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trans-3-(*p*-Chlorophenylthio)-1,4,6-trimethylpiperazine-2,5-dione

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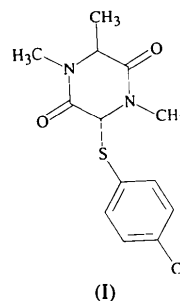
Abstract

The title compound, $C_{13}H_{15}ClN_2O_2S$, assumes a shallow boat conformation where the methyl and 4-chlorothiophenyl substituents in the α -positions are situated *trans* to one another, and the latter is folded across the piperazinedione ring.

Comment

As part of our continuing studies on piperazinediones (Chai & Page, 1993; Chai, King & Hockless, 1995), the structure of the title compound (I) was undertaken to establish the relative stereochemistry of the substituents at the C^α positions. The crystal structure reveals a shallow boat conformation [$\beta = -10.95^\circ$ in the Hooker notation, defined as the dihedral angle between the two amide planes $C(3)–C(2)–N(1)–C(6)$ and $C(3)–N(4)–C(5)–C(6)$] (Hooker, Bayley, Radding & Schell-

man, 1974) with the thiophenyl ligand occupying a pseudo-axial position, and the methyl C atom pseudo-equatorial.



Conformational parameters (in accord with the IUPAC–IUB Commission on Biochemical Nomenclature, 1970) were calculated as follows: $\omega_1 [C(3)–C(2)–N(1)–C(6)] = 8.1(4)$, $\psi_1 [N(1)–C(6)–C(5)–N(4)] = 5.5(3)$, $\varphi_1 [C(2)–N(1)–C(6)–C(5)] = 0.0(4)$, $\omega_2 [C(6)–C(5)–N(4)–C(3)] = -20.1(3)$, $\psi_2 [N(4)–C(3)–C(2)–N(1)] = -20.8(3)$, $\varphi_2 [C(5)–N(4)–C(3)–C(2)] = 27.7(3)^\circ$. Although bond lengths and angles are generally as expected, the significant differences in equivalent torsion angles suggest a substantial twist in conformation, which presumably reflects some flexibility in the molecule, enabling it to rotate and deform in order to minimize any unfavourable intramolecular interactions. Like other compounds of this type containing phenyl substituent side chains

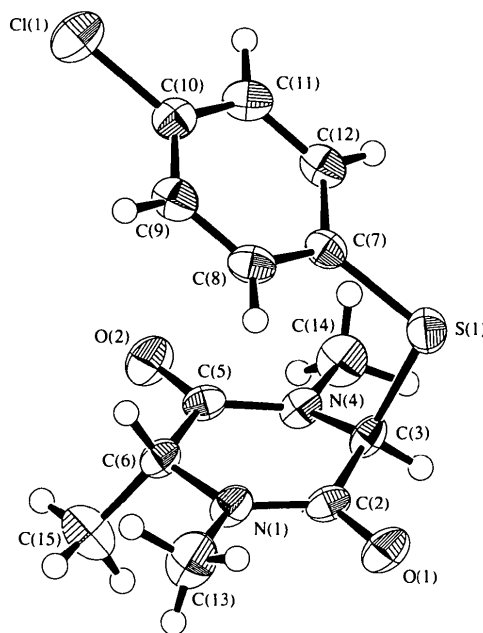


Fig. 1. View of the title compound showing the labelling of all non-H atoms. Displacement ellipsoids are shown at 50% probability levels. H atoms are drawn as circles of arbitrary radii.

(Benedetti, Marsh & Goodman, 1976; Lin & Webb, 1973), the *p*-chlorothiophenyl group at C(3) is folded over the piperazinedione ring, where the dihedral angle between the best planes through these two residues is just 36°. Indeed, NMR results and minimum energy calculations have predicted the preference for such conformations in the solid state (Kopple & Ohnishi, 1969; Kopple & Marr, 1967). There are no interesting or short (below 3.60 Å) contacts to the S atom.

Experimental

3-(*p*-Chlorophenylthio)-1,4,6-trimethylpiperazine-2,5-dione was synthesized by treatment of 3-bromo-1,4,6-trimethylpiperazine-2,5-dione with 4-chlorothiophenol and pyridine (1:1 mol equivalents) in dichloromethane. A 6:1 mixture of the diastereomeric thioethers was obtained. The major component (I) crystallized preferentially from a solvent mixture of ethyl acetate and petroleum spirit.

