4,6-trithiophenobarbital [5-ethyl-1-methyl-5-phenylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trithione], C₁₃H₁₄N₂S₃, preserve the heterocyclic ring puckering observed for *N*-methylphenobarbital (a half-chair conformation), whereas in *N*-methyl-2,4-dithiophenobarbital [5-ethyl-1-methyl-5-phenyl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidine-6(5*H*)-one], C₁₃H₁₄N₂O₂S₂, significant flattening of the ring was detected. The number and positions of the sulfur substituents influence the packing and hydrogen-bonding patterns of the derivatives. In the cases of the 2-thio, 4-thio and 2,4,6-trithio derivatives, there is a preference for the formation of a ring motif of the *R*₂²(8) type, which is also a characteristic of *N*-methylphenobarbital, whereas a *C*(6) chain forms in the 2,4-dithio derivative. The preferences for hydrogen-bond formation, which follow the sequence of acceptor position 4 > 2 > 6, confirm the differences in the nucleophilic properties of the C atoms of the heterocyclic ring and are consistent with the course of *N*-methylphenobarbital thionation reactions.

Comment

Barbiturates are a widespread group of compounds with various pharmacological activities. In particular, phenobarbital, thiopental and pentobarbital have been the subjects of extensive research due to their anaesthetic, sedative,

hypnotic, amnesiac and anticonvulsant properties (Kushikata *et al.*, 2003; Huber *et al.*, 2009). The structures of numerous barbituric acid derivatives, such as phenobarbital, have been studied with respect to their ability to form polymorphs (Williams, 1973, 1974; Platteau *et al.*, 2005; Day *et al.*, 2007). However, there are only a few examples of sulfur analogues of barbiturates. Recently, the crystal structure of 5-benzyl-1,3,5-trimethyltrithiobarbiturate was reported (Takechi *et al.*, 2007).



In this paper, we present the crystal structures of four thio derivatives of *N*-methylphenobarbital, all crystallizing in the centrosymmetric space group *P*2₁/*n*. The structural formulae of the derivatives are given in the scheme. The asymmetric units of *N*-methyl-2-thiophenobarbital, 2-TP, *N*-methyl-4-

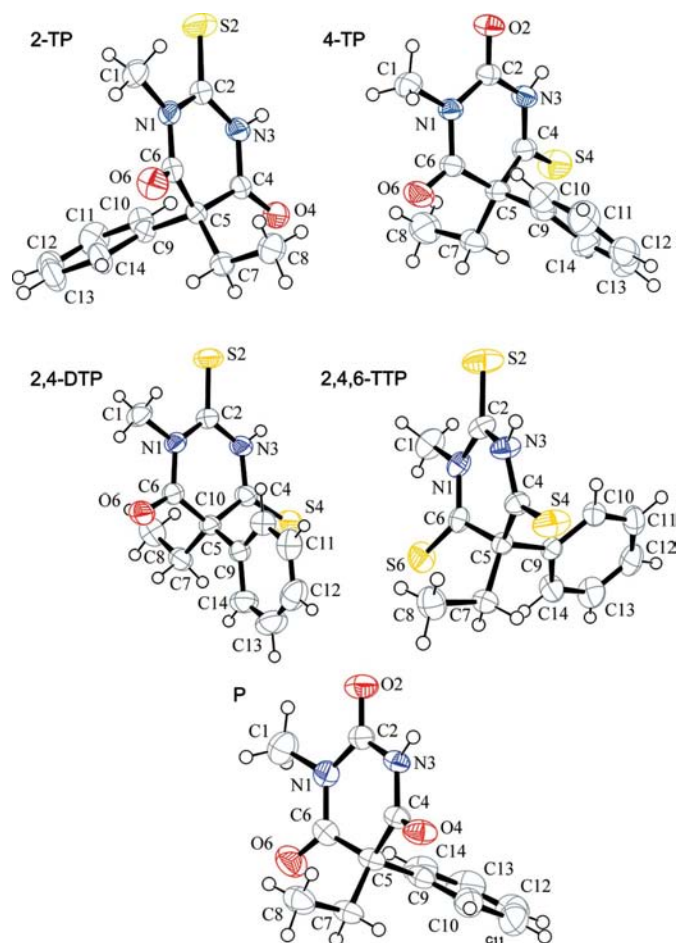


Figure 1
The asymmetric units of 2-TP, 4-TP, 2,4-DTP, 2,4,6-TTP and P, showing the atom-numbering schemes. Displacement ellipsoids are drawn at the 50% probability level.

