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Crystals of 5-phenylbarbituric acid, **2**, are monoclinic, space group  $C2/c$ . There are 8 molecules in the unit cell of dimensions  $a = 20.218(3)$ ,  $b = 7.477(1)$ ,  $c = 12.443(2)$ ,  $\beta = 111.54^\circ$  and  $V = 1749.6(4) \text{ \AA}^3$ . Full-matrix least-squares refinement has reached  $R = 0.039$ . This is the first barbiturate reported to exist in the enol form in the solid state. There is extensive hydrogen bonding between adjacent molecules which gives rise to very dense crystals. The  $^{13}\text{C}$ -nmr spectroscopy shows that **2** exists in both enol and keto forms in DMSO solution.

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### Introduction.

Koffer [3] has determined the  $\text{pK}_a$ s of several 5-alkylbarbituric acids and 5-phenylbarbituric acid, **2**, by means of relaxation techniques. 5-Methylbarbituric acid, **3**, and 5-ethylbarbituric acid, **4**, were found to be stronger acids than barbituric acid, **1** which is in contrast to the +I effect of these two substituents. The kinetic measurements

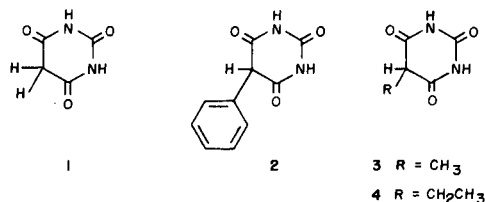


Table I

Fractional atomic coordinates and thermal parameters ( $\times 10^4$ ) for non-hydrogen and ( $\times 10^3$ ) for hydrogen atoms. (The estimated standard deviations are given in parenthesis and refer to the last positions of respective values.)

The expression for the thermal parameters with U values in  $\text{\AA}^2$  is:

$$T = \exp\{-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hfa^*c^* + 2U_{23}kfb^*c^*)\}$$

Atom	x	y	z	U11	U22	U33	U12	U13	U23
N(1)	933(1)	9210(3)	818(2)	231(10)	402(13)	265(11)	-12( 9)	74( 8)	63( 9)
C(2)	568(1)	8691(3)	1486(2)	247(12)	350(14)	238(13)	-20(11)	63(10)	-2(11)
O(2)	-80(1)	8838(2)	1183(1)	183( 9)	627(12)	361(10)	22( 8)	76( 7)	127( 8)
N(3)	978(1)	7985(3)	2519(1)	252(10)	377(12)	276(11)	5( 9)	147( 9)	39( 9)
C(4)	1697(1)	7748(3)	2872(2)	242(13)	288(13)	231(12)	35(11)	77(10)	-12(10)
O(4)	1947(1)	6911(2)	3870(1)	264( 8)	414(10)	265( 9)	88( 7)	108( 7)	90( 7)
C(5)	2064(1)	8369(3)	2223(2)	241(12)	272(14)	234(13)	13(10)	87(10)	-3( 9)
C(6)	1665(1)	9205(3)	1154(2)	267(13)	270(13)	265(14)	-40(10)	107(11)	-54(10)
O(6)	1916(1)	9927(2)	483(1)	275( 9)	405(10)	288( 9)	-52( 7)	109( 7)	31( 7)
C(1')	2851(1)	8307(3)	2611(2)	265(12)	248(14)	323(13)	1(10)	114(10)	31( 9)
C(2')	3187(1)	7616(4)	1906(2)	353(13)	354(15)	409(16)	-5(12)	170(13)	25(12)
C(3')	3914(1)	7643(4)	2257(3)	361(14)	453(18)	650(20)	44(15)	281(16)	82(13)
C(4')	4322(2)	8351(4)	3309(3)	240(14)	475(19)	813(24)	30(17)	152(15)	74(13)
C(5')	4001(1)	9021(4)	4025(3)	273(14)	455(17)	478(18)	-41(14)	3(14)	79(13)
C(6')	3273(1)	9018(3)	3679(2)	334(14)	339(15)	352(15)	23(12)	106(12)	29(11)
H(1)	69(1)	974(4)	18(2)	50( 8)					
H(3)	79(1)	777(3)	297(2)	19( 5)					
H(4)	237(1)	640(3)	404(2)	48( 7)					
H(2')	291(1)	709(3)	118(2)	27( 6)					
H(3')	413(2)	715(5)	178(3)	90(12)					
H(4')	480(2)	838(4)	354(3)	67(10)					
H(5')	431(1)	941(4)	476(3)	46( 8)					
H(6')	306(1)	948(3)	416(2)	26( 6)					

