Acta Chemica Scandinavica B 31 (1977) 756—760

^{13}C Nuclear Magnetic Resonance Spectra of Some 3-Acyltetronic Acids

JENS PETER JACOBSEN, TORSTEN REFFSTRUP and PER M. BOLL

Department of Chemistry, Odense University, DK-5000 Odense, Denmark

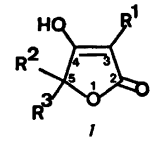
3-Acyltetronic acids (*1c*–*1h*) have been shown to exist in two monoenolic forms. The two forms give rise to two separate sets of signals in deuteriochloroform; in deuteriomethanol only one set of the lines is observed due to a fast interconversion between the two forms. This is opposite to the situation in tetronic acid (*1a*) and 5-methyltetronic acid (*1b*) in which only one form has been observed. The ^{13}C NMR spectra of the anions in alkaline solution show a high degree of delocalization of the excess charge.

Tetronic acid and substituted tetronic acids are normally formulated as having an enolic group at C-4 (*1*).[1] Several other enolic structures are possible, especially in the case of the 3-acetyltetronic acids. Recently Keukeleire *et al.*[2] have reported that a 300 MHz ^1H NMR spectrum of a 3-acyltetronic acid gave rise to two doublets at δ 4.61 and 4.48, respectively, each accounting for approximately half a proton. The spectrum of this product is explained on the basis of a 1:1 mixture of two enol forms.

As part of our interest in the structure of the naturally occurring tetronic acids we report the ^{13}C NMR spectra of several 3-acyl-5-methyltetronic acids together with a few other related tetronic acids (*cf.* Table 1). The assignments of the lines are based upon gated decoupled spectra and chosen so as to obtain internal consistency.

DISCUSSION

The ^{13}C NMR spectra of tetronic acid (*1a*) and 5-methyltetronic acid (*1b*) in deuteriomethanol show that these molecules exist in only one form. Five possibilities exist for the structure of this form, a keto form, three monoenolic forms, and a doubly-enolic form. From the gated decoupled spectrum of (*1b*) it can be established that one hydrogen is attached to C-3 as well as to C-5. This excludes in accordance with the recorded ^1H NMR spectra [2] the keto form, the doubly-enolic form, and one of the mono-enolic forms. Normal α,β-unsaturated ketonic carbon atoms give lines in the area downfield to δ 195.[4,5] Since neither *1a* nor *1b* give rise to any lines of this area, the second mono-enolic form with a keto group at C-4 can also be disregarded, implying that the structures of *1a* and *1b* indeed are represented by *1*. By accepting this structure the chemical shifts of the respective carbon atoms in *1a* and *1b*, given in Table 1, are in



1

	R^1	R^2	R^3	Ref.
1a	H	H	H	9
1b	H	CH_3	H	9
1c	$COCH_3$	CH_3	H	10
1d	$COCH_2CH_3$	CH_3	H	10
1e	$CO(CH_2)_2CH_3$	CH_3	H	10
1f	$COCH(CH_3)_2$	CH_3	H	10
1g	$COCH_2C_6H_5$	CH_3	H	10
1h	COC_6H_5	CH_3	CH_3	
1i	$OCOC_2H_5$	CH_3	H	12
1j	$CO(CH_2)_2CH_3$	CH_2COOH	H	

Table 1. ^{13}C chemical shifts, δ,[a] of substituted tetronic acids.[b]

Compound	C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′	C-4′	[α]/[β]
1a [c]	178.35	88.95	182.57	69.85					
1b [c]	177.25	88.30	185.57	77.51					
1b [d]	177.96	73.68	193.00	74.46					
1c (α)	175.75	97.26	195.24	81.87	188.43	19.56			0.71
1c (β)	167.70	100.19	200.24	76.34	194.46	22.35			
1d (α)	176.14	96.16	194.98	81.74	192.97	26.31	9.55		0.57
1d (β)	167.63	99.67	199.14	75.89	199.27	29.56	8.32		
1e (α)	175.88	96.35	194.72	81.48	191.93	34.18	19.23	13.38	0.71
1e (β)	167.31	99.41	199.99	75.89	197.65	36.90	18.19	13.38	
1e [c]	172.44	99.93	197.70	78.75	196.48	38.33	19.62	13.97	
1e [d]	172.37	91.03	194.92	72.45	195.37	36.97	13.77	8.75	
1f (α)	176.66	95.18	194.72	81.67	196.67	31.32	18.58		0.63
1f (β)	167.44	98.69	200.44	75.87	202.58	33.72	18.26		
1g (α)	176.07	96.61	195.05	81.93	188.43	38.40			0.45
1g (β)	167.63	99.73	199.86	75.95	195.05	41.78			
1h (α)	177.96	97.46	195.24	87.97	183.55				1.0
1h (β)	166.33	94.40	206.10	82.65	188.68				
1i (β)	166.33	94.60	192.19	73.75	166.14				
1j [c,e]	172.90	100.45	194.20	79.33	197.58	36.90	20.14	13.97	
1j [d,f]	177.57	96.61	198.23	78.94	200.44	41.97	18.78	13.32	
2	182.57	88.30	193.75	84.40	161.85				
3 [g]	161.20	99.93	181.21	101.49	205.25	20.73			
4 [h]	164.45	103.50	195.18	39.57	201.28	20.60			