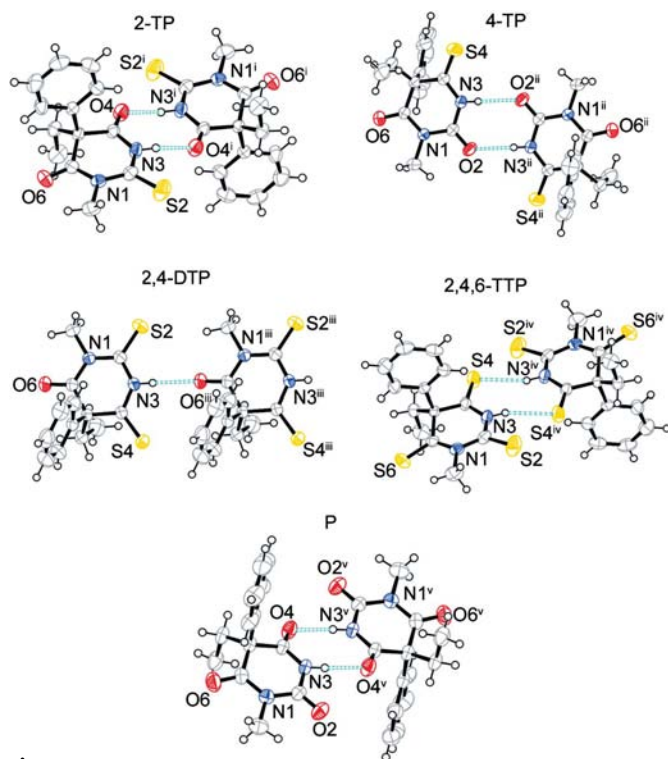


Figure 2

Hydrogen-bond motifs observed in the crystal structures of 2-TP, 4-TP, 2,4-DTP, 2,4,6-TTP and P. [Symmetry codes: (i) $2 - x, 1 - y, -z$; (ii) $2 - x, 1 - y, 1 - z$; (iii) $1 + x, y, z$; (iv) $1 - x, 2 - y, 1 - z$; (v) $-x, -y, 1 - z$.]

thiophenobarbital, 4-TP, *N*-methyl-2,4-dithiophenobarbital, 2,4-DTP, *N*-methyl-2,4,6-trithiophenobarbital, 2,4,6-TTP, and *N*-methylphenobarbital, P, are shown in Fig. 1. The structure of the latter compound was redetermined at 293 (2) K, to enable all five structures to be compared under the same conditions. The previously published data for *N*-methylphenobarbital were obtained at 163 K by Lewis *et al.* (2005) and refined to $R = 0.042$. A determination at 295 K by Bideau *et al.* (1969) was a low-quality determination with $R = 0.107$.

Selected geometric parameters at 293 (2) K for the crystal structures of the thio derivatives are given in Table 1, together with the values observed for *N*-methylphenobarbital at 293 (2) K and also at 163 (2) K (Lewis *et al.*, 2005). The C–N bond lengths are similar to those found in β -lactams ($Csp^2-Nsp^2 = 1.385$ Å; Allen *et al.*, 1995), indicating that the lone pairs of the N1 and N3 atoms are conjugated with the carbonyl or thiocarbonyl groups, which results in the C2–N1–C6 and C2–N3–C4 angles being greater than 120° [the average values are 123.4 (3) and 127.8 (7) $^\circ$, respectively], whereas the mean value of the C4–C5–C6 angle at the chiral centre is 112.8 (11) $^\circ$. The heterocyclic ring in all the crystal structures adopts a half-chair conformation; the torsion angles and ring-puckering parameters are given in Table 1. The set of torsion angles defining the heterocyclic ring conformation was found to be similar for 2-TP, 2,4,6-TTP, 4-TP and P, whereas for 2,4-DTP all the torsion angles are close to zero, which indicates that the ring is significantly flattened. The geometric parameters of P at 293 (2) K are comparable with those found at 163 (2) K.

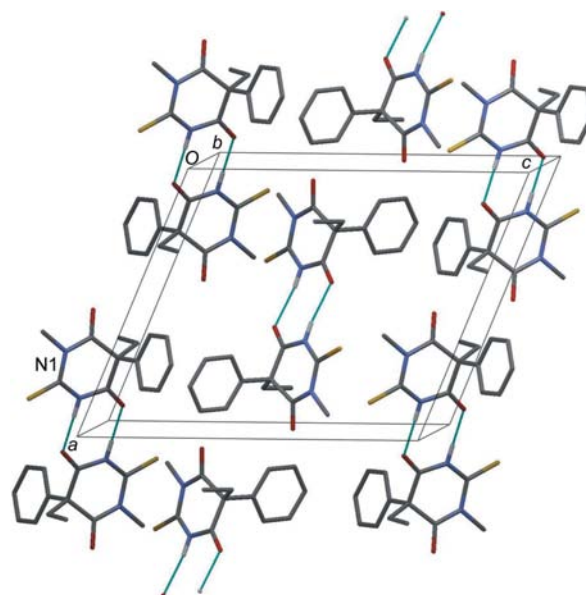


Figure 3

The packing of the molecules in 2-TP with the N3–H3...O4 $R_2^2(8)$ -type hydrogen-bond system. H atoms, except for those involved in the moderate hydrogen bonds, have been omitted for clarity.

