Acta Cryst. (1998). B**54**, 162–173

Pseudoacids. I. 4- and 5-Oxoacids

EDWARD J. VALENTE,* JASON F. FULLER AND JASON D. BALL

Department of Chemistry, Mississippi College, Clinton, MS 39058, USA. E-mail: valente@mc.edu

(*Received 13 March 1997; accepted 26 August 1997*)

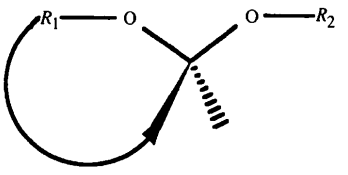
Abstract

Certain 4- and 5-oxoacids may exist in their cyclic lactol (or pseudoacid) forms. These commonly occur in compounds with proximate carboxylic acid and carbonyl (aldehyde or ketone) functions for the formation of five- or six-membered rings. Examples include *trans*-2,3-disubstituted aliphatic, (*Z*)-2,3-olefinic and *o*-disubstituted aromatic acids. Crystal structures of compounds in these categories are reported: *trans*-4-methyl-3-oxo-6-hydroxytetrahydropyran-3-carboxylic acid (6), monoclinic, $C2/c$, a = 25.412 (5), b = 6.291 (1), c = 10.757 (2) Å, β = 104.84 (3)°; penicillic acid (7), 4-methoxy-5-hydroxy-5-(2′-propenyl)dihydrofuran-2-one, tetragonal, $P4_2/n$, $a = b$ = 15.83 (2), c = 7.016 (11) Å; mucochloric acid (8), (*Z*)-3,4-dichloro-5-hydroxydihydrofuran-2-one, triclinic, $P\bar{1}$, a = 6.227 (5), b = 8.085 (5), c = 12.369 (9) Å, α = 99.50 (5), β = 102.38 (6), γ = 90.29 (6)°; 2-methanoylbenzoic acid (9), 3-hydroxy-1-(3*H*)-isobenzofuranone, monoclinic, $P2_1$, a = 4.006 (1), b = 11.489 (2), c = 7.347 (1) Å, β = 97.50 (3)°; 2-ethanoylbenzoic acid (10), 3-hydroxy-3-methyl-1-(3*H*)-isobenzofuranone, orthorhombic, $P2_12_12_1$, a = 5.199 (6), b = 9.651 (14), c = 15.950 (17) Å; 2-(2′-oxoethyl)benzoic acid (11), 3-hydroxy-3,4-dihydroisobenzopyran-1-one, monoclinic, $P2_1/n$, a = 4.651 (3), b = 11.886 (7), c = 14.312 (11) Å, β = 90.86 (6)°. These compounds also exist in the cyclic forms in chloroform solution. A trimeric cyclic trioxane structure, analogous to paracetaldehyde, is confirmed as the solid form of 5-oxopentanoic acid (1), triclinic, $P\bar{1}$, a = 5.640 (4), b = 8.571 (8), c = 18.962 (13) Å, α = 78.68 (6), β = 84.34 (5), γ = 80.38 (6)°. In solution (NMR), mixtures of the open aldoacid, trimeric acid and cyclic pseudoacid exist. In both furanoid and pyranoid pseudoacids, endocyclic lactol C—O bond lengths are lengthened (1.46–1.48 Å), while the exocyclic C—O(H) bonds are shortened (1.38 Å). Pseudoacids commonly form hydrogen-bonded chains linking the lactol hydroxy and carbonyl groups, but 3-hydroxy-3,4-dihydroisobenzopyran-1-one forms distinctive hydrogen-bonded dimers.

1. Introduction

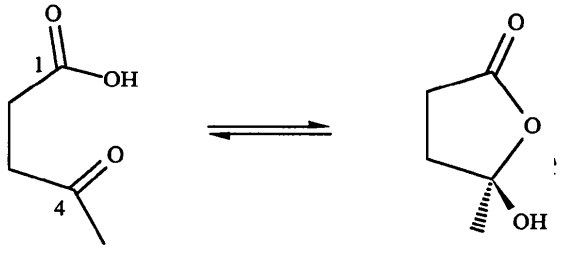
Certain γ- and δ-oxoacids may exist in their cyclic 'lactol' forms. As summarized by Jones (1963), ring tautomers gain stability from their ability to form five- and six-membered rings and the proximity of the interacting groups. Oxoacids may be thought to be analogous to the γ- and δ-hydroxyaldehydes/-ketones (carbohydrates) with the salient functional groups each in the next higher carbon oxidation state. The parent cyclic acids were named 'pseudosäure' (pseudoacid). For the 4-ketoacids, the cyclic form of levulinic acid (4-oxopentanoic acid) was recognized more than a century ago as the potential intermediate in its acid-promoted dehydration to α-angelica lactone (Bredt, 1886). In solution, levulinic acid exists in the open form, although substitution at the positions between the carbonyls apparently shifts the solution equilibria toward the cyclic forms (Pascual *et al.*, 1964; Claeson & Thalen, 1967). The *cis*-unsaturated analogs, such as mucochloric acid (Mowry, 1950), penicillic acid (Birkinshaw *et al.*, 1936) and 4-oxypentenoic acid derivatives (Sheffold & Dubs, 1967) have open-cyclic equilibria which favor the cyclic forms. In the case of penicillic acid, the cyclic lactol form is given credit in part for its carcinogenic activity (Dickens, 1964, 1965). Among the aromatic analogs, the 'hydroxyphthalide' or cyclic structures of 2-methanoylbenzoic acids were assigned by de Diesback & Riat (1937), and the cyclic forms of 2-methanoyl- and 2-ethanoylbenzoic acid could be inferred from low-resolution NMR spectra in solution and their solid-state IR spectra (Tyman & Najam, 1977). Studies have addressed groups of related compounds (Bhatt & Kamath, 1968; Bowden & Malik, 1993). In solution, the cyclic forms of 2-acylbenzoic acids are usually favored, except for *o*-benzoylbenzoic acid (Lalancette *et al.*, 1990). Concerning 5-ketoacids, relatively little has appeared. Isolevulinic acid (5-oxopentanoic acid) was reported with m.p. 401 K (Mikhno *et al.*, 1962), although its structure was thought to be the cyclic trimeric trioxane, analogous to paracetaldehyde (Piacenti & Pino, 1961). Its analog *o*-carboxyphenylethanal was reported as an open structure, but without structural characterization (Schöpf & Kühne, 1950). Shemyakin (1943) speculated that many aldehydoacids crystallized in their cyclic hydroxylactone forms.

Springing from our continuing interest in the structures of compounds with two competing oxygen leaving groups substituted at a single carbon, we have been exploring the geometries and the C—O bond lengths in the general series in which the intermediates are cyclic.



R_1-O$^-$	R_2-O$^-$
Conjugate acid	Conjugate acid
R-OH	*R*-OH, H_2O, Ar-OH, RCO_2H
C=C-OH, Ar-OH	*R*-OH, H_2O, Ar-OH, RCO_2H
RCO_2H	*R*-OH, H_2O, Ar-OH, RCO_2H

Cyclic ground-state structure and reactivity is strongly influenced by the relative leaving group tendencies. Among the tetrahydropyranyl ethers and esters (R_1OH=*R*OH), structures with better R_2-O^- leaving groups have longer exocyclic and shorter endocyclic C—O bonds (Briggs *et al.*, 1984), which correlates with the kinetic data for their hydrolysis (Allen & Kirby, 1984). Among derivatized dihydropyranyl hemiketals, ethers and esters (R_1OH = enol), the noticeable structural effects of strong exocyclic leaving groups (R_2-O^-) on the six-membered rings is a flattening of the ring in concert with a shortening of the endocyclic C—O bond (Ruggiero *et al.*, 1990). In the present contribution, we report the solid-state and solution structural characterizations of a number of pseudoacids (R_1OH = RCO_2H, R_2OH = H_2O).



In an attempt to find structures within the aliphatic 4-oxoacid group, we examined solid 5-oxopentanoic acid (1), which is found in a cyclic s-trioxane form. Several other similar examples were prepared. Among olefinic and aromatic 4-oxoacids, we report the structures of penicillic acid (7), mucochloric acid (8), 2-methanoylbenzoic acid (9) and 2-ethanoylbenzoic acid (10). In the 5-oxoacid group, we report the cyclic structures of *trans*-2-carboxy-3-methyl-5-oxopentanoic acid (6) and *o*-carboxyphenylethanal (11).

