

Stereochemical Aspects of a Substituted Bicyclo[4.2.0]octane

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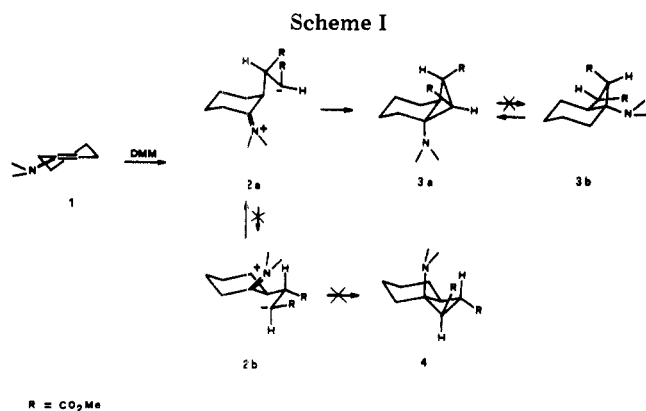
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1-Morpholinocyclohexene reacts with dimethyl maleate (or dimethyl fumarate) under mild reaction conditions to yield a bicyclo[4.2.0]octane derivative. X-ray analysis of this compound shows that it is cis fused, as previously found in anancomeric systems of the same type.

Recently, x-ray studies of some bicyclo[4.2.0]octane systems, derived from enamines, have revealed the preferred cis fusion of the two rings.^{1,2} However, the cases reported dealt with anancomeric enamines as starting materials. It seemed therefore interesting to investigate the stereochemistry of a cyclic adduct derived from a nonbiased enamine. The structure determination seemed also of interest because of the relatively few stereochemical data available in the literature about the bicyclo[4.2.0]octane derivatives.

The reaction between 1-morpholinocyclohexene (1) and dimethyl maleate (DMM) or dimethyl fumarate (DMF) yields the cyclic product 3 in both cases (Scheme I).



Experimental Section

Spectral data were obtained with a Perkin-Elmer 257 infrared spectrometer and a JEOL JNM-C-60 HL NMR spectrometer.

Preparation of Dimethyl *r*-1-Morpholino-*c*-6*H*-bicyclo[4.2.0]octane-*c*-7,*t*-8-dicarboxylate (3). A solution of 9.6 g (65.8 mmol) of DMM (or DMF)³ in dry acetonitrile was added dropwise to a solution of 11.0 g (65.8 mmol) of 1-morpholinocyclohexene in the same solvent, at 25 °C. After 3 days, the reaction mixture was worked up by the method of Brannock et al.⁴ 3 (10.0 g, 48%) was obtained and crystallized from light petroleum: mp 78–80 °C; IR (CHCl₃) 1725 cm⁻¹ (CO₂Me); NMR (CDCl₃) δ 3.60 (m, 4 H, CH₂OCH₂), 3.05 (m, 3 H, H₆, H₇, H₈), 2.60 (m, 4 H, CH₂NCH₂), 1.50 [bm, 8 H, (CH₂)₄].

Anal. Calcd for C₁₆H₂₅NO₅: C, 61.7; H, 8.09; N, 4.50. Found: C, 61.5; H, 8.11; N, 4.42.

Crystal Data for Compound 3 (C₁₆H₂₅NO₅). Weissenberg and precession photographs taken with the Mo K α radiation ($\lambda = 0.7107$ Å) indicated that the crystals were monoclinic, space group *P*2₁/*n*. A crystal of approximately 0.26 × 0.26 × 0.7 mm was mounted on a Siemens automatic diffractometer, with the needle axis [001] along the spindle axis. The following lattice parameters were obtained by hand centering of 15 reflections with the Mo K α radiation: *a* = 13.258 (6), *b* = 13.856 (6), *c* = 9.249 (4) Å, $\beta = 98.59$ (5)°; *Z* = 4; *d*_{calcd} = 1.27 g/cm³; *d*_{meas} = 1.26 (1) g/cm³; μ (Mo K α) = 0.98 cm⁻¹.

Data Collection and Structure Determination. Intensity data were collected with a Siemens automatic diffractometer with the Mo-zirconium filtered radiation ($\lambda = 0.7107$ Å) and the ψ -2 θ scan technique. A total of 2593 independent reflections was collected with the integrating method of the "five-value measurement"; 1545 reflections with *I* > 3 σ _{*I*}, up to $\psi = 26^\circ$, were corrected for Lorentz and polarization factors and used in all subsequent calculations. No correction for absorption ($\mu R \approx 0.026$) or extinction was applied.