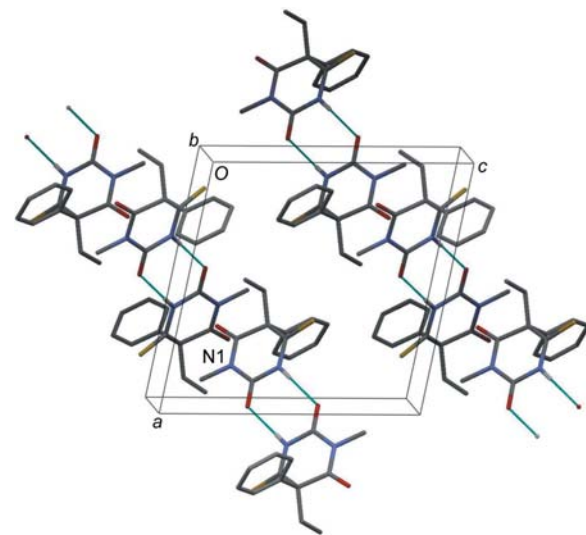
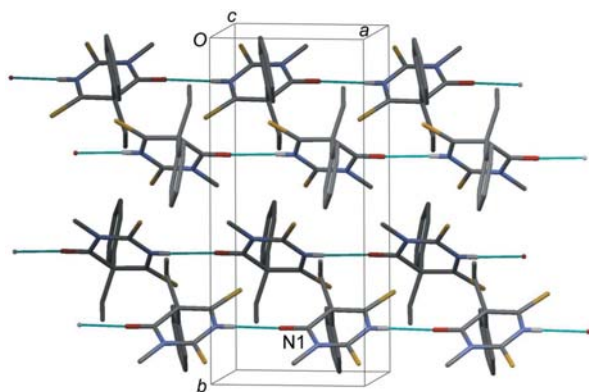


Figure 4

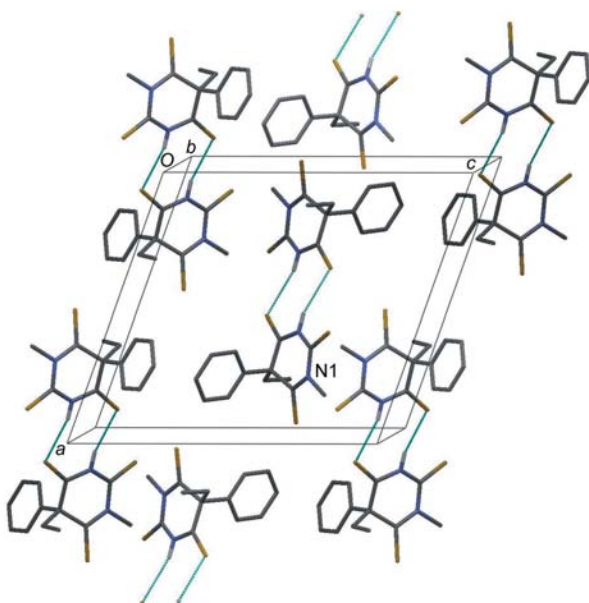
The packing of the molecules in 4-TP with the N3–H3...O2 $R_2^2(8)$ -type hydrogen-bond system. H atoms, except for those involved in the moderate hydrogen bonds, have been omitted for clarity.

The C=S bond lengths in the thio derivatives are significantly shortened [range 1.630–1.646 Å, average 1.639 (6) Å, see Table 1] compared with the value characteristic for thioureas (1.681 Å; Allen *et al.*, 1995) and are similar to those observed in 5-benzyl-1,3,5-trimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trithione (Takechi *et al.*, 2007). The average value of the C=O bond lengths was found to be 1.212 (5) Å, which is also relatively short compared with the values observed in ureas (Allen *et al.*, 1995).

Both P and its thio derivatives possess only one hydrogen-bond donor (the N3–H3 amide group), despite an excess of acceptor groups, which limits the number of possible moderate hydrogen bonds. The analysis of the hydrogen-bond para-


Figure 5

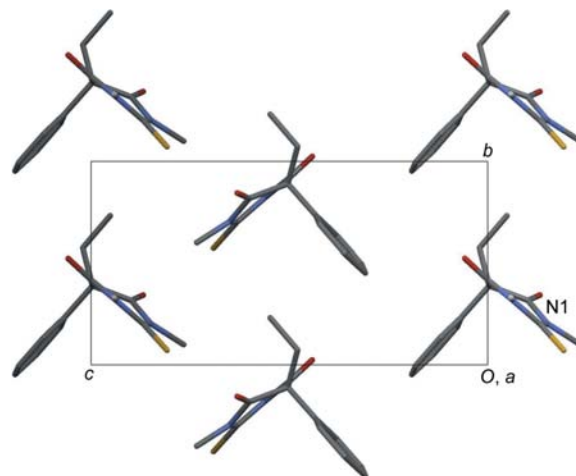
The packing of the molecules in 2,4-DTP with the N3—H3···O6 hydrogen bonds forming a $C(6)$ -type chain along the a direction. H atoms, except for those involved in the moderate hydrogen bonds, have been omitted for clarity.


