The Crystal Structure of a Trisisoxazole Compound: 3-(3-Methyl-5-isoxazolyl)methyl-5-(3-methyl-5-isoxazolyl)methylisoxazole

A. Albinati, S. Brückner, L. Malpezzi and S. V. Meille

Istituto di Chimica, Politecnico Piazza Leonardo da Vinci, 32, 20133 Milano, Italy
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The crystal structure of a trisisoxazole derivative is described. The crystals are monoclinic, space group P2$_1$/c (Z = 4) with cell dimensions: a = 8.846(4), b = 26.688(7), c = 9.081(4) Å, β = 142.82(7)°. The structure was refined by full matrix least squares to a final R of 0.060. The molecule is non-planar and the bond lengths and angles are in the expected range for isoxazole derivatives.

Introduction.

The methylene-polyisoxazole compounds present considerable chemical interest being readily converted to polyketones, which are suitable starting compounds for various cyclization reactions (1,2). The synthesis of methylene polyisoxazoles with three and four rings has recently been achieved (3).

To clarify the geometry and the conformation in these types of compounds, in which various possible relative orientations of the rings may be expected, we have undertaken a crystallographic study of one member of the polyisoxazole series: *i.e.*, that containing three isoxazole rings.

EXPERIMENTAL

Crystal Data.

The compound has the molecular formula $C_{13}H_{13}N_3O_3$, molecular weight 259.26, and occurs as monoclinic crystals with cell dimensions: a = 8.846(4), b = 26.688(7), c = 9.081(4) Å, β = 142.82(7)° (from least squares refinement of 2θ values of 20 reflections). The crystals are in the space group P2$_1$/c, V = 1295.5 Å^3, D$_x$ = 1.33 g. cm^{-3} (Z = 4). A crystal of approximate dimensions 0.2 × 0.1 × 0.2 mm was used for the data collection.

The intensities of 2265 independent reflections were collected up to 2θ = 50° (graphite monochromated MoK$\bar{\alpha}$ radiation, λ = 0.71069 Å) using a Philips automated four circle diffractometer. An $\omega/2\theta$ scan technique (scan speed 0.03°/second^{-1}, scan range 1.0°) was used. For each reflection two background counts (10 seconds at each side of the peak)

Table I

Final Positional and Thermal Parameters (a,b)

	x	y	z	B$_{11}$	B$_{22}$	B$_{33}$	B$_{12}$	B$_{21}$	B$_{23}$
N(1)	0.2989(6)	0.3274(1)	0.6829(6)	4.7(2)	4.6(2)	4.1(2)	−1.4(3)	6.5(3)	−1.6(2)
N(2)	−0.1972(5)	0.1449(1)	0.2720(5)	3.9(1)	2.6(1)	3.7(1)	−0.8(2)	5.9(3)	0.5(2)
N(3)	−0.4212(6)	0.0010(1)	−0.1605(6)	3.8(1)	4.1(1)	4.2(2)	0.5(2)	6.1(3)	−1.0(3)
O(1)	0.2448(5)	0.2886(1)	0.5382(5)	3.9(1)	4.6(1)	5.1(1)	0.7(2)	6.6(2)	0.1(2)
O(2)	−0.0559(5)	0.1861(1)	0.3267(5)	4.4(1)	4.5(1)	3.8(1)	−1.6(2)	5.8(2)	−1.3(2)
O(3)	−0.3850(4)	0.0403(1)	−0.0293(4)	3.1(1)	4.3(1)	3.5(1)	−0.1(2)	4.3(2)	−1.7(2)
C(1)	0.0870(9)	0.3976(1)	0.6317(8)	7.0(3)	4.0(2)	6.0(3)	−1.6(4)	9.1(5)	−2.3(3)
C(2)	0.0920(7)	0.3532(1)	0.5364(7)	4.0(2)	3.0(1)	3.8(2)	−1.0(3)	6.2(3)	−0.3(3)
C(3)	−0.0984(7)	0.3326(1)	0.2977(6)	3.0(2)	3.2(1)	3.1(2)	0.2(3)	4.4(3)	1.0(3)
C(4)	0.0028(7)	0.2936(1)	0.3087(6)	3.5(2)	2.8(1)	3.6(2)	−1.3(3)	5.5(3)	−0.5(3)
C(5)	−0.0947(8)	0.2556(1)	0.1260(8)	6.2(2)	4.5(2)	4.9(2)	−2.7(3)	9.3(4)	−2.6(4)
C(6)	−0.2023(7)	0.2107(1)	0.1157(7)	4.9(2)	2.5(1)	4.0(2)	−0.2(3)	7.4(3)	−0.7(3)
C(7)	−0.4254(7)	0.1873(1)	−0.0690(7)	4.3(2)	2.8(2)	3.5(2)	−0.7(3)	5.8(3)	0.2(3)
C(8)	−0.4152(6)	0.1473(1)	0.0359(7)	3.6(2)	2.4(1)	4.3(2)	0.6(2)	6.3(3)	0.2(3)
C(9)	−0.6081(7)	0.1076(1)	−0.0803(7)	3.9(2)	3.6(2)	4.8(2)	−0.2(3)	7.2(4)	−0.5(3)
C(10)	−0.6064(6)	0.0650(1)	−0.1856(7)	3.1(1)	3.1(1)	4.7(2)	0.1(2)	6.7(3)	0.9(3)
C(11)	−0.7792(6)	0.0042(1)	−0.4052(6)	3.0(1)	3.2(1)	2.6(1)	−0.3(2)	3.8(3)	−0.6(3)
C(12)	−0.6543(7)	0.0045(1)	−0.3798(6)	3.4(2)	3.2(1)	3.1(2)	−1.1(3)	4.8(3)	−0.7(3)
C(13)	−0.7616(8)	−0.0321(2)	−0.5724(8)	4.8(2)	5.0(2)	4.9(2)	−0.5(3)	7.3(4)	−1.7(4)

