

## On the Preferred Protonation Site in Furan and Vinyl Alcohol. An *Ab Initio* Study†

Minh Tho Nguyen and Anthony F. Hegarty\*

Department of Chemistry, University College, Belfield, Dublin 4, Ireland

Tae-Kyu Ha

Laboratory of Physical Chemistry, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zurich, Switzerland

George R. De Maré

Laboratoire de Chimie Physique Moléculaire, Université Libre de Bruxelles, C.P. 160, B-1050 Bruxelles, Belgium

The geometries of furan and vinyl alcohol and their  $C_\alpha$ -,  $C_\beta$ -, and  $O$ -protonated forms have been optimized completely using the 3-21G basis set and analytic gradient (force) methods. The relative energies obtained with the 3-21G basis set were checked by 6-31G\*\*//3-21G (furan and vinyl alcohol species) and 6-31G\*\*//3-21G (vinyl alcohol and its protonated forms) computations. The  $C_\alpha$ -protonated furan and the  $C_\beta$ -protonated vinyl alcohol are found to be the most stable forms, in agreement with experimental results. The preferred reaction site ( $C_\alpha$  or  $C_\beta$ ) upon electrophilic substitution has been rationalized in terms of simple resonance structure arguments supported by MCSCF calculations.

The electrophilic substitution of five-membered heterocyclic compounds such as furan and pyrrole has been the subject of considerable interest and attention. It is well established that the electrophilic substitution of these compounds in solution takes place predominantly at the  $C_\alpha$  position.<sup>1,2</sup> Recent ion cyclotron resonance (i.c.r.) experiments have confirmed that the preferred protonation site in these compounds in the gas phase is also the  $C_\alpha$  position.<sup>3-5</sup> Thus the proton affinity (PA) for the  $C_\alpha$ -protonation, for example 196 kcal mol<sup>-1</sup> for furan, is *ca.* 2.8–4.6 kcal mol<sup>-1</sup> more than the PA value for the  $C_\beta$ -protonation.<sup>3,4</sup>

Different theoretical approaches have been used to interpret the relative reactivities or to predict the preferred protonation site in furan and other heterocyclic compounds.<sup>4,6,7</sup> Most of these theoretical interpretations are based on the correlation of reactivity with the electronic charge density, the electrostatic potential, or on the correlation between the gas-phase PA with the (1s) binding energies in these compounds. As demonstrated in our previous study,<sup>8</sup> protonation frequently induces dramatic changes in both molecular structure and electronic charge distribution and protonation on the most basic centre does not necessarily lead to the most stable protonated form.

In view of these uncertainties, we have carried out *ab initio* SCF determinations of the equilibrium geometries and energies of furan and its three protonated species ( $C_\alpha$ -,  $C_\beta$ -, and  $O$ -protonated) to study the extent of structural changes upon protonation and their effect on the relative thermodynamic stabilities. In contrast to the preferred  $C_\alpha$ -protonation in furan (and in other heterocyclic five-membered compounds), it is known that the  $C_\beta$ -protonation is favoured in the enol ether species<sup>3</sup> and in ketenimine.<sup>8,9</sup> As a continuation of our previous theoretical study,<sup>8</sup> vinyl alcohol was chosen to represent this second category of molecules, and similar comparative *ab initio* calculations have been performed on the neutral and the protonated species.

### Calculations

*Ab initio* SCF calculations of geometrical structures and electronic properties have been carried out by using split-valence 3-21G<sup>10</sup> and 4-31G<sup>11</sup> and extended 6-31G\*<sup>12</sup> (with *d*

functions on C and O) and 6-31G\*\* (with *d* functions on C and O and *p* functions on H) basis sets.

The molecular geometries of furan and vinyl alcohol and their conjugate acids were optimized by the force method with analytical gradient,<sup>13</sup> as implemented in the MONSTER-GAUSS program system.<sup>14</sup> For a systematic comparison of the geometrical parameters of all the species, a complete geometry optimization has been carried out with the 3-21G basis set throughout, and the optimizations were terminated when the gradient length was reduced below  $5 \times 10^{-4}$  mdyne.

