X-Ray Structure of 6(\textit{E})-[2(Z)-(Hydroxyimino)-2-phenylethylidene]-7,7,8,8,9,9-hexamethyl-3-phenyl-1,2-oxazaspiro[4.4]non-2-ene

Teresa Borowiak\textsuperscript{a}, Irena Wolska\textsuperscript{a}, Herbert Mayr\textsuperscript{b}, and Janusz Baran\textsuperscript{c}

\textsuperscript{a} Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland
\textsuperscript{b} Institute of Organic Chemistry, University of Munich, Butenandtstr. 5 - 13 (Haus F), D-81377 München, Germany
\textsuperscript{c} Institute of Fundamental Chemistry, Technical University of Szczecin, Aleja Piastów 42, 70-065 Szczecin, Poland

Reprint requests to Prof. T. Borowiak. E-mail: borowiak@main.amu.edu.pl

Z. Naturforsch. 56 b, 354–358 (2001); received November 27, 2000

1,3-Dipolar Cycloaddition Product, Oxime, Isoxazoline

The X-ray crystallographic structure of the title compound, a product of a 1,3-dipolar cycloaddition reaction of benzonitrile oxide to 3,3,4,4,5,5-hexamethyl-1,2-bis(methylene)cyclopentane, has been determined. Colourless plates crystalize in the orthorhombic space group \textit{Pbca} with cell dimensions \(a = 13.698(2)\), \(b = 11.836(2)\), \(c = 29.157(4)\) Å, \(V = 4727.2(1.2)\) Å\(^3\), \(Z = 8\), 3736 reflections, final \(R(F) = 0.063\) and \(wR(F^2) = 0.166\). The crystals are racemic, the molecules of opposite chirality form centrosymmetric dimers via intermolecular hydrogen bonds O-H - N between their oxime groups. The molecules are highly strained and the geometrical consequences of the steric strain are discussed.

Introduction

The 1,3-dipolar cycloaddition of nitrile oxides to olefines or alkynes leads to \(\Delta^2\)-isoxazolines or isoxazoles, respectively [1]. In the latter case concomitant formation of oximes has been observed [2]. This result prompted the suggestion that 1,3-dipolar cycloaddition was a stepwise process [3], but the biradical mechanism proposed there was criticized later [4].

Compounds 2 and 3 (and 4, the reaction is not enantiospecific, see Scheme 1), are the first oximes obtained from an olefinic dipolarophile, when 3,3,4,4,5,5-hexamethyl-1,2-bis(methylene)cyclopentane (1) is combined with benzonitrile oxide [5]. The formation of the oxime 2 can be rationalized by intramolecular hydrogen transfer in a diradical produced as an intermediate during the 1,3-dipolar cycloaddition [6]. A similar reaction has also been observed when C,N-diphenylnitrone was used as a 1,3-dipole [7].

The oxime 3 arises from the oxime 2 by cycloaddition of another nitrile oxide molecule to the remaining exo-methylene group in 2.

Elucidation of the stereochemistry of these unusual reaction products would give more information on the configuration of the intermediate diradical and thus provide a better insight into the mechanism of Scheme 1.

\begin{align*}
\text{benzonitrile} & \quad \text{oxide} \\
\text{N} & \text{H} \\
\text{O} & \text{N} \\
\text{H} & \text{O} \\
\text{H} & \text{N} \\
\text{benzonitrile} & \quad \text{oxide} \\
\text{N} & \text{H} \\
\text{O} & \text{N} \\
\text{H} & \text{O} \\
\text{H} & \text{N} \\
\text{N} & \text{H} \\
\text{H} & \text{N} \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
\text{Ph} & \\
Table 1. Crystal data, data collection and structure refinement.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{11}H_{12}N_{2}O_{2}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>416.55</td>
</tr>
<tr>
<td>Temperature</td>
<td>293(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P bca</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>13.698(2) Å</td>
</tr>
<tr>
<td>b</td>
<td>11.836(2) Å</td>
</tr>
<tr>
<td>c</td>
<td>29.157(4) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>4727.2(12) Å</td>
</tr>
<tr>
<td>Z, Calculated density</td>
<td>8.1.171 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.074 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1792</td>
</tr>
<tr>
<td>θ-Range for data collection</td>
<td>1.40 - 24.08°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>0 ≤ h ≤ 15, 0 ≤ k ≤ 13, -33 ≤ l ≤ 0</td>
</tr>
<tr>
<td>Refls collected / unique</td>
<td>3736 / 3736 [R(int) = 0.000]</td>
</tr>
<tr>
<td>Data / restraints / params</td>
<td>3730 / 0 / 342</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.369</td>
</tr>
</tbody>
</table>