2. Experimental

Solvents and reagents were of the highest available purity. Penicillic acid (7), mucochloric acid (8), 2-methanoylbenzoic acid (9) and 2-ethanoylbenzoic acid (10) were obtained from Aldrich Chemical Co. They were recrystallized from ether (7), water (8) or ethyl ethanoate (9,10). Proton NMR spectra were recorded at GE-300 MHz and are given in p.p.m. (δ) downfield from tetramethylsilane reference. Melting temperatures were determined on a Shimadzu DSC-5 calorimeter under nitrogen.

2.1. *General procedure for preparation of aliphatic 4- and 5-oxoacids*

2.1.1. *5-Oxopentanoic acid (1).* To a stirred mixture of diethyl malonate (10.8 g, 67 mmol) and sodium ethoxide (100 mg) in 55 ml CCl_4 at 273 K, propenal (3.75 g, 67 mmol) dissolved in CCl_4 was added slowly and the mixture allowed to warm to room temperature while stirring for 12 h. The mixture was then treated with 2 equiv. of aqueous acid and the organic phase was extracted with ether, separated, dried over anhydrous Na_2SO_4 and evaporated to produce a syrup containing the intermediate substituted malonate ester. After distillation under reduced pressure (500 mtorr), hydrolysis and decarboxylation were effected in one step by placing the substituted malonate ester in a porcelain cup within a stainless steel bomb (75 mL volume) together with 3.0 mL of water, and heating for 3 h under the pressure developed at 493 K. After cooling, water was removed from the product aqueous solutions in a stream of nitrogen followed by pumping *in vacuo* for several hours leaving colorless oils. These were distilled under reduced pressure. 5-Oxopentanoic acid (1) from propenal crystallized as a colorless solid, m.p. 401 K (DSC peak), ^{1}H NMR (in $CDCl_3$, a mixture of open, cyclic trimer and pseudoacid isomers), open: 10.9, broad singlet, CO_2H; 9.8, broad singlet, C*H*O; cyclic trimer: 10.9, broad singlet, CO_2H; 4.9, triplet, J = 6 Hz, $HCCH_2$; pseudoacid: 9.4, broad singlet, C—O*H*; 6.6, triplet, J = 6 Hz, $HCCH_2$; all: 2.4, multiplets, O_2C-CH_2; 1.8, multiplets, CH_2-CH_2-CH. In our hands, the air-oxidative synthesis of (1) from air oxidation of cyclohexanone in the presence of $Mn(NO_3)_2$ (Becke & Flemming, 1952) produced adipic acid.

The analogous oxoacid 2-methyl-5-oxopentanoic acid (2) is prepared from propenal and diethyl methylmalonate; 3-methyl-5-oxopentanoic acid (3) from butenal and diethyl malonate; 3,3-dimethyl-5-oxohexanoic acid (4) from mesityl oxide and diethyl malonate; 2,3-dimethyl-5-oxopentanoic acid (5) from butenal and diethyl methylmalonate. Each was an oil. ^{1}H NMR (δ, in $CDCl_3$) for (2): a mixture of open form (28%), cyclic trimer (39%) and pseudoacid (33%) isomers; open: 9.80, triplet, J = 3 Hz, C*H*O; trimer: 5.88, triplet, J = 6 Hz, CHO_2; pseudoacid: 6.63, triplet, J = 6 Hz, CHO_2; open and trimer: 9.2, broad singlet, CO_2H; all: overlapped multiplets: 2.5, $CHCO_2$; 1.8, CH_2CH; 1.6, $CHCH_3$; 1.2, CH_3. For (3): 9.75, singlet (broad), C*H*O; 9.4, singlet (broad), CO_2H; 2.5–2.3, overlapped multiplets, CH_2CHCH_2; 1.11, doublet, J = 7 Hz, CH_3. For (4): 9.3, singlet (broad), CO_2H; 2.62, singlet, CH_2CO_2; 2.51,

singlet, CH_2CO; 2.15, singlet, CH_3CO; 1.13, singlet, CH_3's. For (5): a mixture of open form (80%) and cyclic trimer (20%); open: 9.70, singlet (broad), *CHO*; trimer: 5.95, singlet (broad), CHO_2; both: 9.9, singlet (broad), CO_2H; 2.4–2.2, overlapping multiplets, $CHCHCH_2$; 1.20, 1.05, multiplets, CH_3's. Percentages, where given, are based on integrations of the aldehyde proton in its various forms.

2.1.2. *trans-2-Carboxy-3-methyl-5-oxopentanoic acid (6) or trans-3-carboxy-4-methyl-6-hydroxytetrahydropyran-2-one.* As in the general procedure above, the intermediate ester from reaction of 3-buten-2-al, diethyl 2-methyl-2-(4′-oxobut-2′-yl)pentandioate was treated with 10% aqueous NaOH solution at room temperature for 10 min. The mixture was then acidified with an equivalent of aqueous HCl and extracted with ether (3×); the pooled ether extracts were then dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* whereupon the product mixture partially crystallized. The colorless solid was the *trans* cyclic pseudoacid diastereomer and the colorless oil the *cis* open diastereomer.

2.1.3. *2-Methanoylbenzoic acid (9) or 3-hydroxy-1-(3H)-isobenzofuranone.* ^{1}H NMR (in $CDCl_3$, 303 K): 7.82, doublet, J_{67} = 7.5 Hz, H7; 7.56, triplet, $J_{45} = J_{56}$ = 7.5 Hz, H5; 7.61, doublet of doublets, J_{45} = 7.5 Hz, J_{46} = 1.0 Hz, H4; 7.69, doublet of triplets, $J_{56} = J_{67}$ = 7.5 Hz, J_{46} = 1.0 Hz, H6; 6.64, singlet, HCO_2, 5.07, singlet, broad, OH. ^{13}C NMR (in $CDCl_3$, 303 K): 169.2 (carbonyl C), 146.29 (C7a), 134.69, 130.84, 126.69 (C3a), 125.37, 123.41, 97.83 (lactol C).

2.1.4. *2-Ethanoylbenzoic acid (10) or 3-hydroxy-3-methyl-1-(3H)-isobenzofuranone.* Cell reported by Gupta & Prasad (1970): orthorhombic, $P2_12_12_1$, a = 9.53, b = 5.22, c = 15.82 Å. ^{1}H NMR (in $CDCl_3$, 303 K): 7.78, doublet, J_{67} = 7.5 Hz, H7; 7.68, triplet, $J_{45} = J_{56}$ = 7.5 Hz, H5; 7.58, doublet, J_{45} = 7.5 Hz, H4; 7.54, triplet, $J_{56} = J_{67}$ = 7.5 Hz, H6; 4.55, singlet, broad, OH; 1.87, singlet, CH_3. ^{13}C NMR (in $CDCl_3$, 303 K): 168.7 (carbonyl C), 146.60 (C7a), 134.71, 130.51, 126.00 (C3a), 125.54, 122.03, 106.04 (lactol C), 26.04 (methyl C). These may be compared with lower resolution spectra or partial spectra reported by Tyman & Najam (1977), Jones & Desio (1965), Erley *et al.* (1964) and Finkelstein *et al.* (1967).

2.1.5. *2-(2-Oxoethyl)benzoic acid (11) or 2-carboxyphenyethanal, 3-hydroxy-3,4-dihydroisobenzopyran-1-one.* Following the procedure of Schöpf & Kühne (1950) (11) is obtained as a white crystalline solid, m.p. 368.9 K (DSC peak); literature: 403–413 K (Warnell & Shriner, 1957), 644–645 K (Schöpf & Kühne, 1950). ^{1}H NMR (223 K in $CDCl_3$): 6.94; 7.99, doublet of doublets, J_{78} = 7.5, J_{68} = 1.0 Hz, H8; 7.53, doublet of triplets, $J_{67} = J_{65}$ = 7.5, J_{68} = 1.0 Hz, H6; 7.34, triplet, $J_{78} = J_{67}$ = 7.5 Hz, H7; 7.26, doublet, J_{56} = 7.5 Hz; 6.94, singlet broad, OH; 5.94, doublet of doublets, J_{34A} = 3.1 Hz, J_{34B} = 4.5 Hz, H3; 3.26, doublet of doublets, J_{gem} = 16.6 Hz, J_{34A} = 3.1 Hz, H4*A*; 3.09, doublet of doublets, J_{gem} = 16.6 Hz, J_{34A} = 4.5 Hz, H4*B*; unanalyzed, but $\Delta\nu/J$ = 3.2. Signal from OH broadens and shifts with increasing temperature: 243 K, δ 6.66; 273 K, δ 5.9; 292 K, δ 5.4.