(a) A table of observed and calculated structure factors, and of refined positional and isotropic thermal factors for the hydrogen atoms may be obtained on request from the authors. (b) The e.s.d.'s are given in parentheses; anisotropic temperature factors are in the form: B = [exp − ¼ (B$_{11}$a^{*2}h^2 + B$_{22}$b^{*2}k^2 + B$_{33}$c^{*2}l^2 + 2B$_{12}$a*b*hk + 2B$_{13}$a*c*hl + 2B$_{23}$b*c*kl)].
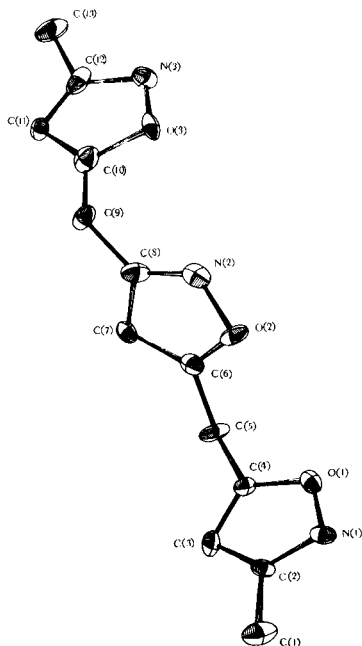
Figure 1. A perspective view of the molecule with the numbering scheme; hydrogens have been omitted for clarity.

Table II

Bond Lengths (Å) and Bond Angles (°) (a)

N(1)-O(1)	1.423(6)		
N(1)-C(2)	1.310(5)		
N(2)-O(2)	1.424(5)		
N(2)-C(8)	1.316(4)		
N(3)-O(3)	1.419(6)	N(1)-O(1)-C(4)	107.8(3)
		N(1)-C(2)-C(3)	110.1(4)
N(3)-C(12)	1.297(4)	N(1)-C(2)-C(1)	119.6(3)
O(1)-C(4)	1.354(3)	N(2)-O(2)-C(6)	107.3(3)
		N(2)-C(8)-C(7)	111.4(4)
O(2)-C(6)	1.351(5)	N(2)-C(8)-C(9)	118.6(3)
O(3)-C(10)	1.362(5)	N(3)-O(3)-C(10)	108.0(3)
		N(3)-C(12)-C(11)	112.6(3)
C(1)-C(2)	1.488(9)	N(3)-C(12)-C(13)	119.8(4)
		O(1)-N(1)-C(2)	106.0(3)
C(2)-C(3)	1.422(6)	O(1)-C(4)-C(3)	109.7(3)
		O(1)-C(4)-C(5)	116.6(4)
C(3)-C(4)	1.324(7)	O(2)-N(2)-C(8)	105.7(3)
		O(2)-C(6)-C(7)	109.8(4)
C(4)-C(5)	1.498(8)	O(2)-C(6)-C(5)	117.4(3)
		O(3)-N(3)-C(12)	104.8(4)
C(5)-C(6)	1.486(8)	O(3)-C(10)-C(9)	116.2(3)
		O(3)-C(10)-C(11)	109.9(4)
C(6)-C(7)	1.350(6)	C(1)-C(2)-C(3)	130.3(6)
		C(2)-C(3)-C(4)	106.4(4)
C(7)-C(8)	1.385(8)	C(3)-C(4)-C(5)	133.7(5)
		C(4)-C(5)-C(6)	113.0(5)
C(8)-C(9)	1.509(6)	C(5)-C(6)-C(7)	132.8(4)
		C(6)-C(7)-C(8)	105.8(6)
C(9)-C(10)	1.494(8)	C(8)-C(9)-C(10)	113.5(6)
		C(9)-C(10)-C(11)	133.8(5)
C(10)-C(11)	1.328(6)	C(10)-C(11)-C(12)	104.7(8)
C(11)-C(12)	1.411(7)	C(11)-C(12)-C(13)	127.6(6)
C(12)-C(13)	1.506(8)		
C-H (b)	1.01(12)		

