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CRYSTALLOGRAPHIC ANALYSIS OF STRUCTURAL EFFECTS ASSOCIATED WITH SYMMETRICAL 1,3-BRIDGING OF FIVE-MEMBERED RINGS BY CARBONYL SPACERS

Changfu Xu,[1a] Jon Clardy,*[1a] Richard V. C. Carr,[1b] Hermann Künzer,[1b,c] Koichi Nakamura,[1b,d] and Leo A. Paquette*[1b]

Department of Chemistry-Baker Laboratory, Cornell University, Ithaca, NY 14853 and
Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

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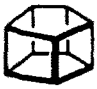
Abstract: The crystal and molecular structures of tricyclo[7.2.1.$0^{3,6}$]decane-2,8-dione (4), its 4,5-benzo fused homologue (5), and tetracyclo[7.2.1.$0^{4,11}$.$0^{6,10}$]-dodeca-2,7-diene-5,12-dione (6) have been determined. The conformations adopted by the saturated and unsaturated five-membered rings in these molecules have been determined. The significantly different angles adopted by the carbonyl groups of the central ring in each of these diketones were also accurately measured. In order to evaluate these relationships, a companion MM2-based computational study was undertaken simultaneously and relevant comparisons are made. The range covered by this triad of molecules provides insight into structural factors that contribute to the preferred ground-state conformations of bridged diquinane systems.

Polycyclopentanoid systems have attracted considerable attention during the last decade.[2] Experimental and theoretical studies have both emphasized the unique properties that five-membered rings can bring to various classes of compounds. The family of hydrocarbons that includes pentaprismane (1),[3] hypostrophene (2),[4] the head-to-head [4+4] dimer of cyclopentadiene (3),[5] its head-to-tail isomer, and related saturated congeners[5,6] have been of interest for a number of reasons.[7]

Despite the high level of fascination with these molecules, detailed structural information is available for only a very limited number of compounds. Recently, we have found it possible to prepare the triad of diketones 4-6 and noted that their crystal habits were suitable for X-ray analysis. Accordingly, their three-dimensional structures have been determined and detailed MM2 calculations of their ground-state geometries have been performed for comparison. The varied degrees of unsaturation and number of interconnective bonds provide informative insight into the static and dynamic stereochemistries adopted by the individual quinane subunits.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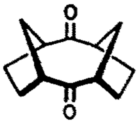
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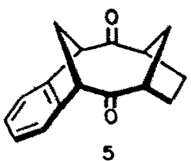
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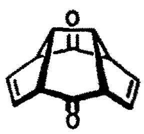
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Results

Synthesis. Diketone 4 was prepared by epoxidation[8] of *syn*-sesquinorbornene[9] and periodic acid cleavage[10] of the oxirane ring. Compound 5 was prepared by air oxidation of *syn*-benzosesquinorbornene as previously described.[11] Access to 6 was gained by oxidative decarboxylation of dimethyl *exo,exo*-5,12-bis(methylthio)tetracyclo[7.2.1.$0^{4,11}$.$0^{6,10}$]dodeca-2,7-diene-5,12-dicarboxylate.[12,13]

