

Article

Crystal Structure and Semi-Empirical Quantum Chemical Calculations Related to the Stability of N,N'-(2'- (2'-furfurylidene)bis(morpholine)

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A estrutura cristalina e cálculos quânticos semi-empíricos de N,N'-(2'-furfurilideno)bis(morfolina), C₁₃H₂₀N₂O₃, mostram que: i) o valor de 115,1(2)° do ângulo entre o carbono centro da reação e o nitrogênio de uma morfolina; ii) o carbono centro da reação está fora do plano de mínimos quadrados do anel furano, e estes dois fatos explicam a alta instabilidade observada na síntese e conservação do composto. A estrutura cristalina do composto foi determinada por difração de raios-X, no sistema cristalino monoclinico, grupo espacial C2/c (No. 15) e dimensões de cela a = 18,824(4), b = 7,039(1) c = 20,644(4) Å, β = 97,32(3)°, V = 2713(2) Å³, Z = 8, D_{calc} = 1,235 Mg m⁻³, λ(MoKα) = 0,71073 Å, μ = 0,088 mm⁻¹, F(000) = 1088, T = 295 K, R = 4,35% (wR = 13,3%), com 2454 reflexões medidas, 2376 reflexões independentes, 1731 com I > 2σ(I) e 206 parâmetros refinados. A molécula exibe contatos intramolecular dos tipos C-H...O e C-H...N. O empacotamento molecular envolve contatos intermoleculares do tipo C-H...O.

The crystal structure and semi-empirical quantum chemical calculations of N,N'-(2'-furfurylidene)bis(morpholine), C₁₃H₂₀N₂O₃, show that: i) the value of 115.1(2)° for the angle between the carbon atom center of the reaction and the nitrogen atom of one morpholine and ii) the carbon atom center of the reaction is outside the least-squares plane of the furan ring, and these two facts explain the high instability observed in the synthesis and conservation of this compound. The crystal structure of the compound was determined *via* X-ray diffraction in the monoclinic crystal system, space group C2/c (Nr. 15) and cell dimensions a = 18.824(4), b = 7.039(1) c = 20.644(4) Å, β = 97.32(3)°, V = 2713(2) Å³, Z = 8, D_{calc} = 1.235 Mg m⁻³, λ(MoKα) = 0.71073 Å, μ = 0.088 mm⁻¹, F(000) = 1088, T = 295 K, R = 4.35% (wR = 13.3%), with 2454 measured reflections, 2376 independent reflections, 1731 with I > 2σ(I) and 206 refined parameters. The molecule has C-H...O and C-H...N intramolecular contacts. The molecular packing involves C-H...O intermolecular contacts.

Keywords: *N,N'-(2'-furfurylidene)bis(morpholine), stability, X-ray analysis, semi-empirical quantum chemical calculations*

Introduction

Some authors have observed that in the reaction of furfural with two mols of aromatic amines different products are formed depending on the nature of the amine¹⁻³. Reisch and Mahran have shown, more recently, that the reaction of furfural with two mols of methyl anthranilate

and methyl 2-aminonicotinate leads to 2,4- and 4,5- di(2-methoxycarbonylanilino) cyclopent-2-enone and to N-N'-(2'-furfurylidene)bis(methyl-2-aminonicotinate), respectively⁴. Lewis and Mulquiney obtained the dicyclopentapyrrolone in the reaction of furfural with 3-4 mols of aniline⁵. When an excess of furfural was used, they

obtained a polymeric product. Seeboth and Hoffmann showed that the condensation of furfural with two equiv. of α -amino-N-heterocycles (1:1) gave azomethine. However, similar condensation of furfural with two α -amino-N-heterocycles (1:2) gave N,N-acetals⁶.

It is interesting to note that the reaction of furfural with 2 mols of morpholine in 95% ethanol, heating for five minutes in a steam-bath and cooling in an ice-bath, gave the corresponding N,N-acetal that is readily hydrolyzed, while the azomethine was isolated when 1 mol of morpholine was added slowly and with agitation to 1 mol of furfural at 0 °C⁷.

These different types of behaviour of the reaction of furfural with amines with respect to the obtained products do not have a clear explanation. In order to obtain some insight into the above mentioned problem, the reaction of furfural and morpholine was studied in order to observe the synthesis and especially the instability of the structure of N,N'-(2'-furfurylidene)bis(morpholine) (Fig. 1), analyzed by X-ray diffraction and by semi-empirical quantum chemical calculations.

Experimental

Materials

Morpholine and 2-furaldehyde were commercially available products and were redistilled prior to use.