2.2. *Crystallography*

A summary of the crystal data and data collection and refinements for (1) and (6)–(11) are given in Table 1. Scattering factors were from *International Tables for Crystallography* (1992, Vol. C). In every case, structures were discovered by application of direct methods (Sheldrick, 1985). Models including coordinates and anisotropic displacement parameters for all non-H atoms were refined by full-matrix least-squares minimizing F^2 differences (Sheldrick, 1993). With the exceptions noted below, all reflections were used in the refinements. H atoms, with the exception of hydroxy H atoms, were placed at calculated positions, riding on the non-H atoms to which they are attached. For H atoms, isotropic displacement parameters were fixed at 120% of the equivalent isotropic displacement parameters of the attached atoms. Hydroxy H atoms were found in difference-Fourier maps and their positions refined through a torsional parameter. In a few cases, an extinction correction was applied, but absorption corrections were not made. Disorder in one of the side chains of (1), a trigonal disorder of methyl group H atoms in (6) and (7), and a twofold disorder in the orientation of the carboxylate in (6) were modeled.

For (8) crystals were apparently composed in various proportions of aggregates of stacked crystallites. After recrystallizations from water, very thin specimens were examined and found to suffer essentially the same effects. Examination of a number of specimens revealed the likely triclinic cell and enabled a systematic data collection. However, the presence of two independent molecules in the asymmetric unit and what appears to be a class of systematically absent reflections (*h*0*l*, *h* odd absent) made the cell assignment suspect. The distribution of intensities is hypercentrosymmetric. No cell of higher symmetry or additional internal symmetry could be found; reflections displaying 2/*m* equivalence are not apparent. While the results are hardly comparable in accuracy with the other structures reported, (8) refined satisfactorily and the molecular structure and intermolecular interactions are chemically reasonable. Residuals are variously plagued by intensity contributions from other crystallites, however, only a few (7) omissions were made and these were among stronger low-order reflections ($2\bar{1}1$, $1\bar{1}2$, $1\bar{1}1$, $\bar{1}11$, $\bar{1}10$, 110, 210) based solely on obvious interferences detected by reviewing the reflection scan profiles. In the structure chlorines were found in pairs of positions approximated by x, z and $\frac{1}{2}+x$, z, where $x \simeq \{-0.27, 0.18\}$ and $z \simeq 0.87$. Similar correlations exist for the comparative positions of the C, H and O atoms. As a result, odd

Table 1. *Experimental details*

	(1)	(6)	(7)	(8)
Crystal data				
Chemical formula	$C_{15}H_{24}O_9$	$C_7H_{10}O_5$	$C_8H_{10}O_4$	$C_4H_2Cl_2O_3$
Chemical formula weight	348.36	174.15	170.16	168.96
Cell setting	Triclinic	Monoclinic	Tetragonal	Triclinic
Space group	$P\bar{1}$	$C2/c$	$P4_2/n$	$P\bar{1}$
a (Å)	5.640 (4)	25.412 (5)	15.834 (23)	6.277 (5)
b (Å)	8.571 (8)	6.2910 (10)		8.085 (5)
c (Å)	18.962 (13)	10.757 (2)	7.016 (11)	12.369 (9)
α (°)	78.68 (6)			99.50 (5)
β (°)	84.34 (5)	104.84 (3)		102.38 (6)
γ (°)	80.37 (6)			90.29 (6)
V (Å^3)	884.1 (12)	1662.3 (5)	1759.0 (45)	604.2 (8)
Z	2	8	8	4
D_x (Mg m^{-3})	1.309	1.392	1.285	1.857
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
No. of reflections for cell parameters	30	30	30	40
θ range (°)	10–20	15.0–22.5	12.5–20	12.5–22.5
μ (mm^{-1})	0.109	0.120	0.104	0.994
Temperature (K)	295 (2)	295 (2)	295 (2)	294 (2)
Crystal form	Prism	Thin rhomb	Prism	Thin plate
Crystal size (mm)	0.40 × 0.30 × 0.10	1.00 × 0.80 × 0.06	0.30 × 0.10 × 0.10	0.40 × 0.40 × 0.05
Crystal color	Colorless	Colorless	Colorless	Colorless
Data collection				
Diffractometer	Scintillation counter, PH analysis	Scintillation counter, PH analysis	Scintillation counter, PH analysis	Scintillation counter, PH analysis
Data collection method	ω scans	ω scans	ω scans	ω scans, 3.0° scans
Absorption correction	None	None	None	None
No. of measured reflections	3118	3826	7107	3903
No. of independent reflections	2698	1907	2051	3526
No. of observed reflections	1032	1191	577	1999
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.0185	0.0324	0.0751	0.0265
θ_{max} (°)	25.00	27.59	27.5	30.09
Range of h, k, l	$0 \rightarrow h \rightarrow 6$ $-10 \rightarrow k \rightarrow 10$ $-22 \rightarrow l \rightarrow 22$	$-32 \rightarrow h \rightarrow 31$ $-8 \rightarrow k \rightarrow 8$ $0 \rightarrow l \rightarrow 13$	$-20 \rightarrow h \rightarrow 20$ $-20 \rightarrow k \rightarrow 20$ $0 \rightarrow l \rightarrow 9$	$0 \rightarrow h \rightarrow 8$ $-11 \rightarrow k \rightarrow 11$ $-17 \rightarrow l \rightarrow 17$
No. of standard reflections	3	3	3	3
Frequency of standard reflections	Every 97 reflections	Every 97 reflections	Every 97 reflections	Every 97 reflections
Intensity decay (%)	−2.5 (20)	−0.1 (20)	−2.5 (5)	−3.2 (14)
Refinement				
Refinement on	F^2	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$	0.0415	0.0362	0.0557	0.1174
$wR(F^2)$	0.1182	0.1051	0.1406	0.3437
S	1.081	1.095	1.481	1.225
No. of reflections used in refinement	2698	1907	2046	3519
No. of parameters used	265	132	111	165
H-atom treatment	H atoms fixed, calculated	H atoms fixed, calculated	H atoms fixed, calculated	H atoms fixed, calculated
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0712P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0606P)^2$ <?h 3pt>$+ 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0364P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.2416P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.000	0.000	0.000	0.000
$\Delta\rho_{max}$ (e Å^{-3})	0.155	0.150	0.184	1.996
$\Delta\rho_{min}$ (e Å^{-3})	−0.158	−0.148	−0.168	−0.736
Extinction method	None	None	*SHELXL*93 (Sheldrick, 1993)	None
Extinction coefficient	–	–	0.0155 (17)	–

Table 1 (*cont.*)

	(1)	(6)	(7)	(8)
Source of atomic scattering factors	*International Tables for Crystallography* (1992, Vol. C)	*International Tables for Crystallography* (1992, Vol. C)	*International Tables for Crystallography* (1992, Vol. C)	*International Tables for Crystallography* (1992, Vol. C)
Computer programs				
Data collection	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)
Cell refinement	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)
Data reduction	*XDISK* (Siemens, 1989*b*)	*XDISK* (Siemens, 1989*b*)	*XDISK* (Siemens, 1989*b*)	*XDISK* (Siemens, 1989*b*)
Structure solution	*SHELXS*86 (Sheldrick, 1985)	*SHELXS*86 (Sheldrick, 1985)	*SHELXS*86 (Sheldrick, 1985)	*SHELXS*86 (Sheldrick, 1985)
Structure refinement	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)
Molecular Graphics	*XP* (Siemens Analytical X-ray Instruments Inc.)	*XP* (Siemens Analytical X-ray Instruments Inc.)	*XP* (Siemens Analytical X-ray Instruments Inc.)	*XP* (Siemens Analytical X-ray Instruments Inc.)
Preparation of material for publication	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)

