118. Glycosylidene Carbenes

Part 8

Crystal Structure of a Cyclic, *N*-Acetylallosamine-Derived Alkoxy-alkyl-diazirine

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The crystal structure of 2-acetamido-1,5-anhydro-1-azi-3-*O*-benzyl-4,6-*O*-benzylidene-1,2-dideoxy-D-allitol (**6**) is reported, and the structural parameters of the diazirine moiety are compared with those of other free diazirines for which structural information has been determined or calculated previously. Lengthening of the N=N bond and shortening of the C–N bonds can be observed as the substituents at the C-atom of the diazirine ring become more electronegative and/or stronger π-electron donors. This is consistent with descriptions of the bonding nature of diazirines and similar observations made on substituted cyclopropanes.

Introduction. – Glycosylidene-derived diazirines, such as **1** [1], **5** [2], or **6** [3] (see *Scheme*), are precursors of glycosylidene carbenes, such as **3**, and may be used for a mild, promoter-free, thermal or photochemical glycosidation, especially of acidic, non-nucleophilic alcohols [4] and for the synthesis of cyclopropanes [3] [5].

Scheme

We have hypothesized that the thermal transformation of these diazirines to carbenes occurs stepwise *via* zwitterions of type **2**, possessing cationic character at the anomeric center [2b]. Indeed, the thermal stability of **1**, **5**, and **6** decreases in the order **6** > **5** > **1** [6]. Thus, it is qualitatively inversely correlated with the anticipated stability of the glycosyl cations corresponding to **2**, as one would expect, if **2** is an intermediate. The thermal stability of these alkoxy-alkyl-diazirines thus depends on the nature of the protecting group and, for **6**, on the torsional strain imposed on the zwitterionic intermediate by the annulated dioxolane ring [7].

We wondered if structural parameters might indicate a preference for the initial cleavage of one of the C(1)−N bonds (anomeric effect) and show the influence of the diazirine substituents on the thermal stability of diazirines. Unfortunately, of the diazirines **1**, **5**, and **6**, only **6** yielded suitable crystals, so that a correlation of the differences of thermal stability with structural parameters is not yet feasible. Since very few X-ray analyses of diazirines are known, and none of alkoxy-substituted and spiro-annulated derivatives, the structure of **6** is of considerable interest.

Discussion. – A view of the molecule of **6** is shown in the *Figure*, experimental and structural parameters are listed in *Table 1* and selected bond lengths and angles in *Table 2*. The structure does not show any distinctly unusual features, and the fused rings adopt chair conformations. The bond lengths of and the angles within the diazirine ring, as discussed below, are in agreement with values found for other diazirines. Neither of the N-atoms attempt to adopt a truly axial or equatorial position; the mid-point of the N=N bond almost bisects these positions. The angle between the planes O(1)−C(1)−C(2) and C(1)−N(1)−N(2) is 88.8°, which indicates no significant distortion of the diazirine ring from perpendicularity with respect to the lie of the sugar ring. The plane of the diazirine ring almost bisects the O(1)−C(1)−C(2) angle and, if anything, is distorted slightly away

Table 1. *Data Collection and Structure Refinement Parameters*

Empirical formula	$C_{22}H_{23}N_3O_5 \cdot CH_2Cl_2$	X-ray wavelength (MoK_α) [Å]	0.71069
Formula weight	458.92	D_x [g·cm^{-3}]	1.266
Crystal colour, habit	colourless, plate	Linear absorption coeff. [cm^{-1}]	1.917
Crystal dimensions [mm]	$0.07 \times 0.33 \times 0.40$	2θ(max) [°]	55
Crystallised from	CH_2Cl_2/pentane	Total reflections measured	3528
Data collection temperature	173 ± 1 K	Unique reflections	3344
Crystal system	monoclinic	R_{int}	0.020
Space group	$P2_1$	Reflections observed ($I > 2\sigma(I)$)	2100
Unit-cell parameters[a]): a [Å]	11.758(3)	Parameters refined	323
b [Å]	8.229(3)	R	0.0562
c [Å]	12.822(3)	wR	0.0521
β [°]	104.08(2)	Goodness of fit s	1.974
V [Å^3]	1203.4(6)	Data/parameter ratio	6.50
Z	2	Final Δ_{max}/σ	0.001
		$\Delta\rho$(max) [e Å^{-3}]	0.48 (near Cl)

[a]) The cell dimensions were obtained from 23 accurately centered reflections with $20° < 2\theta < 23°$.