Synthesis

N,N'-(2'-furfurylidene)bis(morpholine) was prepared by slow addition of 3.5 g of morpholine (0.04 mol) to a solution of 2.5 g of furfural (0.02 mol) in 60 mL of hexane, or toluene, at -10 °C. After the extraction with ethyl acetate, the product was crystallized at 0 °C. Under these conditions, the compound is stable. However, at 25 °C this compound hydrolyses in a few hours. Using hexane or toluene, the yield and the stability is significantly higher than when ethanol 95% is used as in the method of Henry and Dehn⁷.

Calculations

Semi-empirical quantum chemical calculations at the PM3 level⁸ were made using a MOPAC⁹ program package (version 6.0).

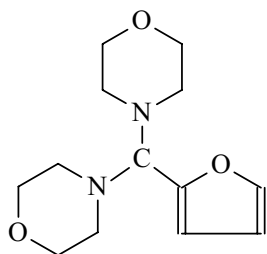


Figure 1. Bidimensional drawing of the title compound.

X-ray Crystallography

A colourless prismatic single crystal of dimensions 0.33 x 0.50 x 0.50 mm was mounted on a glass fiber and used to collect data on a Nonius CAD-4 diffractometer¹⁰ with graphite-monochromated Mo K α radiation and $\omega - 2\theta$ scan. The unit cell and the orientation matrix for the data collection were obtained by a least-squares fit of 25 centered reflections ($9.96 < \theta < 18.17^\circ$). The intensities of three standard reflections were measured every 60 min and varied -13.6%. The intensity data was corrected for Lorentz and polarization effects. A linear decay correction was applied with max. and min. correction factors of 1.07602 and 1.00060. The number of measured reflections was 2454 in the range $0 \leq h \leq 22$, $0 \leq k \leq 8$, $-24 \leq l \leq 24$, with 2376 unique reflections, and 1731 were above the significance level of $2\sigma(I)$. The maximum value of 2θ was 24.97° . The systematic absences were $hkl: h + k = 2n + 1$ and $h0l: l = 2n + 1$, consistent with the space group C2/c. Equivalent reflections were merged with $R_{\text{int}} = 1.7\%$. The structure was solved by means of direct methods using SHELXS97¹¹. The structure was refined by full-matrix least-squares techniques using F² with SHELXL97¹². Anisotropic displacement parameters were used for all non-hydrogen atoms. The disordered atoms C7, O2, C8, C7', O2' and C8' were refined anisotropically using the constraints SADI and SIMU of SHELXL97 (with fixed occupancy factors of 0.524 and 0.476, for unprimed and primed atoms, respectively). H atoms were placed geometrically except those involved in H-bonds which were positionally refined. The number of refined parameters was 206, and the goodness of fit was 1.058. At the end of the refinement an extinction correction parameter $x = 0.015(1)$ was applied, where F_c is multiplied by $k[1+0.001x F_c^2 \lambda^3/\sin(2\theta)]^{-1/4}$ where k is the overall scale factor. Residual densities of 0.155 and -0.196 e⁻ Å⁻³ were found in the final difference map. Examination of the structure with PLATON¹³ showed no solvent-accessible voids in the crystal lattice. The final refinement gave $R = 4.35\%$, $wR = 13.31\%$ and all parameter shifts were less than 0.10 of the corresponding standard deviation. Scattering factors were taken from International Tables for Crystallography (Vol. C). Calculations were performed on a DEC 3000 AXP computer using the MolEN package¹⁴ for data reduction and a PC486 computer for solution and refinement.

Results and Discussion

Table 1 reports the final atomic coordinates, while Fig. 2 shows the ZORTEP¹⁵ of the title molecule with the atom-numbering scheme. Selected bond distances and angles are given in Table 2.

The low stability of N-N'-(2'-furfurylidene) bis (morpholine), shown in its synthesis and conservation, is explained by the semi-empirical chemical calculations. The semi-empirical quantum chemical calculations of the ΔH° of the reaction is -2.69 Kcal/mol, but considering the ΔS° (-48.39 u.s.), the free energy ΔG° gives a value of 11.73 Kcal/mol that explains the strong tendency of this product to go back to reagents. It should be noted that this calcula-

Table 1. Atomic coordinates (10^4) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$).

	x	y	z	U(eq)
O1	1125(1)	4726(2)	7219(1)	63(1)
O2	1730(6)	5755(15)	4801(5)	84(3)
O2'	1981(6)	5131(18)	4841(6)	94(3)
O3	-525(1)	-1014(2)	6473(1)	79(1)
N1	1353(1)	3643(3)	5912(1)	60(1)
N2	726(1)	1073(2)	6318(1)	50(1)
C1	1343(1)	5199(3)	7859(1)	63(1)
C2	1823(1)	3996(3)	8127(1)	63(1)
C3	1933(1)	2663(3)	7635(1)	63(1)
C4	1506(1)	3141(3)	7096(1)	50(1)
C5	1371(1)	2236(3)	6432(1)	53(1)
C6	1292(1)	2748(4)	5266(1)	80(1)
C7	1207(9)	4270(2)	4758(5)	90(5)
C7'	1296(13)	4190(3)	4729(8)	126(8)
C8	1792(10)	6428(17)	5461(5)	91(3)
C8'	2044(11)	6230(2)	5434(6)	131(8)
C9	1971(2)	4903(4)	5982(1)	90(1)
C10	53(1)	2030(3)	6384(1)	59(1)
C11	-556(1)	737(3)	6133(1)	70(1)
C12	135(2)	-1917(4)	6431(2)	85(1)
C13	762(1)	-681(3)	6693(1)	70(1)

$$*U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

Table 3. Hydrogen-bonding geometry (\AA , $^\circ$).