	(9)	(10)	(11)
Crystal data			
Chemical formula	$C_8H_6O_3$	$C_9H_8O_3$	$C_9H_8O_3$
Chemical formula weight	150.13	164.15	164.15
Cell setting	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1$	$P2_12_12_1$	$P2_1/n$
a (Å)	4.0060 (10)	5.199 (6)	4.651 (3)
b (Å)	11.489 (2)	9.651 (14)	11.886 (7)
c (Å)	7.3470 (10)	15.950 (17)	14.312 (11)
β (°)	97.50 (3)		90.86 (6)
V (Å^3)	335.25 (11)	800.3 (17)	791.1 (9)
Z	2	4	4
D_x (Mg m^{-3})	1.487	1.362	1.378
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
Wavelength (Å)	0.71073	0.71073	0.71073
No. of reflections for cell parameters	30	30	30
θ range (°)	12.5–22.5	12.5–22.5	12.5–22.5
μ (mm^{-1})	0.115	0.103	0.104
Temperature (K)	294 (2)	294 (2)	294 (2)
Crystal form	Plate	Irregular	Prism
Crystal size (mm)	0.60 × 0.40 × 0.10	0.40 × 0.30 × 0.20	0.80 × 0.32 × 0.20
Crystal color	Colorless	Colorless	Colorless
Data collection			
Diffractometer	Scintillation counter, PH analysis	Scintillation counter, PH analysis	Scintillation counter, PH analysis
Data collection method	ω scans	ω scans	ω scans
Absorption correction	None	None	None
No. of measured reflections	1697	3366	2550
No. of independent reflections	1537	2451	2297
No. of observed reflections	1017	1591	1161
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.0147	0.0194	0.0141
θ_{max} (°)	34.99	35.03	29.99
Range of h, k, l	$0 \rightarrow h \rightarrow 6$ $0 \rightarrow k \rightarrow 18$ $-11 \rightarrow l \rightarrow 11$	$-8 \rightarrow h \rightarrow 8$ $0 \rightarrow k \rightarrow 15$ $0 \rightarrow l \rightarrow 25$	$0 \rightarrow h \rightarrow 6$ $0 \rightarrow k \rightarrow 16$ $-20 \rightarrow l \rightarrow 20$
No. of standard reflections	3	3	3
Frequency of standard reflections	Every 97 reflections	Every 97 reflections	Every 97 reflections
Intensity decay (%)	−0.2 (10)	−0.1 (10)	0.0 (2)
Refinement			
Refinement on	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$	0.0445	0.0409	0.0323
$wR(F^2)$	0.1297	0.0935	0.0860
S	1.102	1.093	1.042
No. of reflections used in refinement	1537	2451	2297

Table 1 (*cont.*)

	(9)	(10)	(11)
No. of parameters used	102	111	111
H-atom treatment	H atoms fixed, calculated	H atoms fixed, calculated	H atom fixed, calculated
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0831P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0493P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0469P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.000	0.000	0.000
$\Delta\rho_{max}$ (e Å^{-3})	0.252	0.198	0.135
$\Delta\rho_{min}$ (e Å^{-3})	−0.249	−0.156	−0.145
Extinction method	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)
Extinction coefficient	0.0174 (215)	0.0449 (55)	0.0216 (29)
Source of atomic scattering factors	*International Tables for Crystallography* (1992, Vol. C)	*International Tables for Crystallography* (1992, Vol. C)	*International Tables for Crystallography* (1992, Vol. C)
Computer programs			
Data collection	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)
Cell refinement	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)	*P3/PC* (Siemens, 1989*a*)
Data reduction	*XDISK* (Siemens, 1989*b*)	*XDISK* (Siemens, 1989*b*)	*XDISK* (Siemens, 1989*b*)
Structure solution	*SHELXS*86 (Sheldrick, 1985)	*SHELXS*86 (Sheldrick, 1985)	*SHELXS*86 (Sheldrick, 1985)
Structure refinement	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)

orders of *h*0*l* are accidentally weak. Molecules form hydrogen-bonded helices down the *b* axis, which form slightly interpenetrating columns along the *a* axis with the (*Z*)-dichloro molecular feature oriented away from the helix. Along **c**, interpenetrating columns alternate with Cl···Cl interactions between adjacent pairs of columns. These alternating stronger and weaker interactions may contribute to minute orientational disorder which appear as relatively somewhat broadened Bragg profiles and the polycrystallinity of larger specimens. Larger difference Fourier residuals are found near the Cl and O atoms as usual for essentially ordered structures, a conventional model and lacking an absorption correction. Stacking disorder and its attendant diffuse scattering has not been examined, but the commensurate part of the scattering seems to be satisfactorily represented by this anorthic model.

Atom coordinates and equivalent isotropic vibrational parameters for the non-H atoms and the pseudoacid hydroxy H atoms for structures (1) and (6)–(11) are given in Tables 2–8.†

Table 2. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2) for (1)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	U_{eq}
O1	−0.0385 (3)	0.6819 (2)	0.27776 (10)	0.0651 (6)
O2	0.2258 (3)	0.4990 (2)	0.35237 (9)	0.0691 (6)
O3	0.2922 (3)	0.5302 (2)	0.22924 (10)	0.0664 (6)
C1	0.0661 (5)	0.6491 (4)	0.3448 (2)	0.0632 (8)
C2	−0.1249 (4)	0.6303 (3)	0.40503 (14)	0.0626 (8)
C3	−0.3184 (4)	0.7751 (3)	0.40836 (13)	0.0589 (7)
C4	−0.4965 (4)	0.7333 (3)	0.47189 (14)	0.0656 (8)
C5	−0.7111 (4)	0.8575 (4)	0.4818 (2)	0.0590 (8)
O4	−0.7427 (3)	0.9911 (3)	0.44348 (11)	0.0826 (7)
O5	−0.8600 (3)	0.8081 (2)	0.53437 (11)	0.0817 (7)
C6	0.4046 (5)	0.4962 (4)	0.2947 (2)	0.0669 (9)
C7	0.5537 (5)	0.3325 (4)	0.30205 (14)	0.0692 (8)
C8	0.7496 (5)	0.3259 (3)	0.2411 (2)	0.0749 (9)
C9	0.9275 (5)	0.1730 (4)	0.2475 (2)	0.0849 (10)
C10	1.1163 (6)	0.1752 (5)	0.1877 (2)	0.0852 (11)
O6	1.0906 (4)	0.2753 (4)	0.13077 (14)	0.1217 (10)
O7	1.3064 (4)	0.0745 (3)	0.19813 (13)	0.1041 (8)
C11	0.1466 (5)	0.6835 (4)	0.2213 (2)	0.0725 (9)
C12	0.0395 (6)	0.7190 (4)	0.1499 (2)	0.0913 (11)
C13†	0.2580 (12)	0.7369 (10)	0.0913 (3)	0.081 (2)
C14†	0.1770 (9)	0.7759 (8)	0.0161 (3)	0.101 (2)
C15†	0.3741 (11)	0.8032 (10)	−0.0410 (4)	0.087 (2)
O8†	0.3428 (9)	0.8988 (7)	−0.0954 (3)	0.094 (2)
O9†	0.5721 (13)	0.7120 (12)	−0.0312 (4)	0.181 (4)
C13*A*†	0.147 (4)	0.682 (2)	0.0760 (7)	0.117 (8)
C14*A*†	0.289 (3)	0.822 (2)	0.0604 (10)	0.096 (6)
C15*A*†	0.453 (3)	0.809 (3)	−0.0100 (11)	0.090 (7)
O8*A*†	0.432 (4)	0.917 (3)	−0.0602 (12)	0.121 (7)
O9*A*†	0.603 (4)	0.675 (2)	−0.0064 (12)	0.120 (7)

† Partial occupancy: major isomer 0.739 (8), minor isomer designated *A*.

3. Discussion

Within the classes of oxoacids capable of forming five- and six-membered rings, three categories which provide proximity to carboxylate and keto(aldehydo) functions were examined: substituted aliphatic, (*Z*)-olefinic and *o*-disubstituted aromatic.

3.1. *Substituted aliphatic*

Levulinic acid (4-oxopentanoic acid), m.p. 305 K, exists in the open form in solution, as indicated from its proton NMR and solid-state IR spectra (Pascual *et al.*, 1964). Its isomer 5-oxopentanoic acid (1) has been synthesized as an oil which crystallizes to form a solid with m.p. 401–403 K (Mikhno *et al.*, 1962). An earlier report found evidence that (1) has a trimeric s-trioxane

† Lists of atomic coordinates, anisotropic displacement parameters, complete geometry and structure factors have been deposited with the IUCr (Reference: FR0001). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²) for (6)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
O1	0.20225 (4)	0.2070 (2)	0.64927 (10)	0.0537 (3)
O2	0.16128 (4)	0.5006 (2)	0.67070 (12)	0.0722 (4)
C2	0.16313 (5)	0.3457 (2)	0.60523 (14)	0.0462 (4)
C3	0.12299 (4)	0.3107 (2)	0.47617 (14)	0.0423 (3)
C4	0.11971 (5)	0.0796 (2)	0.43089 (14)	0.0489 (4)
C5	0.17764 (5)	0.0034 (2)	0.44530 (15)	0.0509 (4)
C6	0.21044 (5)	0.0089 (2)	0.58233 (15)	0.0485 (4)
O6	0.26499 (4)	0.0024 (2)	0.58737 (11)	0.0612 (3)
C7	0.06827 (5)	0.3968 (2)	0.48513 (15)	0.0476 (4)
O8†	0.0437 (4)	0.313 (2)	0.5520 (11)	0.071 (2)
O9†	0.0481 (5)	0.5526 (18)	0.4131 (14)	0.077 (3)
O8*A*†	0.0581 (4)	0.5826 (15)	0.4411 (15)	0.061 (2)
O9*A*†	0.0396 (6)	0.273 (3)	0.5378 (15)	0.071 (3)
C10	0.08546 (7)	0.0592 (3)	0.2927 (2)	0.0777 (6)

† Partial occupancy: major isomer 0.56 (3), minor isomer designated *A*.