Figure 6

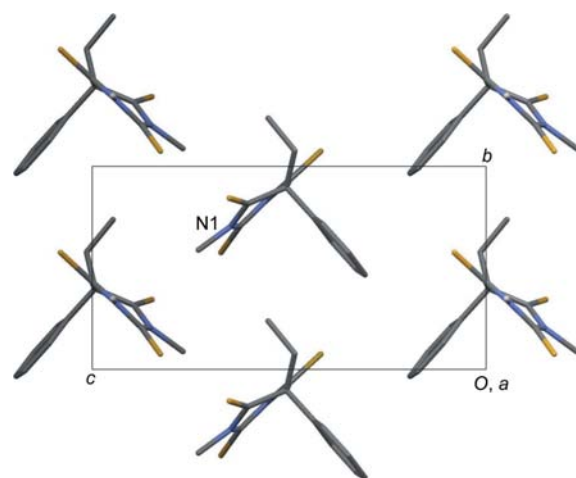
The packing of the molecules in 2,4,6-TTP with the N3—H3···S4 $R_2^2(8)$ -type hydrogen-bond system. H atoms, except for those involved in the moderate hydrogen bonds, have been omitted for clarity.

eters (Table 2) indicates the preferential acceptor properties of the O atom in position 4. If position 4 is occupied by an S atom, the role of the acceptor is taken over by the O atom in position 2 (as in 4-TP). In the case of the 2,4-dithio derivative, only the O atom in position 6 is available as the strong acceptor (the electronegativity of the O atom is 3.44 whereas that for the S atom is 2.58, which is comparable with that of a C atom, 2.55). When all the O atoms are replaced by S atoms in 2,4,6-TTP, position 4 is preferred again for the N—H···S hydrogen bond.

As can be seen in Fig. 2, the structures of 2-TP, 4-TP and 2,4,6-TTP contain centrosymmetric hydrogen-bonded dimers, like those observed in P, formed by the intermolecular N3—H3···O or N3—H3···S interactions across a centre of inversion. This hydrogen-bond motif can be recognized as the typical $R_2^2(8)$ according to the graph-set approach (Etter *et al.*, 1990; Bernstein *et al.*, 1995). The type of hydrogen-bond


Figure 7

Edge-to-face interactions stabilizing the crystal structure of (2-TP). Only the H atom at N3 is shown.


Figure 8

Edge-to-face interactions stabilizing the crystal structure of (2,4,6-TTP). Only the H atom at N3 is shown.

system determines the specific packing pattern in the structures of the thio derivatives. The $R_2^2(8)$ ring composed of N3—H3···O4ⁱ [symmetry code: (i) $2 - x, 1 - y, -z$] hydrogen bonds in 2-TP and that of N3—H3···S4^{iv} [symmetry code: (iv) $1 - x, 2 - y, 1 - z$] in 2,4,6-TTP enforce the same molecular packing arrangement shown in Figs. 3 and 6, respectively. Although the $R_2^2(8)$ system is also observed in the structure of 4-TP, the packing of the molecules is different (Fig. 4) because of the different acceptor type in the N3—H3···O2ⁱⁱ [symmetry code: (ii) $2 - x, 1 - y, 1 - z$] hydrogen bond. In 2,4-DTP the $R_2^2(8)$ ring is not preserved because the donor and acceptor functional groups are not in adjacent positions on the heterocyclic ring. Instead, the packing of the molecules (Fig. 5) is dominated by a $C(6)$ chain formed by the N3—H3···O6ⁱⁱⁱ [symmetry code: (iii) $x + 1, y, z$] hydrogen bond (Fig. 2).

The preference of the moderate hydrogen-bond formation seems to follow the acceptor atom position in the heterocyclic ring according to the sequence $4 > 2 > 6$, which corresponds with the nucleophilic properties of the heterocyclic ring C atoms. This finding is consistent with the order of the S atom

substitution in the thionation of *N*-methylphenobarbital, in which the amount of the thio derivatives of P in the reaction product was found to be: 4-TP 26% > 2,4-DTP 22% > 2-TP 16% (Stasiewicz-Urban *et al.*, 2004).

Because the moderate hydrogen bonds form only discrete dimers or one-dimensional chains, the three-dimensional architecture of the molecular packing has to be provided by weak intermolecular interactions, the geometric parameters of which are summarized in Table 3. In the structures of 2-TP and 2,4,6-TTP, with the substituent in position 4 (O4 and S4, respectively) serving as the acceptor for the N–H group, the hydrophobic layers (depicted in Figs. 7 and 8) are formed as a result of weak C–H... π edge-to-face interactions between the benzene rings of adjacent molecules. Similar behaviour of the molecules is observed in the structure of (P).

