Table 5. *Hydrogen-bond lengths* (Å) *and angles* (°)

$D-H\cdots A$	Position of acceptor atom	$D\cdots A$	$H\cdots A$	$\angle D-H\cdots A$	$\angle H-D\cdots A$
$N-H(N)\cdots Cl(1)$	x, y, z	3·17	2·30	151·0	21·0
$N-H'(N)\cdots Cl(2)$	x, y, z	3·17	2·29	161·2	13·5
$N-H''(N)\cdots Cl(2)$	$x, 1-y, \frac{1}{2}+z$	3·22	2·58	133·3	35·0
$O-N(O)\cdots Cl(1)$	$\frac{1}{2}-x, \frac{1}{2}+y, z$	3·04	2·09	172·0	5·5

Conformation

Fig. 3 is an *ORTEP* plot of the molecule. The conformation of the ethylamine side chain and its relation to the benzene ring in tyramine hydrochloride are described by torsion angles τ_1 and τ_2 involving atoms C(4)–C(3)–C(7)–C(8) and C(3)–C(7)–C(8)–N respectively, the values of τ_1 and τ_2 being 69 and 178° respectively. These values agree well with those of most of the other sympathomimetic amines investigated. The phenethylamine side chain in the molecule is maximally extended (*trans* conformation) and the distance of the N atom from the centre of the ring has been found to be 5·14 Å, as in some other sympathomimetic amines, *e.g.* 5·14 Å in dopamine (Bergin & Carlström, 1968), 5·2 Å in hydroxy-ephedrine (Dattagupta & Saha, 1977) and 5·2 Å in phenylephrine (Bhaduri & Saha, 1975). In most of the sympathomimetic amines so far studied as well as in some structurally dissimilar sympathomimetic amines (Post & Kennard, 1974; Giesecke, 1973), this distance of the N atom from the centre of the benzene ring has been found to be around 5 Å. This distance appears to be a significant requirement for a compound to have sympathomimetic properties.

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The Conformation and Crystal Structure of *meso*-2,10-Dimethyl-3,11-dimethoxycarbonyl-1,6,9,13-tetraoxadispiro[4.2.4.2]tetradeca-2,10-diene

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Abstract

The crystal and molecular structure of the title compound, $C_{16}H_{20}O_8$, has been determined by single-crystal X-ray diffraction. The compound crystallizes in the monoclinic space group $P2_1/c$ with two molecules in a cell of dimensions $a = 9\cdot199$ (1), $b = 12\cdot423$ (1), $c = 8\cdot047$ (1) Å, and $\beta = 114\cdot87$ (1)°. The structure was solved by direct methods (*MULTAN*). Full-matrix least-squares refinement gave a final agreement index of $R = 0\cdot054$ for 1166 observed reflections. The six-membered ring adopts the chair conformation around a

symmetry centre. The conformation of the five-membered rings is nearer to a twist than to an envelope, the approximate twofold axis passing through the C(4) atom. The endocyclic C—O bonds are asymmetric and the C=C distance is longer than expected for a double bond. Crystal packing is due to van der Waals interactions only.

Introduction

The 'Knoevenagel reaction' of carbonyl compounds with active methylene groups is a very useful instrument of organic synthesis for carbon—carbon bond formation, and, along with the Doebner modification, it has been applied in many cases. The application of the Knoevenagel reaction to the carbohydrate field offers new routes for the synthesis of furane compounds starting from monosaccharides. However, in some cases it shows some peculiarities and the structure of the resulting products is different from that expected from the usual reaction.
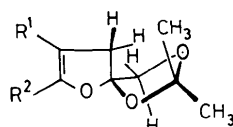

