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Racemic 1,2,4-Trimethylurazole

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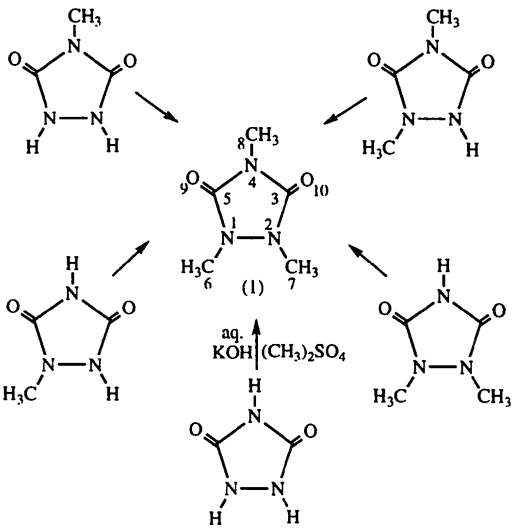
Abstract

The structural and stereochemical parameters of 1,2,4-trimethyl-1,2,4-triazolidine-3,5-dione, $C_5H_9N_3O_2$, (1), were examined in view of the contrast between its physical properties and those of urazoles having one or more unsubstituted NH groups. The X-ray structure shows that (1) is devoid of intermolecular hydrogen bonding but retains the structural features of strongly hydrogen-bonded urazoles. Its *trans*-H_3C—N—N—CH_3 torsion angle of 72.3 (5)° is slightly larger than the corresponding angle in urazoles having an unsubstituted or monomethylated N—N function, but smaller than that in urazoles monosubstituted with bulkier groups. Like other crystalline urazoles, (1) is racemic by virtue of N1 and N2 chirality. In its packing pattern of parallel molecular sheets, two pass through the unit cell; within a sheet, each molecule is surrounded by two of its own chirality and four of opposite chirality. While physical properties of crystalline urazoles can be associated with their degree of intermolecular hydrogen bonding, this study shows that their chirality is an intrinsic molecular phenomena.

Comment

Urazole, 1-methyl-, 4-methyl-, 1,2-dimethyl- and 1,4-dimethylurazole have relatively high melting points, which correlate with their possibilities for intermolecular hydrogen bonding, which, in turn, correlate with the number of free NH groups (Meyers, Lutfi, Hou & Robinson, 1995). The crystalline urazoles possessing NH groups that we have studied previously exhibit chirality and the molecular packing of their racemic mixtures is enantiospecific with respect to their intermolecular hydrogen-bonding patterns (Meyers, Lutfi, Kolb & Robinson, 1994; Robinson, Meyers, Kolb & Colloton, 1996; Meyers, Lutfi, Hou & Robinson, 1995; see also Kolb, Colloton, Robinson, Lutfi & Meyers, 1996). We questioned whether the chirality and the enantiospecific packing patterns of these urazoles were intrinsic molecular features or characteristics engendered by the hydrogen bonding. The X-ray crystal structure of 1,2,4-trimethylurazole, (1), which would be devoid of hydrogen bonding, was therefore investigated. For this study, (1) was synthesized directly from urazole, unlike earlier syntheses utilizing monomethyl or dimethylurazoles.



The X-ray structure of (1) and the atom numbering is shown in Fig. 1. It is clear from the calculated parameters that crystalline (1) does not exhibit intermolecular hydrogen bonding. The hydrazidic N1 and N2 atoms are pyramidal and, with C3, N4, and C5, form a relatively flat five-membered ring with a mean deviation of 0.050 (4) Å. Their methyl substituents (C6 and C7), however, are substantially out-of-plane and *trans* disposed, with deviations from planarity of −0.624 (5) and 0.633 (5) Å, respectively. The imidic N4 atom is trigonal planar. This information illustrates that the structural parameters of (1) differ only slightly from those of related urazoles having NH functional groups and exhibiting strong intermolecular hydrogen bonding. The effect of vicinal steric repulsion is noticeable, however. The torsion angle subtended by the two *trans*-methyl groups and hydrazidic N atoms (C—N1—N2—C) is substantially greater than the corresponding torsion angle of urazoles having a single hydrazidic methyl substituent or no hydrazidic substituent, but smaller than that in urazoles having a single bulky hydrazidic substituent; compound (1): C6—N1—N2—C7 72.3 (5)°; 1-methylurazole: C6—N1—N2—H2 −49 (2)° (Meyers, Lutfi, Kolb & Robinson, 1994); urazole: H1—N1—N2—H2 65° [calculated from the X-ray parameters reported by Belaj (1992)]; (1*R*,2*R*)-urazole-α-D-pyranosyl-2-deoxyriboside: C1′–N1—N2—H2 −74.6 (19)° (Robinson, Meyers, Kolb & Colloton, 1996); 4-phenyl-*t*-1-octylurazole: C6—N1—N2—H2 −82.35° [calculated from the X-ray parameters (H atoms not refined) reported by Baker, Timberlake, Alender, Majeste & Trefonas (1982)].