In all the structures studied, the methyl group in position 1 seems to be engaged as the donor in weak intramolecular C–H...O or C–H...S hydrogen bonds. The differences in the values of the torsion angle defining the spatial arrangement of the substituents at position 5 (C4–C5–C7–C8 and C4–C5–C9–C10, Table 1), observed even in the structures with similar packing patterns, may be attributed to the resultant effect of the different set of weak attractive, weak repulsive and steric interactions. In the structure of 4-TP, atom O6 is close to the centre of the neighbouring pyrimidine heterocyclic ring [Cg2 at $(-x + \frac{3}{2}, y + \frac{1}{2}, -z + \frac{1}{2})$; 3.214 (2) Å]. A similar observation can be made for the O2 atom in the structure of P [Cg2 at $(-x, y - \frac{1}{2}, -z + \frac{3}{2})$; 2.921 (2) Å].

Experimental

The title compounds were obtained by the thionation of *N*-methylphenobarbital with Lawesson's reagent (Stasiewicz-Urban *et al.*, 2004). Crystals suitable for X-ray diffraction were grown by slow evaporation at room temperature from a mixture of *n*-hexane and ethyl acetate in the ratio 3:1 for 2-TP and 4-TP, from cyclohexane for 2,4-DTP, from *n*-hexane for 2,4,6-TTP and from ethanol for P.

2-TP

Crystal data

C ₁₃ H ₁₄ N ₂ O ₂ S	$V = 1301.52 (6) \text{ \AA}^3$
$M_r = 262.32$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 12.9315 (3) \text{ \AA}$	$\mu = 0.24 \text{ mm}^{-1}$
$b = 7.1804 (2) \text{ \AA}$	$T = 293 (2) \text{ K}$
$c = 15.2362 (5) \text{ \AA}$	$0.35 \times 0.30 \times 0.12 \text{ mm}$
$\beta = 113.077 (1)^\circ$	

Data collection

KappaCCD diffractometer	4964 measured reflections
Absorption correction: multi-scan (DENZO and SCALEPACK; Otwinowski & Minor, 1997)	2978 independent reflections 2293 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.924, T_{\max} = 0.976$	$R_{\text{int}} = 0.021$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.045$	164 parameters
$wR(F^2) = 0.111$	H-atom parameters constrained
$S = 1.02$	$\Delta\rho_{\text{max}} = 0.24 \text{ e \AA}^{-3}$
2978 reflections	$\Delta\rho_{\text{min}} = -0.28 \text{ e \AA}^{-3}$

4-TP

Crystal data

C ₁₃ H ₁₄ N ₂ O ₂ S	$V = 1269.13 (6) \text{ \AA}^3$
$M_r = 262.32$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 11.5609 (3) \text{ \AA}$	$\mu = 0.25 \text{ mm}^{-1}$
$b = 9.5538 (3) \text{ \AA}$	$T = 293 (2) \text{ K}$
$c = 11.7268 (3) \text{ \AA}$	$0.32 \times 0.30 \times 0.07 \text{ mm}$
$\beta = 101.521 (2)^\circ$	

Data collection

KappaCCD diffractometer	5542 measured reflections
Absorption correction: multi-scan (DENZO and SCALEPACK; Otwinowski & Minor, 1997)	3381 independent reflections 2494 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.929, T_{\max} = 0.980$	$R_{\text{int}} = 0.021$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.050$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.145$	$\Delta\rho_{\text{max}} = 0.37 \text{ e \AA}^{-3}$
$S = 1.04$	$\Delta\rho_{\text{min}} = -0.41 \text{ e \AA}^{-3}$
3381 reflections	
168 parameters	

2,4-DTP

Crystal data

C ₁₃ H ₁₄ N ₂ OS ₂	$V = 1330.47 (13) \text{ \AA}^3$
$M_r = 278.38$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 6.9600 (3) \text{ \AA}$	$\mu = 0.39 \text{ mm}^{-1}$
$b = 14.9407 (7) \text{ \AA}$	$T = 293 (2) \text{ K}$
$c = 13.1556 (10) \text{ \AA}$	$0.25 \times 0.15 \times 0.10 \text{ mm}$
$\beta = 103.454 (2)^\circ$	

Data collection

KappaCCD diffractometer	5152 measured reflections
Absorption correction: multi-scan (DENZO and SCALEPACK; Otwinowski & Minor, 1997)	2856 independent reflections 2309 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.916, T_{\max} = 0.955$	$R_{\text{int}} = 0.032$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.046$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.114$	$\Delta\rho_{\text{max}} = 0.21 \text{ e \AA}^{-3}$
$S = 1.06$	$\Delta\rho_{\text{min}} = -0.29 \text{ e \AA}^{-3}$
2856 reflections	
168 parameters	

