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Dipropyl 3,6-diphenyl-1,2-dihydro-1,2,4,5-tetrazine-1,2-dicarboxylate

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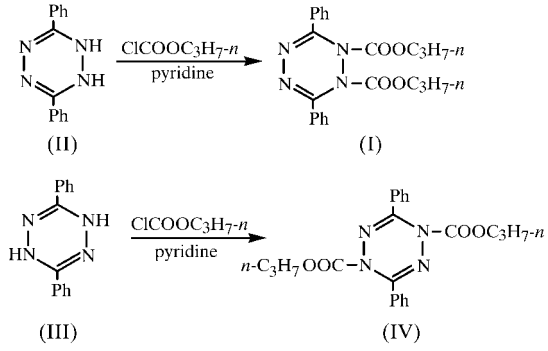
The title compound, $C_{22}H_{24}N_4O_4$, was prepared from propyl chloroformate and 3,6-diphenyl-1,2-dihydro-*s*-tetrazine. This reaction yields the title compound rather than dipropyl 3,6-diphenyl-1,4-dihydro-*s*-tetrazine-1,4-dicarboxylate. The 2,3-diazabutadiene group in the central six-membered ring is not planar; the C═N double-bond length is 1.285 (2) Å, and the average N—N single-bond length is 1.401 (3) Å, indicating a lack of conjugation. The ring has a twist conformation, in which adjacent N atoms lie ±0.3268 (17) Å from the plane of the ring. The molecule has twofold crystallographic symmetry.

Comment

s-Tetrazine derivatives have a high potential for biological activity, possessing a wide range of antiviral and antitumor properties, and these derivatives have been widely used in pesticides and herbicides (Sauer, 1996). Dihydro-*s*-tetrazine has four isomers, namely 1,2-, 1,4-, 1,6- and 3,6-dihydro-*s*-tetrazine. In almost all the cases that have been studied by X-ray diffraction, the dihydro derivatives were best described as 1,4-dihydro isomers, with the 1,2-dihydro isomer being very rare. There still seems to be much confusion over the structure of 1,2- and 1,4-dihydro-*s*-tetrazine isomers. Every compound should have a unique CAS number in *Chemical Abstracts*, but some 1,2- and 1,4-dihydro-*s*-tetrazine compounds have the same CAS number. For example, the CAS number of both 3,6-diphenyl-1,2-dihydro-*s*-tetrazine, (II), and 3,6-diphenyl-1,4-dihydro-*s*-tetrazine, (III), is 14478-73-0 (see *Chemical Abstracts*, **72**, 90413a; **70**, 20031). Some scientists believe that rearrangement can occur between (II) and (III), so that compounds can contain a mixture of the two isomers (Neunhoeffer, 1984).

In a continuation of our work on the structure–activity relationship of *s*-tetrazine derivatives (Hu *et al.*, 2001, 2002), we have obtained a colourless crystalline compound that was the sole product of the reaction of propyl chloroformate and 3,6-diphenyl-1,2-dihydro-*s*-tetrazine. The latter was prepared according to the procedure of Abdel-rahman *et al.* (1968). If 3,6-diphenyl-dihydro-*s*-tetrazine is present as a mixture of forms (II) and (III), two products, (I) and (IV), should be obtained on reaction with propyl chloroformate. If only isomer (II) is present, product (I) should be obtained on reaction with propyl chloroformate, and if only isomer (III) is present, product (IV) should be obtained. However, IR, ^{1}H NMR and MS studies failed to prove whether the *N*,*N*′-substituents were located at the 1,2- or 1,4-positions. The structural identity of our product, (I), was resolved using single-crystal X-ray diffraction.



The molecular structure of (I) is illustrated in Fig. 1. Selected bond lengths, angles and torsion angles are listed in Table 1. In (I), the two C7═N1 bonds [1.285 (2) Å] correspond to typical C═N double bonds, and the C7—N2 [1.416 (2) Å], N1—N1^i [1.406 (3) Å] and N2—N2^i [1.395 (3) Å] bond lengths [symmetry code: (i) $2-x, \frac{3}{2}-y, z$] correspond to typical single bonds. [Typical C═N, C—N and N—N bond lengths are 1.279–1.329, 1.336–1.416 and 1.366–1.454 Å, respectively (Allen *et al.*, 1987).] Therefore, the tetrazine ring corresponds to 1,2-dihydro-*s*-tetrazine and the *N*,*N*′-substituents are at the 1,2-positions, thus proving that (I) is dipropyl 3,6-diphenyl-1,2-dihydro-*s*-tetrazine-1,2-dicarboxylate. It is then clear that the raw material prepared according to the Abdel-rahman procedure was (II), rather than (III) or a mixture of the two isomers, and that there is no rearrangement between the two isomers.