(I) $R^1 = COR'$
      $R^2 = CH_3$ or Ph

By reaction of O-isopropylidene-D-glyceraldehyde with β-diketones or β-ketoesters, unsaturated compounds having the structure of a spiroketal (I) are obtained as a result of intramolecular cyclization. Its structure has been deduced from spectroscopic data, degradation reactions and functional-group interconversion. A new type of cyclization yielding dispiroketals is easily performed by treating (I) with acid in an aprotic solvent.
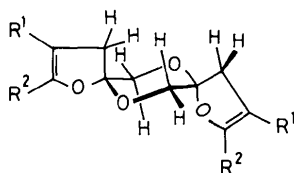
(II)
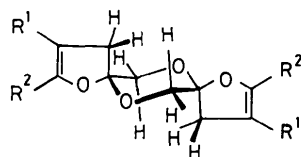
(III)

In spite of their optical inactivity, two isomeric forms (II) and (III) are possible owing to the existence of two chiral centres. Mass spectroscopy data (López-Aparicio, López-Herrera & Sanchez-Ballesteros, 1978) suggest the centrosymmetric trans configuration (III) but this result is subject to personal interpretation according to a hypothetical fragmentation process.

As mentioned above, the Knoevenagel reaction in the organic chemistry field requires a more detailed study and a better knowledge of the structures of the compounds produced. For this reason an X-ray study of the title compound was undertaken at the suggestion of Professor F. J. López-Aparicio of the Organic Chemistry Department, University of Granada, and is now reported.

Experimental

The compound was in the form of colourless prismatic crystals. Preliminary unit-cell dimensions and space-group information were obtained from oscillation and Weissenberg photographs taken with Cu $K\alpha$ radiation. With two molecules in the unit cell, it was necessary to place the molecule centre on a symmetry centre. Accurate cell dimensions (Table 1) were obtained by least-squares refinement of the θ values of 50 reflexions measured on a Philips PW 1100 automated four-circle diffractometer. Intensity data were also collected on this instrument using graphite-monochromated Cu $K\alpha$ radiation and the ω–2θ step scanning mode. Intensity data were collected over the range $2° < \theta < 65°$ to give a total of 1386 independent reflexions of which 1166 were classified as observed by the criterion $I > 2\sigma(I)$.

Structure determination

The structure was solved by a weighted multisolution tangent refinement (MULTAN, Main, Lessinger, Woolfson, Germain & Declercq, 1977). 172 reflexions with $|E| > 1.40$ (approximately fourteen reflexions for non-hydrogen atoms in the asymmetric unit) were used and a choice of phasing was possible based on FOM's; the highest combined figure of merit derived using unit weights for the components was 2·0. An E map computed with this phase set had distinguishable peaks for all non-hydrogen atoms.

Table 1. *Crystal data*

Formula	$C_{16}H_{20}O_8$
Space group	$P2_1/c$ (C_{2h}^5, No. 14)
a	9·199 (1) Å
b	12·423 (1)
c	8·047 (1)
β	114·87 (1)°
V	834·32 Å^3
Z	2
D_{cal}	1·35 Mg m^{-3}
D_{exp}	1·37 (2) Mg m^{-3}
$F(000)$	680

Refinement proceeded by the full-matrix least-squares method, using only the observed reflexions and initially with all non-hydrogen atoms treated isotropically, to give an R value of 0·11. A difference Fourier synthesis showed electron density maxima in the vicinity of the H-atom calculated positions. Further refinement with non-hydrogen atoms treated anisotropically, and hydrogen atoms isotropically (the H positions and their isotropic temperature factors were also included in the refinement) produced convergence with $R = 0·054$. The weighting scheme $w = 1/\sigma^2(F)$, where $\sigma^2(F)$ is derived from $\sigma^2(I)$, was employed. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974) and computing programs of the XRAY system (1970) were used. The final positional parameters for non-hydrogen atoms are in Table 2. Positional and thermal parameters for hydrogen atoms are in Table 3.*

Description of the structure

The bond lengths and angles involving non-hydrogen atoms are illustrated in Fig. 1. Displacements of the