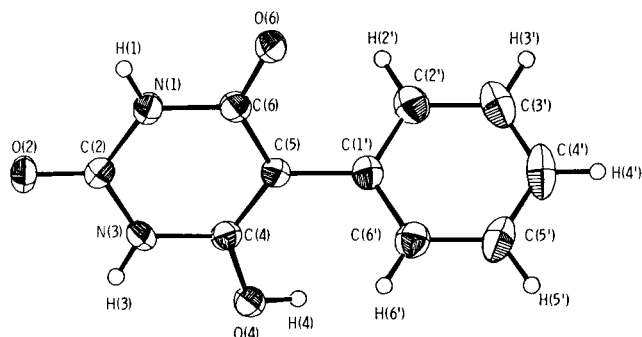


Fig. 1. ORTEP drawing of the molecule. Thermal ellipsoids are scaled at 50% probability level. The hydrogen atoms are represented as circles of arbitrary radius.

indicated that the influence of the substituent on protolysis could be explained more satisfactorily by the structure of solvent, water, rather than by the inductive effect of the alkyl groups. By analyzing the kinetic data, Koffer was able to calculate enol-keto equilibrium constants which were in the range of 0.04 to 0.003 for the 5-alkyl-substituted acid indicating that protolysis of these acids involved essentially the *C*-acid (keto form).

On the other hand, the greater acidity of 5-phenylbarbituric acid, **2**, ( $pK_a = 2.54$ ) as compared to **1** was in accord with the inductive effect of the phenyl group. The calculated enol/keto ratio for compound **2** was 1.2 suggesting that protolysis involved predominately the *O*-acid (enol) form. Since this type of ionization of a barbiturate was unprecedented in the literature, we decided to seek experimental evidence for the enol form of **2**.

This paper presents  $^{13}\text{C}$ -nmr spectroscopic evidence for enol/keto tautomerism of **2** in DMSO and the x-ray structural analysis of the title compound in the solid state.

## EXPERIMENTAL

### Crystal Data.

The crystals of **2** were recrystallized from water to yield colorless transparent plates. A crystal of approximate size  $0.33 \times 0.33 \times 0.06$  mm was selected for the determination of unit-cell parameters and the intensity measurements. Accurate unit-cell dimensions were obtained by least-squares fit of 15 reflections with  $2\theta$  values ranging from  $20^\circ$  to  $39^\circ$ , measured on a Syntex P2, automatic diffractometer with graphite monochromatized  $\text{MoK}\alpha$  radiation. The crystals are monoclinic, space group *Cc* or *C2/c* from the systematic absences ( $hkl$ ,  $h+k = 2n+1$ ;  $hol$ ,  $l = 2n+1$ ), the latter being confirmed by the successful solution and refinement of the structure. The unit-cell parameters are  $a = 20.218(3)$ ,  $b = 7.477(1)$ ,  $c = 12.443(2)$  Å,  $\beta = 111.54(1)^\circ$  and volume  $V = 1749.6(4)$  Å<sup>3</sup>. The formula weight of **2**,  $\text{C}_{10}\text{H}_8\text{O}_3\text{N}_2$  is 204.2. The density of 1.550 g/cm<sup>3</sup> calculated for 8 molecules per cell is in good agreement with the value of 1.53 g/cm<sup>3</sup> measured by flotation. The intensity data were collected in the  $\theta/2\theta$  scanning mode. A total of 1153 unique reflections was measured to  $2\theta = 45^\circ$ , of which 830 were considered as observed by the criterion  $I > 3\sigma(I)$ , where  $\sigma(I)$  was determined by counting statistics. The intensity data were reduced to structure amplitudes by application of the Lorentz and polarization factors. No absorption correction was applied ( $\mu_{\text{MoK}\alpha} = 0.73$  cm<sup>-1</sup>).