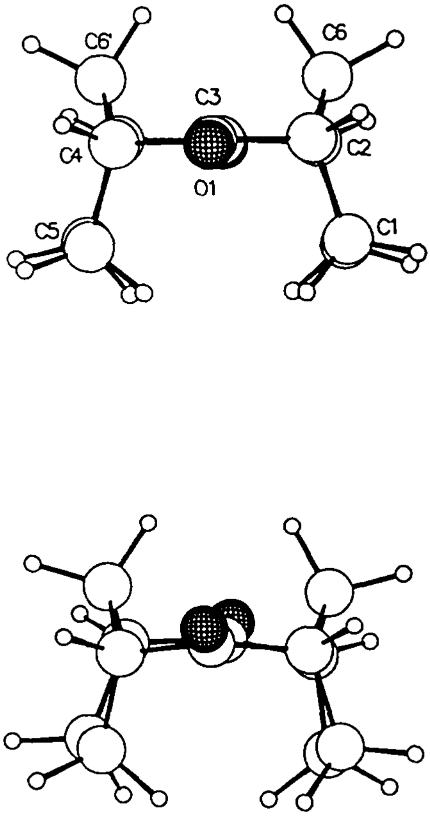
Experimental and Calculated Conformations of 4. A computer-generated perspective drawing of the final x-ray model of 4 is given in Figure 1a. The molecule has a crystallographically required two-fold axis and approximate $\underline{C}_{2\underline{v}}$ point group symmetry. Atoms related by the two-fold axis are designated with a prime ('). The conformation of 4 was the crucial point of interest. As can be appreciated from Figure 1a, atoms C2, C3, O1, C4, C2', C3', O1', and C4' are planar within experimental error. The conformation of the five-membered ring is best described as a slightly distorted envelope or mirror conformation. Usually, the shapes of five-membered rings are discussed in terms of two ideal conformations - the envelope conformation with mirror symmetry and the skew conformation with two-fold symmetry.[14] These conformations are quantitatively assessed using the ring torsional angles. Mirror symmetry requires that one torsional angle be 0°, the two flanking torsional angles be approximately + and -24°, and the remaining two angles - and +38°, respectively. The exact angles could vary in magnitude, but symmetry requires equal magnitudes and opposite signs for the pairs. In the case of 4, this would correspond to the following torsional angles: C1-C5' = 0°, C5'-C4 = +24°, C1-C2 = -24°, C4'-C6 = -38°, and C2-C6 = +38°. This would represent the envelope conformation with C6 serving as the flap. Atoms C1, C2, C4', and C5' would be planar, and C6 would be projected out of the plane away from C3.

This is close to what is actually observed for 4. The two-fold conformation would require a relatively large torsional angle for C1-C5' of approximately 45°, values of -37° for C1-C2 and C5'-C4', and +14° for C2-C6 where planar, and C2 and C4' were above and below this plane. In actual fact, cyclopentanes rarely adopt one of the two ideal conformations. In the present case, the cyclopentane rings adopt mirror conformations with a slight two-fold distortion. The ideally 0° torsional angle for C1-C5' is observed to be 4.5°. Using the fact that the flanking torsional angles in the two-fold conformer are roughly 80% of this value, the flanking torsional angles should be adjusted by -3.7° (80% of 4.5°). The flanking angles should differ in absolute value by 7.4°. The observed value of C5'-C4 is 13.4°, and C2-C6, -20.6°. The remaining two torsional angles should be adjusted by roughly 1.5° (32% of 4.5°) in the positive sense. The observed values are -27.1° for C4'-C6 and +29.3° for C2-C6.

The conformational preferences of 4 were also explored with molecular mechanics using the MM2 series of programs. The results of this study are shown in Figure 1b. In general the agreement is good, but the MM2 conformation has a greatly enhanced two-fold distortion. The C1-C5' torsional angle is predicted to be +14.2° - roughly three times larger than the observed value. The MM2 conformation also puckers the central ring so that the oxygens of the carbonyl are pointing toward the methano bridges (see Figure 1b). The H-H distance between the two closest hydrogens on the methano bridges is predicted to be 2.08 Å. The observed distance is 1.94 Å, but this is subject to an experimental error of 0.3 Å.

The Effect of Benzo Annulation. Figure 2 is a computer-generated perspective drawing of the final x-ray model of 5. Interatomic distances and angles are quite reasonable for the left-hand portion of the molecule, but there is evidence for substantial disorder in the right-hand portion. This is most clearly demonstrated by the C1-C10 distance of 1.334(14) Å - a shortening of this bond from the standard value by some 0.2 Å. The C1-C2 and C9-C10 bonds are also too short by about 0.1 Å. The C2-C1-C10-C9 torsional angle is roughly 0°. The x-ray temperature factors, measures of the spatial distribution of an atom, for C1 and C10 are the largest in the structure with values of 11.1 and 10.7, respectively. The benzene ring, for purposes of comparison, has an average temperature factor of 6.8(1.1). Presumably the C1-C10 bond has a large torsional motion which is well known to lead to unreasonably short distances.

