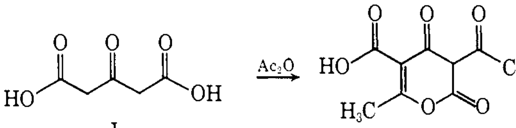
The Crystal Structure of the Product of the Reaction of Acetonedicarboxylic Acid with Acetic Anhydride.

Sr. Jo Ann Jansing[1] and J. G. White*

Contribution from the Chemistry Department, Fordham University, New York, New York 10458. *Received February 13, 1970*

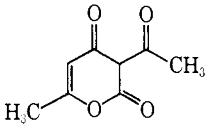
Abstract: Crystals of the the compound $C_9H_8O_6$, prepared by condensation of acetic anhydride and acetonedicarboxylic acid, are orthorhombic with $a = 6.416 \pm 0.006$, $b = 7.204 \pm 0.007$, and $c = 19.20 \pm 0.02$ Å. The space group is *Cmcm* with four molecules per unit cell. The structure was determined using visually estimated film data, and refined by full-matrix least-squares methods using anisotropic temperature factors. In the solid state the molecule is planar, excluding hydrogen atoms, and is symmetrical with respect to acetyl and keto groups in the two halves of the molecule. The bond distances are very well explained by a model in which there is spatial disorder of two mirror-image tautomers of 3-acetyl-2,4-dioxo-4-hydroxy-5-hydroxyethylidenepyran.

In a series of papers on the reaction products of α-oxyacids, von Pechmann and Neger[2] published details of a reaction in which acetic anhydride reacetd with acetonedicarboxylic acid (I) to give a product of formula $C_9H_8O_6$, mp 154°. These authors proposed that the unknown product was a 5-carboxy derivative (II) of dehydroacetic acid (III) which reacted easily with bases



I

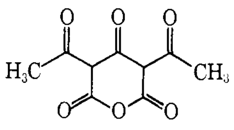
II



III

such as ammonia, aniline, and phenylhydrazine. Dehydroacetic acid is a very useful reagent in synthetic organic chemistry and is frequently prepared from von Pechmann's compound. It has also been studied recently because of its structural similarity to the fungal metabolite radicinin.[3]

However, a new structure for von Pechmann's compound has been proposed on the basis of nmr and ir studies.[4] This is the symmetrical structure 3,5-diacetyl-2*H*-pyran-2,4,6(3*H*,5*H*)-trione (IV).



IV

The X-ray investigation described in the present paper was undertaken in order to resolve the conflicting evidence, and to decide between structures II and IV. Each of these two structures represents several different keto and enol tautomers, only one of which might be expected to exist in the crystal. The crystal data are ($C_9H_8O_6$, mol wt 212.2): unit cell dimensions, $a = 6.416 \pm 0.006$, $b = 7.204 \pm 0.007$, $c = 19.20 \pm 0.020$ Å; volume of cell, 887.6 Å^3; d_c 1.59 g cm^{-3}; d_{meas} 1.61 g cm^{-3}; orthorhombic, absent spectra *hkl* when $h + k$ is odd, *h*0*l* when *l* is odd; space group *Cmcm* ($D_{2h}{}^{17}$); four molecules per cell; absorption coefficient for Cu Kα radiation, $\mu = 10.5$ cm^{-1}.

Experimental Section

The compound was prepared by Bertani[3] and crystals were grown by slow evaporation of an acetone–water solution. The melting point was 158–159°. Since this was rather higher than that previously reported, the identity of the crystals and the original material was checked by X-ray powder diffraction. The density of the crystals was determined by flotation in methyl iodide–carbon tetrachloride solutions. The crystals were platelike, usually elongated along the *a* axis with the shortest dimension being in the direction of the *c* axis. For the X-ray measurements three separate crystals were used for rotation about the three axes. Each was cut to a length of about 0.5 mm (along the rotation axis) and a square cross section of about 0.2 mm on edge.

