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cis-3-Azabicyclo[3.2.0]heptane-2,4-dione

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Key indicators

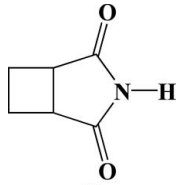
Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.049
wR factor = 0.134
Data-to-parameter ratio = 13.0

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

The title compound, $C_6H_7NO_2$, was synthesized from *cis*-1,2-cyclobutanedicarboxylic anhydride by reaction with ammonium acetate under microwave conditions. The crystal structure of the compound shows that the cyclobutane ring is planar with angles ranging from 89.64 (12) to 90.37 (12)°. The *cis*-3-azabicyclo[3.2.0]heptane-2,4-dione molecules are linked into a chain formation through hydrogen N—H···O=C bonds. Parallel packing is seen between two cyclobutane rings related by inversion symmetry.

Comment

The synthesis and biological evaluation of the title compound, 3-azabicyclo[3.2.0]heptane-2,4-dione, (I), and its analogues are of interest to synthetic medicinal chemists. Previous syntheses of the title compound used ammonia gas, urea (Crockett & Koch, 1977), and ammonium hydroxide (Rice & Grogan, 1957). However, this is the first microwave synthesis of this compound.



(I)

Cyclic imides and their derivatives are known to possess many structural (Lewis *et al.*, 2002), photophysical (Giaimo *et al.*, 2002) and pharmaceutical properties (Britton *et al.*, 2001). Specifically, intermediates of the title compound are currently used for the creation of the topisomerase inhibitors (Axelle *et al.*, 2003; Hasinoff *et al.*, 1997), and antitumor pharmaceuticals (Ren & Lien, 2004; Moore *et al.*, 1990). While the structures of several derivatives of 3-azabicyclo[3.2.0]heptane-2,4-dione have been determined (Ichimura *et al.*, 1980; Chow & Naguib, 1984; Deutsch *et al.*, 1984; Shimo *et al.*, 1998; Warrener *et al.*, 1994; Booker-Milburn *et al.*, 2002; Zhang *et al.*, 2003; Booker-Milburn *et al.*, 2001; Obata *et al.*, 2001; Usman *et al.*, 2001; Edwards *et al.*, 1996), the structure of the title compound has not been established. The *cis* formation is evident with the sp^3 configuration at C1—C2—C3 and C6—C5—C4, maintaining angles of 114.58 (15) and 114.57 (14)°, respectively. The cyclobutane group is planar with bond angles between 89.64 (12) and 90.37 (12)°. Parallel packing is seen between two cyclobutane ring systems related by inversion symmetry, with N—H···O=C hydrogen bonds being formed between alternating molecules down the *a* axis.

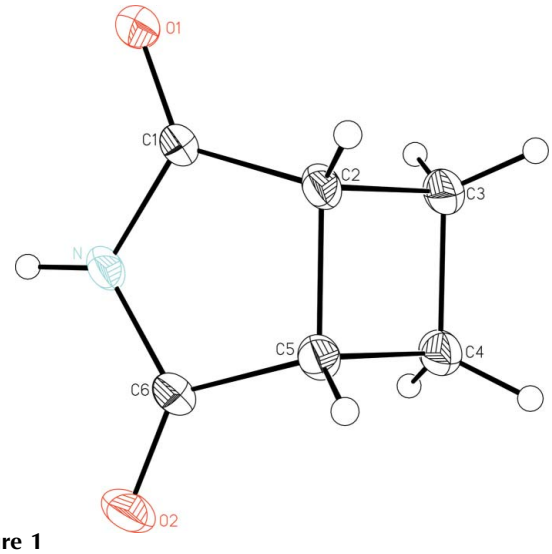


Figure 1
A view of the molecule, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 20% probability level. H atoms are represented by circles of arbitrary size.

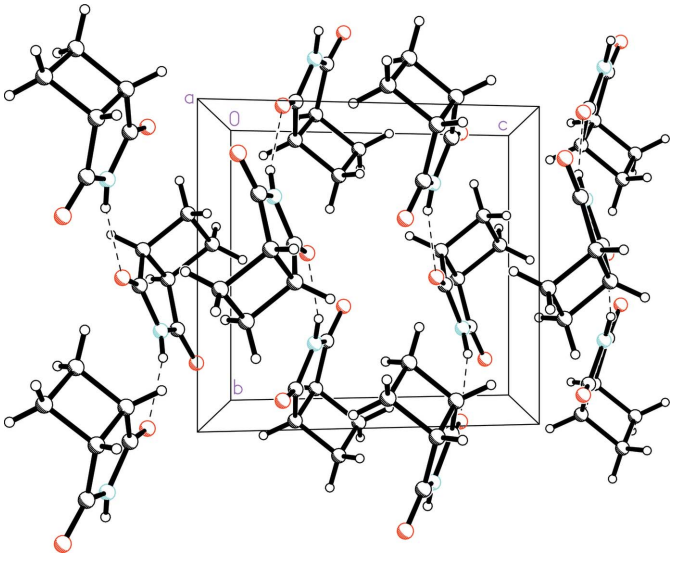


Figure 2
The molecular packing viewed down the *a* axis. Hydrogen bonds are shown as dashed lines.