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34021 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Atomic coordinates ($\times 10^4$) for non-hydrogen atoms

	x	y	z
O(1)	8391 (3)	9272 (2)	−2666 (3)
O(2)	9129 (3)	9230 (2)	472 (3)
O(3)	3556 (3)	8105 (2)	−4882 (4)
O(4)	3377 (3)	9332 (2)	−2934 (3)
C(1)	6914 (4)	8813 (3)	−3605 (5)
C(2)	5831 (4)	9144 (3)	−3013 (5)
C(3)	6578 (4)	9958 (3)	−1508 (5)
C(4)	8345 (4)	9866 (3)	−1125 (5)
C(5)	10794 (4)	9077 (3)	943 (5)
C(6)	6844 (6)	8054 (4)	−5047 (6)
C(7)	4173 (4)	8787 (3)	−3738 (5)
C(8)	1739 (6)	9017 (5)	−3462 (9)

Table 3. Coordinates ($\times 10^3$) and thermal parameters ($\times 10^2$) for the hydrogen atoms

	x	y	z	U (Å²)
H(31)	621 (5)	1068 (3)	−183 (5)	2 (1)
H(32)	644 (4)	976 (3)	−41 (5)	1 (1)
H(51)	1096 (4)	859 (3)	−3 (5)	1 (1)
H(52)	1121 (5)	860 (3)	205 (6)	3 (1)
H(61)	722 (6)	837 (4)	−596 (6)	6 (1)
H(62)	565 (6)	775 (4)	−580 (7)	5 (1)
H(63)	769 (6)	747 (4)	−454 (6)	4 (1)
H(81)	128 (6)	949 (4)	−304 (7)	5 (1)
H(82)	177 (7)	814 (4)	−278 (7)	6 (1)
H(83)	128 (6)	884 (5)	−440 (9)	6 (2)

atoms from the least-squares planes through some atomic groups are given in Table 4. Torsional angles defining the configuration and conformation are listed in Table 5.

The six-membered ring adopts the chair conformation. It is puckered in such a manner that the four atoms O(2), O(2'), C(5) and C(5') lie on a plane but the atoms C(4) and C(4') are substantially displaced from this plane on either side, as observed from least-squares plane I (Table 4). The values of torsional angles through the ring bonds do not show significant deviations from their average value of 53·7°. The endocyclic C—C bond length of 1·508 (4) Å agrees with the average value reported for analogous rings and the two C—O bonds are equal within experimental error (2σ). The internal ring angles agree with the standard value of 111·5° (Dunitz, 1968) but the C—O—C angle is significantly larger.

The puckering of the five-membered rings is intermediate between a twist and an envelope conformation. In terms of the pseudorotational description proposed

Table 4. Least-squares planes through some atomic groups

(a) Equations of the planes in direct space

$$\text{I} \quad -1·410x + 5·809y + 6·874z = 4·400$$
Atoms defining the plane: O(2), O(2'), C(5), C(5').

$$\text{II} \quad 0·193x + 9·351y − 4·875z = 10·132$$
Atoms defining the plane: O(1), C(1), C(2).

$$\text{III} \quad 0·173x + 8·556y − 5·355z = 9·604$$
Atoms defining the plane: O(3), O(4), C(7), C(8).

(b) Deviations of atoms (Å $\times 10^3$)

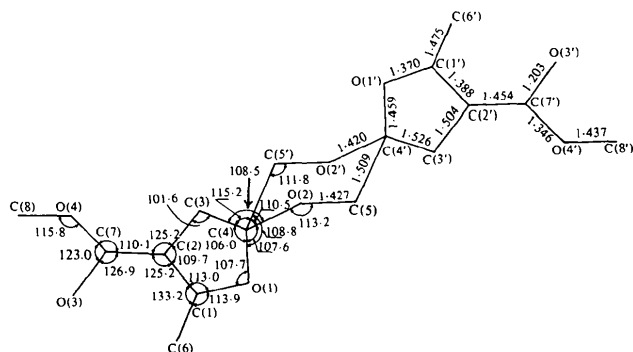| I		II		III	
O(2)	0	O(1)	0	O(3)	6
O(2')	0	C(1)	0	O(4)	10
C(5)	0	C(2)	0	C(7)	−12
C(5')	0	C(3)	42	C(8)	−5
C(4)	−618	C(4)	−196	C(2)	−66
C(4')	618	C(7)	−12	C(3)	−162
C(3)	−579	C(6)	−7	C(1)	−13
O(1)	−2029				