The relative energies of the neutral and three protonated species for both molecules have also been calculated employing the extended basis sets: 6-31G\* for furan and 6-31G\*\* for vinyl alcohol. The MCSCF calculations have been performed by using the split-valence 4-31G basis set.

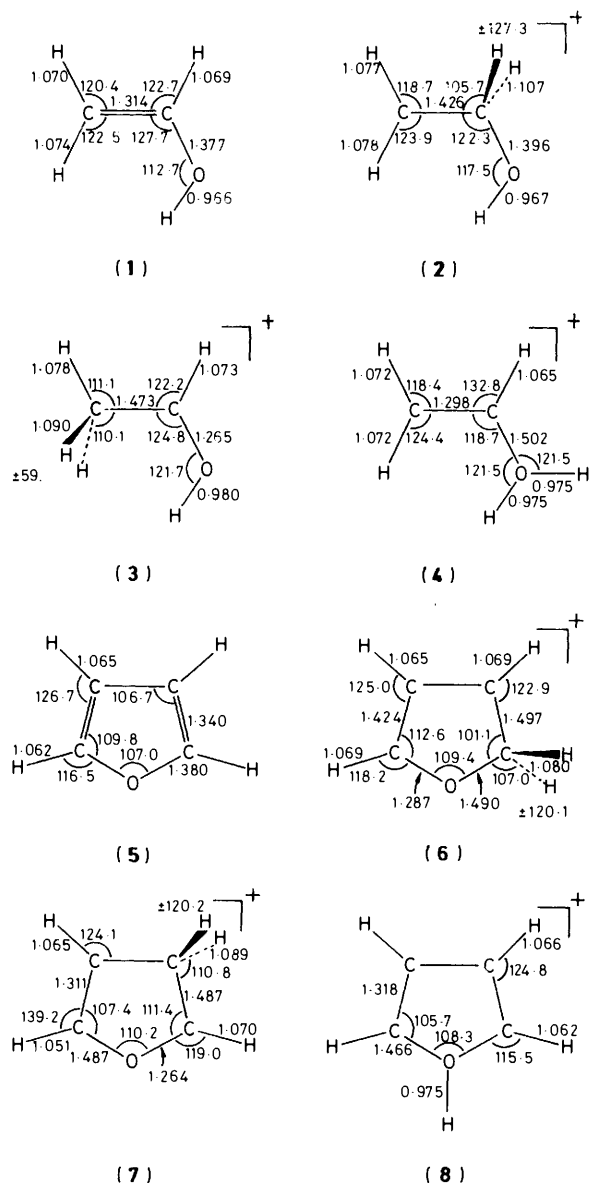
### Results and Discussion

The 3-21G optimized geometries (1)–(8) of vinyl alcohol and furan and their three protonated species are shown. The total SCF energies and the relative energies with respect to the neutral species of both molecules are given in Table 1. In order to ensure that the calculated relative stabilities are not an artefact of the geometry optimization procedures using the rather small split-valence basis set, single-points 6-31G\*\*//3-21G and 6-31G\*\*//3-21G computations were performed on vinyl alcohol and its protonated species and 6-31G\*//3-21G computations on furan and its conjugate acids.

The calculated relative energies of furan species listed in Table 1 clearly show that the  $C_\alpha$ -protonated form is predicted to be the most stable followed by the  $C_\beta$ - and  $O$ -protonated species. The calculated protonation energy, defined as the energy difference between the protonated and non-protonated forms, is 214.7 kcal mol<sup>-1</sup> (6-31G\*) for the  $C_\alpha$ -protonated species. This is larger than those of  $C_\beta$ - and  $O$ -protonated forms by 13.6 and 39.0 kcal mol<sup>-1</sup>, respectively. This result confirms the favoured site of protonation in furan is the  $C_\alpha$  position corresponding to the species which was observed experimentally in the gas phase,<sup>3</sup> in solution,<sup>1</sup> and in the condensed phase.<sup>15</sup>

In contrast, the 3-21G, 6-31G\*, and 6-31G\*\* computations all predict the  $C_\beta$ -protonated form of vinyl alcohol to be the most stable one. The proton affinity for the  $C_\beta$ -protonated vinyl alcohol, 210.9 kcal mol<sup>-1</sup> (6-31G\*\*) is larger than those of the

† Non-S.I. unit employed: 1 cal  $\approx$  4.184 J.