### Structure Determination.

The structure was solved by direct methods using MULTAN 78 [4] which showed the positions of all non-hydrogen atoms. Full-matrix least-squares refinements were carried out using SHELX 76 [5]. The non-hydrogen atoms were refined with anisotropic temperature factors. All hydro-

Table II

Bond lengths (Å) and bond angles ( $^\circ$ ) with estimated standard deviations in parentheses.

Bond Lengths					
N(1)	-	C(2)	1.355(3)		
N(1)	-	C(6)	1.382(3)		
C(2)	-	O(2)	1.228(3)		
C(2)	-	N(3)	1.355(3)		
N(3)	-	C(4)	1.367(3)		
C(4)	-	O(4)	1.315(3)		
C(4)	-	C(5)	1.363(3)		
C(5)	-	C(6)	1.422(3)		
C(5)	-	C(1')	1.484(3)		
C(6)	-	O(6)	1.248(3)		
C(1')	-	C(2')	1.391(3)		
C(1')	-	C(6')	1.394(3)		
C(2')	-	C(3')	1.371(4)		
C(3')	-	C(4')	1.372(5)		
C(4')	-	C(5')	1.375(5)		
C(5')	-	C(6')	1.373(4)		
Bond Angles					
C(2)	-	N(1)	-	C(6)	125.3(2)
N(1)	-	C(2)	-	O(2)	123.1(2)
N(1)	-	C(2)	-	N(3)	114.3(2)
O(2)	-	C(2)	-	N(3)	122.6(2)
C(2)	-	N(3)	-	C(4)	124.3(2)
N(3)	-	C(4)	-	O(4)	111.1(2)
N(3)	-	C(4)	-	C(5)	120.8(2)
O(4)	-	C(4)	-	C(5)	128.1(2)
C(4)	-	C(5)	-	C(6)	117.3(2)
C(4)	-	C(5)	-	C(1')	123.3(2)
C(6)	-	C(5)	-	C(1')	119.4(2)
N(1)	-	C(6)	-	C(5)	117.4(2)
N(1)	-	C(6)	-	O(6)	116.7(2)
C(5)	-	O(6)	-	O(6)	125.8(2)
C(5)	-	C(1')	-	C(2')	121.3(2)
C(5)	-	C(1')	-	C(6')	120.4(2)
C(2')	-	C(1')	-	C(6')	118.2(2)
C(1')	-	C(2')	-	C(3')	120.5(2)
C(2')	-	C(3')	-	C(4')	120.6(3)
C(3')	-	C(4')	-	C(5')	119.8(3)
C(4')	-	C(5')	-	C(6')	120.2(3)
C(1')	-	C(6')	-	C(5')	120.6(2)

### Hydrogen bonding contacts

N(1) ... O(2)'	2.855(3)	N(1)-H(1)-O(2)'	172(3)
H(1) ... O(2)'	2.00(3)		
N(3) ... O(2)''	2.909(3)	N(3)-H(3)-O(2)''	145(2)
H(3) ... O(2)''	2.23(2)		
O(4) ... O(6)'''	2.603(2)	O(4)-H(4)-O(6)'''	164(3)
H(4) ... O(6)'''	1.75(3)		

Superscripts refer to atoms in the following positions:

I -  $x, 2-y, -z$  II -  $x, y, \frac{1}{2}-z$  III  $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}-z$   
IV (see Fig. 2)  $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$

rogen atoms were located in a difference Fourier map and were allowed to refine with isotropic temperature factors. The weighting scheme used in the least-squares was  $w = 1/(\sigma^2 F_o + 4.95 \times 10^{-3} F_o^2)$  and the quantity minimized was  $\Sigma w(|F_o| - |F_c|)^2$ . The final agreement factors are  $R = 0.039$  and  $R_w = 0.041$  for the 830 observed reflections. The final difference Fourier map showed a maximum residual electron density of  $0.21 \text{ e}/\text{\AA}^3$ . The scattering factors for all atomic species were taken from the International Tables for X-ray Crystallography [6]. The final atomic coordinates and temperature factors are given in Table I.