Table 4. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²) for (7)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
O1	0.57045 (11)	0.63111 (9)	0.1480 (3)	0.0666 (6)
C2	0.6354 (2)	0.6633 (2)	0.0471 (4)	0.0632 (8)
O2	0.69962 (12)	0.62236 (12)	0.0200 (3)	0.0855 (7)
C3	0.6154 (2)	0.7460 (2)	−0.0188 (4)	0.0637 (8)
C4	0.5385 (2)	0.7631 (2)	0.0412 (4)	0.0572 (7)
O4	0.49019 (11)	0.83009 (11)	0.0179 (3)	0.0704 (6)
C5	0.50203 (14)	0.6926 (2)	0.1563 (5)	0.0596 (8)
O5	0.48727 (11)	0.71303 (12)	0.3449 (3)	0.0764 (7)
C6	0.4243 (2)	0.6559 (2)	0.0658 (5)	0.0687 (9)
C7	0.4342 (2)	0.6170 (2)	−0.1207 (6)	0.1150 (14)
C8	0.3498 (2)	0.6646 (2)	0.1526 (7)	0.1073 (12)
C9	0.5259 (2)	0.8957 (2)	−0.0988 (5)	0.0852 (10)

Table 5. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²) for (8)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
Cl3*A*	−0.2724 (3)	−0.5265 (2)	0.87440 (11)	0.0552 (5)
Cl4*A*	0.1760 (3)	−0.2753 (2)	0.87187 (11)	0.0561 (5)
O1*A*	−0.1813 (7)	−0.4889 (4)	0.5781 (3)	0.0395 (9)
O2*A*	−0.4475 (8)	−0.6416 (6)	0.6141 (3)	0.0524 (11)
C2*A*	−0.2888 (9)	−0.5479 (6)	0.6465 (4)	0.0360 (10)
C3*A*	−0.1793 (9)	−0.4787 (6)	0.7630 (4)	0.0367 (10)
C4*A*	−0.0105 (9)	−0.3825 (6)	0.7623 (4)	0.0350 (10)
C5*A*	0.0062 (9)	−0.3798 (6)	0.6434 (4)	0.0374 (10)
O5*A*	−0.0226 (8)	−0.2197 (5)	0.6189 (3)	0.0481 (10)
Cl3*B*	0.2277 (3)	0.2209 (2)	0.87484 (11)	0.0570 (5)
Cl4*B*	0.6754 (3)	−0.0321 (2)	0.87141 (11)	0.0542 (5)
O1*B*	0.3191 (7)	0.0307 (4)	0.5782 (3)	0.0388 (8)
O2*B*	0.0523 (9)	0.2020 (6)	0.6141 (4)	0.0552 (11)
C2*B*	0.2086 (10)	0.1260 (6)	0.6475 (4)	0.0369 (11)
C3*B*	0.3216 (9)	0.1178 (6)	0.7636 (4)	0.0351 (10)
C4*B*	0.4875 (9)	0.0211 (6)	0.7616 (4)	0.0350 (10)
C5*B*	0.5031 (9)	−0.0457 (6)	0.6432 (4)	0.0372 (11)
O5*B*	0.4789 (8)	−0.2166 (5)	0.6188 (3)	0.0481 (11)

Table 6. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²) for (9)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
O1	0.3206 (6)	−0.25259 (15)	0.3665 (2)	0.0633 (6)
O2	0.5301 (4)	−0.0718 (2)	0.3932 (2)	0.0513 (4)
O3	0.3665 (4)	0.12161 (12)	0.3371 (2)	0.0474 (4)
C1	0.3698 (6)	−0.1595 (2)	0.2972 (3)	0.0434 (5)
C3	0.5500 (6)	0.0311 (2)	0.2766 (3)	0.0409 (4)
C3*A*	0.3892 (5)	−0.0098 (2)	0.0922 (2)	0.0336 (3)
C4	0.3400 (6)	0.0477 (2)	−0.0735 (3)	0.0431 (4)
C5	0.1731 (6)	−0.0110 (2)	−0.2225 (3)	0.0480 (5)
C6	0.0608 (6)	−0.1239 (2)	−0.2071 (3)	0.0467 (5)
C7	0.1124 (5)	−0.1820 (2)	−0.0417 (3)	0.0411 (4)
C7*A*	0.2803 (5)	−0.12234 (15)	0.1069 (2)	0.0328 (3)

Table 7. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²) for (10)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

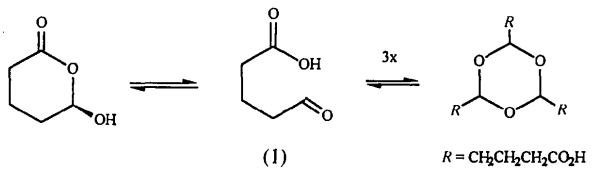
	x	y	z	U_{eq}
C1	0.1103 (3)	−0.07445 (14)	0.64980 (8)	0.0336 (3)
O1	−0.0431 (2)	−0.16872 (11)	0.64862 (6)	0.0474 (3)
O2	0.1316 (2)	0.01116 (9)	0.71621 (5)	0.0383 (3)
C3	0.3342 (3)	0.11738 (14)	0.70252 (8)	0.0336 (3)
O3	0.2190 (2)	0.24596 (10)	0.69650 (6)	0.0449 (3)
C3*A*	0.4374 (3)	0.07743 (14)	0.61718 (8)	0.0312 (3)
C4	0.6315 (3)	0.13720 (15)	0.57065 (9)	0.0409 (4)
C5	0.6794 (3)	0.0821 (2)	0.49192 (10)	0.0483 (4)
C6	0.5398 (3)	−0.0295 (2)	0.46132 (10)	0.0514 (4)
C7	0.3491 (4)	−0.0904 (2)	0.50834 (9)	0.0437 (4)
C7*A*	0.3010 (3)	−0.03385 (14)	0.58666 (8)	0.0322 (3)
C8	0.5194 (3)	0.1042 (2)	0.77436 (10)	0.0484 (4)

Table 8. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²) for (11)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C1	0.0788 (2)	−0.04561 (9)	0.14177 (8)	0.0549 (3)
O1	0.0291 (2)	−0.14165 (7)	0.11647 (6)	0.0752 (3)
O2	0.2340 (2)	0.01940 (6)	0.08564 (5)	0.0611 (2)
C3	0.2385 (2)	0.14085 (9)	0.10154 (8)	0.0575 (3)
O3	−0.0215 (2)	0.18673 (7)	0.07251 (6)	0.0596 (2)
C4	0.2888 (2)	0.16706 (10)	0.20289 (8)	0.0590 (3)
C4*A*	0.0859 (2)	0.10280 (9)	0.26337 (8)	0.0492 (3)
C5	−0.0015 (3)	0.14103 (11)	0.34979 (9)	0.0633 (3)
C6	−0.1833 (3)	0.07793 (12)	0.40339 (9)	0.0752 (4)
C7	−0.2806 (3)	−0.02469 (12)	0.37240 (10)	0.0752 (4)
C8	−0.1985 (3)	−0.06461 (10)	0.28696 (9)	0.0620 (3)
C8*A*	−0.0149 (2)	−0.00074 (9)	0.23201 (8)	0.0484 (3)

(Piacenti & Pino, 1961) rather than a cyclic pseudoacid structure. From the proton NMR of (1) at 298 K in $CDCl_3$ solution, we find evidence for the open cyclic pseudoacid and cyclic trimer forms. A characteristic of the cyclic pseudoacid form from aldehydoacids is the methine H found around δ 6.6. The methine H of the aldehyde trioxanes resonates at a higher field, nearer δ



5, and the open-chain aldehyde downfield from both of these at δ 9.8.

