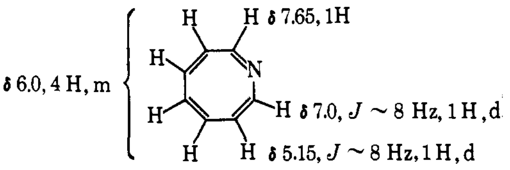
the temperature of the probe was increased. No other changes, however, were observed in the spectrum which could be ascribed to conformational, double-bond, or bicyclic isomers.

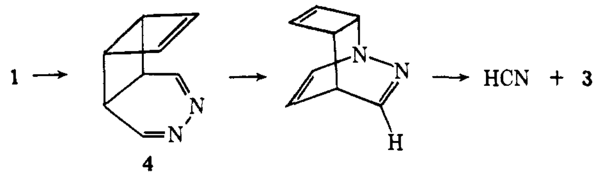


The mass spectrum (50 eV) of azocine consists of the following major ions (*m/e*, relative abundance): 105, 87; 104, 100; 78, 93; 52, 81; 51, 89; 50, 66; 39, 55. Its ionization potential (8.5 eV) and thermal behavior in our mass spectral reactor corresponded to that previously determined by pyrolysis of **1**.

Chemical evidence for **3** was obtained by its reduction to the dianion[6] using potassium in liquid ammonia. The white salt was hydrolyzed with aqueous ethanol and the resulting solution was reduced with hydrogen over platinum oxide. Heptamethylenimine was obtained, although in low yields, as evidenced by glpc–mass spectrometry.

We propose the following scheme for the thermal generation of azocine by analogy with the recently elucidated thermal rearrangement of basketene.[7] A similar scheme has been proposed for the boron trifluoride induced rearrangement of the *N*-oxide of **1** to benzaldehyde oxime.[8] It is probable that the explusion of hydrocyanic acid occurs in the oven. No evidence has been obtained so far regarding the possible initial formation of a bicyclic isomer of azocine.[9]

Obviously, one factor favoring the retro Diels–Alder reaction to give **4** rather than nitrogen extrusion must be strain release; however, a strain-releasing retro Diels–Alder reaction to give nitrogen and the syn dimer of cyclobutadiene is also possible for **1**, but does not occur. The totality of structural features governing the reaction course remains to be assessed.



Acknowledgment. We thank Professor Farnum for suggesting this problem to us and for providing us with samples of diazabasketene.

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Conformations of Cyclic Dipeptides. Structure of *cyclo*-Glycyl-L-tyrosyl (L-3-(4-Hydroxybenzyl)-2,5-piperazinedione)[1]

Sir:

The current interest[2-10] in conformations of cyclic dipeptides (2,5-piperazinediones) makes timely the study of the interactions between α-carbon substituents and the dipeptide (diketopiperazine) ring. We report here the structural and conformational analysis of *cyclo*-glycyl-L-tyrosyl (*c*-Gly-L-Tyr) as determined by single-crystal X-ray diffraction.[11]

The structure was solved by direct methods with the symbolic addition procedure[12] and tangent formula refinement of phases.[13] The crystals are orthorhombic, space group $P2_12_12_1$ with $a = 7.775 \pm 0.003$, $b = 21.475 \pm 0.011$, $c = 6.170 \pm 0.001$ Å; $Z = 4$; $\rho_{\text{calcd}} = 1.418$ g/cm^3; and $\rho_{\text{obsd}} = 1.415$ g/cm^3. The 1045 independent integrated intensities with $2\theta < 135°$ were measured by the θ–2θ scan technique with Ni-filtered Cu Kα radiation on a Picker FACS-I diffractometer. Refinement of the structure by full-matrix least squares included anisotropic temperature factors for all but the hydrogen atoms. Positional parameters for all hydrogen atoms were derived from difference Fourier syntheses, but were kept fixed in the refinement. Comparison of calculated structure factors with the 1023 equally weighted observed structure factors gives a conventional R factor of 0.105.[14]

Bond distances and bond angles are shown in Figure 1. These values are generally not significantly different from those reported for other diketopiperazines;[4,9,10,15] our present estimated standard deviations range from 0.011 to 0.015 Å and from 0.8 to 1.0°. The internal angles at C^α follow the expected trend correlating increased substitution with lower angle. The corresponding angles in *c*-L-Ala-L-Ala are 112.0 and 110.5°,[4] whereas in unsubstituted diketopiperazine they are 115.1°.[15]

The overall shape of the molecule is best described in terms of the three possibilities shown in Figure 2. Without departing from amide planarity, the DKP ring can be planar (Figure 2A) or assume two possible

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(1) This work was begun with Research Corporation assistance and completed under NSF Grant No. GB-7376 and NSF Instrumentation Grant No. GP-10343.