Intensity data were collected using the equiinclination Weissenberg technique and a multiple film method. Ni-filtered Cu Kα radiation was used. The reciprocal lattice levels *h*0*l*–*h*6*l*, 0*kl*–5*kl*, and *hk*0 were recorded. The intensities of 193 independent nonzero reflections, 42% of the available data, were estimated visually by comparison with a time-calibrated intensity strip. Absorption corrections were not made since these were found to be negligible. A set of F_0 values was derived after application of Lorentz-polarization corrections, and these were brought to a common scale by cross-correlation of the different sets through common reflections.

Structure Determination and Refinement

From the systematically absent reflections three space groups are formally possible, *Cmc*2$_1$, *Cmcm*, and *C*2*cm* (axes transferred from *Ama*2). The space groups *Cmc*2$_1$ and *Cmcm* would both require a planar molecule (excluding hydrogen atoms). Since a nonplanar molecule was regarded as a distinct possibility, with the nonmethyl hydrogen atoms attached to ring carbon atoms, initial trials were carried out in the space group *C*2*cm*. In this space group a molecular mirror plane is required and it was reasonable to place the molecules such that their long dimension lay along the *c* axis perpendicular to the mirror plane.

The section of the three-dimensional Patterson function at $x = 0$ was calculated with data sharpened to correspond approximately to that from atoms at rest. This Patterson section was used as a guide to restrict the

---

* To whom correspondence should be addressed.

(1) This manuscript is based on the Ph.D. Dissertation of J. A. J., Fordham University, 1969.

(2) H. von Pechmann and F. Neger, *Ann.*, 273, 194 (1893).

(3) L. Bertani, Ph.D. Dissertation, Fordham University, 1968 (directed by D. D. Clarke).

(4) T. Kato and Y. Kubota, *Chem. Pharm. Bull.*, **14**, 931 (1966).

Table I. Refined Positional and Thermal Parameters for $C_9H_8O_6$ with Standard Deviations

Atom	y	z	U_{11}	U_{22}	U_{33}	U_{23}
C(1)	0.3040 (24)	0.2500 (0)	0.066 (12)	0.024 (7)	0.139 (23)	0.000 (0)
C(2)	0.2064 (16)	0.1865 (11)	0.068 (8)	0.035 (5)	0.137 (13)	−0.001 (4)
C(3)	0.0028 (20)	0.1863 (10)	0.071 (7)	0.036 (6)	0.135 (15)	0.003 (4)
C(4)	0.2974 (20)	0.1210 (13)	0.060 (9)	0.056 (8)	0.216 (23)	0.007 (5)
C(5)	0.2055 (22)	0.0489 (8)	0.138 (15)	0.081 (10)	0.092 (13)	−0.003 (3)
O(1)	0.4855 (14)	0.2500 (0)	0.098 (9)	0.012 (5)	0.182 (17)	0.000 (0)
O(2)	0.9191 (18)	0.2500 (0)	0.081 (9)	0.038 (8)	0.128 (15)	0.000 (0)
O(3)	0.8979 (12)	0.1367 (6)	0.114 (8)	0.044 (5)	0.156 (13)	−0.007 (2)
O(4)	0.4845 (12)	0.1214 (6)	0.079 (5)	0.050 (5)	0.167 (13)	0.007 (2)

possible number of molecular positions. These turned out to be only three, related by different translations along y, while in all cases the mean molecular plane was kept perpendicular to a. Detailed calculations showed that only one of these could account quantitatively for the outstanding features of the intensity data.