2,4,6-TTP

Crystal data

C ₁₃ H ₁₄ N ₂ S ₃	$V = 1406.56 (9) \text{ \AA}^3$
$M_r = 294.44$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 13.8686 (2) \text{ \AA}$	$\mu = 0.51 \text{ mm}^{-1}$
$b = 7.2346 (4) \text{ \AA}$	$T = 293 (2) \text{ K}$
$c = 14.9844 (5) \text{ \AA}$	$0.19 \times 0.15 \times 0.05 \text{ mm}$
$\beta = 110.681 (1)^\circ$	

Data collection

KappaCCD diffractometer	5585 measured reflections
Absorption correction: multi-scan (DENZO and SCALEPACK; Otwinowski & Minor, 1997)	3201 independent reflections 2587 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.905, T_{\max} = 0.975$	$R_{\text{int}} = 0.025$

Table 1

A comparison of selected geometric parameters and ring-puckering parameters (Å, °) for the thio derivatives of *N*-methylphenobarbital.

Ring-puckering parameters, defined according to Cremer & Pople (1975), were calculated using the *PARST* program (Nardelli, 1983).

	2-TP	4-TP	2,4-DTP	2,4,6-TTP	P	P†
N1–C2	1.371 (2)	1.382 (2)	1.371 (2)	1.377 (3)	1.384 (2)	1.391 (2)
C2–N3	1.371 (2)	1.372 (2)	1.377 (3)	1.376 (3)	1.377 (2)	1.379 (2)
N3–C4	1.364 (2)	1.366 (2)	1.361 (3)	1.352 (3)	1.363 (2)	1.365 (2)
C4–C5	1.512 (2)	1.527 (2)	1.525 (3)	1.520 (3)	1.525 (2)	1.528 (2)
C5–C6	1.526 (2)	1.529 (2)	1.523 (3)	1.543 (3)	1.525 (2)	1.528 (2)
N1–C6	1.402 (2)	1.381 (2)	1.389 (3)	1.383 (3)	1.380 (2)	1.386 (2)
C2–O2/S2	1.6436 (17)	1.218 (2)	1.646 (2)	1.640 (2)	1.2072 (19)	1.2095 (19)
C4–O4/S4	1.2147 (19)	1.6297 (18)	1.635 (2)	1.643 (2)	1.2176 (19)	1.2184 (19)
C6–O6/S6	1.2039 (19)	1.211 (2)	1.210 (2)	1.632 (2)	1.221 (2)	1.2126 (19)
C2–N1–C6	122.93 (14)	123.39 (14)	123.81 (17)	123.34 (18)	124.52 (13)	124.39 (13)
N1–C2–N3	116.44 (14)	117.06 (14)	116.82 (17)	115.95 (19)	116.54 (13)	116.52 (13)
C2–N3–C4	127.72 (14)	126.67 (15)	128.56 (18)	128.24 (19)	126.16 (13)	126.06 (13)
N3–C4–C5	116.20 (13)	114.43 (15)	116.46 (17)	115.71 (18)	116.05 (13)	116.23 (13)
C4–C5–C6	111.91 (13)	112.66 (14)	114.50 (16)	111.90 (16)	112.05 (13)	111.91 (13)
N1–C6–C5	117.04 (14)	118.75 (14)	119.70 (16)	116.81 (18)	118.19 (13)	118.20 (13)
N1–C2–N3–C4	10.4 (3)	5.2 (3)	2.4 (3)	13.8 (4)	–5.4 (2)	5.9 (2)
C2–N3–C4–C5	3.4 (2)	–25.1 (3)	–1.0 (3)	0.9 (3)	–23.0 (2)	–23.0 (2)
N3–C4–C5–C6	–23.72 (19)	30.1 (2)	1.1 (3)	–23.0 (3)	–29.38 (19)	29.84 (18)
C4–C5–C6–N1	32.14 (18)	–19.2 (2)	–2.7 (3)	32.1 (2)	22.8 (2)	–23.27 (19)
C5–C6–N1–C2	–20.9 (2)	–0.1 (3)	4.5 (3)	–19.9 (3)	–7.5 (2)	8.1 (2)
C6–N1–C2–N3	–0.8 (2)	8.6 (2)	–4.1 (3)	–3.1 (3)	–2.8 (2)	2.2 (2)
C4–C5–C7–C8	61.7 (2)	–66.7 (2)	–58.9 (2)	61.5 (2)	63.76 (19)	–63.03 (19)
C4–C5–C9–C10	–3.4 (2)	111.14 (19)	66.3 (2)	–15.5 (3)	59.16 (18)	–59.21 (17)
C4–C5–C9–C14	177.55 (15)	–69.7 (2)	–113.3 (2)	165.6 (2)	–121.73 (16)	–121.60 (15)
q_2	0.251 (1)	0.232 (2)	0.019 (2)	0.269 (2)	0.198 (1)	
q_3	0.120 (2)	0.117 (2)	0.023 (2)	–0.107 (2)	–0.136 (2)	
φ_2	80.9 (4)	–154.1 (4)	–11 (5)	80.8 (5)	37.5 (5)	
Q_r	0.278 (2)	0.260 (2)	0.030 (2)	0.289 (2)	0.240 (2)	
θ_2	115.5 (3)	63.3 (4)	39 (4)	111.8 (4)	124.6 (3)	

† The crystal structure of *N*-methylphenobarbital at 163 K was reported by Lewis *et al.* (2005) with $R = 4.21\%$; Cambridge Structural Database (Allen, 2002) refcode: MEPBAB01.