We have attempted to explore this phenomenon with MM2 calculations. The minimum energy structure is shown in Figure 2b. As can be seen, the minimum energy conformation also has an essentially 0° C1-C10 torsional angle. The calculations did indicate that torsion about this bond would be a relatively low energy process. For example, a torsional angle of 26°, shown in Figure 2c, raised the calculated energy by only 0.9 kcal/mol. In view of this evidence for disorder, further attempts to analyze the conformation of 5 did not appear warranted.



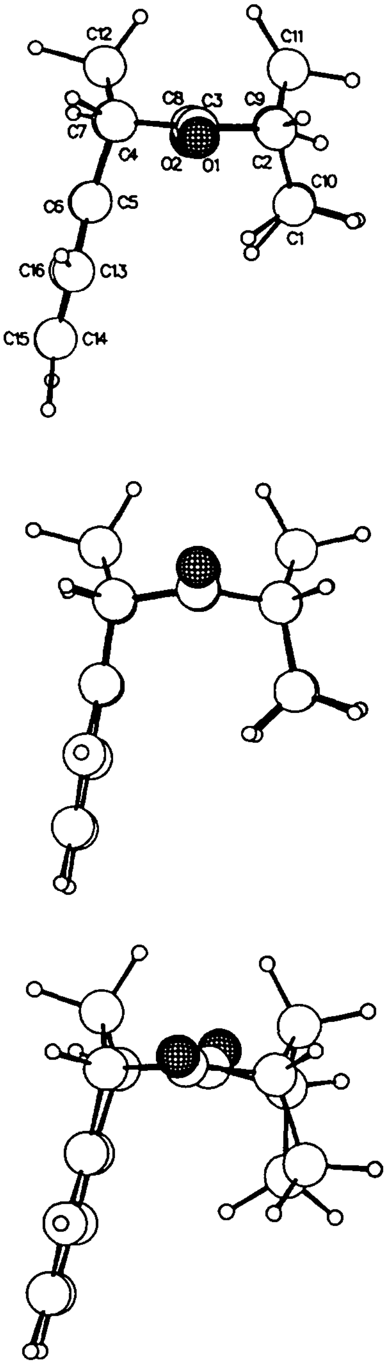


Figure 1. At the top (1a) is a computer-generated perspective drawing of the final x-ray model of **4**. The molecule has a crystallographic two-fold axis. At the bottom (1b) is the MM2 model of **4**. Note the puckering of the carbonyl groups and the larger torsional angle of the ethano bridges.

Figure 2. At the top (2a) is a computer-generated perspective drawing of the final x-ray model of **5**. Note the small torsional angle about the C1-C10 bond. In the center (2b) is a drawing of the minimum energy conformation found by MM2 calculations. At the bottom (2c) is a drawing of the conformation with a 26° C1-C10 torsional angle that is only 0.9 kcal/mol higher in energy than 2b.

The Consequences of Additional Interplanar Bonding. A computer-generated perspective of **6** is given in Figure 3a and the MM2 model in Figure 3b. In general the agreement is good, but there are some differences. Both the calculated and experimental structures have essentially planar cyclopentene rings. The C11-C12 distance is observed to be 1.563(5) Å, and the calculated value

