Tetronic Acids and Derivatives. Part XI (1). Structure of Coupling Products of Tetronic Acids with Benzenediazonium Sulfate

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^{13}C Nmr, ^{1}H nmr and ir parameters of coupling products of tetronic acids (4-hydroxy-5*H*-furan-2-ones) with benzene diazonium sulfate are only consistent with a phenylhydrazone formulation with an almost equal ratio of the *syn* and *anti* configurations. These results contrast with those of coupling products of acyclic 3-ketoesters, existing mainly as *anti* tautomers, and more sharply with the 3-parabromophenylhydrazone of L-dehydro ascorbic acid, which is exclusively *syn*.

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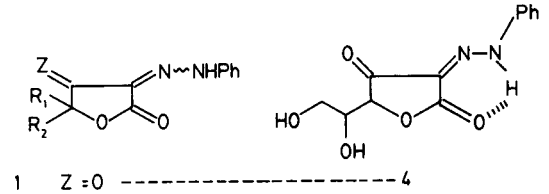
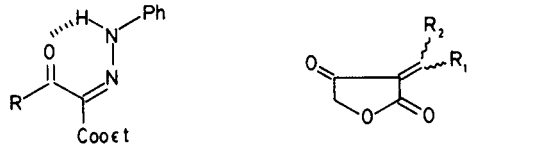
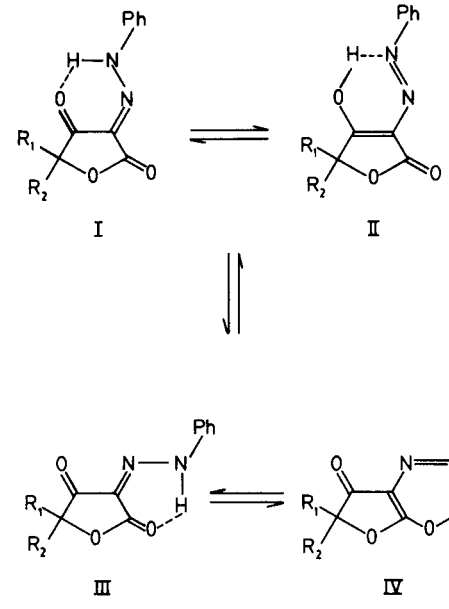
Our current interest to the chemistry of tetronic acids led us to prepare 3-phenylhydrazonotetronic acids as starting materials for heterocyclic nitrogen derivatives (2). These compounds were eventually converted to the corresponding oxime **2** and phenylhydrazone **3**, two useful model systems for a definitive structural elucidation of the osazone of ascorbic acid (3). In a very recent communication, the closely related 3-parabromophenylhydrazone of L-dehydroascorbic acid **4** was shown by ^{13}C and ^{1}H nmr to exist in a single configuration, presumably *syn* (4), according to a previous X-ray crystallographic analysis (5). This unquestionnable result sharply contrasts with those of coupling products of acyclic 3-ketoesters, usually represented as hydrogen-bonded anti tautomers **5** (6-9) and with all known examples of tetronic acids bearing at C-3 an exocyclic double bond such as 3-benzylidene tetronic acids **6** (10) or 3-acyl tetronic acids **7** (1,11) which exist in an almost equal ratio of both syn and anti tautomers. This apparent discrepancy prompted us to examine the spectral parameters of compounds **1** and we were gratified to find the first structural difference between a tetronic and an ascorbic derivative presumably arising from the somewhat particular sugar residue at C-5 in the latter.



1 Z = O ---------- 4
2 Z = NOH
3 Z = NNHPh



5 ---------- 6 R_1 = H, R_2 = Ph
7 R_1 = OH, R_2 = CH_3



I II III IV

	R_1	R_2
a	H	H
b	H	CH_3
c	CH_3	CH_3

As cyclic 1,2,3-triketone derivatives, compounds **1** can exist in four tautomeric forms I-IV (Scheme 2). Their current formulation as in I (or III) is only supported by an extension of well established results with acyclic analogues (6-9) and by some unconclusive chemical proofs such as the absence of coloration with ferric chloride (12). It has been also pointed out that compounds **1** are weak acids and their sodium salts would be as in II or IV (13). A methyl enol ether was also claimed to be available by reaction of diazomethane on compound **1b** (14). Among the

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Table I

^{13}C Chemical Shifts (chloroform)

Carbon	Tautomer I	Tautomer III	I/III ratio	**4** (a)	Azobenzene	Acetone Phenylhydrazone	Acetophenone Phenylhydrazone
C-2	166.2	165.1	2.5	165.9			
C-3	127.6	128.0	1.1	122.4			
C-4	194.4	193.2	1.9	193.8			
C-5	81.2	81.2	/	82.6			
C-6 (CH_3)	16.9	16.9	/	—			
C'-1	139.9	139.9	/	141.3	152.3	143.2	140.7
C'-2,6	117.1	117.1	/	119.5	123.0	112.8	112.8
C'-3,5	129.5	129.5	/	133.1	129.9	128.9	128.9
C'-4	119.5	119.5	/	119.8	131.8	119.0	119.0

(a) In dimethylformamide, from reference 4.

spectroscopic techniques, ^{13}C nmr should be a sensitive molecular probe to study the tautomerism of compounds **1** since a marked difference is expected between the two tautomeric pairs I-III and II-IV in the chemical shifts of aryl carbons which are respectively within a phenyl hydrazono or a phenylazo moiety (3).