Atoms C7, N1, N1^i and C7^i are not coplanar, which demonstrates the lack of conjugation in the C═N—N═C group. Theoretically, in (I), the N1—N1^i bonds should be shorter than the N2—N2^i bonds, since N1 and N1^i form C═N

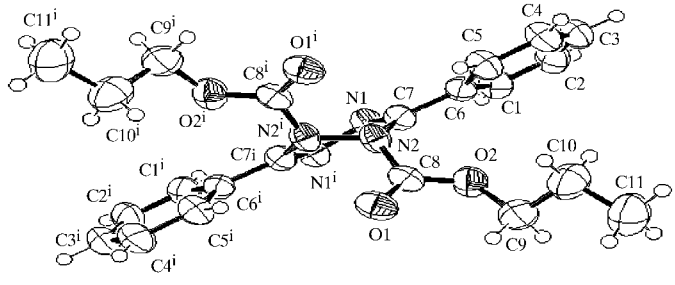


Figure 1
View of a molecule of (I), showing the atomic numbering scheme. Displacement ellipsoids are shown at the 30% probability level for non-H atoms. [Symmetry code: (i) $2-x, \frac{3}{2}-y, z$.]

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double bonds with atoms C7 and C7^{i}. However, the N1—N1^{i} bonds are actually longer, because of the stereo-effect of the 1,2-substituents.

The molecule has twofold crystallographic symmetry, with the twofold axis passing through the centres of the N1—N1^{i} and N2—N2^{i} bonds. The central ring has a twist conformation, in which atom N2 lies 0.3268 (17) Å out of the central least-squares plane and the adjacent N2^{i} atom lies at an equal distance on the opposite side.

Experimental

Compound (II) (1.0 g, 4.2 mmol), prepared according to the procedure of Abdel-rahman *et al.* (1968), was dissolved in dichloromethane (40 ml) with stirring. Propyl chloroformate (0.96 ml, 8.5 mmol) and pyridine (0.68 ml, 8.5 mmol) were added to the mixture in an ice bath. The mixture was stirred at room temperature for 6 h and dried *in vacuo* to give a light-red solid, (I) (1.1 g, yield 64%), which was then recrystallized from ethanol to give colourless prisms (m.p. 384–385 K).

Crystal data

$C_{22}H_{24}N_4O_4$
M_r = 408.45
Tetragonal, $I4_1/a$
a = 15.655 (13) Å
c = 16.869 (13) Å
V = 4134 (5) Å^3
Z = 8
D_x = 1.313 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 11.5–13.5°
μ = 0.09 mm^{-1}
T = 293 (2) K
Prism, colourless
0.60 × 0.40 × 0.38 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
8309 measured reflections
1873 independent reflections
1404 reflections with $I > 2\sigma(I)$
R_{int} = 0.046
θ_{max} = 25.2°
$h = -16 \rightarrow 18$
$k = -18 \rightarrow 16$
$l = -16 \rightarrow 20$
3 standard reflections
frequency: 60 min
intensity decay: 0.3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.111
S = 1.05
1873 reflections
139 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0477P)^2 + 2.1561P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0062 (6)

H atoms were added at calculated positions and refined using a riding model. H atoms were given isotropic displacement parameters equal to 1.2 (or 1.5 for methyl H atoms) times the equivalent isotropic displacement parameters of their parent atoms, and C—H distances were restrained to 0.93 Å for phenyl H atoms, 0.96 Å for methyl H atoms and 0.97 Å for the remaining H atoms.

Table 1
Selected geometric parameters (Å, °).

N1—C7	1.285 (2)	N2—N2^{i}	1.395 (3)
N1—N1^{i}	1.406 (3)	N2—C7	1.416 (2)
C7—N1—N1^{i}	117.70 (10)	N1—C7—N2	119.29 (15)
N2^{i}—N2—C7	111.29 (11)		
N1^{i}—N1—C7—N2	−9.8 (3)	C7^{i}—N1^{i}—N1—C7	32.0 (3)
N2^{i}—N2—C7—N1	−31.5 (2)	C7^{i}—N2^{i}—N2—C7	50.9 (3)

Symmetry code: (i) $2-x, \frac{3}{2}-y, z$.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1397). Services for accessing these data are described at the back of the journal.

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