The 3-21G-optimized geometries (1)–(8) of vinyl alcohol and furan and their various protonated species obtained using the analytic gradient method

C<sub>α</sub>- and O-protonated forms by 51.7 and 27.5 kcal mol<sup>-1</sup>, respectively. It is interesting to note that in vinyl alcohol, the O-protonated form is more stable than the C<sub>α</sub>-protonated form, while in furan the O-protonated form is the least stable one.

A similar situation as in vinyl alcohol was observed in our previous study for ketenimine (CH<sub>2</sub>=C=NH).<sup>8</sup> The C<sub>β</sub>-protonated ketenimine (CH<sub>3</sub>-C=NH<sup>+</sup>) was found to be the most stable form followed by the N-protonated one (CH<sub>2</sub>=C=NH<sub>2</sub><sup>+</sup>), and the C<sub>α</sub>-protonated form (CH<sub>2</sub>=CH=NH<sup>+</sup>) represented the least stable form.<sup>8</sup>

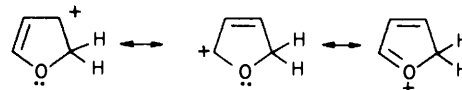
As shown in (1)–(8), the changes in all geometrical parameters upon protonation are very large in both molecules. Upon protonation at the C<sub>α</sub> position in furan, for example, one of the C<sub>α</sub>-O distances (1.38 Å in furan) becomes very short (1.287 Å) while the other one becomes much larger (1.424 and 1.497 Å from 1.34 Å, respectively). Similar changes in the ring structures are observed in the other protonated species. The drastic changes in the C-C and C-O bond distances upon

### Furan

#### Neutral



#### C<sub>α</sub>-Protonation

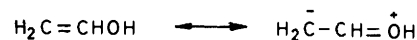


#### C<sub>β</sub>-Protonation



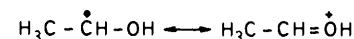
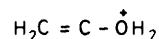
### Vinyl alcohol

#### Neutral



#### O-protonation

#### C<sub>β</sub>-protonation



### Scheme.

protonation are also found to be the very important in vinyl alcohol, similar to the large changes observed on protonation in the C-C and C-N distances in ketenimine.<sup>8</sup> The major changes in geometrical parameters of the molecules upon protonation are responsible for the failure of correlation between the most reactive centre in the electrophilic substitution and the electronic charge density, 1s-binding energy, or the molecular electrostatic potential, as attempted in most previous studies.<sup>6,7</sup>

Some relevant molecular properties for vinyl alcohol and furan were calculated using the 6-31G\* basis set and are given for comparison in Table 2. The most basic position is without doubt the O-atom site followed by the C<sub>β</sub> and C<sub>α</sub> sites as the calculated net charges, 1s binding energies, and the electronic potentials ( $\langle 1/r \rangle$ ) indicate. According to these properties, both vinyl alcohol and furan should behave almost identically in the electrophilic proton substitution. This is not the case as the present calculations of relative stabilities of the protonated species and the previous experimental studies have shown. The importance of severe geometry relaxation upon protonation has also been studied previously for large heterocyclic compounds by employing semi-empirical MO methods.<sup>7,16</sup>

In summary, attempts to correlate in a semi-quantitative way the preferred protonation site with the intrinsic basicity of the neutral species are only partially successful. In contrast, there exists a qualitative and elementary reason which could rationalize the difference in protonation sites. Thus the preference for C<sub>α</sub> over C<sub>β</sub> proton substitution in furan and for C<sub>β</sub> over C<sub>α</sub> proton substitution in vinyl alcohol can be rationalized in a simple way in terms of the resonance structures of the species in the Scheme.

