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A THEORETICAL STUDY OF TAUTOMERISM IN DEHYDROASCORBIC ACID OSAZONE AND RELATED TETRONIC ACID DERIVATIVES

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ABSTRACT

The HMO method has been used to study tautomerism in diazonium coupling-products of tetronic acids (**1**) and their 4-phenylhydrazones **15**, model compounds for dehydroascorbic acid osazone. In addition, HMO calculations have been performed for 2,5-bis(phenylhydrazono)cyclopentanone (**28**) and 1,3-bis(phenylhydrazono)-2-indanone (**32**). The results are consistent with the chelated phenylhydrazone structure **12** and the dichelated bis(phenylhydrazone) structure **19**, in agreement with the ^{13}C-n.m.r. spectral data reported by Gelin and Pollet.

INTRODUCTION

There are several contradicting reports on the tautomeric structure of the diazonium coupling-products of tetronic acids (**1**, R = H, Me, Ph) in the literature. These compounds are currently formulated as **7** by analogy with acyclic analogs **14** and on the basis of such inconclusive chemical tests as the absence of coloration with ferric chloride[1–5]. On the other hand, Haynes and Plimmer[6] pointed out that compounds **1** (R = H) are weak acids and that their sodium salts should correspond to the structures **9** and/or **10**. A methyl enol ether was also claimed[7] to have been obtained by reaction of diazomethane with **1** (R = Me).

A similar controversy exists over the structure of dehydroascorbic acid osazone (**15**, R = $CHOHCH_2OH$)[8–10]. For example, whereas Roberts[8] assigned structure **20** for this osazone on the basis of its electronic-absorption spectral data, Rao and Nair[9] conducted i.r. spectral studies of this compound and favored the dichelated bis(phenylhydrazone) structure **19**. More recently, Pollet and Gelin[11] have examined the ^{13}C-n.m.r. spectrum of **15** and indicated that their data seem to support structure **19** rather than **20**.

This apparent controversy prompted us to re-examine the tautomerism of **1** and **15** from a quantum-chemical point of view. In the present contribution, the relative stabilities of the possible tautomeric forms of the model compounds **1**

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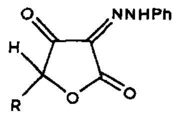

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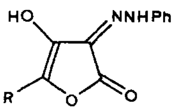

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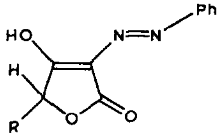

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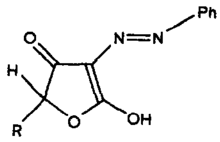

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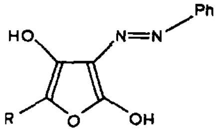

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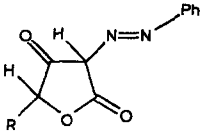

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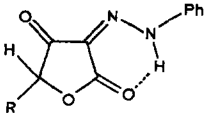

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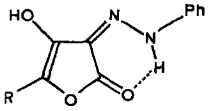

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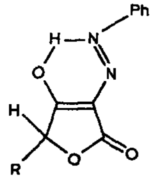

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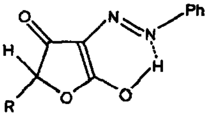

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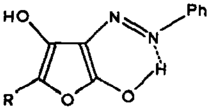

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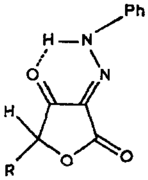

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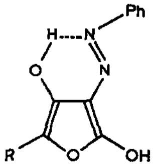

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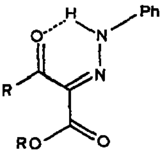

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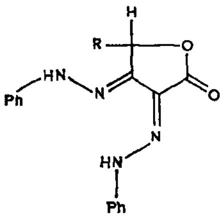
(R = H) and **15** (R = H) and the effect of intramolecular hydrogen-bonding have been investigated by using the Hückel molecular orbital (HMO) method. This approach has been found successful in study of the tautomerism of diazonium coupling-products of phenolic compounds[12] and of heterocyclic systems having an active methylene group[13-16].