Refinement was first carried out on the $0kl$ projection and R was reduced to 0.21, but further improvement did not seem feasible due to the large amount of overlapping. During this refinement it had become clear that the molecule was essentially planar and therefore that there could be no hydrogen atoms bonded directly to ring carbon atoms. However, the y,z coordinates would not be sensitive to moderately small tilts of the molecular planes with respect to the a axis—which would still require the space group *C*2*cm*. However, an inspection of the $h00$ reflections showed that this was quite unlikely. These reflections were extremely intense and fell off uniformly with scattering angle. According to the absolute scale derived from the $0kl$ calculated structure factors all were close to an absolute maximum of F for their scattering angles and it was clear that the molecules were, in fact, lying in the (200) planes. Accordingly, three-dimensional refinement was carried out in the centrosymmetric space group *Cmcm* with the atoms in the following special positions: $0,0,0$; $^1/_2,^1/_2,0$ + O(1), C(1), O(2) in (c) $0,y,^1/_4$; $0,\bar{y},^3/_4$; C(2), C(3), C(4), C(5), O(3), O(4) in (f) $0,y,z$; $0,\bar{y},\bar{z}$; $0,y,^1/_2 - z$; $0,\bar{y},^1/_2 + z$ (see Figure 2 for numbering scheme).

The structure first was refined by Fourier methods in the section $x = 0$. This was followed by full-matrix least-squares refinement. Three cycles using isotropic refinement reduced R to 0.252. At this point anisotropic refinement was begun. For all atoms lying in the mirror plane at $x = 0$, β_{12} and β_{13} are required to be zero, while for the three atoms C(1), O(1), and O(2) which lie also in the mirror plane at $z = {}^1/_4$, β_{23} is also zero. Four cycles varying all free parameters reduced R to 0.115. After omitting the low-angle reflections 200, 400, and 002 which showed evidence of extinction, two further cycles were carried out giving a conventional R of 0.084. Refinement was based on F. The weighting scheme used in the final stages of least-squares refinement was obtained by a straight-line fit of a plot of $|\Delta F|$ *vs.* $|F_\sigma|$. The best mean line was defined $|\Delta F| = a + b|F_\sigma|$, with $a = 0.64$ and $b = 0.046$. The $|\Delta F|$ calculated by this relation was set equal to σ for each reflection. Values of both the positional and thermal parameters are given in Table I with their standard deviations. The thermal parameters U_{11}, etc., are the mean-square amplitudes of vibration in ångströms^2. The table of final calculated and observed values of the structure factors has been deposited with the ASIS National Auxiliary Publications Service.[5] The scattering factors used were those given in the International Tables.[6] The magnitudes of the parameters U_{11} (Table I) are normal for vibration components perpendicular to the molecular plane and their distribution gives no indication of a molecular tilt with respect to a. Accordingly the mirror plane perpendicular to a appears valid. However, the large values of the U_{33} parameters, discussed in detail below, raised the question of whether the mirror plane perpendicular to c was in fact only an approximation. If the two halves of the molecule were different in an ordered way the true space group would be *Cmc*2$_1$. To test this possibility a least-squares refinement was carried out in this space group.

Since even a pseudomirror plane in the molecule would cause correlation of parameters related by the plane all parameters could not be varied simultaneously. Isotropic temperature factors had to be used because of the correlation of positional deviations in the two halves of the molecule with anisotropic components. The coordinates were first changed slightly to correspond to those expected for fixed double and single bonds. Refinement was carried out on each half of the molecule in turn with the three atoms on the center line being included in both cycles. Convergence was obtained when R was reduced only to 0.206 and the bond distances were physically quite unreasonable. It was therefore concluded that the space group was in fact *Cmcm*.

Attempts to locate the hydrogen atoms in the molecule by difference Fourier methods were not completely successful. The two strongest peaks in the difference maps were at or near plausible hydrogen atom positions. One peak of 0.46 e/Å^3 was close to the position predicted for a methyl hydrogen but was extremely elongated. The other, 0.33 e/Å^3, was between O(1) and O(4) and could correspond to a hydrogen atom involved in hydrogen bonding as discussed below. However, the other methyl hydrogen atoms were not clearly defined probably because of high thermal motion or spatial disorder.

The spatial relations of the four molecules in the unit cell are shown in Figure 1. The main cleavage plane of the crystal, perpendicular to c, is clearly due to the poor packing in this direction. The interatomic distances

---

(5) For this table order NAPS Document No. NAPS-01063 from the ASIS National Auxiliary Publications Service, c/o CCM Information Corp., 909 3rd Ave., New York, N. Y. 10022, remitting $2.00 for microfiche or $5.00 for photocopies. Advance payment is required. Makes checks or money orders payable to ASIS-NAPS.