In the structures in the Scheme, the relative intrinsic basicity of C<sub>α</sub> and C<sub>β</sub> positions in both neutral molecules become more obvious: the C<sub>β</sub> sites in vinyl alcohol and the C<sub>α</sub> site in furan representing the most basic site. In the same vein, extra resonance structures are available for C<sub>β</sub>-protonation of vinyl alcohol and C<sub>α</sub>-protonation of furan favouring these reaction sites.

In both neutral species, the charged resonance forms are due to the interaction of the lone-pair orbital of oxygen with the π-orbital of the C=C double bond. These structures can thus be

**Table 1.** Calculated total and relative energies of vinyl alcohol and furan and their protonated species

Species	Total energies (a.u.)			Relative energies (kcal mol <sup>-1</sup> )		
	3-21G//3-21G	6-31G*//3-21G	6-31G**//3-21G	3-21G	6-31G*	6-31G**
Vinyl alcohol (1)	-152.041 40	-152.887 56	-152.899 63	0.0	0.0	0.0
C <sub>α</sub> -Protonated	-152.281 60	-153.138 87	-153.153 30	-150.7	-157.7	-159.2
Vinyl alcohol (2)						
C <sub>β</sub> -Protonated	-152.366 42	-153.221 01	-153.235 72	-203.9	-209.2	-210.9
Vinyl alcohol (3)						
O-Protonated	-152.349 55	-153.172 52	-153.191 97	-193.4	-178.8	-183.4
Vinyl alcohol (4)						
Furan (5)	-227.350 83	-228.622 69		0.0	0.0	
C <sub>α</sub> -Protonated	-227.679 22	-228.964 80		-206.1	-214.7	
Furan (6)						
C <sub>β</sub> -Protonated	-227.659 30	-228.941 62		-193.6	-200.1	
Furan (7)						
O-Protonated	-227.650 44	-228.902 76		-188.0	-175.7	
Furan (8)						

**Table 2.** A comparison of some calculated properties of vinyl alcohol and furan (6-31G\*)

		Vinyl alcohol	Furan
Net charge	C <sub>α</sub>	+0.216	+0.125
	C <sub>β</sub>	-0.495	-0.272
	O	-0.732	-0.574
C(1s) orbital energy <sup>a</sup>	C <sub>α</sub>	-11.2945	-11.2833
	C <sub>β</sub>	-11.2094	-11.2261
Electric potential (<1/r> <sup>a</sup> )	C <sub>α</sub>	-14.6643	-14.6755
	C <sub>β</sub>	-14.7507	-14.7342
	O	-22.2839	-22.2542

<sup>a</sup> Atomic units.

regarded as the excited states involving pairwise excitations which exhibit appreciable contributions to the electronic structures of relevant species.

In order to verify the above elementary consideration, a set of MCSCF calculations has been performed using the 4-31G basis set. While the lone-pair- $\pi$ -orbital interaction may be described by the HOMO ( $1a''$ ) and LUMO ( $2a''$ ) excitations in vinyl alcohol which represent the C=C bonding and anti-bonding  $\pi$ -orbitals, five orbitals of  $\pi$  symmetry including the lone-pair orbitals of oxygen are involved in furan; three occupied orbitals ( $1b_1$ ,  $2b_1$ , and  $1a_2$ ) and two virtual orbitals ( $3b_1$  and  $2a_2$ ), among which the  $1a_2$  and  $2a_2$  orbitals are shown to be the pure  $\pi$ -orbitals without contribution of the lone pair of oxygen. The calculated MCSCF wavefunctions for vinyl alcohol and furan result in the contributions of the following pairwise excitations of electrons [equations (1) and (2)].