#### Preparation of 5-Phenylbarbituric Acid. 2.

5-Phenylbarbituric acid was prepared by the condensation of urea with diethyl phenylmalonate in the presence of sodium ethoxide in ethanol in a manner described previously [7].

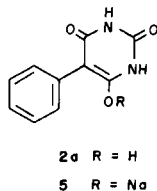
#### $^{13}\text{C}$ NMR Spectroscopy.

The decoupled and coupled  $^{13}\text{C}$ -nmr spectra of **2** were recorded in  $d_6$ -DMSO (1.0 mmole in 1.5 ml  $d_6$ -DMSO) using the solvent as reference (39.5 ppm). The  $^{13}\text{C}$  spectra of the anion of **2** were recorded in 0.5 mmol of sample in 2 ml 2 M NaOD solutions with an external  $d_6$ -DMSO reference standard (coaxial capillary tube). All spectra were obtained using a WP 200-SY Bruker spectrometer operating at a frequency of 50.327 MHz. Spectral widths of 220 ppm were employed using 2 s relaxation delays. Data was collected with 16K data points (1.35 Hz/pt) with a pulse width of 10  $\mu\text{s}$  corresponding to a tip angle of  $33^\circ$ . The spectra with smaller spectral widths ( $\sim 1500$  Hz) were used to evaluate the coupling constants and to measure precisely chemical shifts with resolution of  $\pm 0.15 - 0.18$  Hz per data point.

#### Results and Discussion.

##### X-ray Analysis.

The identification of the atoms and the configuration of the molecule are shown in the ORTEP [8] drawing of Figure 1. The bond lengths and bond angles with their standard deviations are given in Table II. The distance C(4)-C(5) and C(5)-C(6), which should be equivalent if the molecule was symmetrical and existed in the keto form, are quite different in the enol form. Thus, the distance C(4)-C(5) of  $1.363(3) \text{ \AA}$  has a much greater double bond character than the bond C(5)-C(6) of  $1.422(3) \text{ \AA}$ . Similarly, the C(6)-O(6) distance of  $1.248(3) \text{ \AA}$  is substantially shorter than  $1.315(3) \text{ \AA}$  found for the C(4)-O(4) bond. These distances are consistent with the enol structure of 5-phenylbarbituric acid, **2a**, shown below.



The planarity of the two 6-membered rings can be estimated from Table III. The angle between these two planes is  $51.7(1)$ . The torsion angles involving the C(5)-C(1') bond are: C(4)-C(5)-C(1')-C(6) =  $52.8(4)^\circ$ , C(4)-C(5)-C(1')-C(2') =  $130.1(3)^\circ$ , C(6)-C(5)-C(1')-C(2') =  $57.3(4)^\circ$  and C(6)-C(5)-C(1')-C(6') =  $123.4(3)^\circ$ .

Table III  
Least-Squares Planes

Deviation ( $\text{\AA}$ ) of atoms from least squares planes (\* refers to atoms excluded from the calculation of the least-squares plane).

Atom	Deviation	Atom	Deviation
N(1)	-0.044(3)	C(1')	0.000(3)
C(2)	0.005(3)	C(2')	-0.002(4)
N(3)	0.027(3)	C(3')	0.001(4)
C(4)	-0.033(3)	C(4')	0.006(5)
C(5)	-0.004(3)	C(5')	-0.008(4)
C(6)	0.041(3)	C(6')	0.002(3)
O(2)*	0.023(3)	C(5)*	0.063(4)
O(4)*	-0.098(4)		
O(6)*	0.141(4)		
C(1')*	0.064(4)		

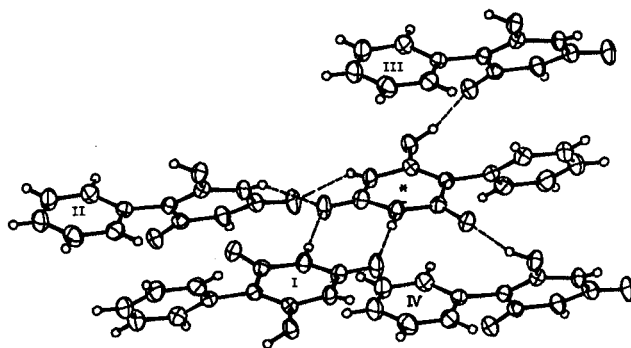


Fig. 2. Hydrogen bonding between neighboring molecules. Molecules marked with Roman numerals are generated through the symmetry operators given in Table 2. That marked with an asterisk has coordinates (xyz).