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C1-H1...O3 ⁱ	0.93(2)	2.53(2)	3.453(3)	172(2)
C12-H12B...O1 ⁱⁱ	0.97(3)	2.55(3)	3.306(3)	135(2)
C(6)-H(6A)...N(2)	0.98(3)	2.41(3)	2.800(3)	103(2)
C(9)-H(9A)...O(1)	0.97(3)	2.57(3)	3.179(3)	121(2)
C(10)-H(10A)...N(1)	0.99(3)	2.56(2)	2.973(3)	105(2)

Symmetry codes: (i) -x,y+1,-z+3/2
(ii) x,y-1,z

tion corresponds to the compounds in the gaseous state, and that these results are similar to those of the experimental synthesis that was made in non-polar and non-hydroxylic solvents.

The semi-empirical quantum chemical calculations using MOPAC gave 111.44, 113.58 and 110.01 $^\circ$ for the bond angles C4-C5-N1, C4-C5-N2 and N1-C5-N2, respectively. It is interesting to note the coincidence of these results with those of Table 2.

Table 2. Selected bond lengths (\AA) and bond angles ($^\circ$).

N2-C5	1.459(2)
C4-C5	1.504(2)
C5-N1	1.458(2)
N1-C5-N2	108.7(2)
N1-C5-C4	111.7(2)
N2-C5-C4	115.1(2)

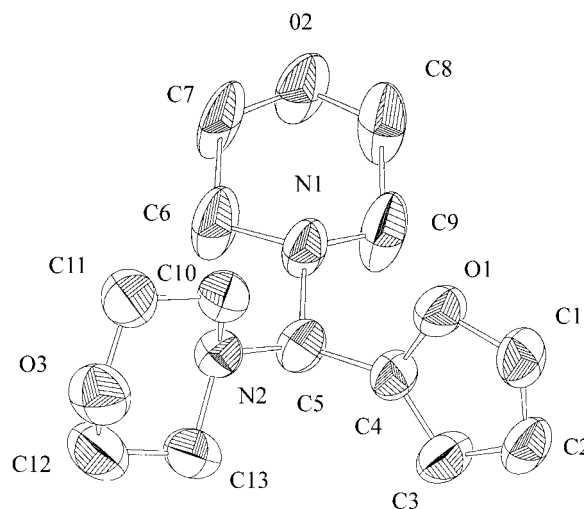


Figure 2. A ZORTEP plot of the title molecule, showing the atom-labeling scheme. Displacement ellipsoids are shown at the 50% probability level. The H atoms and the disordered C7', O2' and C8' atoms were omitted for clarity.

Three lines of reasoning from these data lead to an explanation of the low stability of the compound (the crystals become opaque):

i) Considering the “normal” bond angles such as tetrahedral (109.5°)¹⁶ for the tetracoordinated C5, or those corresponding to acyclic species that presumably are unstrained such as propane (112°)¹⁶, it is evident that the value of the angle C4-C5-N2 (113.58° calc., $115.1(2)^\circ$ cryst.) indicates the existence of some angle strain.

ii) The semi-empirical quantum chemical calculation and the crystallographic data show that C5 is $0.040(6)$ Å outside the least-squares plane of the furan ring (O1-C1-C2-C3-C4), indicating that there should exist a strong strain over the C4-C5 bond.

iii) The ring N1-C6-C7-O2-C8-C9 has the following puckering coordinates $Q(\text{Å})$, $\theta(^\circ)$, $\phi(^\circ)$ ¹⁷⁻¹⁸: $0.584(9)$, $11(1)$, $318(5)$ which is indicative of a distorted chair conformation. The ring N2-C10-C11-O3-C12-C13 with the puckering coordinates $0.579(2)$, $3.0(2)$, $354(4)$ has a chair conformation.

The molecule has C-H...O and C-H...N intramolecular contacts. The molecular packing involves C-H...O intermolecular contacts. They are listed in Table 3.

Supplementary Material

The list of bond distances, bond angles, anisotropic temperature factors, hydrogen coordinates and observed and calculated structure factors, is available from the authors (I. V.) upon request.

Acknowledgments

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