RESULTS AND DISCUSSION

The diazonium coupling-products of tetronic acid **1** may exist in six different tautomeric forms **1–6**. In addition, the forms **1** and **5** may each exist in two chelated forms, **7** and **12**, and **11** and **13**, respectively. These chelated structures are expected to prevail in nonpolar solvents as they are stabilized by intramolecular hydrogen-bonds. Each of the other forms **2–4** can have only one chelated structure, namely, **8–10**, respectively. The form **6**, in comparison with the other structures **1–5** or **7–13**, is clearly the most unstable because of interrupted conjugation between the phenylazo group and the heterocyclic portion of the molecule.



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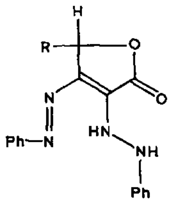

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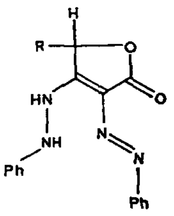

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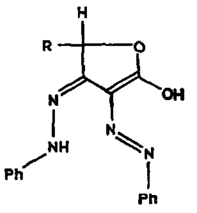

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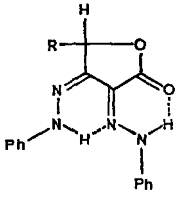

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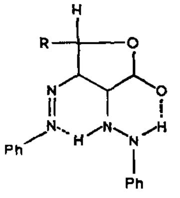

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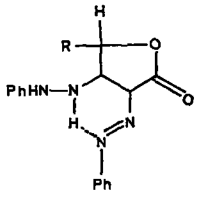

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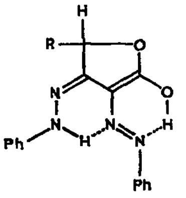

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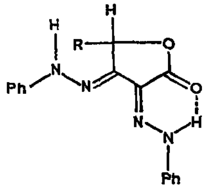

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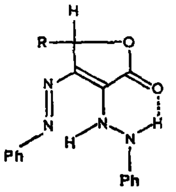

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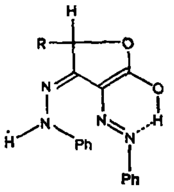

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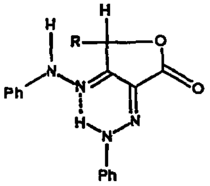

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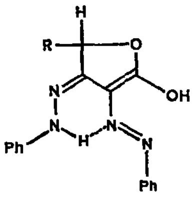

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The values of the bonding energies, *BE*, calculated for these tautomeric forms of 3-phenylazotetronic acid are given in Table I. For a given tautomeric pair, it is sufficient to compare the bonding energies of the two tautomers provided they have the same number of π-electrons. However, for systems having different numbers of π-electrons, the bonding energy per π-electron, BE/n, is the more appropriate quantity to be used for comparison. The BE/n values for all tautomeric forms among **1–14** are presented in the third column of Table I. Generally, a positive value of ΔBE_{i-j} or $\Delta(BE/n)_{i-j}$ indicates greater stability of the *i*-form, whereas negative value indicates that the *j*-form is more stable. From our previous experience, one tautomer will preponderate when $|\Delta(BE/n)|$ is larger than 0.002 β.

Examination of the data in Table I reveals that the order of stability of the unchelated tautomers of **1** is **1** > **4** > **3** > **2** > **5**. The form **6** is expected to be the

TABLE I

ENERGY CHARACTERISTICS[a] OF TAUTOMERS OF **1**

Tautomer	BE	n	BE/n	*HOMO*	*LUMO*	$E(N \rightarrow V_1)$
1	16.308	16	1.019	0.750	−0.199	0.949
2	16.474	18	0.915	0.469	−0.275	0.944
3	15.116	16	0.945	0.610	−0.348	0.958
4	16.140	16	1.008	0.565	−0.405	0.970
5	16.157	18	0.897	0.347	−0.413	0.760
7	16.539	16	1.034	0.746	−0.230	0.976
8	16.709	18	0.928	0.494	−0.300	0.794
9	16.239	16	1.015	0.665	−0.350	1.015
10	16.255	16	1.016	0.620	−0.388	1.008
11	16.246	18	0.903	0.333	−0.384	0.717
12	16.538	16	1.034	0.757	−0.232	0.989
13	16.272	18	0.904	0.369	−0.399	0.768

[a] *BE*, bonding energy; *n*, number of π-electrons; *BE/n*, bonding energy per π-electron; HOMO and LUMO, the energies of the highest occupied and of the lowest unoccupied π-molecular orbital, respectively; $E(N \rightarrow V_1)$, energy of the $N \rightarrow V_1$ transition (β units). Because of the interrupted conjugation, no calculation has been conducted for the tautomer **6**.

least stable one for reasons already discussed. The data also suggest that **1** is the preponderant form for the diazonium coupling-product of tetronic acids.