Fig. 1. Bond lengths (Å) and angles (°) for non-hydrogen atoms. (E.s.d.'s are 0·004 Å for bond lengths and 0·3° for angles.)
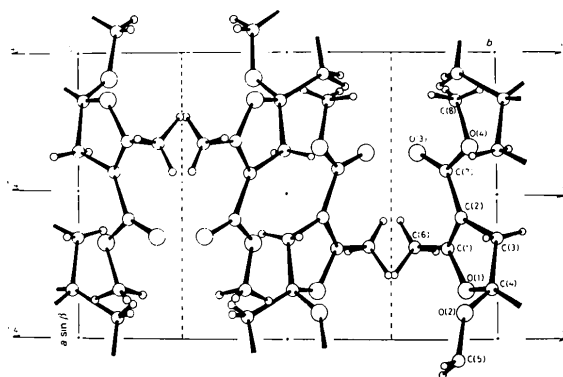
Table 5. *Selected torsional angles in the molecule* (°)

(E.s.d.'s are 0·5°.)

(*a*) Six-membered ring

C(4)–O(2)–C(5)–C(4')	54·4
O(2)–C(5)–C(4')–O(2')	−52·9
C(5)–C(4')–O(2')–C(5')	53·8

(*b*) Five-membered ring

O(1)–C(1)–C(2)–C(3)	1·7
C(1)–C(2)–C(3)–C(4)	−10·1
C(2)–C(3)–C(4)–O(1)	14·3
C(3)–C(4)–O(1)–C(1)	−14·2
C(4)–O(1)–C(1)–C(2)	8·1

(*c*) Junction of the rings

O(1)–C(4)–O(2)–C(5)	64·8
O(1)–C(4)–C(5')–O(2')	−65·0
C(3)–C(4)–O(2)–C(5)	179·1
C(3)–C(4)–C(5')–O(2')	176·3

(*d*) Carboxyl group

C(3)–C(2)–C(7)–O(3)	−176·5
C(3)–C(2)–C(7)–O(4)	3·2
C(1)–C(2)–C(7)–O(3)	4·8
C(1)–C(2)–C(7)–O(4)	−175·5

Fig. 2. A view of the structure down the *c* axis.

by Altona, Geise & Romers (1968), the 'phase angle' is $\Delta = 48·3°$ and the 'amplitude of puckering' $\varphi_m = 15·2°$. In this description we select $\Delta = 0°$ corresponding to a twofold rotation axis passing through O(1) and the mid-point of C(2)–C(3). The least-squares plane through O(1), C(1) and C(2) atoms (II) and the deviations of ring atoms from this plane are indicated in Table 4. The endocyclic C(1)–O(1) of 1·370 (3) Å and C(4)–O(1) of 1·459 (4) Å are asymmetric. The asymmetry of the endocyclic C–O bonds is observed in some pyranose derivatives (Sundaralingam, 1968) but in 1,2 unsaturated aldopyranose it is still more pronounced due to the influence of the C–C double bond. The C(1)–C(2) bond of 1·388 (5) Å is longer than expected for a double bond which suggests resonance forms involving the ring atoms. The junction of the five- and six-membered rings can be characterized by the torsional angles around C(4), with the C(4)–C(3) and C(4)–O(1) bonds in quasi-equatorial and axial positions, respectively. As in 1,4,9,12-tetraoxadispiro[4.2.4.2]tetradecane (Chadwick, Dunitz & Schweizer, 1977), the conformation of the ring is nearer to a twist than an envelope, but the approximate twofold axis passes now through the C(4) atom.