The structure was solved by direct methods using the MULTAN

program.⁵ The *E* map, based on the phases obtained for 240 reflections with $|E| > 1.80$, revealed all nonhydrogen atoms. An isotropic refinement reduced the agreement indices *R*₁ and *R*₂⁶ to 0.14 and 0.19, respectively. After anisotropic block-diagonal matrix least-squares refinement (*R*₁ = 0.084, *R*₂ = 0.12), a difference Fourier map was calculated to locate the hydrogen atoms. The final least-squares cycles were performed with isotropic temperature factors for the hydrogen atoms, so that *R*₁ and *R*₂ were reduced to 0.04 and 0.055, respectively.⁶ Positions of the hydrogen atoms all occurred in the expected regions, the mean value of the C–H distance being 0.99 (4) Å and with approximately tetrahedral angles.

Fractional coordinates are reported in Table I¹² with the estimated standard deviations in parentheses. They were calculated from the residuals and the diagonal elements of the inverse matrix of the last least-squares cycle. The numbering scheme for the atoms is shown in Figure 1 together with the bond lengths. Table II¹² lists the angles of interest.

Results and Discussion

X-ray analysis of the resulting bicyclo[4.2.0]octane has shown that once again the rings are cis fused. The methoxy carbonyl groups are mutually trans and in equatorial conformation. The group at C7 is exo with respect to the cyclohexane ring, while that at C8 is trans with respect to the morpholine ring. Cotton's prediction, relative to the favorite conformation of the cyclobutane ring in fused systems, is verified.⁷ The angle of puckering of the cyclobutane ring (dihedral angle between the C1, C6, C8 and C6, C8, C7 planes) is at its ideal value of 25.2° in spite of the steric interactions of the methoxycarbonyl group at C8 with the cyclohexane ring. More dramatic seem to be the steric interactions between the methoxycarbonyl groups. The C2...C9 distance in fact is 2.986 (3) Å, shorter than the sum of the respective van der Waals radii. Thus the relative positions of the methoxycarbonyl groups (torsion angle C11–C7–C8–C9, 98.7°) appear essentially due to a compromise between the steric interactions of the group at C8 with the cyclohexane ring and the interactions of the same group with the other methoxycarbonyl group [C9...C11, 3.511 (4) Å] and with the morpholine ring [C9...N, 3.651 (3) Å].

The overall geometry of the four-membered ring is similar to that found in analogous compounds, the bond lengths and angles, as well as the internal twist angles, being in the usual ranges. No short intermolecular contact has been observed. The conformation of the six-membered ring appears intermediate between the twist and chair form, as a consequence of the cis junction itself, which causes dramatic bond angle deformations, mainly at the C6 position. The value of the C1–C6–C7 bond angles is 120.7°, close to that found in cis-fused compounds,^{1,2} but much greater than that found in the trans-fused system described by Barnett and Davies.⁸ This situation results also in a smaller value of the torsional angle C2–C1–C6–C5 (27.5°) when compared with the value of 62.9° found in the above-mentioned trans-fused compound.⁸

As to the reaction mechanism, the first step in the addition of the electrophile to the enamine is generally regarded as the formation of a zwitterionic intermediate.^{9,10} The usual stereoelectronic axial attack of DMM (or DMF) on 1 leads to 2a, from which 3 is obtained as a single product. The lack of