It should be pointed out that changes in the values of the Coulomb and the resonance integrals used in the calculations (see Methods and Calculations) by ±10–25% do not affect the foregoing order of stabilities of the tautomers.

The effect of intramolecular hydrogen-bonding upon the stabilities of the various forms of **1** was also examined in an attempt to shed some light on their structures. The treatment used here is similar to that developed by Pullman and Pullman[17] and employed in our previous work[14]. The results of the calculations are summarized in Table I. Inspection of the data indicates that intramolecular hydrogen-bonding increases the stability of all tautomers. However, the added stability in form **1** (hydrogen-bonded tautomers **7** and **12**) is more than twice as large as that for the next most stable tautomer **4** (hydrogen-bonded form **10**). Furthermore, both structures **7** and **12** appear to possess identical stabilities.

As an additional step, we have considered the effect of intermolecular hydrogen-bonding and thus examined the effect of protic solvents on the tautomeric structure of **1**. The results of this study are summarized as follows:

Solvated tautomer	BE,β	BE/n,β	$E(N \rightarrow V_1)$,β
1	16.590	1.036	0.913
2	16.639	0.924	0.727
3	16.309	1.019	0.958
4	16.237	1.015	0.975
5	16.217	0.900	0.720

It is obvious that intermolecular hydrogen-bonding exerts a stabilizing effect on all of the tautomers, with the solvated hydrazone tautomer **1** being still the most stable.

The foregoing results indicate that the diazonium coupling-products of tetronic acids exist mainly in the hydrazone form. Inspection of the relative values of *BE* of the various hydrazone tautomers suggests an equilibrium between two or more forms, depending on the medium. In the solid state or in nonpolar media, a 1:1 equilibrium mixture of the chelated forms **7** and **12** is expected, whereas the form **12** and the solvated form **1** would preponderate in polar solvents. In fact, Gelin and Pollet[18] have recently shown that **1** (R = H or Me) exist in chloroform or in acetonitrile as a mixture of the two tautomers **1** and **12** in 9:11 ratio. The solid-state spectrum of **1** (R = Me) is also compatible with these results. It shows three carbonyl absorption-bands near 1775, 1715, and 1675 cm^{-1}, and a weak, broad NH band at 3300–3100 cm^{-1}. In principle, for the equilibrium **7** $\rightleftharpoons$ **12** four CO bands would be expected because of the free and bonded keto and lactone CO groups. The observation of only three CO bands may arise from the overlap of two of the expected four bands. Generally, α,β-unsaturation and intramolecular hydrogen-bonding effects may combine in lowering the CO stretching frequency by[19,20] 40–60 cm^{-1}. Accordingly, the bands at 1775 and 1675 cm^{-1} may be assigned to the vibrations of the free-lactone and bonded-keto CO groups in **12**, whereas the vibration at 1715 cm^{-1} arises from the bonded- and free-keto CO group in **7**.

Following the same procedure as just described, the bonding energies of various possible forms of the 3,4-bis(phenylhydrazone) derivative of tetronic acid **15** (R = H) were calculated. The results are summarized in Table II. It is obvious that the most

TABLE II

ENERGY CHARACTERISTICS[a] OF TAUTOMERS OF **15**

Tautomer	BE	n	BE/n	*HOMO*	*LUMO*	$E(N\rightarrow V_1)$
15	24.643	24	1.027	0.569	−0.305	0.874
16	16.060	16	1.004	0.599	−0.140	0.739
17	16.099	16	1.006	0.598	−0.346	0.944
18	24.386	24	1.016	0.378	−0.412	0.790
19 *(ZZ)*	24.998	24	1.041	0.587	−0.300	0.887
20	16.190	16	1.012	0.653	−0.140	0.793
21	16.238	16	1.014	0.657	−0.356	1.013
22	24.610	24	1.025	0.401	−0.359	0.760
23 *(ZE)*	24.866	24	1.036	0.566	−0.330	0.896
24	16.197	16	1.012	0.625	−0.111	0.736
25	24.513	24	1.021	0.423	−0.407	0.830
26 *(EE)*	24.805	24	1.033	0.618	−0.330	0.948
27	24.480	24	1.020	0.349	−0.364	0.713

