Tetrahedron Letters Vol. 21, pp 4491 - 4494
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0040-4039/80/1115-4491$02.00/0

TAUTOMERISM IN ACYL TETRONIC ACIDS

S. Gelin*

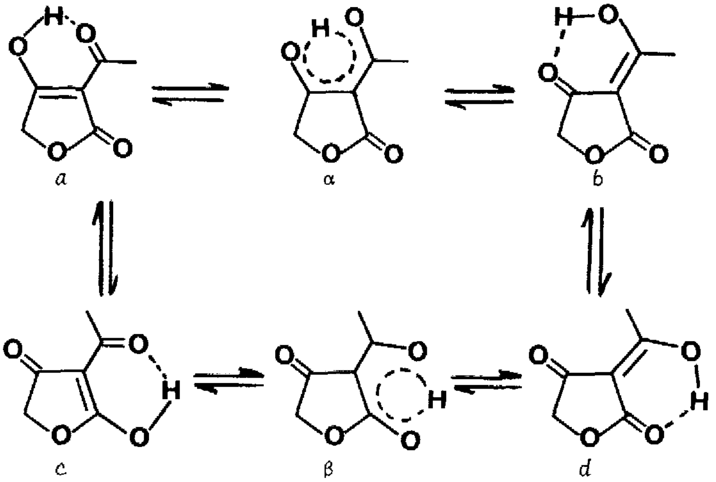
Laboratoire de Chimie Organique, Institut National des Sciences Appliquées
Villeurbanne, 69621 F

P. Pollet

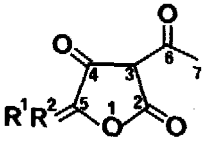
Department of Chemistry, University of Petroleum and Minerals, P.O. Box 298,
Dharan, Saudi Arabia

The tautomeric structures of some acetyl tetronic acids are studied by NMR *analysis.*

The studies of the tautomeric structures of acyl tetronic acids has been recently investigated[1-4]. These compounds could possibly exist in four tautomeric forms. The equilibria between the external tautomers *a*,*b*$\rightleftharpoons$c,*d* are expected to be slow, with regard to spectra averaging and the equilibria between the internal tautomers *a*$\rightleftharpoons$*b*, c$\rightleftharpoons$*d* fast. Highly delocalized forms α and β has been postulated as the best description of each tautomeric pair[4]. However, there is a clear conflict regarding the assignment in the ^{1}H-NMR spectra of the observed two sets of signals arising from the splitting of the methylene or the methine protons at C-5 in each external tautomeric pair. The downfield signal has been attributed either to the c,*d* forms on the basis of a diamagnetic effect of the ring carbonyl[1,2], or to the *a*,*b* forms since the C-5 proton (s) next to the carbonyl function would resonate at higher field compared to the corresponding proton (s) next to a double bond[3].



In order to clarify this discrepancy, we report here the results of an investigation by 350 ^{1}H-NMR and ^{13}C-NMR of some acetyl tetronic acids[5,6] (3-acetyl-2,4-oxolanediones) 1-3.



1 $R^1 = R^2 = H$
2 $R^1 = H$, $R^2 = Me$
3 $R^1R^2 = CHPh$

Strikingly, the 350 MHz ^{1}H-NMR spectra of compounds 1 and 2 display two sets of lines as a reflect of the tautomeric equilibria. The ratio of the tautomers is roughly the same 60/40, regardless of the nature of the C-5 substituents. In contrast, no tautomeric equilibrium is detected for 5-benzylidene-3-acetyl-2,4-oxolanedione 3, which shows a single set of signals (table 1).

In deuteriochloroform solution, the ^{13}C-NMR spectrum of 2 gives rise to two resonances for all the carbon atoms in a 60/40 ratio; whereas, for compound 1 the carbonyl lines sequence were too broad to be seen. Compound 3 shows only one set of sharp lines. In DMSO-d_6 solution, compound 2 exhibits only seven distinct peaks for seven types of carbon atoms. The straithforward assignment, summarized in table 2 is based on off-resonance decoupling and examination of the gated decoupled spectra. In the gated decoupled spectrum of 2, the quartets (^2J=6 Hz) at δ 194.68 and 188.55 arise from the C-6 carbon atom. The signals at δ 200.32 and 195.47 were assigned to the C-4 carbon. This carbon is coupled with the H-5 proton (doublet ^2J=4 Hz) and with the C-5 methyl group (quartet ^3J=2 Hz). The C-2 carbon resonances at δ 167.85 and 175.92 appear as a doublet (^3J=2 Hz). In the spectrum of 3, the quadruplet at δ 197.25, ^2J=6.5 Hz, the singlet at 164.67 and the doublet at 181.02 were assigned to the carbon atoms at the position C-6, C-2 and C-4 respectively.