The carboxyl group is planar as expected (maximum atomic deviation from the least-squares plane III of Table 4 is 3σ). The mean plane is quasi-coplanar with the five-membered ring [the maximum torsional angle around C(7)–C(2) is 8°]. Bond lengths and angles agree with the standard values for this group except that the C(7)–C(2) bond is now shortened by the influence of the C–C double bond. Bond distances and angles involving H atoms show a reasonable agreement. Average values are 0·99 (5) Å for C–H bonds and 112 (3) for H–C–C, 109 (3) for H–C–O and 107 (3)° for H–O–C angles; the greatest deviations from these average values are smaller than 4σ for the bond lengths and 3σ for the bond angles. The maximum dispersion in H–C bond distances corresponds to the C(8)(methyl)–H and this could indicate a thermal motion effect.

The molecular packing in the crystal is illustrated in Fig. 2. The intermolecular distances do not give any evidence of hydrogen bonds. As can be seen from Fig. 2, the molecules pack in layers approximately parallel to (010). Molecules are held together by van der Waals interactions only and there are no intermolecular contacts that are significantly shorter than the sum of the corresponding van der Waals radii.

All calculations were carried out on a DCT 2000 terminal of the Centro de Calculo of this University, connected to a Univac 1108 computer.

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α-D-Glucose: Further Refinement Based on Neutron-Diffraction Data*

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Abstract

Precise translations were determined for α-D-glucose, $C_6H_{12}O_6$, (orthorhombic, $P2_12_12_1$) as follows: $a = 10.3662$ (9), $b = 14.8506$ (16), $c = 4.9753$ (3) Å at 294–296 K based on $\lambda(Cu\ K\alpha_1) = 1.54051$ Å. The structure has been further refined using neutron-diffraction data previously obtained [Brown & Levy (1965). *Science*, **147**, 1038–1039] and the full-matrix least-squares method, with anisotropic extinction corrections. The fit to the observations is much improved [$R(F) = 0.048$; standard deviation of fit = 1.053], and the parameter errors are slightly smaller. Parameter changes are slight and of no chemical significance. The segmented-body model has been used to calculate corrections to the bond lengths and valence angles for the effects of thermal motion. Bond lengths, valence angles, torsion angles, and details of hydrogen bonding are tabulated.

Introduction

Thirteen years ago (Brown & Levy, 1965) we reported atomic coordinates and selected derivative structural parameters for α-D-glucose from a fairly precise refinement, based on neutron-diffraction data, of the structure of McDonald & Beevers (1952). The data used in the 1965 work appear to be of high quality by present standards; but there are considerable extinction effects, and the least-squares refinement procedure did not include adjustment of extinction parameters. Instead,

we had attempted to minimize the effects of extinction by the somewhat unsatisfactory method of giving zero weights to the 37 observations of $|F_o|^2$ corresponding to the highest observed intensities. Because of the biochemical importance of α-D-glucose, we have now completed the refinement using our original data and applying anisotropic extinction corrections (Coppens & Hamilton, 1970). Shifts from the old parameters (Brown & Levy, 1965) are small (see below), but there is striking improvement in the fit to the observations, and there are slight decreases in the standard errors of the parameters. We have used the segmented-body model (Johnson, 1970) to analyze the new thermal parameters and thereby provide corrections to the bond lengths and valence angles for the effects of thermal motion. The bond length and angle data are also rendered more precise, and presumably more reliable, by use of the new, more precisely determined cell parameters which we also report here.

Data and refinement

The revised cell parameters (see *Abstract*) were determined, with the assistance of R. D. Ellison, by the least-squares method from the Bragg angles of 11 high-angle reflections ($138 \leq 2\theta \leq 165°$) from a small crystal on an X-ray diffractometer. In every significant detail the procedures in recording neutron-diffraction data and in preliminary data reduction were as in our work on sucrose (Brown & Levy, 1972). A total of 2168 intensity measurements were made for the 1656 independent reflections with indices all positive or zero to the limit 0.760 Å^{-1} in (sin $\theta)/\lambda$ ($\lambda = 1.078$ Å, $\theta_{max} = 55.0°$). For the absorption corrections (Busing & Levy, 1957) the coefficient was $\mu = 0.28$ mm^{-1}; the minimum