β -DIKETONE INTERACTIONS Part 10. The structure and properties of 3-(2',4'-dimethoxyphenyl)pentane-2,4-dione; enol ring symmetry and other hydrogen bond parameters

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ABSTRACT

The X-ray crystal structure of the title compound shows it to be the enol tautomer and with two molecules in the unit cell, with hydrogen bond lengths, $R(0 \cdot \cdot 0)$, of 2.446 and 2.474 Å. These and other hydrogen bond parameters $(\delta, \Delta\delta(H-D)$ and $\nu_{OHO})$ of similar compounds are compared and attempts made to relate them to Q, which is derived from the bond asymmetry of the enol ring.

INTRODUCTION

The enol tautomers of the β -diketones offer rare examples of strong hydrogen bonds in a neutral environment [1]. Pentane-2,4-dione (PD) itself has only a moderately strong bond judged by its $R(O \cdot O)$ of 2.535 Å, which was measured when this molecule fortuitously turned up in crystals of a drug complex [2]. On the other hand some 3-substituted derivatives of PD whose structures have been analysed, show OHO bonds significantly shorter than this [3-7], with $R(O \cdot O)$ below 2.45 Å, establishing them as strong hydrogen bonds [8].

Recently we have reported the structure, IR and NMR properties of 3-(4methoxyphenyl)pentane-2,4-dione [5]. To check the relative importance of steric and electronic factors on the hydrogen bond we have been able to synthesise the related molecule 3-(2,4-dimethoxyphenyl)pentane-2,4-dione and obtain crystals suitable for X-ray analysis. The structure, IR and NMR properties of this compound are now reported and compared not only with the mono-methoxy derivative, but with other 3-substituted β -diketones.

EXPERIMENTAL

3-(2',4'-Dimethoxyphenyl)pentane-2,4-dione, ($C_{13}H_{16}O_4$)

2,4-Dimethoxyphenyllead triacetate was prepared by the method of De Vos et al. [9] and Bell et al. [10]. 1,3-Dimethoxybenzene (4.5 g, 32.6 mmol) was added dropwise to a benzene solution of lead tetraacetate (10 g, 22.4 mmol) and dichloroacetic acid (9 g, 95 mmol). The mixture was stirred for 20 h, until all the lead tetraacetate had reacted. It was then washed with 100 cm³ water and hexane was added. The precipitated solid was filtered and dried. This was converted to the triacetate by stirring with 50 cm³ acetic acid in 40 cm³ chloroform for 1 h until the solution became clear. Hexane was added to precipitate the triacetate as yellow crystals (8.31 g, 72.6%).

2,4-Dimethoxyphenyllead triacetate (3.5 g, 6.7 mmol) and pyridine (2 cm³) were dissolved in CHCl₃ (14 cm³). Pentane-2,4-dione (0.7 g, 7.0 mmol) was added dropwise with stirring. The mixture was stirred at 40 °C for 48 h according to the method of Pinhey and Rowe [11]. The resultant solution was washed with water (20 cm³) and twice with 3 M H₂SO₄ (2×20 cm³) to remove the lead salt. The aqueous and acid solutions were extracted separately with CHCl₃ (10 cm³). The combined extracts were washed with water (2×25 cm³), dried over MgSO₄ and stripped of solvent to give a yellow solid. This was purified using a silica column with 10% ethyl acetate in 40/60 petroleum/ether as the eluant. The first fraction was collected and stripped of solvent to yield colourless crystals of 3-(2',4'-dimethoxyphenyl)pentane-2,4-dione (0.89 g, 56% yield) that were recrystallised from methanol, m.p.=64-66°C. Found: C, 65.94; H, 6.86%. C₁₃H₁₆O₄ requires: C, 66.09; H, 6.83%.

NMR spectra were recorded on a Bruker WM250 spectrometer (¹H at 250 MHz; ²H at 38.4 MHz). $\delta_{\rm H}/\rm{CDCl}_3$: 1.85 (s, 6H, MePD), 3.77 (s, 3H, OMe), 3.84 (s, 3H, OMe), 6.51 (m, 2H, 3,5-C₆H₂), 6.98 (d, 1H, 6-C₆H) and 16.65 (s, 1H, OHO). There was also evidence of a small amount of the keto tautomer at 2.16 (s, Me), 3.79 (s, OMe), and 3.82 (s, OMe) corresponding to ca. 2.5%. The keto CH and aromatic protons of this tautomer could not be clearly differentiated.