In solution, a three-component mixture is also observed for 2-methyl-5-oxopentanoic acid (2). Open forms are seen in 2,3-dimethyl-5-oxopentanoic acid (3), 3-methyl-5-oxopentanoic acid (4) and 3,3-dimethyl-5-oxohexanoic acid (5), with a small amount of the cyclic trimer present in (3). In the solid state (1) has the cyclic trioxane structure (Fig. 1). The average of the six ether C—O bond lengths is 1.417 (8) Å. The alkyl carboxylic acid groups are all disposed in equatorial conformations on the C atoms of the trioxane ring. The major (*anti*) conformer has all three side chains with the six C—C—C—C torsion angles from 173.4 (3) to −176.2 (2)° and has occupancy 0.739 (8). The minor conformer has one of the three side chains (C12–C15, O8, O9) in one of the almost energetically equivalent *gauche* (synclinal) arrangements, with this side chain having the torsions −79.2 (15) and 173.0 (15)°. Nevertheless, the terminal carboxylic acid groups of the disordered chain are displaced by ~0.8 Å relative to each other and have similar orientations.

Carboxylic acid groups of (1) are hydrogen bonded to others in neighboring molecules across inversion centers in the usual pairwise manner. The H···O distances are 1.74 (8) (using an average for the disordered carboxyl), 1.69 (1), 1.69 (1) Å, and the angles at H are 163 (10), 169 (1), 168 (1)°, respectively (after normalizing the O—H distances to 0.96 Å). The O···O contacts range from 2.54 to 2.87 Å, with the longer among them belonging to the disordered carboxylates.

In the course of synthesis of 3-methyl-5-oxopentanoic acid (3), a mixture of the intermediate diastereomeric 2-carboxy-3-methyl-5-oxopentanoic acids (6) gave crystals of the *trans*-pseudoacid. The structure of *trans*-(6) is shown in Fig. 2. The tetrahydropyran ring adopts a distorted half-chair form, flattened at the ring carboxyl group. Methyl and carboxylate substituents are *trans*, equatorial and pseudoequatorial, respectively. The hydroxy group is equatorial, corresponding to one of the two commonly encountered stable anomeric forms of 2-hydroxytetrahydropyrans. In the half-chair conformation, four of the ring atoms describe a plane [mean atomic deviation 0.004 (2) Å] and the remaining two lie above [C5, +0.289 (3) Å] and below [C4, −0.470 (3) Å]. The torsions $C—O_n—C—O_x$ and $C—O_n—C—H_x$ are +133 (1) and −109 (1)°, respectively. In the *cis* isomer, the cyclic pseudoacid structure would require the methyl and carboxyl substituents to have axial/pseudoequatorial or equatorial/pseudoaxial orientations, respectively. To relieve unfavorable 1,3-diaxial (carboxyl···H and methyl···H or OH) interactions, the equilibrium may shift toward the open form with perhaps a lower melting point.

Since the open form of (6) is a 2-substituted malonic acid, its cyclic pseudoacid has both carboxylic acid and pyranoid lactol groups. The carboxylic acid forms a typical strong dimer through hydrogen bonding with a neighboring inversion-related molecule. The disordered H···O distance has an average length of 1.79 (3) Å and the average angle at H is 149 (4)°; the O···O distances are 2.60 (2) and 2.70 (2) Å. The lactol carbonyl and hydroxy groups are also hydrogen bonded, forming chains through the structure; the H···O distance is 1.85 (1) Å and the angle at H is 166 (1)°. The lactol ring oxygen does not engage in hydrogen bonding.

3.2. *(Z)-Olefinic pseudoacids*

Two compounds in this category were examined: penicillic acid (7) and mucochloric acid (8). The latter is clearly in the cyclic form in solution from the lack of an

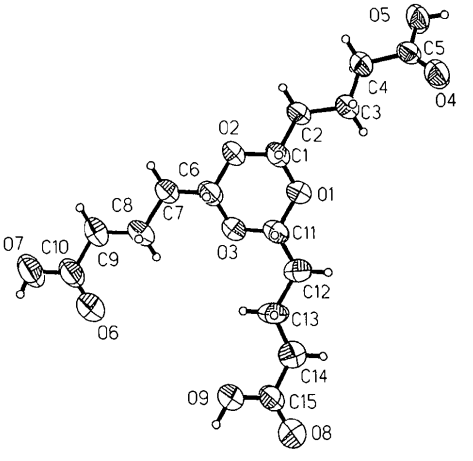


Fig. 1. Thermal ellipsoid plot (50%) of the major conformer of 5-oxopentanoic acid trimer (1) with atom designations.

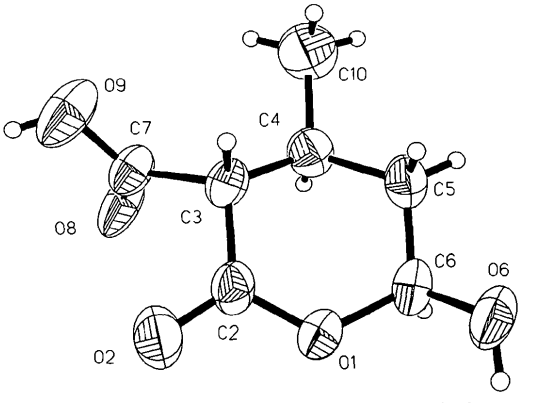


Fig. 2. Thermal ellipsoid plot (50%) of the pseudoacid of the major conformer of *trans*-2-carboxy-3-methyl-5-oxopentanoic acid (6).

aldehyde H resonance and the presence of the methine H at δ 6.09 (Pouchert, 1983). Figs. 3 and 4 show the molecular structures in the crystals. In each, the five-membered pseudoacid ring is essentially planar with the deviations of the non-H atoms from the mean plane being 0.003 (1) and 0.004 (2) Å in (8) and 0.005 (3) Å in (7). Hydroxy groups have a common conformation. Carbonyl O atoms are hydrogen bonded with lactol hydroxy groups forming chains extending through the structures. In (7) the H···O distance is 1.76 (1) Å and the angle at H is 173 (1)°. In (8) the hydrogen bonding links carbonyl and lactol hydroxy groups alternating between the two independent molecules. The H···O distances are 1.92 (3) and 1.94 (3) Å, and the angles at H are 154 (3) and 170 (3)°, respectively.

3.3. *o-Disubstituted aromatic*

Three compounds in this category were examined: 2-methanoylbenzoic acid (9), 2-ethanoylbenzoic acid (10) and *o*-carboxyphenylacetaldehyde (11). Acids (9) and (10) are known to exist in the cyclic pseudoacid forms in $CDCl_3$ solution (Tyman & Najam, 1977). For (9), the methine H is found at δ 6.64 (298 K), which is consistent with the lactol structure. In the carbon NMR, methine C in (9) is found at δ 97.8 p.p.m. and in (10) at δ 106.0 p.p.m. Carbon chemical shifts around 100 p.p.m. are consistent with hemiacetal and hemiketal structures (Levy & Nelson, 1972) and clearly distinguished from those expected from open aldehyde or ketone carbonyl resonances. Figs. 5 and 6 show the structures of the five-membered ring pseudoacids (9) and (10), respectively. The five-membered pseudoacid rings are essentially planar with mean deviations of the non-H atoms of 0.009 (4) (9) and 0.008 (4) Å (10). Hydrogen-bonded chains link the hydroxy groups with the carbonyl O atoms of neighboring molecules. In (9) and (10) the H···O distances are 1.83 (1) and 1.80 (1) Å, and the angles at H are 167 (2) and 178 (2)°, respectively.

For pseudoacid (11), the compound exists in the cyclic form in $CDCl_3$ solution from 223 to 292 K and the distinctive methine H signal is at δ 5.94 (292 K). The small and almost equal vicinal coupling between the

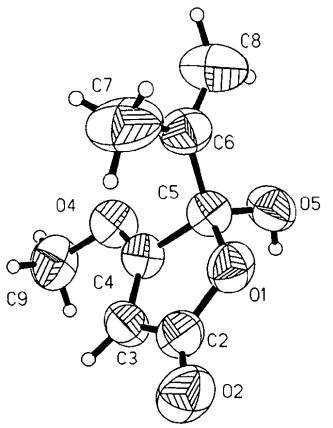


Fig. 3. Thermal ellipsoid plot (50%) of the major conformer of penicillic acid (7).

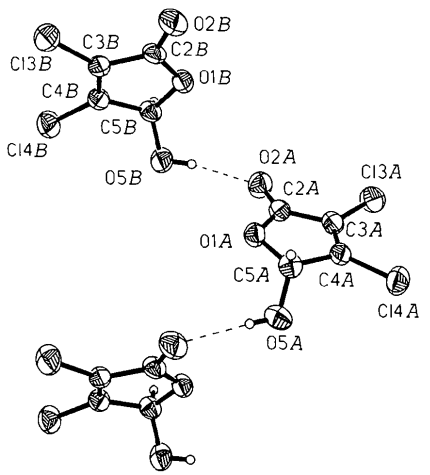


Fig. 4. Thermal ellipsoid plot (50%) of mucochloric acid (8), showing both molecules in the asymmetric unit and the hydrogen-bonding chain extending along the *b* axis.