(6) "International Tables for X-ray Crystallography," Vol. III, Kynoch Press, Birmingham, 1962, pp 202–204.

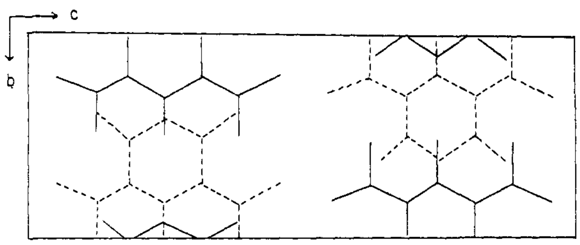


Figure 1. The packing arrangement of the four molecules in the unit cell. Full lines represent molecules at $x = 0$, dotted lines molecules at $x = {}^1/_2$.

between different molecules, which are less than 3.5 Å, are given in Table II and show no abnormalities.

Table II. Intermolecular Approach Distances <3.5 Å[a]

Atoms	Distance, Å
C(1A)–O(2B)	3.31
O(1A)–O(2B)	3.24
O(3A)–O(4B)	3.28
O(3A)–C(4B)	3.30
C(3A)–O(1B)	3.44
C(3A)–O(4B)	3.44

[a] Molecule A has the coordinates of Table I; molecule B is translated by ${}^1/_2, {}^1/_2, 0$.

All computations were carried out on an IBM 360/40 computer. Modified versions of Busing, Martin, and Levy's least-squares and function and error programs[7,8] were used. Other programs originated in the Chemistry Department of Fordham University.

Discussion

The bond distances and bond angles for $C_9H_8O_6$ calculated from the coordinates of Table I are shown in Figure 2. The critical point of the investigation, the distinction between the groups or atoms attached to C(2) and C(3), seems settled, in the solid state at least, in favor of formula IV, although not that particular tautomer. The crystallographic requirement (in space group *Cmcm*) of a mirror plane through the center of the molecule perpendicular to the *c* axis was never regarded as deciding this question conclusively. A planar form of formula II might be sufficiently similar to its mirror image for disordering to occur, resulting in a statistical mirror plane. However, in this case atoms C(5) and O(3) would each appear as one-half methyl and one-half oxygen (or hydroxyl). The average bond distances in such a situation would be very different from the values found, 1.535 Å for C(4)–C(5) and 1.216 Å for C(3)–O(3), which are almost exactly in accordance with the proposed assignment. In addition, if C(5) were actually half oxygen it might be expected to have an unusually low-temperature factor and O(3) an unusually high one. In the isotropic refinement the reverse was the case, C(5) having a higher temperature factor than O(3).

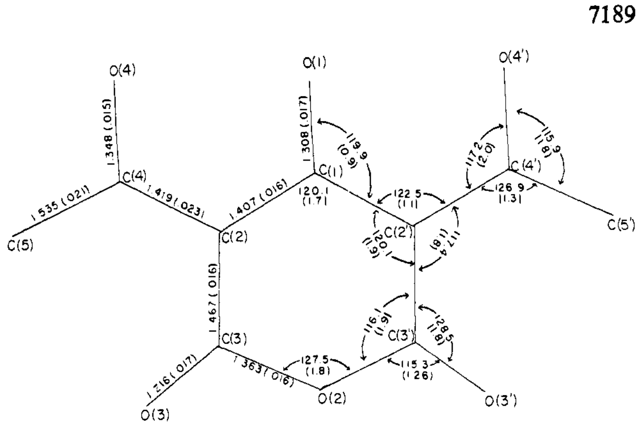
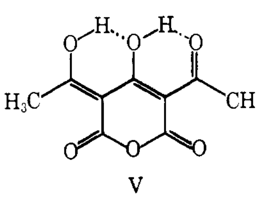


Figure 2. The bond distances and bond angles in $C_9H_8O_6$ with their standard deviations.