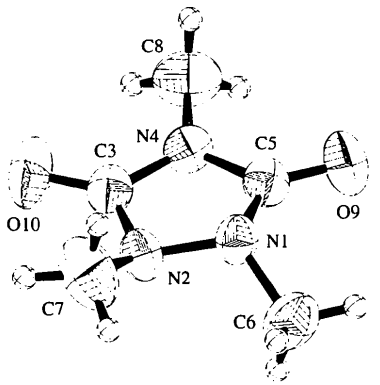


Fig. 1. The molecular configuration of an *S,S* enantiomer of (1) and the atom-numbering scheme, with displacement ellipsoids at the 30% probability level. H atoms are shown as isotropic spheres of arbitrary radii.

Crystalline (1) is racemic, as are 1-methylurazole (Meyers, Lutfi, Kolb & Robinson, 1994) and 4-methylurazole (Meyers, Lutfi, Hou & Robinson, 1995), and is composed of parallel molecular sheets, one of which is shown in Fig. 2. Two such sheets pass through the unit cell and are parallel to (100). Within a sheet, each molecule is surrounded by two molecules of its own chirality and four of opposite chirality. Racemic pairs are clearly identifiable in Fig. 2, a shorter distance separating the antipodes of a pair than any two molecules of the same chirality or one antipode pair from another. A crystal structure analysis of crystals grown from chloroform was attempted, but a refinement suitable for publication could not be attained because disordered chloroform solvate was incorporated into the structure.

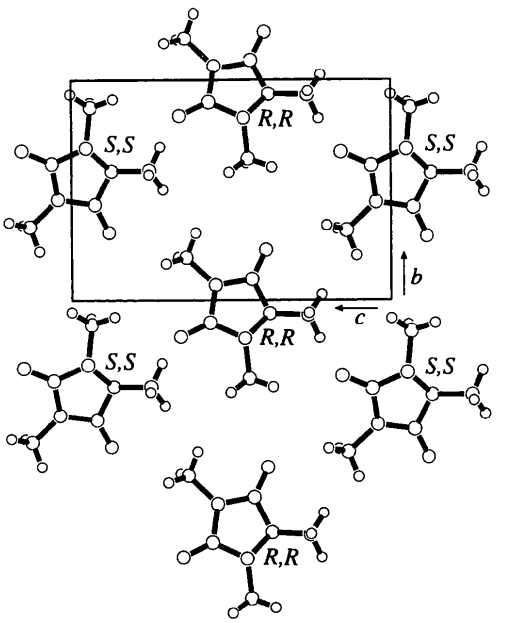


Fig. 2. A view of one of the molecular sheets which make up the structure of (1). Two such sheets, related by a symmetry center at $(\frac{1}{2},\frac{1}{2},\frac{1}{2})$, pass through the unit cell. Racemic pairs are clearly identifiable.

These chiral-specific packing patterns of (1) are an intrinsic molecular characteristic, whereas the chiral-specific packing patterns exhibited by 1-methylurazole (Meyers, Lutfi, Kolb & Robinson, 1994) and 4-methylurazole (Meyers, Lutfi, Hou & Robinson, 1995) are intimately associated with their three-dimensional intermolecular hydrogen bonding. The strong tendency of the C=O functions of urazoles to form hydrogen bonds is generally satisfied in the crystalline state through intermolecular interactions with the NH functions. Such interactions cannot occur with crystalline (1), which results in its low melting point and ease of sublimation under ambient conditions and, *via* hydrogen bonding of its C=O functions, gives rise to its ready solubility in proton-donating solvents and its hygroscopicity, compared with less substituted urazoles. Indeed, crystalline (1) absorbs moisture from the air and assumes a liquid aspect within a few minutes, a fact which would account for the large variation in melting points (see *Experimental*).

Experimental

After a stirred mixture of urazole (0.486 g, 4.81 mmol) and water (3 ml) was gently heated until solution was complete, a solution of potassium hydroxide (0.325 g, 5.79 mmol) in 2 ml of water was added. When the solution cooled to room temperature, dimethyl sulfate (2.57 g, 20.39 mmol) was added and stirring continued. Small amounts of potassium hydroxide were added at intervals to keep the reaction mixture slightly basic. The progress of the reaction was monitored by TLC [silica gel, $CHCl_3$:EtOH (4:1)]. More dimethyl sulfate (4.67 g, 36.99 mmol) was added in portions during the course of the reaction. At the end of 12 h, ammonium hydroxide was added to destroy residual dimethyl sulfate and the resulting basic solution was neutralized with dilute hydrochloric acid and rotary evaporated to dryness. This solid residue was triturated with mixed hexanes, then with chloroform, which proved to be the better solvent. The combined solutions, dried (anhydrous $MgSO_4$) and rotary evaporated, provided colorless microcrystals of (1) (0.593 g, 86.2% yield, m.p. 345–346 K) unsuitable for X-ray diffraction. Crystallization from hexane afforded long thin needles (m.p. 334–335 K) which were also unsuitable for X-ray study. The addition of several drops of chloroform to the microcrystals and refrigeration of the mass provided small cubic crystals (m.p. 331–333 K), which were used for the X-ray analysis. Because the crystals of (1) were hygroscopic, the crystal used for data collection was coated with vacuum grease and sealed in a glass capillary. The thin needles, kept in a sealed flask over a period of several months at room temperature, sublimed onto the walls as clusters of small prisms (m.p. 329–330 K). Literature m.p.: 332–334 K (Bausch *et al.*, 1991); 337–339 K (Jacobson, D'Adamo & Cosgrove, 1972; Arndt, Loewe & Tarlan-Akon,