As can be seen in Fig. 2, there is extensive intermolecular hydrogen bonding in the crystals. All potential sites participate in hydrogen bonding of the type  $\text{NH}\cdots\text{O}$  and  $\text{OH}\cdots\text{O}$ . The enol hydrogen attached to O(4) is involved in

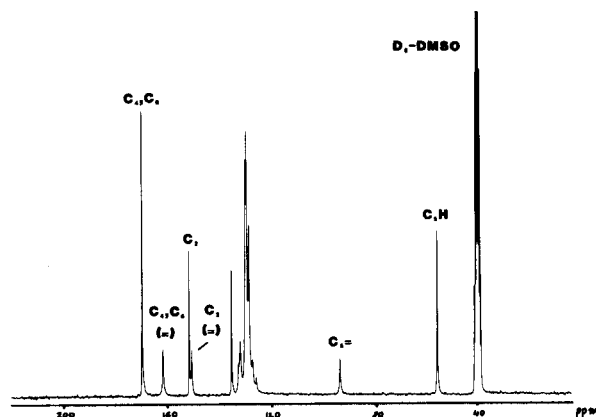


Fig. 3a. The  $^1\text{H}$ -decoupled  $^{13}\text{C}$  spectrum of 5-phenylbarbituric acid (spectral width 220 ppm).

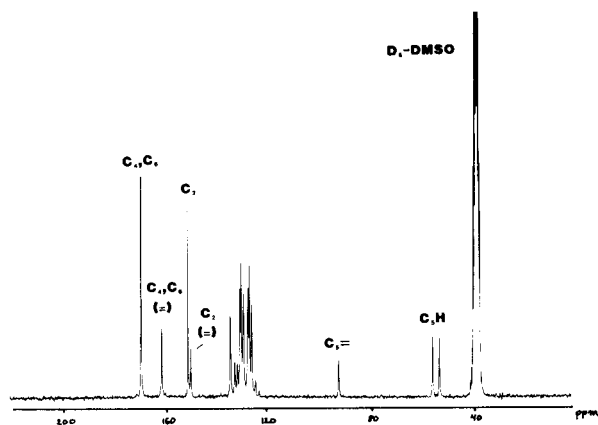


Fig. 3b. The  $^1\text{H}$ -coupled  $^{13}\text{C}$  spectrum of 5-phenylbarbituric acid (spectral width 220 ppm).

a strong hydrogen bond linking two molecules through a 2<sub>1</sub>-screw axis. The distance O(4)···O(6') is 2.603(2) Å. Each nitrogen atom participates in a pair of hydrogen bonds either across a center of symmetry for N(1) or a diad axis for N(2). The distances N(1)···O(2) and N(3)···O(2) are 2.855(3) Å and 2.909(3) Å, respectively. More details about the geometry of these hydrogen bonds are given in Table 2. The density of the crystals of **2** is extremely high and reflects the extensive intramolecular hydrogen bonding within the crystals.

#### $^{13}\text{C}$ NMR Spectroscopy.

The  $^1\text{H}$ -decoupled and  $^1\text{H}$ -coupled  $^{13}\text{C}$ -nmr spectrum of **2** in  $d_6$ -DMSO are shown in Figs. 3a and 3b, respectively. They indicate clearly the presence of both keto and enol forms;  $^{13}\text{C}$  chemical shift assignments are shown in Table 4. The signal at 55.1 ppm in the decoupled spectrum, which is split into a doublet in the coupled spectrum, is assigned to C-5 of the keto form of **2**, whereas the resonance signal in both spectra at 92.8 ppm is assigned to the C-5 of the enol form, **2a**. To confirm these assignments, the decoupled and coupled  $^{13}\text{C}$  nmr spectra of 5-phenylbarbituric enolate anion, **5**, were recorded in 2M NaOD and are shown in Figs. 4a and 4b, respectively. The absence of the resonance at 55.1 and the presence of the resonance at 93.3 ppm support the  $^{13}\text{C}$  chemical shift assignments of C-5 of the enol and keto forms of **2**.