In a previous ^{13}C-NMR study of a series of tetronic acids[4], it was claimed that the predominant tautomeric species is the β-form, by considering, for example in compound 2, the α-form as giving the lower field signal at δ 175.75. However, it is known that a hydrogen-bonded carbonyl resonates at lower field than a corresponding free carbonyl[7]. Therefore, it can be assumed that the predominant tautomer is the α (or *a*,*b*) form(s) and consequently, the chemical shifts previously erroneously attributed to the β (or *c*,*d*) form(s) are those to the α (or *a*,*b*) form(s). Subsequently, in the ^{1}H-NMR spectra, the most intense downfield of the two resonances for the C-5 proton(s) must be attributed to the *a*,*b* forms according to[3] and not to the *c*,*d* forms as previously assigned[1,2].

The direction of enolization of a number of β-di-or-tricarbonyl systems has been studied by ^{1}H or ^{13}C-NMR spectroscopy[8-11]. Of particular interest are the ^{13}C-NMR results obtained from 2-acetylcyclopentanone[11] and 2-acetylcyclopentan-1,3-dione[10], in which the carbons chemical shifts can be related to the tautomeric form. It can be observed that the methyl carbon resonance of the side chain is shielded of 4.8 ppm by the change of a free

Table 1 - 350 MHz ^{1}H-NMR of tetronic acids 1-3; δ ($CDCl_3$)(a)

Compound	H (C-5)	CH_3 (C-7)	R^2	OH (enol)
1 *a*,*b* 59%	4.67 (s)	2.56 (s)		11.7
1 c,*d* 41%	4.56 (s)	2.57 (s)		11.7
2 *a*,*b* 60%	4.83 (q)	2.57 (s)	1.51 (d)	12.2
2 c,*d* 40%	4.71 (q)	2.57 (s)	1.53 (d)	12.2
3 *a*	(b)	2.57		11.5

(a) recorded on a 350 MHz Cameca spectrometer.
(b) 6.62 (1H,s); 7.3-7.5 (2H,m); 7.7-7.9 (3H,m).

Table 2 - ^{13}C-chemical schifts for derivatives of tetronic acids 2,3 (a)

Compound	Solvent	C-2	C-3	C-4	C-5	C-6	C-7	R^2
2 *a*,*b* 60%	$CDCl_3$	167.85	100.37	200.32	76.40	194.68	22.39	16.81
2 c,*d* 40%		175.93	97.40	195.47	81.98	188.55	19.54	17.17
2	DMSO-d_6	170.19	98.95	194.4	76.26	190.80	24.00	17.00
3 *a*	$CDCl_3$	164.67	100.43	181.02	140.61	197.25	25.15	(b)

(a) recorded on a Brucker WP80 spectrometer with respect to Me_4Si, t ≈ 30° ; samples were dissolved in $CDCl_3$ or DMSO-d_6 (300 mg/3 ml).
(b) = CH 113.44 C_6H_5 : C'1 not observed; C'2,6 129.13; C'3,5 131.70; C'4 130.43

carbonyl by an enolized carbonyl group; 2-(1-hydroxyethylidene)-cyclopentanone, δ = 20.3, and 2-acetyl-1-hydroxycyclopent-1-ene, δ = 25.1 . Furthermore, the magnitude of the chemical shift of a methyl carbon α to an hydrogen-bonded carbonyl is quite close in o-hydroxyacetophenone (δ = 25.4)[7] or in 2-acetylcyclopentan-1,3-dione (δ = 25.6)[10], which is reported to exist predominantly as 2-acetyl-3-hydroxycyclopent-2-ene-1-one form. These findings seem to indicate that the shift of this methyl carbon is fairly independant of the other moiety of the molecule. It may be, therefore, assumed that the compound 3 is best represented as tautomeric form *a* (δ CH_3 = 25.15). In the other hand, the chemical shift of the C-7 methyl carbon (δ = 19.54) in the tautomeric pair 2c⇄2*d*, clearly argues for the predominant, if not all, form *d*, having an exocyclic double bond at C-3.

Using the values of 3*a* and 2*b* as endo and exo tautomers, the population of the tautomers 2*a* ⇄ 2*b* could be tentatively estimated from the observed chemical schift (δ = 22.39), the mole fraction x of the *a* and *b* tautomers at equilibrium given by :

$$22.39 = x_a(25.15) + x_b(19.54) \qquad x_a = 0.5$$

This result may reflect either the symmetrical structure α or an equal population of the two tautomers 2*a* and 2*b* in rapid equilibrium.

From the presence of only one set of methylene signals in the ^{1}H-NMR spectrum of 1 in DMSO-d_6 solution, it has been concluded that the strong solvatation effect of this polar solvent, rapidly, drives the tautomeric equilibria toward the major tautomers in chloroform, $c \rightleftharpoons d$ forms for the authors[2]. We have presented evidence that, in fact, they are the $a \rightleftharpoons b$ forms. Our ^{13}C-NMR study (C-7 methyl carbon δ 24.0) seems in accordance to a greater population of solvated form 2*a* than 2*b*.

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(Received in France 18 July 1980)