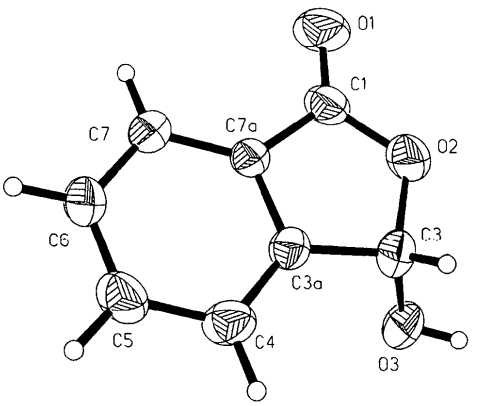


Fig. 5. Thermal ellipsoid plot (50%) of 3-hydroxy-1-(3*H*)-isobenzofuranone (2-methanoylbenzoic acid) (9).

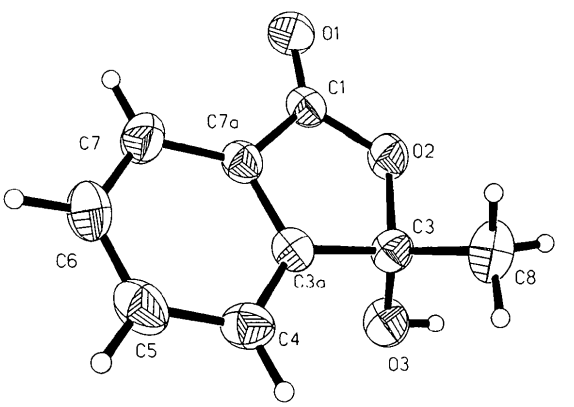


Fig. 6. Thermal ellipsoid plot (50%) of 3-hydroxy-3-methyl-1-(3*H*)-isobenzofuranone (2-ethanoylbenzoic acid) (10).

methine H and the adjacent benzylic H atoms supports an assignment in which the 3-hydroxy group is entirely in the axial conformation in solution. In the solid (Fig. 7), the pyranoid six-membered ring is in the 1,2-diplanar or envelope conformation. The flap atom is the methine C3 and it is substantially out of the plane [−0.61 (2) Å] described by the other non-H benzopyranoid ring atoms [mean atomic deviation 0.02 (2) Å]. The hydroxy group is attached to the flap and disposed axially, a conformation usually described as the α-anomer.

Hydrogen bonding in (11) is distinctively different from that in the others described above. Chains are not found, rather pseudoacids form discrete dimers by hydrogen bonding between the hydroxy groups and carbonyl O atoms across a crystallographic inversion center, as shown in Fig. 7. This arrangement may be considered to be the pseudoacid equivalent of the normal and far more common carboxylic acid dimeric hydrogen-bonding interaction. The H···O distance is 1.81 (1) Å and the angle at H is 167 (1)°. Since the hydroxy group is oriented axially on the dihydroisobenzopyran ring, the hydrogen bond with the adjacent molecule requires that the mean molecular planes of the two heterocycles be parallel but offset, in this case by ~2.75 Å. This dimer is also somewhat weaker than the typical carboxylic acid hydrogen-bonded dimer. This may be rationalized by noting that in the usual carboxylic acid dimer, the π-bond cooperativity involves double-bond/single-bond and single-bond/no-bond resonances. These resonance structures entail no connectivity changes, other than at the hydroxy H, and the resonance contributors are alternate equivalent carboxylic acids. The π systems in the carboxylic acids may be thought to overlap throughout the process. In the pseudoacid dimer, π-bond cooperativity cannot occur since the double-bond/single-bond and single-bond/no-bond resonances involve rehybridization and connectivity changes at lactol C. The migration of the hydroxy H's would result in the open-cyclic equilibrium, not alternate equivalent pseudoacids. In the stronger of the hydrogen-bonded carboxylic acid dimers, O···O contacts are from 2.4 to 2.65 Å. In the pseudoacid dimer there is evidence for the resonance structure drawn in the shortening and lengthening of the C—O bonds (see below). The O···O contact distances are 2.76 (1) Å.

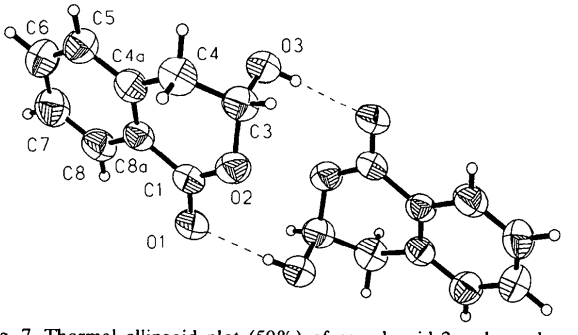
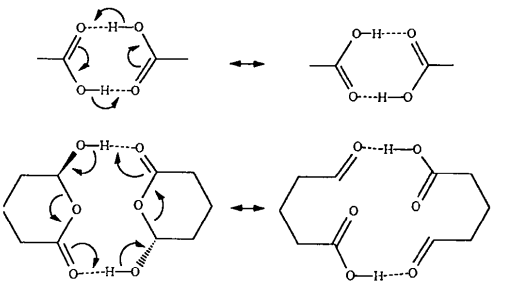
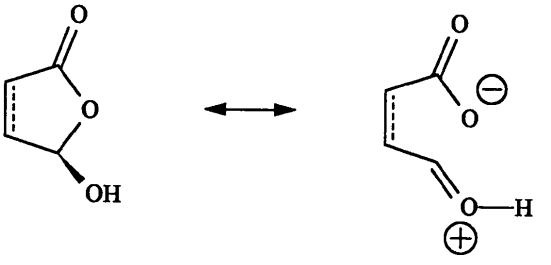


Fig. 7. Thermal ellipsoid plot (50%) of pseudoacid 2-carboxyphenylacetaldehyde (11), showing the hydrogen-bonded dimer.



3.4. *C—O bonds*

Table 9 presents selected bond lengths for the pseudoacids (6)–(11). All of these pseudoacids are *trans*-2,3-disubstituted aliphatic, (*Z*)-olefinic or *o*-disubstituted aromatic oxoacids. Compounds (6) and (11) are 5-oxoacids and form pyranoid pseudoacids; (7)–(10) are 4-oxoacids and form furanoid pseudoacids. The furanoid lactol rings of the latter group are nearly planar. Exocyclic hydroxy groups are necessarily disposed out of the ring plane with a torsion near 115°. Endocyclic C—O bonds (1.46–1.48 Å) are generally ~0.08–0.10 Å longer than the exocyclic C—O(H) (1.36–1.38 Å). This may be rationalized by an increased participation of resonance structures representing the superior leaving group tendency of carboxylate relative to the hydroxide ion attached at the lactol (or former aldehyde/ketone carbonyl) carbon. The endocyclic lactol C—O lengthens while the exocyclic C—O shortens. Effectively, the exocyclic C=O$^+$ contribution acts to somewhat enhance the ionic component of the exocyclic C—O bond relative to that expected from the sum of covalent radii (Schomaker & Stevenson, 1941; Pauling, 1960). Correspondingly, the endocyclic C···O$^-$ contribution acts to offset partially the influence due to the ionic component of the endocyclic C—O bond.