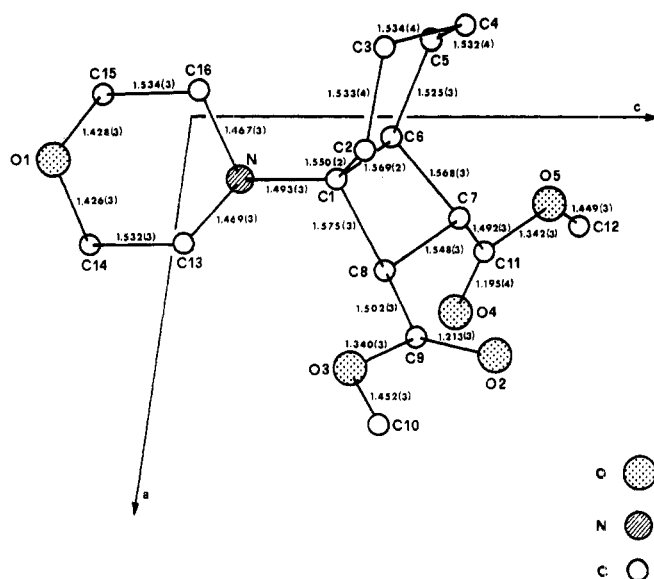


Figure 1. A projection of the molecule along the *b* axis reporting the numbering scheme for the atoms and the bond lengths.

formation of the trans-fused compound **4** might be attributed to the greater stability of **2a** compared with **2b**, owing to the well-known Johnson strains.¹¹ Obviously the reaction is assumed to be under kinetic control, even if no isomerization of **3** is possible because of its great instability.¹⁰ On the other hand, provided that the Curtin-Hammett principle cannot be applied in this case, one can assume that the collapse of the carbon anion onto C1 may be faster than the formation of **2b**. In any case the cis-fused system is the reaction product.

The spectroscopic data relative to **3** indicate that it probably exists as the single conformation **a**, both in solution and in the solid state. Its NMR spectrum in fact is identical with that of the analogous biased compound, thus indicating that no

conformational equilibrium **3a** \rightleftharpoons **3b** is present. On the other hand, strong interactions between the group at C8 and the axial hydrogens of the cyclohexane ring would be present in **3b**. A considerably important 1,3-diaxial interaction between the morpholine ring and the group at C7 would further increase the energy of **3b**.

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Registry No.—1, 670-80-4; 3, 62532-82-5; DMM, 624-48-6; DMF, 624-49-7.

Supplementary Material Available. Tables of temperature factors and torsion angles (3 pages). Ordering information is given on any current masthead page.

References and Notes

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- (6) The agreement indices R_1 and R_2 are defined as follows:

$$R_1 = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|}$$

$$R_2 = \left[\frac{\sum w(|F_o| - |F_c|)^2}{\sum w|F_o|^2} \right]^{1/2}$$

The function minimized was $\sum w(k|F_o| - |F_c|)^2 / \sum w|F_o|^2$, where the weighting factor w was in the form $1/(3.1 + |F_o| + 0.0074|F_o|^2)$. The constants were chosen so as to maintain $w(|F_o| - |F_c|)^2$ essentially constant over all ranges of $|F_o|$ and $\sin \theta/\lambda$. Atomic scattering factors were from F. H. Moore, *Acta Crystallogr.*, **16**, 1169 (1963).

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- (12) See paragraph at end of paper regarding supplementary material.

Synthetic Aspects of the Photochemistry of Keto Imino Ethers.^{1,2} A Facile Synthesis of Functionalized Bicyclo[n.1.0] Systems

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A general method for the synthesis of bicyclo[n.1.0]alkanes functionalized at the one-carbon bridge is described. Bicyclo[n.1.0]alkanes **20–24** were prepared by photorearrangement of keto imino ethers **16–19** in THF solvent. The products were isolated in satisfactory yield as isocyanates (**21, 23, and 24**) or as the dimethylurea derivatives of the isocyanates (**20 and 22**). The required keto imino ethers were prepared by O-alkylation of the silver salts of the corresponding imides **12–15**. The products of the photorearrangement are cyclopropanone derivatives and as such should be useful synthetic intermediates.

We have reported that irradiation of 2-ethoxypyrrrolin-5-one (**1**), prepared by O-alkylation of succinimide, gave in good isolated yield 1-ethoxycyclopropyl isocyanate (**2**) or the *tert*-butyl carbamate (**3**).³ The reaction has been shown to occur from the n, π^* singlet state of **1**, and a Norrish type I cleavage mechanism has been proposed.

Cyclopropanes **2** and **3** are derivatives of cyclopropanone, and derivatives of this type have been used as precursors for a variety of compounds.⁴ For instance, the bicyclo[4.1.0]heptane **4**⁵ has been converted to the β -lactam **5**,⁶ the cyclobutanone **6**,⁷ amino ethers **7**,⁶ the cyclopropanol **8**,⁵ and further derivatives.^{5–7} Photoproducts **2** and **3** have been hydro-