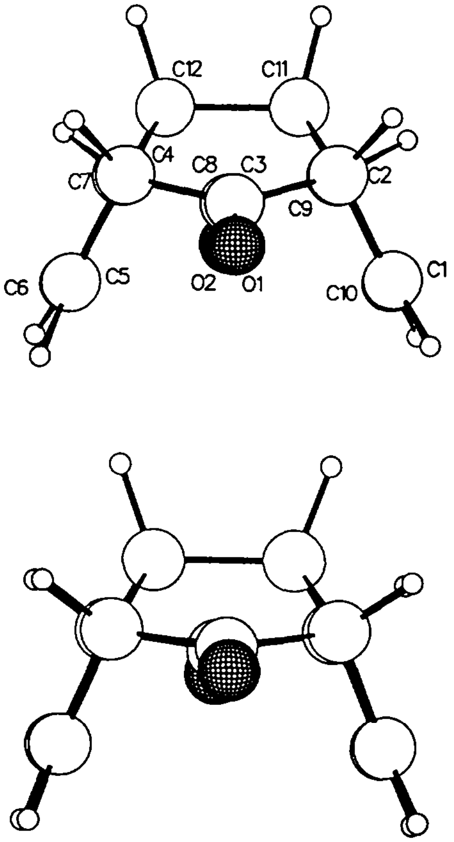


Figure 3. At the top (3a) is a computer-generated perspective drawing of the final x-ray model of **6**. Note the planar cyclopentene rings and the pronounced tilt of the carbonyl groups. At the bottom (3b) is the best MM2 structure.

is 1.549 Å. In the x-ray structure, the carbonyl oxygens are bent downward more than in the calculated structure. The average (four observations) torsional angle (e.g., C11-C2-C2-O1) in the x-ray structure is 171.4(14)°, and the calculated value is 160.0(1)°.

Discussion

The crystallographic data presented herein provide a detailed picture of conformations adopted by saturated and unsaturated five-membered rings when bridged symmetrically in a 1,3-fashion by ketone carbonyl groups. Two important conformationally related issues have been addressed. One is, of course, associated with the extent of folding that occurs in the cyclopentane or cyclopentene subunits. In **4** and **5**, envelope conformations are adopted to different degrees as detailed above. When the pair of atoms that constitute the respective flaps are covalently bonded as in **6**, the five-membered rings develop essentially planar characteristics. In general, good agreement has been found with MM2 computations, although various torsional angles were not always closely reproduced.

As a consequence of these structural studies, it has also become clear that the central oxygen-substituted rings in **4**-**6** develop interesting topological features that are not at all well reproduced by MM2. In diketone **4**, for example, the calculated minimum energy conformation has the two carbonyl oxygens pointing upward toward the methano bridges (Figure 1b). Perhaps to facilitate this flexing, the ethano bridges are made to adopt enhanced two-fold distortion. In the solid state, possible strain relief of this type is not observed and the carbonyl oxygens actually cant in a slightly downward direction (Figure 1a). This divergence is more exacerbated in **5**, as a comparison of Figures 2a and 2b will immediately indicate.[15]

As expected, the downward tilt of the carbonyl oxygens in **6** is highly accentuated (Figure

3a). Although MM2 properly predicts folding in the same direction (Figure 3b), the extent of this deformation is not as severe as it should be. Although perturbations brought on by crystal packing forces need to be factored into the crystallographic data as a whole, it nevertheless remains that the MM2 force field-optimized calculated structures fall somewhat short in arriving at views of the true molecular orientations. With the pending introduction of an additional torsional-stretch term into the force field equations (i.e., the advent of MM3),[16] there is every expectation that discrepancies of the type witnessed above may well be resolved.

Experimental Section

Preparation of Diketone 4. A cold (0 °C), magnetically stirred solution of *syn*-sesquinorbornene (160 mg, 1 mmol) in dry dichloromethane (8 mL) was treated with 1.5 equiv of *m*-chloroperbenzoic acid and stirred at 0 °C for 3 h. Water was added and excess peracid was reduced with aqueous sodium bisulfite solution. Additional CH_2Cl_2 was introduced and the organic phase was washed with sodium carbonate solution, dried, and evaporated. The residual yellow oil was dissolved in 5 mL of 10% aqueous methanol to which 455 mg (2 mmol) of periodic acid was added. The reaction mixture was heated overnight at the reflux temperature, diluted with 50 mL of dichloromethane, and washed with sodium thiosulfate solution and brine prior to drying. After solvent removal, the pale yellow oil solidified. Recrystallization from ethyl acetate-hexane gave 98 mg (51%) of 4 as colorless crystals, mp 192 °C; ^{13}C NMR (75 MHz, $CDCl_3$) ppm 214.53, 54.48, 31.32, 31.16.