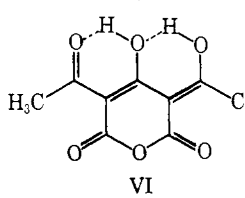
In view of the planarity of the molecule the nonmethyl hydrogen atoms cannot be attached to C(2),-C(2′). The bond distances found make it quite improbable that they are bonded to O(3),O(3′) and therefore they must be associated with the three oxygen atoms O(4), O(1), and O(4′). The only static symmetrical model, with the two hydrogen atoms bonded to O(4) and O(4′), can be rejected by considering the observed bond distances in this part of the molecule. C(1)–O(1) would be a pure double bond, C(1)–C(2) a single bond, and C(2)–C(4) a double bond. None of the experimental distances are in agreement with these assignments.

One of the most striking features of the experimental results is the occurrence of extremely large vibration amplitudes along the crystal *c* axis (Table I). The average root-mean-square amplitude along *c* is 0.385 Å, while that along *b* is 0.199 Å. The differences between U_{22} and U_{33} are roughly constant for all atoms. The effect is contrary to what would occur for a rigid body torsional vibration of the molecule in its own plane. In this case the direction of the long axis of the ellipsoid cross section would change for successive ring atoms. In strictly vibrational terms the data can only be interpreted as a movement of the whole molecule back and forth in the *z* direction. However, an explanation due to disorder is far more probable.

The largest values of U_{33} are for the atoms O(1), O(4), and C(4) all in the region which would be most affected by the positions of the nonmethyl hydrogen atoms. The elongation of the electron density for these atoms was very marked in the Fourier maps. An asymmetry is probably introduced into the molecule by the localization of these hydrogen atoms as in V and VI, possibly with contribution from ionic forms. The compound is thus formulated as 3-acetyl-2,4-dioxo-4-hydroxy-5-hydroxyethylidenepyran. Since structures such as these no longer contain an exact mirror plane perpendicular to the molecular plane their minimum energy positions would not necessarily be with their central lines coinciding with the crystallographic mirror planes, and small displacements to either side could



V



VI

---

(7) W. R. Busing, K. O. Martin, and H. A. Levy, "A Fortran Crystallographic Least Squares Program," Oak Ridge National Laboratory, Oak Ridge, Tenn., Report TM-305, 1962.

(8) W. R. Busing, K. O. Martin, and H. A. Levy, "A Fortran Crystallographic Function and Error Program," Oak Ridge National Laboratory, Oak Ridge, Tenn., Report TM-306, 1964.

result. The observed distributions could result either from dynamic tautomerism in individual molecules or a disordered structure containing both tautomers arranged at random, making the mirror planes perpendicular to *c* statistical only. If, in the dynamic model, the interchange were very fast then it would merely add into the true thermal vibrations which should then show an interpretable pattern. An interchange in individual molecules which is slow compared to thermal vibrations and a spatial disordering of different tautomers would be indistinguishable from the X-ray data. Diffuse scattering observed around the intense reflections is consistent with a disordered structure.

The observed bond distances are very well explained by the above model. The bonds C(1)–C(2) and C(2)–C(4) are 1.41 and 1.42 Å, respectively, very close to the average of carbon–carbon single and double bond distances. The C(2)–C(3) distance of 1.47 Å is of the magnitude expected for a carbon–carbon single bond in a conjugated system.[9] The carbon–oxygen distance in the ring (1.36 Å) is very similar to the bond distance of 1.369 Å found for the equivalent bond in 2,6-dimethyl-γ-pyrone.[10] The bond C(4)–O(4) is intermediate between the carbon–oxygen double bond distance and the carbon–hydroxyl distance. The bond C(1)–O(1) is shorter than that expected for a pure carbon–hydroxyl bond, but this could be due to ionic contribution, or to a partial contribution from the symmetrical structure with a central keto group. The bond angles within the ring are normal with the exception of the C(3)–O(3)–C(3) angle which probably opens to accommodate the oxygen atom within the plane of the ring, thus distorting the angles of the carbonyl configuration slightly. This type of angle opening at the oxygen vertex with corresponding narrowing of the adjacent O–C–C angles was also noted in dehydroacetic acid monimide ligands.[11]