Table 2. Bond lengths [Å] and angles [deg] and selected torsion angles [deg] with e.s.d.'s in parentheses.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length [Å]</th>
<th>Angle [deg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)-C(29)</td>
<td>1.520(4)</td>
<td></td>
</tr>
<tr>
<td>(1)-C(5)</td>
<td>1.560(5)</td>
<td></td>
</tr>
<tr>
<td>(1)-C(12)</td>
<td>1.531(4)</td>
<td></td>
</tr>
<tr>
<td>(2)-C(31)</td>
<td>1.507(5)</td>
<td></td>
</tr>
<tr>
<td>(2)-C(3)</td>
<td>1.553(4)</td>
<td></td>
</tr>
<tr>
<td>(3)-C(4)</td>
<td>1.512(4)</td>
<td></td>
</tr>
<tr>
<td>(4)-C(19)</td>
<td>1.520(4)</td>
<td></td>
</tr>
<tr>
<td>(5)-C(26)</td>
<td>1.517(4)</td>
<td></td>
</tr>
<tr>
<td>(5)-C(27)</td>
<td>1.563(4)</td>
<td></td>
</tr>
<tr>
<td>(6)-C(7)</td>
<td>1.474(4)</td>
<td></td>
</tr>
<tr>
<td>(7)-C(10)</td>
<td>1.480(4)</td>
<td></td>
</tr>
<tr>
<td>(16)-C(17)</td>
<td>1.486(4)</td>
<td></td>
</tr>
<tr>
<td>(17)-C(20)</td>
<td>1.467(4)</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. A view of the S-enantiomer showing the labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

1,3-dipolar cycloadditions of nitrile oxides. In this paper we report the X-ray structure of the oxime 3.

Experimental

Colourless crystals suitable for X-ray analysis were grown from methanol solution by slow evaporation. The data were collected on a kappa-geometry KM4 KUMA diffractometer [8], with graphite monochromated Mo-Kα radiation. The accurate unit cell dimensions were obtained by the least-squares fit of setting angles of 32 reflections (12° < 2θ < 27°). The θ-2θ scan method and a variable scan speed, depending on reflection intensity, were used. Two control reflections were measured after every 100 reflections and showed no systematic changes during data collection. Intensity data were corrected for the Lorentz and polarization effects [8]. The structure was solved by direct methods with the SHELXS86 [9] program and refined by the full-matrix least-squares method...
with the SHELXL93 [10] program. Refinement on $F^2$ was carried out for all reflections, six of them were excluded from the reflection file due to their large ($|F_o| - |F_c|$) differences. The function $\sum w(|F_o|^2 - |F_c|^2)$ was minimized with $w^{-1} = (\sigma^2(F_o)^2 + (0.0430P)^2 + 2.5033P)$, where $P = (F_o^2 + 2F_c^2)/3$.

All non-hydrogen atoms were refined with anisotropic thermal parameters. The coordinates of the hydrogen atoms were calculated in their idealized positions, then H atoms of the methyl groups were refined as a riding model with their thermal parameters calculated as 1.5 times $U_{eq}$ of that of the carrier carbon atom, for the other H atoms their positional and thermal parameters were refined.

The crystallographic data, together with data collection and structure refinement details are listed in Table 1. Selected bond distances, bond angles and torsion angles of 3 are reported in Table 2. The displacement ellipsoid representation of the 4-5 (3) enantiomer, together with the atomic numbering scheme, is shown in Fig. 1. The drawings were performed with a Stereochemical Workstation [11]. Additional crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No CCDC 159938. Copies of the data can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [E-mail: deposit@ccdc.cam.ac.uk].

Results and Discussion

Crystals of the title compound contain pairs of enantiomers, the chiral center being the spirocarbon atom C(4). The further discussion will concern the overall conformation of 3, which is similar to that of 3-phenyl-4,5-dihydro-isoxazole-5-spirocyclopentane [12] (5),

although six methyl groups in 3 introduce much greater steric stress than that existing in the molecule 5. The cycloalkane ring appears to be rigid in the crystal of 3, showing no evidence of disorder. Torsion angles in that ring (Table 2) indicate a conformation close to a half-chair form with a pseudo-axis of symmetry passing through the C(2) atom and the midpoint of the C(4)-C(5) bond, with the asymmetry parameter $\Delta C_2 = 1.3^\circ$. The value of the pseudoradial puckering amplitude, $q$, calculated as the square root of the sum of squares of the atom deviations from the mean plane through the five membered ring is 0.38 Å. A close value, of 0.35 Å has been found for the unsubstituted cyclopentane ring in 5 [12], while the mean of $q$ derived for the unsubstituted cyclopentane molecule in the gas phase equals to 0.43 Å [17]. However, the nature of the steric strain in the cyclopentane region of 3 is quite complex and the puckering amplitude does not provide full information. The bond distances in the cyclopentane ring vary significantly, from 1.512(4) Å for the C(3)-C(4) distance, typical of the Csp$^2$-Csp$^3$ single bond, up to 1.582(4) Å of the Csp$^3$-Csp$^3$ bond distance C(1)-C(2), which is much longer than the bond distances in unsubstituted

Table 3. A comparison of the bond angles $\alpha_{isoax-C\_spiro\_cycloalk}$ in spirocycloalkanes.