[a] For the explanation of symbols, see Table I.

stable forms of this model compound for dehydroascorbic acid osazone (**15**, R = $CHOCH_2OH$) are the dichelated and monochelated bis(phenylhydrazone) structures, **19**, **23**, and **26**. The results of a study of the effect of intermolecular hydrogen-bonding with protic solvents provide further support for the conclusion that the bis(phenylhydrazone) form **15** exhibits maximal stability in this instance.

Solvated tautomer	BE, β	BE/n, β	$E(N \rightarrow V_1)$, β
15	24.837	1.035	0.811
16	16.224	1.014	0.695
17	16.297	1.018	0.939
18	24.482	1.020	0.749

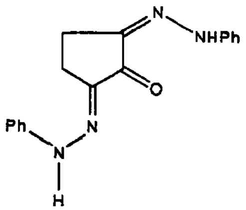
The assignment of structure **20** made by Roberts[8] on the basis of the long-wavelength absorption maximum of **15** (R = $CHOHCH_2OH$) and its similarity to that of the cyclopentane-1,2,3-trione 1,3-bis(phenylhydrazone) **28** seems to be ambiguous. This is because the results of the HMO calculations of the bonding energies of the various tautomers of **28** and its benzo derivative **32** (Table III) indicate that the most stable tautomeric structures of such compounds are the chelated bis(phenylhydrazones) **30** and **34**, respectively. These structures possess higher bonding-energies than the isomeric forms **31** and **35**, respectively, even though the latter have an extra hydrogen bond. Furthermore, spectral evidence for the bis(phenylhydrazone) structure of **28** and **32** has been reported[21]. Moreover, comparison of the values of the energies of the $N \rightarrow V_1$ transitions, $E(N \rightarrow V_1)$, of **28** (0.870 β) and **15** (0.874 β) indicates that they are similar. Thus, it is expected that both compounds will absorb at similar wavelengths (the longest-wavelength absorption band). The same is also true of the pair **19** and **30**.

TABLE III

ENERGY CHARACTERISTICS[a] OF TAUTOMERS OF **28** AND **32**

Tautomer	BE	n	BE/n	*HOMO*	*LUMO*	$E(N \rightarrow V_1)$
28	24.368	22	1.108	0.699	−0.171	0.870
29	24.135	22	1.097	0.456	−0.246	0.702
30	24.598	22	1.118	0.667	−0.185	0.852
31	24.298	22	1.104	0.467	−0.257	0.724
32	33.126	28	1.183	0.592	−0.192	0.784
33	32.910	28	1.175	0.439	−0.199	0.638
34	33.351	28	1.191	0.630	−0.200	0.830
35	33.084	28	1.181	0.471	−0.228	0.699

[a] For the explanation of symbols, see Table I.



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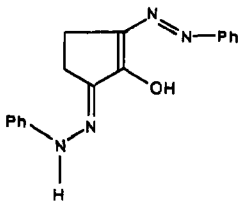

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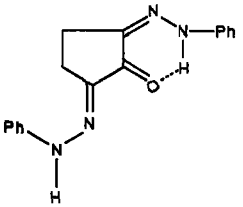

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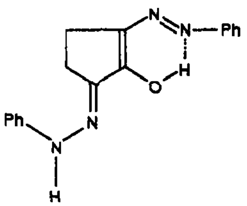

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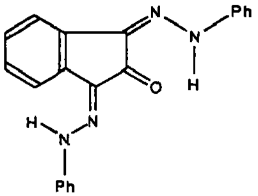

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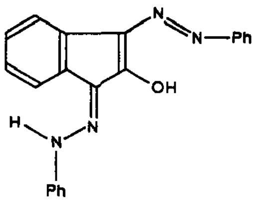

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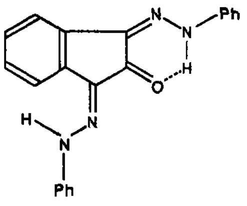