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.048$
 $wR(F^2) = 0.116$
 $S = 1.06$
 3201 reflections
 166 parameters
 1 restraint

H atoms treated by a mixture of independent and constrained refinement
 $\Delta\rho_{\max} = 0.32 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.38 \text{ e \AA}^{-3}$

P

Crystal data

$\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_3$
 $M_r = 246.26$
 Monoclinic, $P2_1/c$
 $a = 13.7063 (5) \text{ \AA}$
 $b = 7.2553 (2) \text{ \AA}$
 $c = 12.6606 (4) \text{ \AA}$
 $\beta = 105.565 (2)^\circ$

$V = 1212.84 (7) \text{ \AA}^3$
 $Z = 4$
 Mo $K\alpha$ radiation
 $\mu = 0.10 \text{ mm}^{-1}$
 $T = 293 (2) \text{ K}$
 $0.30 \times 0.30 \times 0.30 \text{ mm}$

Data collection

KappaCCD diffractometer
 Absorption correction: multi-scan (*DENZO* and *SCALEPACK*; Otwinowski & Minor, 1997)
 $T_{\min} = 0.972$, $T_{\max} = 0.975$

4931 measured reflections
 2756 independent reflections
 2230 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.019$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.051$
 $wR(F^2) = 0.143$
 $S = 1.05$
 2756 reflections
 167 parameters

H atoms treated by a mixture of independent and constrained refinement
 $\Delta\rho_{\max} = 0.37 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.23 \text{ e \AA}^{-3}$

Although all the derivatives studied have a chiral centre at the C5 atom, their crystal structures are centrosymmetric and so the crystals contain racemates. All H atoms were initially located in difference Fourier maps. The H atoms of the methyl (C1 and C8) and methylene (C7) groups and those of the phenyl ring (C10–C14) were subsequently included in the refinement in geometrically idealized positions, with C–H = 0.96, 0.97 and 0.93 Å, respectively, and refined using the riding model with isotropic displacement parameters of $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{parent atom})$. The H atom attached to the N3 atom was constrained to an idealized position for 2-TP, with N–H = 0.86 Å, restrained assuming a target N–H distance of 0.86 (1) Å for 2,4,6-TTP and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$ in both cases. For the remaining structures, the positional and displacement parameters of this H atom were refined freely. In the final stage of the refinement, a few reflections, probably affected by absorption, were omitted (4-TP: reflections 200 and 153; 2,4-DTP: 032, 0121, 793 and 210; 2,4,6-TTP: 200; P: 413, 620 and 114). Additionally, in the case of 2,4-DTP, θ_{\max} was also reduced from 27.41 to 27.00° (97 reflections omitted) which improved the data completeness (0.976 to 0.986).

For all compounds, data collection: *COLLECT* (Nonius, 1997); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003), *ORTEP-3 for Windows* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97*.

Table 2

Hydrogen-bond geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
2-TP N3—H3...O4 ⁱ	0.86	2.12	2.927 (2)	157
4-TP N3—H3...O2 ⁱⁱ	0.83 (3)	2.08 (3)	2.902 (2)	170 (2)
2,4-DTP N3—H3...O6 ⁱⁱⁱ	0.83 (2)	2.15 (2)	2.984 (2)	176 (2)
2,4,6-TTP N3—H3...S4 ^{iv}	0.87 (1)	2.53 (1)	3.376 (2)	164 (2)
P N3—H3...O4 ^v	0.90 (2)	1.99 (2)	2.896 (2)	178 (2)

Symmetry codes: (i) $-x+2, -y+1, -z$; (ii) $-x+2, -y+1, -z+1$; (iii) $x+1, y, z$; (iv) $-x+1, -y+2, -z+1$; (v) $-x, -y, -z+1$.

The authors thank the X-ray Laboratory, Faculty of Chemistry, Jagiellonian University, for use of the Nonius KappaCCD diffractometer.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN3120). Services for accessing these data are described at the back of the journal.