 $C_{13}H_{16}O_4$ is insoluble in water and shaking a solution of it in CDCl₃ with D_2O for 2 days did not effect exchange of the enol proton for deuterium. Shaking with a D_2O solution of K_2CO_3 however did achieve exchange to $C_{13}H_{15}O_4D$. The ²H chemical shifts of this showed the enol deuteron to resonate at 16.02, which represents an upfield shift of +0.63 for $\Delta\delta(H-D)$.

The IR spectrum, run on a Perkin Elmer 983G spectrometer, as a KBr disc, showed absorbances at 3215w,br, 2999m, 2939m, 2835m, 2581w,br, 2069w, 1606vs, 1580vs, 1505vs, 1457vs, 1436s, 1411vs, 1330s, 1301vs, 1276s, 1207vs, 1157vs, 1129s, 1116m, 1050s, 1031s,br, 995m, 971m, 920m, 910m, 847m, 829s, 806m, 739vw, 678w, 657w, 598w, 450w and 385w cm⁻¹. The spectral region 1100–1700 $\rm cm^{-1}$ is underlaid by an intense broad continuum characteristic of strong hydrogen bonding.

X-Ray structure determination

Crystal data: $C_{13}H_{16}O_4$, M = 236.267, triclinic, space group P1, a = 9.196(4), b = 11.209(4), c = 12.874(2) Å, $\alpha = 76.61(2)$, $\beta = 87.08(2)$, $\gamma = 100.17(3)^{\circ}$, U = 1265.02 Å³, Z = 4, $D_c = 1.241$ g cm⁻³, $\lambda = 0.71069$ Å, F(000) = 504.00, μ (Mo $K\alpha$) = 0.86 cm⁻¹, crystal size (0.75×0.63×0.55 mm).

TABLE 1

	x	у	z	
0(1)	1181(3)	3842(3)	5413(2)	
O(2)	2297(3)	3905(3)	3632(3)	
O(3)	-1164(3)	699(2)	4126(2)	
0(4)	-5999(3)	1400(3)	3082(3)	
C(1)	-260(4)	3186(3)	4112(3)	
C(2)	-92(4)	3391(3)	5130(3)	
C(3)	-1342(5)	3100(4)	5975(3)	
C(4)	1017(4)	3444(3)	3377(3)	
C(5)	986(5)	3156(5)	2324(4)	
C(6)	-1742(4)	2690(3)	3820(3)	
C(7)	-2773(4)	3456(3)	3551(3)	
C(8)	-4165(4)	3006(4)	3314(3)	
C(9)	-4583(4)	1765(4)	3345(3)	
C(10)	-6522(5)	119(5)	3149(4)	
C(11)	-3606(4)	955(3)	3605(3)	
C(12)	-2199(4)	1426(3)	3848(3)	
C(13)	-1544(5)	-605(4)	4183(4)	
0(1')	719(3)	-933(3)	1592(2)	
O(2')	-614(3)	832(3)	1207(2)	
O(3')	-3679(3)	-2636(3)	2793(2)	
0(4')	-6988(3)	-4279(3)	525(2)	
C(1')	-1734(4)	-1197(3)	1134(3)	
C(2')	-1758(5)	56(4)	1032(3)	
C(3')	-3053(6)	612(4)	733(4)	
C(4')	-424(4)	-1632(4)	1392(3)	
C(5')	-282(5)	-2942(4)	1419(4)	
C(6')	-3061(4)	-2045(3)	942(3)	
C(7')	-3383(4)	-2169(4)	-69(3)	
C(8')	-4655(4)	-2906(4)	-264(3)	
C(9')	-5656(4)	-3558(3)	596(3)	
C(10')	-7378(5)	-4378(4)	-504(4)	
C(11')	-5362(4)	-3501(4)	1633(3)	
C(12')	-4087(4)	-2763(3)	1799(3)	
C(13')	-4565(5)	-3404(5)	3712(3)	