The data for the 25.2 MHz ^{13}C nmr or compounds **1b, 4** (4) and our three model compounds azobenzene and the phenylhydrazones (15) of acetone and acetophenone are shown in Table I. The proton bearing aryl carbons were easily identified using off-resonnance decoupling technique and from their respective intensities (16). The deviations from the usual chemical shifts of benzene (128.5 ppm) have the same magnitude as those of the two phenylhydrazones and are then incompatible with the presence of a phenylazo group as in II or IV. Particulary noteworthy are the chemical shifts of carbons C'-1 and C'-4 (*para*) at respectively ca 140 and 119 ppm in a phenylhydrazono group and at 152 and 131.8 ppm in a phenylazo. Furthermore, the presence of two tautomeric forms, identified as I and III from the above discussed aryl carbons, is clearly demonstrated by the two signals for each carbon (C-2 through C-4) of the tetronic ring, in an approximate 60/40 ratio in both chloroform and dimethylsulfoxide. The two signals at 194.4 and 193.2 ppm, unambiguously attributable to cyclopentanic ketones (3,11) provide an additional confirmation of the phenylhydrazonoketone structure of the two present tautomers then best represented by I and III. The corresponding signals in the enol form (such as in II or IV) is usually found near 180 ppm (1,11). Since a hydrogen-bonded carbonyl resonnates at lower field than the corresponding free carbonyl (17), we have assigned the major ketonic signal (194.4 ppm) to the tautomer I. Surprisingly, we also found the major lactonic signal (166.2 ppm, attribuable by homogeneity to tautomer I) also deshielded comparing to the minor signal at 165.1 ppm. If hydrogen-bonding was present in both tautomer, this situation should be reversed; we then suspected the absence of intramolecular chelation in one of the tautomeric forms. A routine spectral investigation was then undertaken to elucidate this point and also to have a more reliable determination of the ratio of each species.

^1H nmr spectra of compounds **1a-c** clearly revealed the two species by the two sets of signals observed in chloroform for the C-5 protons. A 55-45 ratio was obtained from the well-separated singlets at 4.71 (major) and 4.76 ppm in compound **1a**; spectrum recorded in dimethylsulfoxide shows a single signal at 4.88 ppm with compound **1a**. Since the two sets of signals are still present in ^{13}C nmr in this solvent, this coalescence cannot be attributed to an interconversion of one tautomer to the other; it must then arise from the breakage of the present H-bonded system accompanied by loss of the shielding effect on the C-5 protons. Unfortunately, the signals for the NH protons are featureless broad bands near 10 ppm.

The presence of the two tautomers is also easily shown by ir spectroscopy. The main features of ir spectra of compounds **1a-c** are: a weak and broad band between 3500 and 2000 cm^{-1}, a single band at 1775 cm^{-1} (five-membered lactone), two absorptions of almost equal intensities at 1715 and 1675 cm^{-1} and finally a broad band at 1540 cm^{-1}. Some confusion exists in the literature about the position of the C=N- band in related acyclic systems, either at 1540 cm^{-1} (6) or in the 1630-1670 region (7). We have verified that the absorption at 1675 cm^{-1} cannot be attributed to an azomethine vibration, since both bands at 1715 and 1675 cm^{-1} faded by converting compounds **1a-c** to oximes **2** or phenylhydrazones **3** (3). They must then correspond to two ketone stretching vibrations; the low wavelength band being attributed to the hydrogen-bonded ketone in tautomer I. The intramolecular nature of this chelation was demonstrated by the insensitivity of the whole spectra by dilution effect in both chloroform and acetonitrile. In contrast, the lactonic band at 1775 cm^{-1} is always sharp in

chloroform, acetonitrile or in solid state; if this lactone was engaged in a chelation (in tautomer III) one can expect a substantial lowering of its stretching band compared with the free lactone in tautomer I and consequently two signals between 1800 and 1740 cm^{-1}; for example, the interconversion of ascorbic acid osazone and of related compounds **2,3** in solution can be monitored by the progressive replacement of a chelated lactone band at 1740 cm^{-1} (the expected wavelength in a chelated tautomer III) by a free lactone band at 1770 cm^{-1} (observed in our case with both tautomers I and III) (3,18). This observation of a chelation only between the phenylhydrazono group and a ketone allow us to assign the deshielded signal in ^{13}C nmr to the H-bonded ketone in tautomer I which is consequently the major (55%) form.

The difference in the tautomeric population of structure I between 3-phenylhydrazonotetronic acids (55%) and 3-phenylhydrazonoascorbic acids (0%) can only be attributed to the dihydroxyalkyl residue at C-5 in the latter. A tentative explanation lies in the absence of interconversion in going from solid state to the solution and then of the prevalence of the stabilizing factors of the crystalline state (19); according to the crystallographic analysis, the *syn* structure of compound **4** is stabilized by both intramolecular chelation between the lactone and the phenylhydrazono proton and intermolecular hydrogen-bonding involving the ketone and one of the hydroxyl group of the sugar like chain at C-5 (5). This favoured molecular packing cannot be found in the tetronic series in which the presence of the two tautomers seems to arise from geometrical factors rather than from hydrogen-bonding reasons, since intramolecular chelation was only found at present in only one tautomer. The emphasis of these factors is currently under examination by a crystallographic study.

EXPERIMENTAL

The ^{13}C nmr spectra were recorded on a Varian XL-100-12-FT spectrometer using the natural abundance at a concentration of 1*M* and a probe temperature of 30°. The ^{1}H nmr spectra were recorded on a Varian A-60 spectrometer and the chemical shifts are given in ppm downfield from tetramethylsilane as internal standard. Ir spectra were obtained using a Beckmann model Acculab 2 and a Perkin Elmer model 180 spectrometer with a R.I.I.C. variable cell (0.025 to 5 mm width) at five successive dilutions from 0.05*M* to 0.0015*M*. Uv spectra were recorded with a Beckmann DB uv-visible spectrophotometer at $3.5 \times 10^{-5}M$ in 95% ethanol. Compounds **1a,b,c** were prepared as previously described (20).

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