References

- Allen, F. H. (2002). *Acta Cryst.* **B58**, 380–388.
- Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1995). *International Tables for Crystallography*, Vol. C, edited by A. J. C. Wilson, ch. 9.5, pp. 685–706. Dordrecht: Kluwer Academic Publishers.
- Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
- Bernstein, J., Davis, R. E., Shimon, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Bideau, J.-P., Marly, L. & Housty, J. (1969). *C. R. Acad. Sci. Ser. C (Chim.)*, **269**, 549–551.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- Day, G. M., Motherwell, W. D. S. & Jones, W. (2007). *Phys. Chem. Chem. Phys.* **9**, 1693–1704.
- Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* **B46**, 256–262.
- Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
- Huber, B., Bocchicchio, M., Hauser, I., Horstmann, V., Jokeit, G., May, T., Meinert, T., Robertson, E., Schorlemmer, H., Schulz, L., Wagner, W. & Seidel, M. (2009). *Seizure Eur. J. Epil.* doi:10.1016/j.seizure.2008.07.006.
- Kushikata, T., Hirota, K., Yoshida, H., Kudo, M., Lambert, D. G., Smart, D., Jerman, J. C. & Matsuki, A. (2003). *Neuroscience*, **121**, 855–863.
- Lewis, W., McKeown, R. H. & Robinson, W. T. (2005). *Acta Cryst.* **E61**, o799–o800.
- Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
- Malone, J. F., Murray, C. M., Charlton, M. H., Docherty, R. & Lavery, A. J. (1997). *J. Chem. Soc. Faraday Trans.* **93**, 3429–3436.

Table 3

Weak interactions (Å, °) and contacts (Å).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>	Notes
Cg1 is the centre of gravity of the C9–C14 benzene ring and Cg2 is the centre of gravity of the heterocyclic ring.					
2-TP C1—H1a...O6	0.96	2.28	2.712 (3)	106	Intra
C8—H8a...Cg1 ^{vi}	0.96	2.85	3.610 (2)	136	III†
C12—H12...Cg1 ^{vii}	0.93	2.73	3.639 (2)	167	Edge-to-face, I†
4-TP C1—H1a...O2	0.96	2.26	2.710 (2)	107	Intra
C1—H1c...Cg1 ^{vii}	0.96	2.81	3.702 (2)	154	II†
O6...C2 ^{viii}			2.949 (2)		
O6...Cg2 ^{viii}			3.214 (2)		
2,4-DTP C1—H1a...O6	0.96	2.22	2.677 (3)	108	Intra
C1—H1b...S4 ^{ix}	0.96	3.00	3.824	144	
2,4,6-TTP C1—H1a...S6	0.96	2.42	2.959 (3)	115	Intra
C8—H8c...S4	0.96	2.87	3.444 (3)	120	Intra
C8—H8a...Cg1 ^x	0.96	2.98	3.687 (3)	132	III†
C12—H12...Cg1 ^{vii}	0.93	2.75	3.620 (3)	156	Edge-to-face, I†
P C1—H1a...O2	0.96	2.28	2.724	108	Intra
C1—H1c...Cg1 ^{xi}	0.96	3.00	3.931	165	II†
C10—H10...O4	0.93	2.59	3.112 (2)	116	Intra
C10—H10...O6 ^{xii}	0.93	2.59	3.436 (2)	151	
C13—H13...Cg1 ^{xiii}	0.93	2.90	3.798 (2)	162	Edge-to-face, I†
O2...C2 ^{xiv}			3.087 (2)		
O2...Cg2 ^{xiv}			2.921 (2)		

† Category of weak H... π interaction according to the classification of Malone *et al.* (1997). Symmetry codes: (vi) $x, y+1, z$; (vii) $-x+\frac{3}{2}, y-\frac{1}{2}, -z+\frac{1}{2}$; (viii) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+\frac{1}{2}$; (ix) $x-\frac{1}{2}, -y+\frac{3}{2}, z-\frac{1}{2}$; (x) $x, y+1, z$; (xi) $x, -y-\frac{1}{2}, z+\frac{1}{2}$; (xii) $x, -y+\frac{1}{2}, z-\frac{1}{2}$; (xiii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$; (xiv) $-x, y-\frac{1}{2}, -z+\frac{3}{2}$.

- Nardelli, M. (1983). *Acta Cryst.* **C39**, 1141–1142.
- Nonius (1997). *COLLECT*. Nonius BV, Delft, The Netherlands.
- Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
- Platteau, C., Lefebvre, J., Hemon, S., Baecht, C., Danede, F. & Prevost, D. (2005). *Acta Cryst.* **B61**, 80–88.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
- Stasiewicz-Urban, A., Kubaszek, M., Żylewski, M., Cegła, M. & Bojarski, J. (2004). *Pol. J. Chem.* **78**, 2105–2115.
- Takechi, H., Kubo, K., Takahashi, H. & Matsumoto, T. (2007). *Acta Cryst.* **E63**, o701–o703.
- Williams, P. P. (1973). *Acta Cryst.* **B29**, 1572–1579.
- Williams, P. P. (1974). *Acta Cryst.* **B30**, 12–17.