Crystal data

C₁₃H₁₅ClN₂O₂S

M_r = 298.79

Monoclinic

*P*2₁/*a*

a = 10.550 (1) Å

b = 9.071 (2) Å

c = 15.146 (2) Å

β = 103.37 (1)°

V = 1410.2 (3) Å³

Z = 4

D_x = 1.407 Mg m⁻³

Cu *K*α radiation

λ = 1.5418 Å

Cell parameters from 25 reflections

θ = 48.4–49.8°

μ = 3.785 mm⁻¹

T = 213 K

Block

0.28 × 0.28 × 0.26 mm

Colourless

Data collection

Rigaku AFC-6R diffractometer

$\omega/2\theta$ scans

Absorption correction:

ψ scan (North, Phillips & Mathews, 1968)

T_{min} = 0.902, *T_{max}* = 1.000

2346 measured reflections

2251 independent reflections

1871 observed reflections

[*I* > 3σ(*I*)]

R_{int} = 0.035

θ_{\max} = 60.07°

h = -11 → 11

k = 0 → 10

l = 0 → 17

3 standard reflections

monitored every 150

reflections

intensity decay: 0.51%

Refinement

Refinement on *F*²

R = 0.036

wR = 0.041

S = 2.99

1871 reflections

233 parameters

All H-atom parameters

refined

$w = 4F_o^2 / [\sigma^2(F_o^2) + (0.009F_o^2)^2]$

(Δ/σ)_{max} = 0.03

$\Delta\rho_{\max} = 0.30 \text{ e } \text{Å}^{-3}$

$\Delta\rho_{\min} = -0.021 \text{ e } \text{Å}^{-3}$

Extinction correction: none

Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U_{eq}</i>
Cl(1)	1.40496 (7)	-0.04753 (9)	0.07130 (5)	0.0513 (2)
S(1)	0.85578 (6)	0.04916 (8)	0.15482 (5)	0.0385 (2)
O(1)	0.7918 (2)	-0.1410 (2)	0.3159 (1)	0.0409 (6)
O(2)	1.2334 (2)	0.1647 (2)	0.3562 (1)	0.0439 (6)
N(1)	1.0115 (2)	-0.1385 (2)	0.3621 (2)	0.0338 (6)
N(4)	1.0142 (2)	0.1575 (2)	0.3131 (1)	0.0296 (6)
C(2)	0.8968 (2)	-0.0780 (3)	0.3226 (2)	0.0299 (7)
C(3)	0.8980 (2)	0.0721 (3)	0.2808 (2)	0.0295 (7)
C(5)	1.1315 (2)	0.0952 (3)	0.3457 (2)	0.0288 (7)
C(6)	1.1374 (2)	-0.0633 (3)	0.3779 (2)	0.0304 (7)
C(7)	1.0118 (2)	0.0182 (3)	0.1330 (2)	0.0304 (7)
C(8)	1.0773 (3)	-0.1152 (3)	0.1537 (2)	0.0353 (8)
C(9)	1.1984 (3)	-0.1366 (3)	0.1351 (2)	0.0369 (8)
C(10)	1.2515 (3)	-0.0239 (3)	0.0943 (2)	0.0342 (8)
C(11)	1.1878 (3)	0.1075 (3)	0.0709 (2)	0.0369 (8)
C(12)	1.0681 (3)	0.1287 (3)	0.0911 (2)	0.0353 (8)
C(13)	1.0139 (4)	-0.2926 (4)	0.3917 (3)	0.055 (1)
C(14)	1.0089 (3)	0.3147 (3)	0.2886 (3)	0.0436 (10)
C(15)	1.2052 (4)	-0.0645 (4)	0.4781 (2)	0.056 (1)

Table 2. Selected geometric parameters (Å, °)

O(1)—C(2)	1.230 (3)	N(4)—C(3)	1.437 (3)
O(2)—C(5)	1.224 (3)	N(4)—C(5)	1.346 (3)
N(1)—C(2)	1.337 (3)	C(2)—C(3)	1.503 (3)
N(1)—C(6)	1.463 (3)	C(5)—C(6)	1.515 (4)
C(2)—N(1)—C(6)	125.1 (2)	N(4)—C(3)—C(2)	115.8 (2)
C(3)—N(4)—C(5)	122.5 (2)	N(4)—C(5)—C(6)	118.9 (2)
N(1)—C(2)—C(3)	117.7 (2)	N(1)—C(6)—C(5)	114.9 (2)

The θ -scan width used was (1.30 + 0.3tan θ)° at a speed of 8.0° min⁻¹ (in ω). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak-to-background counting time. H atoms were allowed to refine isotropically.