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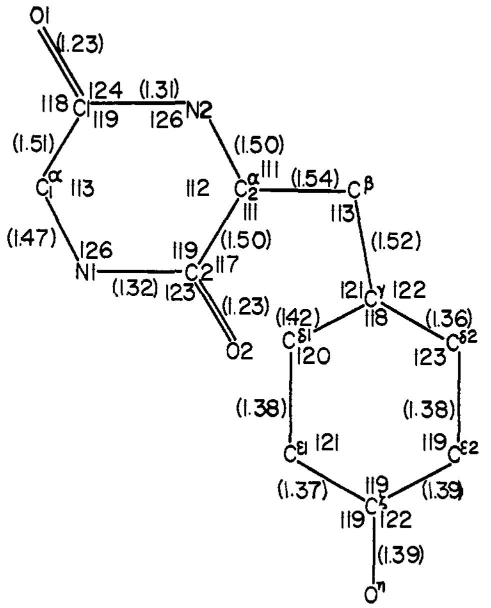

Figure 1. Bond angles and bond distances[10] in *cyclo*-glycyl-L-tyrosyl. Bond distances are shown in parentheses.

boat conformations, one with the benzyl substituent quasiaxial ("flagpole," Figure 2B), and the other with this substituent quasiequatorial ("bowsprit," Figure 2C).[5] We find *c*-Gly-L-Tyr to be buckled to the extent of 10–20° toward the boat conformation (B); the relevant torsional angles are $\phi_1 = 19°$, $\psi_1 = -13°$, $\phi_2 = 16°$, $\psi_2 = -10°$. The ϕ and ψ values are 10–13° smaller and of opposite sign to the corresponding angles in *c*-L-Ala-L-Ala, which is buckled in the opposite direction, with the methyl groups quasiequatorial (Figure 2C).[4,9] The amide groups deviate only slightly from planarity ($\omega_1 = -4°$, $\omega_2 = -7°$) so that there is little "twist" in the boat.

The χ^1 (C^α, C^β) angle is 55° so that the aromatic ring lies directly over the DKP ring (Figure 2B) in agreement with nmr studies in solution which have shown that arylmethyl side chains prefer this folded conformation[2,3,5] (the F rotamer).[3] The 71° $\chi^{2,1}$ angle tilts the aromatic ring plane 19° away from the symmetrical position perpendicular to the $C^\alpha C^\beta C^\gamma$ plane. Pullman and coworkers have assumed a planar DKP ring in molecular orbital calculations on *c*-Gly-L-Phe and found $\chi^1 = 60°$, $\chi^2 = 60°$ for the most stable conformation.[8] Empirical potential energy calculations employing a planar DKP ring give $\chi^1 = 60°$, $\chi^2 = 90°$.[16]

An overall picture of the effect of substituents on the conformation of the DKP ring is beginning to emerge from nmr and X-ray data. Application of a recently developed expression relating the peptide NH-C^αH coupling constant to dihedral angle[17] indicates that, in dimethyl sulfoxide solution, a number of monosubstituted diketopiperazines, including *c*-Gly-L-Tyr, *c*-Gly-L-Phe, *c*-Gly-L-Trp, and *c*-Gly-L-Val, prefer a boat conformation with the substituent in a flagpole type of orientation (Figure 2B).[3,18] This conformation was proposed earlier for *c*-Gly-L-Phe and *c*-D-Ala-L-Phe in trifluoroacetic acid on the basis of aromatic ring shielding effects in the nmr spectra.[5] Figure 2 shows that, for the folded conformation, interaction between the substituent and the DKP ring is greatest for the flagpole orientation (Figure 2B). When the second amino acid has the L configuration as in Figure 2, both substituents may not be able to assume the flagpole orientation, particularly when one substituent is aromatic. Models show that planarity can remove the side-chain interference and still maintain some interaction between a substituent and the DKP ring. The dominance of the planar conformation for *c*-L-Ala-L-Phe has been explained on this basis;[5] *c*-L-Val-L-Tyr also favors the planar conformation found in diketopiperazine itself, *c*-Gly-Gly.[3,18]

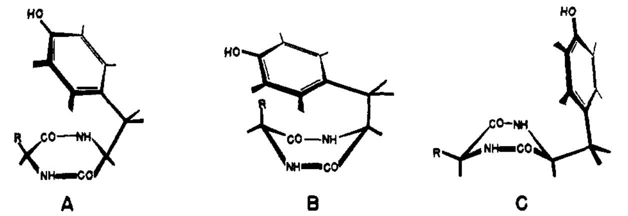

Figure 2. The folded form ($\chi^1 = 60°$) of a tyrosyl residue in cyclic dipeptides with planar and boat conformations of the diketopiperazine ring.

In the absence of aromatic side chains, the lessened importance of intramolecular interactions apparently makes the various DKP ring conformations quite close in energy and makes other effects such as crystal packing forces more important. Thus, one would expect the DKP ring to minimize ring strain by taking whichever boat conformation avoids side chain interference, but in the crystalline state, both planarity[10,15,19] and the bowsprit boat conformation (Figure 2C) have been found.[4,9]

The DKP ring conformation, then, appears to be primarily determined by the maximization of DKP aromatic ring interaction and the avoidance of side-chain interference. Strain in the DKP ring system enters to a lesser extent. The solution of the *c*-L-Ser-L-Tyr crystal structure, now in progress, should allow further evaluation of these effects.

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Photooxidation of Aqueous Benzene. I. Identification of the Product as 1,3-Cyclopentadiene-1-carboxaldehyde[1]

Sir:

Irradiation of benzene at 253.7 nm in aerated water at pH 4–8 has been reported[2] to yield an acidic aldehyde, tentatively identified as 4*H*-pyran-2-carboxaldehyde. A recent communication[3] supporting this assignment

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