The aromatic region in Figs 3a and 3b indicate a mixture of the two forms. The  $^{13}\text{C}$  resonance of the 5-phenyl group were assigned by comparison of the  $^1\text{H}$ -coupled and  $^1\text{H}$ -decoupled spectra. The quaternary carbon (C-1') is distinguished easily from the other aromatic carbon atoms due to the lack of  $^1\text{J}_{\text{C,H}}$  coupling. The three remaining sets were assigned to C-3'(5') (doublet of doublet - one  $^3\text{J}_{\text{C,H}}$ ); C-2'(6') (doublet of triplets - two  $^3\text{J}_{\text{C,H}}$ ); C-4' (doublet of triplets but with half the intensity of the signal assigned to

Table 4

$^{13}\text{C}$  Chemical Shifts of 5-Phenylbarbituric Acid **2**, and its Enolate Anion, **5** [a,b]

Resonance	<b>2a</b>	<b>2</b>	<b>5</b> [c]
C-2	150.0	151.1	159.2
C-4	161.3 [d]	169.3	170.0
C-5	92.8	55.1	93.3
C-6	161.7 [d]	169.3	170.0
C-1'	134.8 [e]	134.6	135.6
C-2'(6')	131.9	129.3	130.4
C-3'(5')	131.1	128.9	126.7
C-4'	126.6	128.0	124.3

[a]  $\delta$  ppm. [b] Downfield from TMS and using the solvent as double reference standard;  $d_6$ -DMSO = 39.5 ppm [c] Measured as 0.75M solution in 2M NaOD and with hexadeuteriomethyl sulfoxide as the external reference. [d] The two assignments could be reversed. [e] Partially overlapped with C-1' of **2**.

to C-2'(6'). The remaining resonances of the keto form of **2** were assigned as follows: C-4 and C-6 carbonyl carbons at 169.3 ppm and C-2 carbonyl carbon at 151.1 ppm, whereas those of the enol form, **2a**, were assigned to C-4 and C-6 enol carbons at 161.3 ppm and 161.7 ppm and to C-2 carbonyl carbon at 150.0 ppm. In the spectrum of enolate anion, **5**, only two resonances appear in the lower field.

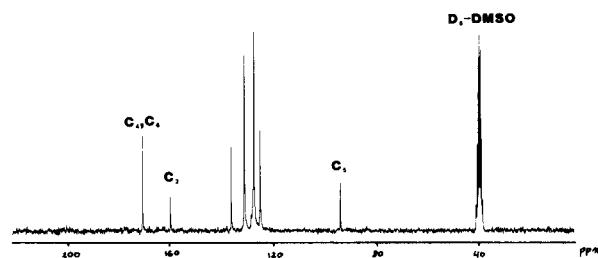


Fig. 4a. The  $^1\text{H}$ -decoupled  $^{13}\text{C}$  spectrum of 5-phenylbarbituric enolate anion (spectral width 220 ppm).

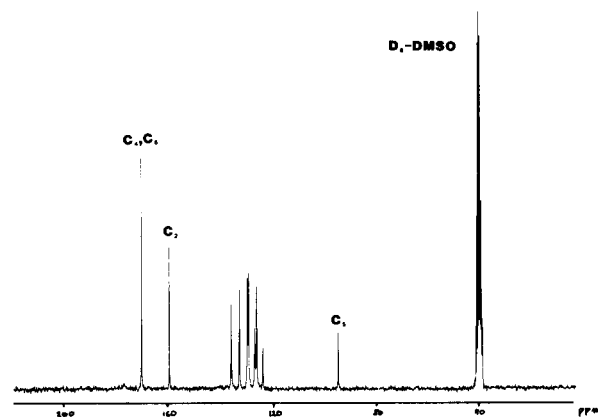


Fig. 4b. The  $^1\text{H}$ -coupled  $^{13}\text{C}$  spectrum of 5-phenylbarbituric enolate anion (spectral width 220 ppm).

The  $^{13}\text{C}$  signal at 170.0 ppm was assigned to the two equivalent C-4 and C-6 carbon atoms and the other 159.2 was assigned to the C-2 carbonyl carbon of **5**.

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