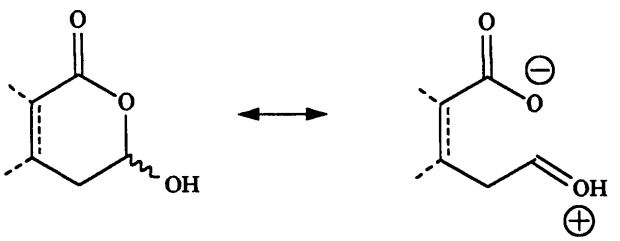


In the two pyranoid or δ-oxoacid structures (6) and (11), each has a 2,3-disubstitution pattern. Again, the endocyclic C—O distances (1.46–1.48 Å) are longer by 0.08–0.09 Å than the exocyclic C—O(H) (1.37–1.38 Å) distances. In the ground state, the increased participation of resonance structures in which carboxylate has

Table 9. *Selected C—O bond lengths (Å), angles (°) and torsions (°) in cyclic 4- and 5-oxoacids (e.s.d.'s in parentheses)*

	Distances				Angles		
	C=O	=C—O_n	O_n—C	C—O_x	O_n—C—O_x	C—O_n—C	τ(C—O_n—C—O_x)
Five-ring, furanoid or γ-pseudoacids							
(7)	1.221 (4)	1.348 (4)	1.457 (3)	1.382 (4)	108.7 (2)	109.6 (2)	−119.2 (2)
(8)*A*	1.204 (7)	1.332 (6)	1.470 (7)	1.382 (6)	108.8 (4)	110.4 (4)	−117.6 (4)
(8)*B*	1.194 (7)	1.361 (6)	1.461 (5)	1.365 (6)	110.4 (4)	110.7 (3)	118.5 (5)
(9)	1.212 (3)	1.344 (3)	1.468 (3)	1.381 (3)	110.3 (2)	110.8 (1)	115.1 (2)
(10)	1.210 (2)	1.348 (2)	1.486 (2)	1.381 (2)	108.8 (2)	111.4 (1)	112.9 (1)
Six-ring, pyranoid or δ-pseudoacids							
(6)	1.210 (2)	1.317 (2)	1.480 (2)	1.374 (2)	105.8 (1)	124.8 (1)	133 (1)
(11)	1.219 (2)	1.334 (1)	1.462 (2)	1.385 (2)	109.4 (1)	119.0 (1)	−74 (1)

superior leaving-group tendencies relative to the hydroxide ion at the (former) carbonyl carbon also provides a rationalization for these C—O distance disparities. According to this model, the partial double-bond character of the exocyclic C—O bond would be facilitated in an equatorial (β) hydroxy conformer relative to an axial (β) form. This C—O length in (6), which has an equatorial OH, is significantly shorter, and the endocyclic C—O length significantly longer, than in (11), which is in the axial conformation. A similar shortening of the β-exocyclic C—O bonds relative to the α orientation has been noted in tetrahydropyranyl acetals (Briggs *et al.*, 1984). In both the five- and six-ring pseudoacids, the endocyclic C—O lengths are consistent with the lengthening seen in γ- and δ-lactones and are among the longer of such examples. The shorter exocyclic C—O lengths are comparable to the exocyclic C—O's in β-pyranoses (1.390 Å) and somewhat shorter than in α-pyranoses (1.409 Å; Bürgi & Dunitz, 1994). The mean values and length disparity between the adjacent C—O's are similar to those for the hemiketals of warfarin (Ruggiero *et al.*, 1990), in which conjugate acids of the respective leaving groups are the warfarin enol (pK_a, observed = 5.5; Stella *et al.*, 1984) and water (pK_a = 15.74). In the pseudoacid series the corresponding groups are carboxylic acids (pK_a's ≃ 3.5–5) and water.



4. Summary

Some substituted aliphatic, as well as (*Z*)-olefinic and *o*-disubstituted, 4- and 5-oxoacids may exist in the form of the cyclic pseudoacids, also called lactols, and in the aromatic case, phthalides. Nominally single Csp^3—O bonds from the lactol carbon show clear disparity which may be modeled by the participation of double-bond/no-bond resonance structures. The pseudoacid endocyclic leaving group (carboxylate) is superior to the exocyclic leaving group (hydroxide) and the endocyclic C—O is longer than the exocyclic C—O distance. In the five-membered ring pseudoacids, the rings are essentially planar and the hydroxy groups typically form intermolecular hydrogen bonds with the lactone-like carbonyl oxygen of adjacent molecules. Six-membered ring pseudoacids are more conformationally flexible and the lactol hydroxy groups may have anomeric conformations. Intermolecular hydrogen bonding between hydroxy and carbonyl groups also occurs and in the case of *o*-carboxyphenylacetaldehyde, a pseudoacid dimer forms.

This contribution is made with thanks to, and in recognition of, Dr Verner Schomaker (Professor of Chemistry, Emeritus, University of Washington). His many valuable contributions to the study of chemical bonding and the understanding of the results of diffraction experiments have enriched science and have stimulated his students. We gratefully acknowledge the National Institutes of Health (AREA grant GM42198), the National Science Foundation (ILI-USE9250769) and the Office of Naval Research (DURIP 88450-0340) for instrumental support, and Dr Jeffrey D. Zubkowski and Mr Ali Jabalameli (Jackson State University).

References

Allen, F. H. & Kirby, A. J. (1984). *J. Am. Chem. Soc.* **106**, 6197–6200.

Becke, F. & Flemming, W. (1952). German Patent 844,293, to BASF; *Chem. Abstr.* 7054*a* (1954).

Bhatt, M. V. & Kamath, K. M. (1968). *J. Chem. Soc. B*, pp. 1036–1044.

Birkinshaw, J. H., Oxford, A. E. & Ratstrick, H. (1936). *Biochem. J.* **30**, 394–411.

Bowden, K. & Malik, F. P. (1993). *J. Chem. Soc. Perkin Trans. 2*, pp. 635–639.

Bredt, J. (1886). *Ann.* **236**, 225–240.

Briggs, A. J., Glenn, R., Jones, P. G., Kirby, A. J. & Ramaswamy, P. (1984). *J. Am. Chem. Soc.* **106**, 6200–6206.
Bürgi, H.-B. & Dunitz, J. D. (1994). *Structure Correlation*, Vol. 2, Appendix A. New York: VCH Publishers.
Claeson, G. & Thalen, A. (1967). *Arkiv Kemi*, **29**, 311–322.
Dickens, F. (1964). *Br. Med. Bull.* **20**, 96–101.
Dickens, F. (1965). *Br. J. Cancer*, **19**, 392–403.
Diesback, H. de & Riat, H. (1937). *Helv. Chim. Acta*, **24**, 1306–1316.
Erley, D. S., Potts, W. J., Jones, P. R. & Desio, P. J. (1964). *Chem. Ind.* pp. 1915–1916.
Finkelstein, J., Williams, T., Toome, V. & Traiman, S. (1967). *J. Org. Chem.* **32**, 3229–3230.
Gupta, M. P. & Prasad, S. M. (1970). *Indian J. Phys.* **44**, 138–140.
Jones, P. R. (1963). *Chem. Rev.* **63**, 461–487.
Jones, P. R. & Desio P. J. (1965). *J. Org. Chem.* **30**, 4293–4298.
Lalancette, R. A., Vanderhoff, P. A. & Thompson, H. W. (1990). *Acta Cryst.* C**46**, 1682–1686.
Levy, G. C. & Nelson, G. L. (1972). *Carbon-13 Nuclear Magneitic Resonance for Organic Chemists*, ch. 8. New York: Wiley Interscience.
Mikhno, S. D., Berezovskii, V. M. & Preobrazhenskii, N. A. (1962). *Zh. Obshch. Khim.* **32**, 2829–2831.
Mowry, D. (1950). *J. Am. Chem. Soc.* **72**, 2535–2537.
Pascual, C., Wegman, D., Graf, U., Sheffold, R., Sonner, P. F. & Simon, W. (1964). *Helv. Chim. Acta*, **47**, 213–221.
Pauling, L. (1960). *The Nature of the Chemical Bond*, 3rd ed., ch. 3. Ithaca, New York: Cornell University Press.
Piacenti, F. & Pino, P. (1961). *Ann. Chim.* **51**, 803–822.
Pouchert, C. J. (1983). Editor. *The Aldrich Library of NMR Spectra*, ed. II, Vol. 1, p. 594*c*. Milwaukee: Aldrich Chemical Co.
Ruggiero, G., Thaggard, A., Valente, E. J. & Eggleston, D. S. (1990). *Acta Cryst.* B**46**, 629–637.
Schomaker, V. & Stevenson, D. P. (1941). *J. Am. Chem. Soc.* **63**, 37–40.
Schöpf, C. & Kühne, R. (1950). *Chem. Ber.* **83**, 390–394.
Sheffold, R. & Dubs, P. (1967). *Helv. Chim. Acta*, **50**, 798–808.
Sheldrick, G. M. (1985). *SHELXS86. Program for Crystal Structure Determination*. University of Göttingen, Germany.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Shemyakin, M. M. (1943). *J. Gen. Chem.* **13**, 290–300 (USSR, English summary).
Siemens (1989*a*). *P3/PC Diffractometer Program*. Version 3.13. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Siemens (1989*b*). *XDISK. Diffractometer Program*. Version 3.11. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Stella, V. J., Mooney, K. G. & Pipkin, J. D. (1984). *J. Pharm. Sci.* **73**, 946–948.
Tyman, J. H. P. & Najam, A. A. (1977). *Spectrochim. Acta A*, **33**, 479–485.
Warnell, J. L. & Shriner R. L. (1957). *J. Am. Chem. Soc.* **79**, 3165–3167.