Experimental

cis-1,2-Cyclobutanedicarboxylic anhydride (1.0 g, 7.90 mmol) and ammonium acetate (NH_4OAc; 0.60 g, 7.9 mmol) were mixed in an 8 ml Teflon-capped vial. The sample was irradiated in a Kennmore microwave (1100 W, frequency 2450 MHz) for 100 s at full power and then cooled to room temperature. The product was purified by flash column chromatography on silica (30 g) eluted with ethyl acetate/hexanes (1:1) yielding 0.71 g of a white solid (72%). M.p. 373–375; ^{13}C NMR (90 MHz, CDCl3) δ 23.14 (CH_2), 40.22 (CH), 182.11 (C═O); MS *m*/*z* 54, 82, 125 (*M* +); IR (chloroform) (ν_{max}, cm^{-1}): 1725.4, 1781.0 (2C═O). In an alternative synthesis, *cis*-1,2-cyclobutanedicarboxylic anhydride (0.20 g, 1.59 mmol) and ammonium acetate (NH_4OAc, 0.15 g, 1.95 mmol) were mixed thoroughly in a CEM-sealed vial with a magnetic stirrer. The sample was heated for 5 min at 423 K in a CEM Discover microwave powered at 150 W. It was then cooled rapidly to 313 K and dissolved in 25 ml of ethyl acetate. The organic layer was washed with distilled water (2 × 5 ml) and dried over sodium sulfate (anhydrous). The dried organic layer afforded 0.14 g of a white solid (71%). MS *m*/*z*: 125 (*M*+), 82, 54. Crystals were grown by slow evaporation of a $CHCl_3$ solution.

Crystal data

$C_6H_7NO_2$
M_r = 125.13
Monoclinic, $P2_1/c$
a = 9.4771 (5) Å
b = 7.6956 (5) Å
c = 8.3279 (5) Å
β = 103.763 (4)°
V = 589.93 (6) Å^3
Z = 4
D_x = 1.409 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 79 reflections
θ = 2.5–27.9°
μ = 0.90 mm^{-1}
T = 293 (2) K
Chunk, colorless
0.58 × 0.55 × 0.40 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: none
1319 measured reflections
1081 independent reflections
1008 reflections with $I > 2\sigma(I)$
R_{int} = 0.079
θ_{max} = 69.0°
$h = -11 \rightarrow 11$
$k = 0 \rightarrow 9$
$l = -10 \rightarrow 10$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.134
S = 1.08
1081 reflections
83 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0725P)^2 + 0.1848P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.078 (12)

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.2146 (19)	C2—C5	1.530 (2)
O2—C6	1.213 (2)	C2—C3	1.547 (2)
N—C6	1.377 (2)	C3—C4	1.531 (2)
N—C1	1.380 (2)	C4—C5	1.554 (2)
C1—C2	1.493 (2)	C5—C6	1.500 (2)
C6—N—C1	113.81 (13)	C3—C4—C5	90.10 (12)
O1—C1—N	123.72 (15)	C6—C5—C2	105.09 (12)
O1—C1—C2	128.14 (15)	C6—C5—C4	114.57 (14)
N—C1—C2	108.11 (13)	C2—C5—C4	89.64 (12)
C1—C2—C5	105.12 (13)	O2—C6—N	124.25 (16)
C1—C2—C3	114.58 (15)	O2—C6—C5	127.86 (16)
C5—C2—C3	90.37 (12)	N—C6—C5	107.87 (13)
C4—C3—C2	89.88 (12)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N—H2*B*···O1^{i}	0.86	2.08	2.9163 (19)	164

Symmetry code: (i) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$.

All H atoms were initially located in a difference Fourier map. They were then placed in geometrically idealized positions and constrained to ride on their parent atoms with C—H distances of 0.97

and 0.98 Å for CH and CH_2, respectively, and $U_{iso}(H) = 1.2U_{eq}(C)$. The N—H distance was constrained to 0.86 Å, with $U_{iso}(H) = 1.2U_{eq}(N)$.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1999); software used to prepare material for publication: *SHELXTL*.

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