It should be noted that the bond distances given above are uncorrected either for thermal motion or corresponding disorder effects. Attempts to correct for thermal motion using the riding model[12] gave less reasonable values than the uncorrected ones, not surprisingly in these circumstances. The simultaneous occurrence of both thermal motion and static disorder of relatively small magnitude creates an indeterminate situation with very high correlation of these variables. The standard deviations computed must therefore be regarded as minimum.

Acknowledgment. The authors wish to thank Dr. L. Bertani for crystals of $C_9H_8O_6$, Dr. D. D. Clarke for much helpful discussion, and the New York State Science and Technology Foundation for a grant for X-ray equipment. One of us (J. A. J.) gratefully acknowledges support under an NDEA Title IV Fellowship.

---

(9) A. I. Kitiagorodskii, "Organic Chemical Crystallography," Consultants Bureau, New York, N. Y., 1955.

(10) G. M. Brown, H. G. Norment, and H. A. Levy, *Acta Crystallogr.*, **10**, 806 (1957).

(11) S. Kiryu, *ibid.*, **23**, 392 (1967).

(12) W. R. Busing and H. A. Levy, *ibid.*, **17**, 142 (1964).

The Alkaline Hydrolysis of *p*-Nitroacetanilide and *p*-Formylacetanilide[1a]

Ralph M. Pollack[1b] and M. L. Bender[1c]

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201. *Received April 10, 1970*

Abstract: The hydroxide ion catalyzed hydrolysis of *p*-nitroacetanilide (I) and *p*-formylacetanilide (II) has been investigated at 25.0° at [OH⁻] ranging from about 10^{-3} to 1 *M*. The rates for both compounds show a very marked dependence on the concentration of hydroxide ion. The kinetic order for I in hydroxide ion varies from 1.8 at low [OH⁻] to 0.4 at high [OH⁻]. The order for II is 1.9 throughout the range investigated. At [OH⁻] below 0.1 *M*, I reacts 25 times faster than II. Both compounds react substantially faster than predicted from a previous study of ring-substituted acetanilides with more electron-donating substituents. These results are interpreted in terms of a mechanism involving nucleophilic attack of hydroxide ion to form a tetrahedral intermediate, followed by ionization to a dianion, and unimolecular breakdown to acetate ion and anilide ion. An inverse solvent isotope effect for *p*-nitroacetanilide ($k_{H_2O}/k_{D_2O} = 0.61$) at $[OD^-] = 4.60 \times 10^{-3}$ *M* supports this mechanism. The varying kinetic order in [OH⁻] for I is explained by a change in the rate-determining step of the reaction at higher concentration of base, in conjunction with ionization of the substrate to give an unreactive anion. The pK_a's of *p*-nitroacetanilide and *p*-formylacetanilide were measured and found to be 13.8 and 14.3, respectively.

In a previous publication from these laboratories,[2] it was proposed that the alkaline hydrolysis of anilides involves a dipolar ion which decomposes to give the carboxylate ion and free amine directly. This proposal was based primarily on the finding that the hydrolysis rates of a series of ring-substituted anilides depend only slightly on substituent, but that the partitioning of the tetrahedral intermediate is markedly influenced by substituent. Subsequent findings of general base catalysis in the hydrolysis of 2,2,2-trifluoroacetanilide,[3] acetanilide,[4] and 2,2,2-trifluoro-*N*-methyl-

---

(1) (a) This research was supported by the National Science Foundation; (b) National Institutes of Health Postdoctoral Fellow, 1968–1970; (c) to whom correspondence should be addressed.

(2) M. L. Bender and R. J. Thomas, *J. Amer. Chem. Soc.*, **83**, 4183 (1961).