[a] Uncertainty ±0.07 ppm. [b] Dissolved in deuteriochloroform unless otherwise stated. The methyl group at C-5 gave δ 17.0±0.5 in all compounds exept in *1h* in which $\delta(CH_3)$ 23.78. [c] Dissolved in deuteriomethanol. [d] 100 mg of the compound dissolved in 1.3 ml D_2O+0.05 ml 40 % NaOD. [e] $\delta(CH_2)$ 36.06 and δ(COOH) 172.18. [f] $\delta(CH_2)$ 39.89 and δ(COOH) 178.55. [g] δ(C-6) 99.93. [h] δ(C-6) 70.30.

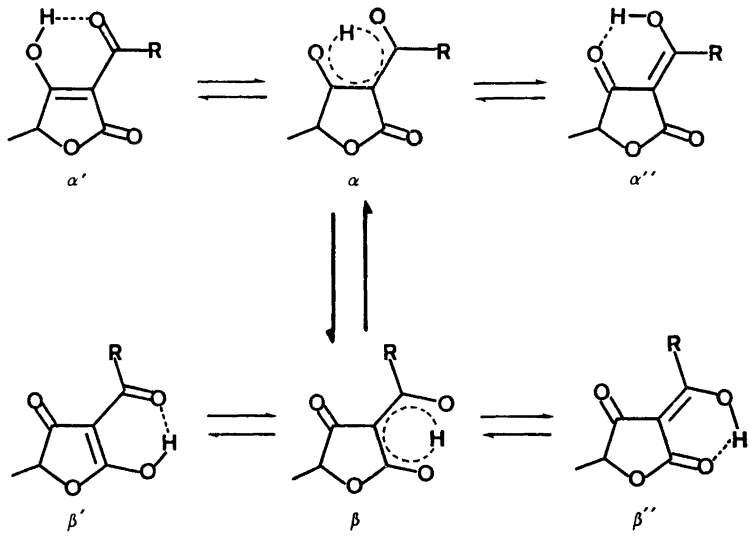
agreement with values found for carbon atoms in other compounds.[4,5] The possibility of the existence of a rapid equilibration between two enolic forms of *1a* and *1b*, as in the case of *1e* in deuteriomethanol, seems unjustified in view of the chemical shifts of C-4 and C-2.

The ^{13}C NMR spectra of 3-acyl-5-methyltetronic acids *1c*–*1h* in deuteriochloroform reveal the existence of two forms occurring in different proportion. The gated decoupled spectra show that C-5 in these compounds is attached to one hydrogen, whereas C-3 carries no hydrogen. This implies that these compounds have to be considered as being of the mono-enolic type. Several types of tautomeric equilibria are conceivable in such a system (Scheme 1).

Each of the equilibria $\alpha' \rightleftharpoons \alpha \rightleftharpoons \alpha''$ and $\beta' \rightleftharpoons \beta \rightleftharpoons \beta''$ will give rise to only one set of NMR signals, since the interconversion between the three forms is fast compared to the time scale in NMR spectroscopy. Shapet'ko *et al.*[6] have suggested the nonexistence of form α' and α'' as well as of β' and β'' in acyclic β-diketones. The enolic form of the latter compounds is completely described by a structure of either the α-type or the β-type. This can be rationalized in the sense of the potential function of the enolic hydrogen having only one minimum. This is contrary to the situation in six-membered cyclic β-ketoaldehydes in which the ^{13}C NMR spectrum has been shown to be a superposition of two forms equivalent to either α' and α'' or β' and β''.[7] The potential function of the enolic proton will in that case contain two minima separated by a small potential barrier. The chemical shifts, δ, of the carbon atoms are then given by [7]

$$\delta = p_a\delta_a + p_b\delta_b \quad [a = \alpha' \text{ (or } \beta'\text{)}, \; b = \alpha'' \text{ (or } \beta''\text{)}]$$

in which δ_a and δ_b are the chemical shifts in the tautomeric forms a and b, whereas p_a and p_b are the temperature dependent probabilities of these forms. A change of the value for the



Scheme 1.