<table>
<thead>
<tr>
<th>$\alpha$</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>116.0(1)°</td>
<td>12</td>
</tr>
<tr>
<td>112.9(5)°</td>
<td>12</td>
</tr>
<tr>
<td>110.0(2)°</td>
<td>this work</td>
</tr>
<tr>
<td>116.19(9)°</td>
<td>12</td>
</tr>
<tr>
<td>110.0(2)°</td>
<td>13</td>
</tr>
</tbody>
</table>
cyclopentane, 1.548(1) Å, derived from the electron diffraction [17]. Also the exocyclic bond angles to the methyl groups are significantly different from the tetrahedral values (see Table 2). This big variety of the deformed geometric parameters found in the cyclopentane ring in 3 should be undoubtedly ascribed, in part at least, to the atom-atom non-bonded repulsions in the highly overcrowded cyclopentane moiety, since the (C···C) mean nonbonded distance in the cyclopentane ring of 3 is equal to 2.45(4) Å, a value comparable with that in the unsubstituted cyclopentane, the later being 2.444 Å, as calculated from the electron diffraction data [17]. Probably, due to the steric reasons, the C(3)=C(6)-C(7)=N(8)-O(9) chain is not flat and no conjugation is observed, the C(3)=C(6) and C(7)=N(8) bond distances being 1.319(4) and 1.278(3) Å, respectively, typical of isolated double bonds. On the other hand, the C(6)-C(7)=N(8)-O(9) group is nearly planar to within 0.03 Å and the configuration of the oxime group is Z (torsion angles: O(9)-N(8)-C(7)-C(6) -6.4(4)° and O(9)-N(8)-C(7)-C(10) 177.7(2)°). The configuration of 3, in relation to the C(3)=C(6) double bond, is E (torsion angles C(7)-C(6)-C(3)-C(4) -174.9(3)° and C(7)-C(6)-C(3)-C(2) 3.7(5)°). Contrary to the other spiro-derivatives of isoxazoline [12 - 15], this spirocycloalkane isoxazolines undergo a thermal rearrangement involving the N-O bond cleavage[12]. The N-O bond length in 3, 1.402(3) Å, is within the experimental error the same as in the other spiroisoxazolines [12 - 15]. It has been suggested [12] that the only geometrical parameter of the molecular structure which might be related to the molecular stability is the stereochemical arrangement around the spiro-carbon atom. We have compared this arrangement in 3 and found that in particular the bond angle Oisoax-Cspiro-Cycloalk is sensitive to the stereochemical requirements of different cycloalkane rings (Table 3), however on account of the scarcity of related crystal structures in the Cambridge Structural Database [18], only a few examples can be quoted.

The molecules of 3 are connected by intermolecular hydrogen bonds O-H···N forming centrosymmetrical dimers (Fig. 2, Table 4).

Table 4. Hydrogen-bonding geometry (Å, deg).

<table>
<thead>
<tr>
<th>D-H···A</th>
<th>D-H</th>
<th>H···A</th>
<th>D···A</th>
<th>D-H···A</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(25)-H(25)···N(18)</td>
<td>0.90(4)</td>
<td>2.60(4)</td>
<td>2.852(4)</td>
<td>97(3)</td>
</tr>
<tr>
<td>O(9)-H(9)···N(8)</td>
<td>0.80(4)</td>
<td>2.02(4)</td>
<td>2.778(3)</td>
<td>159(3)</td>
</tr>
</tbody>
</table>

Symmetry codes: 1 x, y, z; 2 -x, 1-y, 1-z.

The cyclopentane and isoxazoline rings are almost perpendicular, the angle between their mean-squares planes is 81.7(1)°. On the other hand, due to the intramolecular hydrogen bond C-H···N between the hydrogen atom on C(25) of the phenyl group and the nitrogen atom N(18), the isoxazoline and phenyl rings are almost coplanar, with an angle between their mean planes of 19.9(1)° and a distance H(25)···N(18) of 2.60(4) Å.

Spirocycloalkane isoxazolines undergo a thermal rearrangement involving the N-O bond cleavage[12]. The N-O bond length in 3, 1.402(3) Å, is within the experimental error the same as in the other spiroisoxazolines [12 - 15]. It has been suggested [12] that the only geometrical parameter of the molecular structure which might be related to the molecular stability is the stereochemical arrangement around the spiro-carbon atom. We have compared this arrangement in 3 and found that in particular the bond angle Oisoax-Cspiro-Cycloalk is sensitive to the stereochemical requirements of different cycloalkane rings (Table 3), however on account of the scarcity of related crystal structures in the Cambridge Structural Database [18], only a few examples can be quoted.

The molecules of 3 are connected by intermolecular hydrogen bonds O-H···N forming centrosymmetrical dimers (Fig. 2, Table 4).