Table 2. *Selected Bond Lengths* [Å] *and Bond Angles* [°] *for* **6**. E.s.d.'s in parentheses.

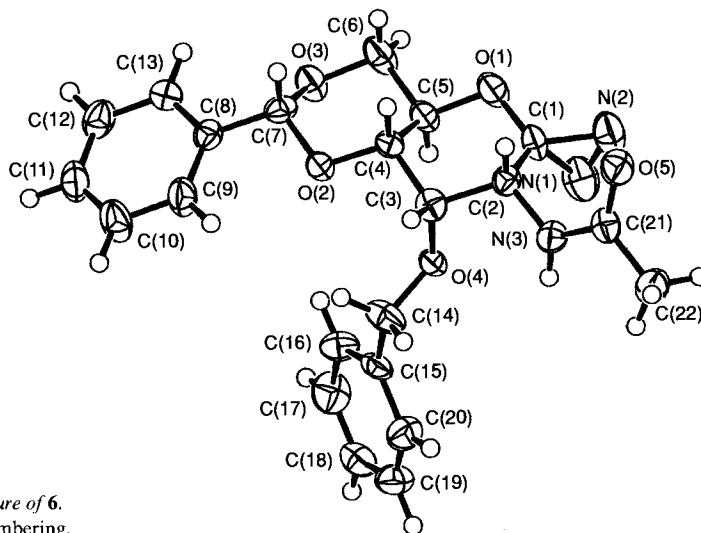|			
N(1)−N(2)	1.258(8)	C(1)−C(2)	1.507(8)
N(1)−C(1)	1.478(8)	C(2)−C(3)	1.527(8)
N(2)−C(1)	1.452(8)	C(3)−C(4)	1.516(8)
O(1)−C(1)	1.373(7)	C(4)−C(5)	1.518(8)
O(1)−C(5)	1.441(7)		
N(1)−C(1)−N(2)	50.8(4)	N(2)−C(1)−C(2)	122.3(5)
N(2)−N(1)−C(1)	63.5(4)	C(1)−O(1)−C(5)	110.5(4)
N(1)−N(2)−C(1)	65.7(4)	C(1)−C(2)−C(3)	111.5(5)
O(1)−C(1)−N(1)	115.9(5)	C(2)−C(3)−C(4)	107.9(4)
O(1)−C(1)−N(2)	114.7(5)	C(3)−C(4)−C(5)	110.7(4)
O(1)−C(1)−C(2)	116.0(5)	O(1)−C(5)−C(4)	109.0(4)
N(1)−C(1)−C(2)	121.4(5)		

Figure.
X-Ray structure of **6**.
Arbitrary numbering.

from the amido group and towards O(1). The angle formed at C(1) between the mid-point
of the N(1)=N(2) bond and C(2) is 125.8°, while the corresponding angle involving the
mid-point of N(1)=N(2) and O(1) is 118.3°. Although this distortion is very small, it could
be the result, on the one hand, of the interaction between the electron donor O(1) and the
orbitals of the diazirine ring or, on the other hand, of a repulsion between the acetamido
group and the diazirine ring. The former interaction will be discussed further below; there
is no evidence for the latter. The difference in length of the C–N bonds of the diazirine
ring is very small and presumably not significant, although it is in the direction which is
expected if electron donation from the O-substituent leads to a more advanced breaking
of the 'pseudoaxial' C–N bond which forms a smaller torsional angle with the predicted
axis of the π-type lone pair on the O-atom.