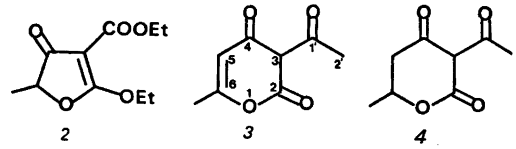
chemical shift, δ, between different temperatures will therefore be observable if two potential minima are present.

The ^{13}NMR spectrum of *1e* in deuteriochloroform has been investigated in the temperature range from −40 to 54 °C. The values of the chemical shifts of all the carbon atoms turned out to be completely independent of the temperature. This indicates that the forms α', α'', β', and β'' are not present in case of *1e*. It seems not unreasonable to extend this conclusion to all the compounds *1c*−*1h*. The two forms present in these compounds are therefore most likely represented by α and β. However, these structures do not imply that the distance from the enolic proton to the two oxygen atoms are equal, but implies the existence of only one potential minimum for the proton.

The assignments of the lines to the carbon atoms of the two forms given in Table 1 are based upon the difference in intensity of the lines. The α-form has been considered to be the form giving δ (C-2) ≈ 175 in order to achieve consistency with *1b*. As can be seen from the table this means that the β-form in most cases is the dominating form in deuteriochloroform ($[\beta] > [\alpha]$).

The effect of different substituents R^1 in *1c*−*1g* is clearly seen to influence the ratio between the two forms ($[\alpha]/[\beta]$) and the value of the chemical shift of C-1′. The chemical shifts of C-4 and C-2 are rather insensitive to changes in R^1. It can, furthermore, be calculated that the difference in the values of C-1′ between the two forms is independent of the nature of the substituent. This suggests that the structures of the two forms are the same for all the compounds and, thus, independent of R^1. The values of δ(C-2), δ(C-4), and δ(C-1′) are most easily rationalized by considering the two O−H distances as being almost identical in the α-form, whereas the β-form is best represented by the structure β' since δ(C-1′) in this form is almost in the area expected for normal α,β-unsaturated ketonic carbon atoms.

3-Ethoxycarbonyl-5-methyltetronic acid (*1i*) exists only in one form in deuteriochloroform. By comparing the value of δ(C-4) for *1i* with the corresponding value for 2-ethoxy-3-ethoxycarbonyl-5-methyl-4,5-dihydrofuran-4-one (*2*) it seems justified to regard *1i* as being of the β-



2 *3* *4*

type. This is opposite to the situation found for the unsubstituted tetronic acid.

The unusual stability as well as the IR and UV spectra of 3-acyltetronic acids [1] are not in agreement with the behaviour of the corresponding six-membered ring compounds, *e.g.* the ^{13}C spectrum of 3-acetyl-6-methyl-2,3-dihydropyran-2,4-dione (*3*) and 3-acetyl-6-methyl-2,3,5,6-tetrahydropyran-2,4-dione (*4*). The latter two exist only in one form in deuteriochloroform (Table 1). The difference in behaviour of these two types of compounds is therefore likely to be connected to the special hydrogen bonding system present in the case of the 3-acyltetronic acids.

The ^{13}C NMR spectrum of *1e* in deuteriomethanol gives rise to only one set of signals (Table 1). This can be explained in terms of a fast interconversion between the α- and β-form due to the exchange of the enolic hydrogen with the solvent. For carlosic acid (*1j*), being almost insoluble in deuteriochloroform, nothing can be said about the possible existence of two forms. Only one form is present in deuteriomethanol (Table 1).

3-Acyltetronic acids are only slightly soluble in water. In alkaline solution the anion is formed. The ^{13}C chemical shift values for the anion of *1b*, *1e* and *1j* are given in Table 1. The values of δ(C-4) and δ(C-1′) are in the area normally found for α,β-unsaturated ketonic carbon atoms, suggesting a high degree of delocalization of the excess charge. This is in agreement with the results obtained for the open form of carolic acid.[8]

We have recently shown [8] that carolic acid has to be considered as a 4:5 mixture of (*E*)- and (*Z*)-methyl-(2′-tetrahydrofurylidene)-tetrahydrofuran-2,4-dione (*5*), respectively. This ratio can be considered quite strange, since steric factors in the proposed hydrated precursor, 3-(ω-hydroxybutyryl)-5-methyltetronic acid, do not give reason for suggesting any deviation from a 1:1 ratio of the two enolic ether forms of carolic acid. We believe that the reason for deviation can be explained from our observation that the 3-acyltetronic acids exist in two forms, α and β, the β-form being the major form present. Therefore, it is suggested that the proportion, in which *5α* and *5β* exist in the solvent, is the main factor controlling the formation of carolic acid (*5*) with an *E*/*Z* ratio of 4:5.