Data collection and cell refinement were performed with *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). The structure was solved by direct methods (*SIR92*; Altomare *et al.*, 1994) and expanded using Fourier techniques (Beurskens *et al.*, 1992). All calculations were performed using *TEXSAN* software (Molecular Structure Corporation, 1993).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PT1026). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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3-Hydroxy-2,6-dinitroacetophenone: an Unusual Substitution Pattern Resulting from Nitration of 3-Hydroxyacetophenone

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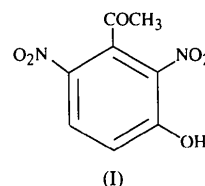
Abstract

Nitration of 3-hydroxyacetophenone gives 2,6-dinitro-3-hydroxyacetophenone, $C_8H_6N_2O_6$, in which the nitro groups have entered the sterically least favourable positions in the aromatic nucleus. None of the expected substitution in the 4-position was observed. The two nitro groups flanking the carbonyl side chain are different in that one is in the plane of the aryl ring but the other is twisted well out of the plane.

Comment

During nitration of 3-hydroxyacetophenone to obtain the previously reported 2-nitro-3-hydroxyacetophenone (Butenandt, Hallmann & Beckmann, 1957), a substantial quantity of a new compound was also isolated. 1H NMR spectroscopy showed that there were two *ortho* H atoms and, by using additivity rules for chemical shifts (Gordon & Ford, 1972), it seemed that the H atoms occupied the 4,5-positions in the aromatic ring indicating that an unexpected substitution had occurred. However, this prediction was not sufficiently clear-cut

to distinguish it from the alternative expected structure with H atoms at the 5,6-positions. X-ray analysis gave the true structure (I) and showed that the NMR prediction had been correct. The relatively high yield of nitration products is unusual in that one nitro group joined the aryl ring *ortho* to the carbonyl and *para* to hydroxyl while the other joined *ortho* to both carbonyl and hydroxyl (a position of sterically restricted access); no nitration was observed in the expected position, *ortho* to hydroxyl and *para* to carbonyl, where there is no steric constraint. This substitution pattern violates the normal rules for electrophilic substitution into a simple aromatic ring (March, 1985) since sterically hindered nitration is highly unfavourable. There are a few examples in the literature exhibiting a similar 'ortho' effect of carbonyl (Ingold, 1954; Rubenstein, 1925; Raiford & Wells, 1935; Ginsburg, 1951). The present result is another even more extreme example of substitution which appears to be governed by transition-state energies rather than the 'normal' ground-state considerations for electrophilic aromatic substitution (Kruse & Cha, 1982).



The structure of the title compound is also unusual in that one nitro group alongside the carbonyl lies planar with the aryl ring whilst the other nitro adjacent to the carbonyl is twisted almost at right angles to it. The aromatic ring remains substantially planar.

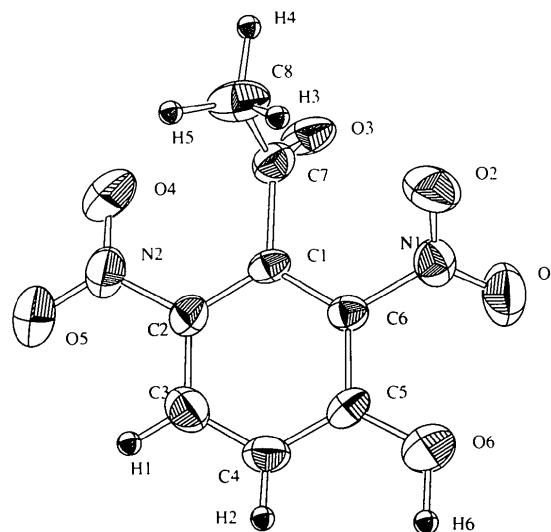


Fig. 1. Molecular structure showing 50% probability displacement ellipsoids.