Fractional atomic co-ordinates $(\times 10^4)$ for $C_{13}H_{16}O_4$

TABLE 2

Bond lengths (Å) and angles (deg) for $\rm C_{13}H_{16}O_4$

Parameter	Value	Parameter	Value
Bond lengths			
C(2) - O(1)	1.296(5)	C(4) - O(2)	1.289(5)
C(12)-O(3)	1.368(5)	C(13)-O(3)	1.425(5)
C(9)-O(4)	1.378(5)	C(10) - O(4)	1.412(6)
C(2)-C(1)	1.393(6)	C(4)-C(1)	1.414(6)
C(6)-C(1)	1.480(5)	C(3)-C(2)	1.480(6)
C(5)-C(4)	1.465(7)	C(7) - C(6)	1.392(5)
C(12)-C(6)	1.396(5)	C(8) - C(7)	1.368(6)
C(9)-C(8)	1.367(6)	C(11)-C(9)	1.387(6)
C(12)-C(11)	1.388(6)	C(4')-O(1')	1.271(5)
C(2') - O(2')	1.306(5)	C(12')-O(3')	1.383(5)
C(13') - O(3')	1.410(6)	C(9')-O(4')	1.363(5)
C(10')-O(4')	1.414(6)	C(2')-C(1')	1.385(6)
C(4')-C(1')	1.405(6)	C(6')-C(1')	1.478(6)
C(3')-C(2')	1.467(7)	C(5')-C(4')	1.489(7)
C(7')-C(6')	1.383(6)	C(12')-C(6')	1.403(6)
C(8')-C(7')	1.378(6)	C(9')-C(8')	1.375(6)
C(11')-C(9')	1.390(6)	C(12')-C(11')	1.367(6)
Bond angles			
C(13)-O(3)-C(12)	118.9(4)	C(10)-O(4)-C(9)	118.4(4)
C(4)-C(1)-C(2)	118.5(4)	C(6)-C(1)-C(2)	120.4(4)
C(6)-C(1)-C(4)	121.1(4)	C(1)-C(2)-O(1)	122.4(4)
C(3)-C(2)-O(1)	114.7(4)	C(3)-C(2)-C(1)	122.9(4)
C(1)-C(4)-O(2)	120.5(5)	C(5)-C(4)-O(2)	116.5(4)
C(5)-C(4)-C(1)	122.9(4)	C(7)-C(6)-C(1)	121.3(4)
C(12)-C(6)-C(1)	121.8(4)	C(12)-C(6)-C(7)	116.9(4)
C(8)-C(7)-C(6)	122.1(4)	C(9)-C(8)-C(7)	119.8(4)
C(8)-C(9)-O(4)	115.8(4)	C(11)-C(9)-O(4)	123.5(4)
C(11)-C(9)-C(8)	120.8(4)	C(12)-C(11)-C(9)	118.6(4)
C(6)-C(12)-O(3)	115.3(4)	C(11)-C(12)-O(3)	122.9(4)
C(11)-C(12)-C(6)	121.8(4)	C(13')-O(3')-C(12')	118.1(4)
C(10')-O(4')-C(9')	118.1(4)	C(4')-C(1')-C(2')	118.9(4)
C(6')-C(1')-C(2')	119.9(4)	C(6')-C(1')-C(4')	121.1(4)
C(1')-C(2')-O(2')	121.8(5)	C(3')-C(2')-O(2')	115.0(5)
C(3')-C(2')-C(1')	123.2(5)	C(1')-C(4')-O(1')	122.4(5)
C(5')-C(4')-O(1')	116.0(5)	C(5')-C(4')-C(1')	121.6(4)
C(7')-C(6')-C(1')	123.0(4)	C(12')-C(6')-C(1')	120.8(4)
C(12')-C(6')-C(7')	116.2(4)	C(8')-C(7')-C(6')	123.6(4)
C(9')-C(8')-C(7')	118.2(4)	C(8')-C(9')-O(4')	124.9(4)
C(11')-C(9')-O(4')	114.6(4)	C(11')-C(9')-C(8')	120.5(4)
C(12')-C(11')-C(9')	119.8(4)	C(6')-C(12')-O(3')	113.6(4)
C(11')-C(12')-O(3')	124.8(4)	C(11')-C(12')-C(6')	121.6(4)
O(2)-H(16)-O(1)	152.1(15)	O(2')-H(16')-O(1')	149.5(14)

Data collection

Unit-cell dimensions were determined and intensity data were collected at room temperature on an Enraf-Nonius CAD4 diffractometer using graphitemonochromated Mo $K\alpha$ radiation and an ω -2 θ scan procedure. A total of 4453 unique reflections were collected $(3 < 2\theta < 50^{\circ})$. The segment of reciprocal space scanned was: $(h) \ 0 \rightarrow 10$, $(k) \ -13 \rightarrow 13$, $(l) \ -15 \rightarrow 15$. The reflection intensities were corrected for absorption using the azimuthal-scan method [12]; maximum transmission factor 0.997, minimum value 0.968.