Single Crystal, X-Ray Diffraction Analysis of 4. Preliminary x-ray photographs displayed orthorhombic symmetry. Accurate lattice constants of a=9.7508(14), b=7.8246(14), and c=12.7704(20) Å were determined from a least-squares fit of fifteen diffractometer measured 2θ-values. The crystal density (ρ_c = 1.31 g/cm^3) and systematic extinctions were accommodated by space group C2cb (Aba2 in an alternate setting) with four molecules in the unit cell. This requires that only one half of the molecule constitutes an asymmetric unit; the remaining portion of the molecule is generated by the two-fold axis. All unique diffraction maxima with $2\theta < 114°$ were collected on a computer controlled four-circle diffractometer using graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω-scans. Of the 354 independent reflections collected in this fashion, 326 (92%) were judged observed ($F_o > 3\sigma(F_o)$) and used in subsequent calculations.[17] The structure was phased uneventfully. Hydrogens were located in a difference synthesis following partial refinement of the nonhydrogen atoms. Block diagonal least-squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogens have converged to a conventional crystallographic residual of 0.0528 for the observed reflections. Additional crystallographic details are available and are described in the paragraph entitled **SupplementaryMaterial Available** at the end of this paper.

Single Crystal X-Ray Diffraction Analysis of 5. Preliminary x-ray photographs displayed monoclinic symmetry. A least-squares fit of fifteen diffractometer measured 2θ-values gave lattice constants of a=10.5990(32), b=9.5540(31), c=12.6706(27) Å, and β=71.990(22)°. A plausible crystal density (ρ_c = 1.30 g/cm^3) and systematic extinctions were uniquely accommodated by the common space group $P2_1/c$ with one molecule of composition $C_{16}H_{16}O_2$ forming the asymmetric unit. All unique diffraction maxima with $2\theta < 114°$ were collected on a computer controlled four-circle diffractometer using graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω-scans. Of the 1666 reflections surveyed in this fashion, 1242 (75%) were judged observed and used in subsequent calculations.[17] The structure was solved uneventfully by direct methods, and the hydrogens were located on a difference synthesis following partial refinement of the nonhydrogen atoms. Block diagonal least-squares refinement with anisotropic nonhydrogen atoms and isotropic hydrogens have converged to the current crystallographic residual of 0.0871. Additional crystallographic details are available and are described in the paragraph entitled **Supplementary Material Available** at the end of this paper.

Single Crystal X-Ray Diffraction Analysis of 6. Preliminary x-ray photographs showed monoclinic symmetry, and accurate lattice constants of a=7.6019(16), b=10.6064(21), c=12.8281(15) Å, and β=102.54(7)° were obtained from a least-squares fit of fifteen diffractometer measured 2θ-values. Systematic extinctions and crystal density (ρ_c = 1.39 g/cm^3) uniquely indicated space group $P2_1/c$ with one molecule of $C_{12}H_{10}O_2$ forming the asymmetric unit. All unique diffraction maxima with $2\theta < 114°$ were collected on a computer controlled diffractometer using graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω-scans. Of the 1197 reflections collected in this way, 1046 (87%) were judged observed ($F_o > 3\sigma(F_o)$).[17] A phasing model was found using direct methods, and hydrogens were found on a difference synthesis. Block diagonal least-squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogens have converged to a conventional crystallographic residual of 0.0884 for the observed data. Additional crystallographic details are available and are described in the paragraph entitled **Supplementary Material Available** at the end of this paper.

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Supplementary Material Available: Atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.

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(1) (a) Cornell University. (b) The Ohio State University. (c) Postdoctoral fellowship awardee of the Deutsche Forschungsgemeinschaft, 1985-1986. (d) On sabbatical leave from the Tochigi Research Laboratories of the Kao Corporation (Japan), 1984-85.

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(17) All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from x-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq and M. M. Woolfson, University of York, England, 1980; BLS78A, an anisotropic block diagonal least squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a locally modified crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985. MM2 calculations were done using the QCPE program as modified by Serena Software.