1948). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.17 (*s*, 6H, N1—CH_3 and N2—CH_3), 3.08 (*s*, 3H, N4—CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.99 (C3 and C5), 32.22 (N1—CH_3 and N2—CH_3), 25.36 (N4—CH_3).

Crystal data

$C_5H_9N_3O_2$
M_r = 143.15
Monoclinic
$P2_1/c$
a = 7.6532 (15) Å
b = 7.769 (2) Å
c = 12.177 (2) Å
β = 98.228 (14)°
V = 716.6 (3) Å^3
Z = 4
D_x = 1.3268 (6) Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 19.56–21.03°
μ = 0.10 mm^{-1}
T = 296 K
Prism
0.46 × 0.41 × 0.39 mm
Colorless

Data collection

Rigaku AFC-5*S* diffractometer
$\omega/2\theta$ scans (rate 6° min^{-1} in ω)
Absorption correction: none
1470 measured reflections
1364 independent reflections
723 observed reflections [$I > 1.8\sigma(I)$]

R_{int} = 0.013
θ_{max} = 25°
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 9$
$l = -14 \rightarrow 14$
3 standard reflections monitored every 100 reflections
intensity decay: −0.5%

Refinement

Refinement on F
R = 0.059
wR = 0.041
S = 3.80
723 reflections
91 parameters
H-atom parameters not refined (riding with C—H = 0.95 Å)
$w = 4F_o^2/\sigma^2(F_o^2)$

$(\Delta/\sigma)_{max}$ = 0.0001
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.3.1)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
N1	0.8299 (4)	0.0728 (5)	0.6018 (3)	0.0474 (12)
N2	0.7027 (4)	0.1807 (4)	0.5398 (3)	0.0493 (14)
C3	0.6579 (6)	0.1087 (6)	0.4374 (4)	0.0514 (19)
N4	0.7294 (4)	−0.0572 (5)	0.4452 (3)	0.0487 (14)
C5	0.8276 (5)	−0.0833 (6)	0.5474 (3)	0.0490 (17)
C6	0.8324 (6)	0.0755 (6)	0.7220 (3)	0.072 (2)
C7	0.7395 (7)	0.3659 (6)	0.5482 (4)	0.091 (2)
C8	0.7056 (6)	−0.1843 (6)	0.3572 (4)	0.080 (2)
O9	0.9012 (4)	−0.2149 (4)	0.5818 (3)	0.0732 (14)
O10	0.5700 (4)	0.1700 (4)	0.3564 (3)	0.0822 (14)

Table 2. *Selected geometric parameters (Å, °)*

O9—C5	1.213 (5)	N2—C3	1.365 (6)
O10—C3	1.209 (6)	N2—C7	1.467 (6)
N1—N2	1.418 (5)	N4—C3	1.398 (6)
N1—C5	1.381 (6)	N4—C5	1.374 (5)
N1—C6	1.461 (5)	N4—C8	1.449 (6)
N2—N1—C5	107.7 (3)	C5—N4—C8	124.3 (4)
N2—N1—C6	115.8 (3)	O10—C3—N2	128.4 (4)
C5—N1—C6	119.4 (4)	O10—C3—N4	125.8 (4)
N1—N2—C3	107.9 (3)	N2—C3—N4	105.7 (4)
N1—N2—C7	115.6 (3)	O9—C5—N1	127.0 (4)
C3—N2—C7	119.1 (4)	O9—C5—N4	127.2 (4)
C3—N4—C5	110.8 (4)	N1—C5—N4	105.8 (4)
C3—N4—C8	124.8 (4)		
C6—N1—N2—C7	72.3 (5)	C8—N4—C5—N1	174.5 (4)
C8—N4—C3—N2	176.3 (4)		

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *PROCESS* in *TEXSAN* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *LS* in *TEXSAN*. Molecular graphics: *ORTEP* (Johnson, 1965) *TEXSAN*. Software used to prepare material for publication: *FINISH* in *TEXSAN*, and *PLATON* (Spek, 1990).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: FG1225). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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