Structure solution and refinement

The structure was solved by the application of routine direct methods (SHELX-86) [13], and refined by full-matrix least-squares (SHELX-76) [14]. The asymmetric unit contains two independent molecules. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined isotrop-



Fig. 1. The molecular structure and numbering scheme of the two molecules of $3 \cdot (2', 4' \cdot dimethoxyphenyl)$ pentane-2,4-dione, (1) and (1'), in the unit cell.



Fig. 2. The unit cell of the crystal viewed (a) along the *a* axis, and (b) along the *b* axis.

ically. The final residuals R and R_G were 0.0510 and 0.0445 for the 435 variables and 2732 data for which $F_0 > 3\sigma(F_0)$. The function minimised was $\sum_w (|F_0| - |F_c|)^2$ with unit weights. All computations were made on a CAS286AT (IBM PC clone) computer with two on-board T800 transputers. Table 1 lists the atomic coordinates and Table 2 the bond lengths and angles. The two kinds of hydrogen bond had $R(0 \cdot 0)$ 2.445 and 2.475 Å respectively. The molecular structure and atom numbering is shown in Fig. 1, and portions of the lattice as viewed down the *a* and *b* axes in Fig. 2. Non-hydrogen atom anisotropic temperature factors, hydrogen fractional atomic coordinates and isotropic temperature factors and selected non-bonded distances are deposited as supplementary data^{*}.

DISCUSSION

We have previously published [5-7] the results of five structural determinations of *para*-substituted derivatives of 3-phenylpentane-2,4-dione, all of which exist as enol tautomers in the solid state. Each exhibited a shorter hydrogen bond length $R(0 \cdot \cdot 0)$ than that of pentane-2,4-dione itself, and this we interpret as the best, but not the only, evidence of strong hydrogen bonding. The substituents on the phenyl ring were 4'-methoxy [5], 4'-biphenyl [6], 4'-nitro, 4'-phenoxy and 4'-isopropyl [7]. Only small variations in hydrogen bond length were observed and these could not be related to the electronic effects of the ring substituents.

The conclusion is that introduction of the phenyl ring at the 3-position of pentane-2,4-dione has the same steric effect in each molecule. The aromatic ring, which is nearly perpendicular to the enol ring in each case, is exerting steric pressure on the methyl groups, and in this way is forcing the "pincers" of the two carbonyl groups closer together to create a shorter hydrogen bond.



This being so, then it was surmised that added leverage could be achieved by having an *ortho* substituent on the phenyl ring. It was hoped that in this way the transition from strong to very strong hydrogen bonding could be achieved. With the 2',4'-dimethoxyphenyl derivative reported here we have achieved our aim, and it too gave crystals suitable for X-ray diffraction analysis.

The structure of $C_{13}H_{16}O_4$ shows it to be entirely in the enol tautomeric

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configuration. In the unit cell there are two molecules with hydrogen bond lengths of 2.445 and 2.475 Å. These values are very similar to the 2.449 Å of the mono-4'-methoxy derivative [5] showing that no extra steric congestion of the molecule has occurred, or if steric pressure has increased then it is dissipated without affecting the hydrogen bond.

The ¹H and ²H NMR spectra of $C_{13}H_{16}O_4$ have the chemical shift of the enol proton at 16.65, exactly the same as the mono-4'-methoxy compound [5], and in accord with a hydrogen bond length of ca. 2.45 Å [7]. Little can be inferred from δ_{OHO} alone. The NMR isotopic shift, $\Delta\delta(H-D)$, is much more informative and in this case is +0.63, which indicates a strong hydrogen bond [1]. This value is greater than the +0.31 of its monomethoxy counterpart, but very like the +0.61 of the biphenyl derivative [6]. Positive $\Delta\delta(H-D)$ proves conclusively that the hydrogen bonding is strong; the proton is easily able to surmount or tunnel through the internal energy barrier but the deuteron is constrained to one well. Negative values of $\Delta\delta(H-D)$ are found when the bond is very strong and both H and D are above the internal barrier [1].

The location of the hydrogen bond proton, as shown by X-ray diffraction indicates an asymmetry of the OHO bond. However it is the more accurately determined heavy atom bond lengths of the enol ring which have excited comment in a recent paper by Gilli et al. [15]. The symmetry of the enol ring is different in our two molecules.