The amido group of **6** provides one acceptor and one donor site for an intermolecular
H-bond. The N(3)–H(3)· · ·O(5′) H-bond[1]) links the molecules into one-dimensional
infinite chains which run parallel to the *y*-axis. The H(3)· · ·O(5′) distance is 2.08(5) Å.

Reports of X-ray structure determinations of diazirines are very few, there being only
one other known determination of a free diazirine, 3-chloro-3-[(naphth-1-yl)methyl]-
diazirine (**7**) [8]. The remaining structure determinations involve diazirines coordinated
via the N-atoms to transition metals [9]. The bonding parameters of diazirine (H_2CN_2)
and those of methyl- and halogeno-substituted diazirines have been calculated from
rotational spectra [10]. The structure of difluorodiazirine has been determined by
electron-diffraction techniques [11]. The structural parameters of the diazirine moiety of
all of these compounds are listed in *Table 3*.

On the basis of the standard deviations for the N=N and C–N bond lengths for the
compounds in *Table 3*, the corresponding bond lengths in **6** are entirely consistent with
those previously observed or calculated. If the transition-metal complexes of diazirines
are excluded, an interesting trend becomes apparent, although the magnitudes of the

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[1])   Atom O(5′) belongs to the molecule in the symmetry-related position: $1 - x, 1/2 + y, 2 - z$.

Table 3. *The Ring Geometry of Diazirines*

	N=N [Å]	C−N [Å]	⊀ (N−C−N) [°]	Reference
F_2CN_2	1.293(9)	1.426(4)	53.9(4)	[11]
6	1.258(8)	1.465(13)	50.8(4)	
7	1.244(10)	1.465(10)	50.3(5)	[8]
$MeClCN_2$	1.241(5)	1.462	50.2(5)	[10a]
$MeBrCN_2$	1.240(5)	1.462	50.2	[10b]
$(Me)_2CN_2$	1.235(5)	1.490(10)	48.9	[10c]
$MeHCN_2$	1.235(5)	1.481(10)	49.3(3)	[10d]
H_2CN_2	1.228(3)	1.482(3)	48.9	[10e]
$[Ru(NH_3)_5(pmd)](PF_6)_2^a)$	1.28(1)	1.46/1.51	50.9(9)	[9a]
$[\{Cr(CO)_4\}_2\{\mu-(\eta^2\text{-pmd})\}_2\{\mu\text{-dppe}\}]^a)$	1.268(8)	1.485(9)	50.6(4)	[9b]
$[\{Cr(CO)_5\}\{\mu-(\eta^2\text{-pmd})\}\{Mo(CO)_5\}]^a)$	1.265(6)	1.493	50.1	[9c]

a) dppe = 1,2-bis(diphenylphosphino)ethane, pmd = 3,3-pentamethylenediazirine.

standard deviations mean that this trend must be treated cautiously. As the substituent(s) at the C-atom of diazirine become more electronegative, the N=N bond becomes longer and, to a lesser extent, the C−N bonds become shorter. The calculated bond lengths for unsubstituted diazirine indicate the shortest N=N bond and, except for dimethyldiazirine, the longest C−N bonds. At the other extreme, difluorodiazirine, which possesses the most electronegative substituents, has the longest N=N bond and the shortest C−N bonds. In between, the monohalogeno-substituted methyldiazirines show the same trends when compared with methyl- and dimethyldiazirine, although the standard deviations make this comparison tenuous. Compound 7 has almost identical N=N and C−N bond lengths as chloro-methyl-diazirine, of which 7 is essentially a derivative. The X-ray analysis of 6 provides the first example of a crystal structure of an alkoxy-substituted diazirine. Since O is between F and Cl in electronegativity, on the basis of the predicted trend, the N=N and C−N bond lengths should lie between those observed for chloro-methyl-diazirine and difluorodiazirine. *Table 3* verifies this. The effect is, of course, most pronounced in difluorodiazirine, and a better comparison would be possible if bond lengths for fluoro-methyl-diazirine were available.