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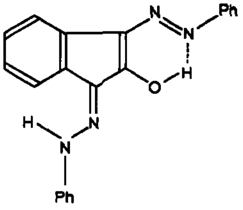

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Inspection of the values of $E(N \rightarrow V_1)$ for **12** (0.989 β) and **19** (0.887 β), which are the most stable structures for **1** and **15**, respectively, shows that the introduction of the second 4-phenylhydrazono group into **1** results in a bathochromic shift equivalent to about 0.102 β. This result suggests that the absorptions of **15**, regardless of the nature of the R group, are not necessarily due to the presence of a five-membered lactone ring adjacent to the chelated system, in agreement with the recent findings of Pollet and Gelin[11].

Further evidence in support of the bis(phenylhydrazono) tautomer is that our data show that the conversion of the dichelated form **19**, which has the *ZZ* geometry $[E(N \rightarrow V_1) = 0.887\ \beta]$ into the monochelated form **26** having the *EE* arrangement $[E(N \rightarrow V_1) = 0.948\ \beta]$ will be accompanied by a hypsochromic shift of the longest-wavelength absorption band. This accounts for the experimental observation that the λ_{max} of **15** (R = Me) in ethanol shifts with time from 468 to 444 nm[11], and that of **15** (R = $CHOHCH_2OH$) likewise[9] from 460 to 440 nm[9]. The small difference between the bonding energies of the two forms, **19** and **26**, suggests that interconversion of these two may occur in solution, with **19** being preponderant in the solid state or in nonpolar solvents. In solvents of intermediate polarity, both forms should coexist. The i.r. data reported for **15** (R = $CHOHCH_2OH$) in 1,4-dioxane and in dimethyl sulfoxide[9] and for **15** (R = Me) in acetonitrile[11] are in agreement with the foregoing conclusions.

METHODS AND CALCULATIONS

To calculate the relative stabilities of the various tautomeric forms of **1**, **15**, **28**, and **32** within the framework of the HMO method, we have used the concept of bonding energy[13,14,22,23] defined by equation (*1*):

$$BE = E_\pi - \sum n_i \alpha_i \qquad (1)$$

where *BE* is the bonding energy, E_π is the total π-electronic energy of the system, n_i is the number of π-electrons contributed by the atom *i* to the system, and α_i is the Coulomb integral of the atom *i*. The quantity *BE* appears to be better founded[13,22,23] than the commonly used delocalization energy[24] because of the uncertainty in defining the correct Kekulé structures. The values of the parameters adopted for all compounds in this work are based on those suggested by Kuder[12] and are summarized in Table IV.

TABLE IV

HMO HETEROATOM PARAMETERS[a]

Azo form		*Hydrazone form*	
$h_{\dot{N}}$	0.5	$h_{\ddot{N}H}$	1.5
$h_{\dot{O}}$ (exocyclic)	2.0	$h_{\dot{N}}$	0.5
$h_{\dot{O}}$ (endocyclic)	2.0	$h_{\ddot{O}}$ (endocyclic)	2.0
		$h_{\dot{O}}$	1.0
k_{CN}	0.9	k_{CN}	0.7
k_{NN}	1.0	k_{NN}	0.7
k_{C-O}	0.8	$k_{C=N}$	1.1
$k_{C=O}$	1.0	$k_{C=O}$	1.0

[a] Coulomb integrals: $\alpha_X = \alpha + h_X\beta$; resonance integrals: $\beta_{XY} = k_{XY}\beta$.

In the treatment of intramolecular hydrogen-bonds, the Coulomb integrals for the centers XH and Y interacting with each other were taken as[17]:

$$\alpha_{XH} = \alpha_X - 0.2\,\beta$$
$$\alpha_{Y\cdots H} = \alpha_X + 0.7\,\beta$$
$$\beta_{X(H)Y} = 0.2\,\beta$$

A similar approach has been used in the treatment of tautomers hydrogen-bonded to solvent molecules, SH, where:

$$\alpha_{XH\cdots SH} = \alpha_X - 0.2\,\beta$$
$$\alpha_{Y\cdots HS} = \alpha_Y - 0.2\,\beta$$

The HMO calculations were performed conventionally by using an IBM 360/65 computer.

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