In Gilli's paper the difference between the carbon-oxygen bond lengths (q_1) and carbon-carbon bond lengths (q_2) around the enol ring is correlated to other structure and energy parameters in what is termed "resonance assisted hydrogen bonding". For 20 compounds with the molecular fragment H-O-C=C-C=O, for which structural data are available, q_1 and q_2 vary from almost zero to 0.12 Å [16]. It was shown that q_1 and q_2 are linearly related, and because this is so their sum, designated Q, is used as the quantity to be correlated with other properties. In ref. 16 a plot of hydrogen bond length, $R(O \cdot O)$, versus Qshowed a relationship.

The types of compound used in ref. 15 included ten β -diketones, chiefly derivatives of dibenzoylmethane, and ten other structures with hydroxy and carbonyl groups suitably orientated to form the same kind of hydrogen bonding. From our results on the structures of pentane-2,4-dione derivatives we are in a position to test Gilli's thesis on a group of six closely related molecules and the data is listed in Table 3. The results are rather disappointing. In Fig. 3 we show a scatter plot of Q for the seven hydrogen bonds of Table 3, together with

Substituent	<i>R</i> (0··0) (Å)	R(C-O) (Å)	R(C=O) (Å)	R(C-C) (Å)	R(C=C) (Å)	q_1	q_2	$egin{array}{c} Q \ (q_1 + q_2) \end{array}$	$\delta_{ m OHO}$	v _{оно}	Ref.
4-Isopropyl	2.419	1.315	1.281	1.404	1.390	0.034	0.014	0.048	16.67	1475	7
4-Phenyl	2.441	1.292	1.290	1.409	1.396	0.002	0.013	0.015	16.72	1485	6
4-Phenoxy	2.443	1.249	1.284	1.418	1.406	0.010	0.012	0.022	16.69	1488	7
4-Nitro	2.445	1.309	1.270	1.432	1.379	0.039	0.053	0.092	16.78	1414	7
2,4-Dimethoxy	2.446	1.296	1.289	1.414	1.393	0.007	0.021	0.028	16.65	1411	This
	2.474	1.306	1.271	1.405	1.385	0.035	0.020	0.055			paper
4-Methoxy	2.449	1.301	1.283	1.406	1.391	0.018	0.015	0.033	16.65	1510	5

Selected data of the phenyl substituted derivatives of 3-phenylpentane-2,4-dione



Fig. 3. Plot of hydrogen bond lengths, $R(0 \cdot \cdot 0)$, versus asymmetry factor, Q, for derivatives of 3-phenylpentane-2,4-dione (\Box) and other β -diketones (\blacksquare).

other β -diketone enol structures [1] in which the enol's carbons are not part of another cyclic system. It requires the eye of faith to see any relationship in this constellation of points.

Inspection of Table 3 also shows that Q does not relate in any meaningful way to the chemical shift of the proton of the hydrogen bond, δ_{OHO} , or its stretching vibrational mode, ν_{OHO} . Although $R(O \cdot \cdot O)$ is not varying a great deal $(2.45 \pm 0.05 \text{ Å})$ the symmetry of the ring does vary and so does Q. Hydrogen bonds are clearly sensitive to the vagaries of crystal forces rather than to "resonance-assistance" from the hydrogen bonding [15].

Vibrational modes

A previous paper [7] argued that early assignments of the stretching mode of the strong hydrogen bonds, ν_{OHO} , of pentane-2,4-dione and its derivatives

substituted at the 3 position were probably wrong, in that they attributed $\nu_{\rm OHO}$ to weak bands at ca. 2500 cm⁻¹. Broad bands underlying the carbonyl modes were shown to be due to $\nu_{\rm OHO}$, and for molecules in which the hydrogen bond is <2.45 Å these bands should come below 1690 cm⁻¹. The IR spectrum of the $C_{13}H_{16}O_4$ shows a broad band over the region 1100–1700 cm⁻¹ with many other bands superimposed upon it.

Since two OHO bond lengths of the unit cell are very nearly the same we cannot expect to differentiate two broad $\nu_{\rm OHO}$ signals. There are three submaxima to the broad band at ca. 1600, 1450 and ca. 1200 cm⁻¹. There is also an underlying broad band at 1030 cm⁻¹. The first of these broad bands is $\nu_{\rm C=0}$, in line with previous assignments for molecules of this kind [7]. The band at 1450 cm⁻¹ is allotted to the $\nu_{\rm OHO}$, leaving the bands at 1200 and 1030 cm⁻¹ for the corresponding in and out-of-plane bending vibrations of the hydrogen bond [1].

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