Detailed discussions of the bonding nature of diazirines can be found elsewhere [12]. *Baird* [12a] indicates that the trend described above can be explained in terms of two contributions. Firstly, replacement of H or Me substituents by an electronegative substituent withdraws electron density from the $2p_\pi$ orbital of the C-atom, which then attempts to regain electron density by combining with the bonding $\pi_{N=N}$ orbital. This results in a small increase in the C−N bond order and a small decrease in the N=N bond order, which is consistent with the observed bond-length changes. Secondly, if a substituent contains a lone pair of electrons, as is the case with halogeno atoms and the O-atom of 6, this substituent acts as an electron donor to the diazirine ring, when the lone pair of the substituent is oriented parallel to the N=N bond. The highest occupied molecular orbital in diazirine is a $3b_2$ type, a *Walsh*-type orbital which is CN bonding and NN antibonding. As a result of the donation, this orbital becomes more heavily nitrogen in character, thus increasing the degree of NN antibonding character and lengthening the N=N bond.

The orbitals involved in the bonding of diazirine are essentially the same as those in cyclopropane, with the addition of two electrons. *Allen* [13] has carried out a detailed

analysis of the bond-length trends in cyclopropanes as a function of the electron-acceptor and -donor nature of the substituents. The trends he observed for electron-donor substituents are the same as those described above for diazirines, with the C—C bond adjacent to the substituent becoming shorter as the electronegativity or donor strength of the substituent increases, and the distal C—C bond (equivalent to the N=N bond in diazirine) becoming longer. The correlation of these observations with the orbital description for cyclopropane has been discussed by *Deakyne et al.* [14].

Experimental Part

Crystal-Structure Determination of **6**. All measurements were made on a *Rigaku AFC5R* diffractometer with graphite-monochromated MoK_α radiation and a 12-kW rotating anode generator. Data collection and refinement parameters are given in *Table 1*[2]). The data were collected using the ω-2θ scan technique. The ω-scan width was $(1.42 + 0.35\tan\theta)°$ and the ω-scan speed $8°$ min^{-1}. The weak reflections $(I < 5\sigma(I))$ were rescanned up to a maximum of 4 scans, and the counts were accumulated. Stationary background counts were recorded on each side of the reflection with a peak/background counting time ratio of 2:1. Neutral atom scattering factors for non-H-atoms were taken from *Cromer* and *Waber* [15a] and the scattering factors for H-atoms from *Stewart et al.* [16]. The scattering factors were corrected for the real and imaginary parts of the anomalous dispersion [17] [15b]. *Lorentz*, polarisation, and absorption corrections (DIFABS [18]) were applied to the intensities. The intensities of three representative reflections which were measured after every 150 reflections decreased by *ca.* 3.5% during the data collection. A linear correction was applied to the data to account for this. The structure was solved by direct methods (SHELXS-86 [19]) which revealed the positions of all non-H-atoms of the fused rings and the phenyl group. The remaining non-H-atoms were located in a subsequent *Fourier* expansion of the structure with the program DIRDIF [20]. The non-H-atoms were refined anisotropically. All H-atoms were visible in a difference *Fourier* map. The H-atom attached to the amide N-atom was placed in the position indicated in the difference *Fourier* map, and its position was allowed to refine. The Me group H-atoms were also placed in the positions indicated in the map, but their positions were not refined. All remaining H-atoms were placed in geometrically calculated positions with a fixed C—H distance of 0.95 Å. Individual isotropic temperature factors were refined for all H-atoms. The structure was refined on F by full-matrix least-squares procedures using the TEXSAN [21] program system. Refinements minimized the function $\Sigma w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + 0.0001F_o^2]^{-1}$. The only significant features in the final difference map were a few peaks of residual electron density in the region of the solvent molecule (max. 0.48 e $Å^{-3}$). The CH_2Cl_2 solvent molecule is undergoing strong thermal motion within its cavity, or is disordered; a disordered model, however, could not be successfully refined. No attempt was made to determine the absolute configuration; the enantiomorph was chosen based on the known configuration of the starting material.

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