EXPERIMENTAL

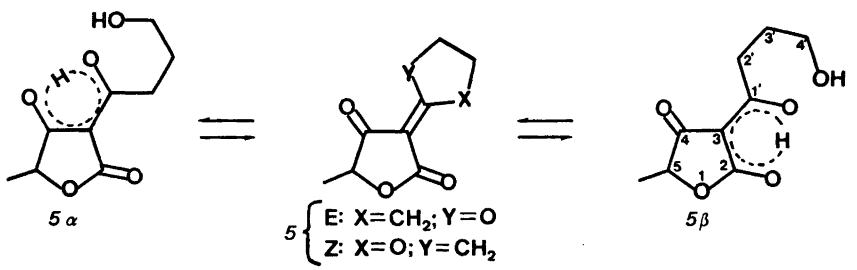
The ^{13}C NMR spectra were recorded on a Jeol FX60 spectrometer. 8K data points were used with a pulse length of 6 μs corresponding to a 60° flip angle. The spectral width was 4000 Hz. The magnetic field was stabilized by internal deuterium lock on the signal from the solvents. The probe temperature was 30 °C. All chemical shifts were measured as δ (ppm downfield to TMS). In case of variable temperature measurement the sample temperature was controlled with a standard variable temperature controller and determined with an accuracy of ±1 °C.

3-Benzoyl-5,5-dimethyltetronic acid (1h). Prepared from 2-chloro-2-methylpropanoyl chloride and ethyl benzoylacetate,[11] m.p. 74–75 °C (Anal. $C_{13}H_{12}O_4$: C, H, O).

Carlosic acid (1j). Isolated from single flask cultures of *Penicillium charlesii* NRRL 1887. Details will be discussed in another paper.[13]

Compound *2* was prepared according to Ref. 11.

3-Acetyl-6-methyl-2,3,5,6-tetrahydropyran-2,4-dione (4). Dehydracetic acid (7.05 g, 0.042 mol) was hydrogenated at room temperature in glacial acetic acid (50 ml) with 0.5 g of 5 % Pd/C as catalyst in a low pressure hydrogenation apparatus. The uptake of 0.042 mol of hydrogen took 4 h. The reaction mixture was poured into water (100 ml) and the pH value



Scheme 2.

was adjusted to 7. Extraction with ether and removal of acetic acid from the etheral phase by extraction with saturated sodium hydrogen carbonate, drying and subsequent evaporation of the solvent under reduced pressure gave 5.3 g (70 %) of crude *4* with m.p. 88 – 92 °C. Recrystallization from ethanol raised the m.p. to 95 – 97 °C (lit.[14] 100 °C).

Acknowledgement. The authors are indebted to Dr. C. W. Hesseltine, U. S. Department of Agriculture, Agricultural Research Service, Peoria, Illinois, for supplying the *Penicillium charlesii* NRRL 1887.

REFERENCES

1. Haynes, L. J. and Plimmer, J. R. *Q. Rev. Chem. Soc. 14* (1960) 292.
2. Keukeleire, D. De, Taeye, S. De and Verzele, M. *Tetrahedron 32* (1976) 2923.
3. Boll, P. M., Sørensen, E. and Balieu, E. *Acta Chem. Scand. 22* (1968) 3251.
4. Stothers, J. B. *Carbon-13 NMR Spectroscopy*, Academic, New York 1972.
5. Breitmaier, E. and Voelter, W. *^{13}C NMR Spectroscopy*, Verlag Chemie, Berlin 1974.
6. Shapet'ko, N. N., Berestova, S. S., Lukovkin, G. M. and Bogachev, Yu. S. *Org. Magn. Reson. 7* (1975) 237.
7. Shapet'ko, N. N., Radushnova, I. L., Bogachev, Yu. S., Berestova, S. S., Potapov, V. M., Kiryushkina, G. V. and Talebarovskaya, I. K. *Org. Magn. Reson. 7* (1975) 540.
8. Jacobsen, J. P., Reffstrup, T. and Boll, P. M. *Acta Chem. Scand. B 31* (1977) 505.
9. Svendsen, A. and Boll, P. M. *Tetrahedron 29* (1973) 4251.
10. Andresen, F. H., Svendsen, A. and Boll, P. M. *Acta Chem. Scand. B 28* (1974) 130.
11. Mulholland, T. P. C., Foster, R. and Haydock, D. B. *J. Chem. Soc. Perkin Trans. 1* (1972) 1225.
12. Benary, E. *Ber. Dtsch. Chem. Ges. 44* (1911) 1759.
13. Reffstrup, T. and Boll, P. M. *In preparation.*
14. Gelin, S. and Gelin, R. *Bull. Soc. Chim. Fr.* (1968) 288.

Received April 22, 1977.