(a) The e.s.d's are given in parentheses. (b) Average value.

were averaged; three standard reflections were measured every 90 minutes to check the stability of the crystal and of the experimental conditions. No significant variations were detected. 964 reflections having I ≥ 3σ (I) were considered as observed; the standard deviations on the intensities were based on counting statistics using the formula $\sigma(I) = (N_T + N_{bg1} + N_{bg2})^{1/2}$ where N_T and N_{bg} are the total peak counts and background counts, respectively. No absorption or extinction corrections were found necessary.

Structure Refinement.

The structure was solved by direct methods using the program MULTAN 74 (4). An E map revealed all the atoms of the molecule but the hydrogens. The structure was refined by full matrix least squares using anisotropic temperature factors for O, N and C. The hydrogens of the three rings and of the methylene groups were located on a Fourier difference map and subsequently refined with isotropic temperature factors.

At this stage a Fourier difference map revealed that the hydrogens of the two terminal methyl groups were disordered between two possible configurations; therefore twelve half-weighted hydrogens were added and their contribution to the structure factors refined; moreover, the presence of structural disorder may account for the fall off of the intensities with increasing 2θ and consequently the large number of unobserved reflections. A Cruickshank (5) weighting scheme was chosen; the scattering factors used were from reference 6. A final difference map showed no significant residual features. The final atomic coordinates are given in Table I, while the relevant bond lengths and

angles are in Table II and III. A perspective view of the molecule is shown in Figure 1.

Discussion.

The molecule is non planar; the two external isoxazole-rings are rotated in opposite directions along the C(4)-C(5) and C(9)-C(10) bonds as can be judged from the values of the dihedral angles C(4)-C(5)-C(6)-C(7) and C(8)-C(9)-C(10)-C(11), −127.2(8)° and 124.0(7)°, respectively.

The geometry of the isoxazole moiety is similar to that found in other isoxazole derivatives. The average C-N bond length, 1.308 (with an average deviation of ± 0.010

Table III

Relevant Internal Rotation Angles (°)(a)

C(1)-C(2)-C(3)-C(4)	180.0(6)
C(2)-C(3)-C(4)-C(5)	−178.7(7)
C(3)-C(4)-C(5)-C(6)	89.5(6)
C(4)-C(5)-C(6)-C(7)	−127.2(8)
C(5)-C(6)-C(7)-C(8)	−179.8(8)
C(6)-C(7)-C(8)-C(9)	179.5(8)
C(7)-C(8)-C(9)-C(10)	−83.6(6)
C(8)-C(9)-C(10)-C(11)	124.0(7)
C(9)-C(10)-C(11)-C(12)	178.9(6)
C(10)-C(11)-C(12)-C(13)	179.9(8)

(a) The e.s.d's are given in parentheses.

Å), is comparable to the values found in the α and β form of 3-hydroxy-5-phenyl isoxazole (7,8) [1.315(7) and 1.313(7) Å, respectively]. The mean value of the C-O bond [1.356(6) Å] is analogous to that of similar rings and consistent with a partial double bond character. In fact, a value of 1.338(3) Å is found in the compound 3-(p-amino-phenyl)-5-phenyl-1,2,4-oxadiazole (9) and an average value of 1.363 Å in the aforementioned hydroxyphenyl-isoxazoles (7,8), while it is 1.368(6) Å in the furan molecule (10).

Moreover, the shortening of some inter-ring bond lengths [e.g., for the C-N bond 1.308(4) Å as compared to 1.475 Å for the same bond when N is sp^2 hybridized (11)] is consistent with some degree of conjugation, which is, however, not extending through the N-O bond. This bond has a mean value of 1.422(6) Å, which is not significantly different from the accepted single bond value 1.41 Å (11).

The bond lengths involving the methyl or methylene carbons [mean value 1.495(7) Å] are in the range expected for bonds involving a sp^2 hybridized carbon. Moreover, there is no significant difference between the other C-C bonds (both single and double) of the three rings.

Values for the ring angles are comparable to those found in other heterocycles. The deformation of the C=C and O-C-C angles [i.e., C(3)-C(4)-C(5), O(1)-C(4)-C(5) and similar angles] from the expected values [average values 132.4° and 117.2° with average deviations of $\pm$ 1.68° and $\pm$ 0.9°, respectively] may be due to the steric requirement of minimizing the interactions between the hydrogens bonded to the ring carbons and those bonded to the methylene groups.

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