Vinyl alcohol

$$\Psi_{\text{MCSCF}} = 0.9789\Phi_0 - 0.2043\Phi(1a'' \longrightarrow 2a'') \quad (1)$$

Furan

$$\Psi_{\text{MCSCF}} = 0.9818\Phi_0 - 0.0729\Phi(2b_1 \longrightarrow 3b_1) - 0.1370\Phi(1a_2 \longrightarrow 3b_1) - 0.0808\Phi(2b_1 \longrightarrow 2a_2) - 0.0747\Phi(1a_2 \longrightarrow 2a_2) \quad (2)$$

The significant contributions from the considered pairwise excitations of the  $\pi-\pi^*$  type in both molecules clearly indicate

that the above simple consideration based on the resonance structure may be supported by a more rigorous theoretical approach such as the multiconfiguration self-consistent field method. Therefore, it may be assumed that, for molecules in which the lone pair and  $\pi$ -orbital interaction is important, the preferred protonation site (C<sub>α</sub> or C<sub>β</sub>) may be determined by considering the possible resonance structure leading to the difference in the intrinsic  $\pi$ -basicity. According to this argument, the five-membered heterocyclic compounds such as furan and pyrrole belong to the favoured C<sub>α</sub>-protonation set, while the open-chain compounds such as vinyl alcohol, enol ethers, and ketenimine belong to the preferred C<sub>β</sub>-protonation set, in agreement with experimental observations.

### Acknowledgements

M. T. N. and A. F. H. are indebted to the Department of Education (Irish Government) for financial support. We thank the Computer centres of E. T. H. and U. L. B. for computer-time grants.

### References

- 1 A. R. Katritzky, and J. M. Lagowsky, 'The Principles of Heterocyclic Chemistry,' Academic Press, New York; R. A. Jones, *Adv. Heterocycl. Chem.*, 1970, **11**, 383; A. Gossauer, 'Die Chemie der Pyrrole,' Springer-Verlag, Berlin, 1974; R. A. Jones and G. P. Bean, 'The Chemistry of Pyrroles,' Academic Press, London, 1977.
- 2 R. Gossauer, E. Krumbholz, and F. W. Steuber, *Liebigs Ann. Chem.*, 1981, 789.
- 3 R. Houriet, H. Schwarz, and W. Zummack, *Angew. Chem.*, 1980, **92**, 934; *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 905.
- 4 R. Houriet, H. Schwarz, W. Zummack, J. A. Andrade, and P. v. R. Schleyer, *Nouv. J. Chim.*, 1981, **5**, 505.
- 5 G. Angelini, G. Lilla, and M. Speranza, *J. Am. Chem. Soc.*, 1982, **104**, 7084, 7091.
- 6 P. Politzer and H. Weinstein, *Tetrahedron*, 1975, **31**, 915; D. Chou and H. Weinstein, *ibid.*, 1978, **34**, 275.
- 7 J. Catalan and M. Yanez, *J. Am. Chem. Soc.*, 1984, **106**, 421; J. Catalan, O. Mo, P. Pérez, and M. Yanez, *Tetrahedron*, 1983, **39**, 2851; J. Catalan, P. Pérez, and M. Yanez, *ibid.*, 1982, **38**, 3693 and references cited therein.
- 8 T.-K. Ha and M. T. Nguyen, *J. Mol. Struct., Theochem.*, 1982, **87**, 355.
- 9 D. G. McCarthy and A. F. Hegarty, *J. Chem. Soc., Perkin Trans. 2*, 1980, 579.
- 10 J. S. Binkley, J. A. Pople, and W. J. Hehre, *J. Am. Chem. Soc.*, 1980, **102**, 939.

- 11 W. J. Hehre, R. Ditchfield, and J. A. Pople, *J. Chem. Phys.*, 1972, **56**, 2257.  
13 H. B. Schlegel, Ph.D. Thesis, Queen's University, Kingston, 1975.  
14 M. R. Peterson and R. A. Poirier, MONSTERGAUSS program, University of Toronto, Toronto, 1981.

- 15 U. E. Wiersum and H. Wynberb, *Tetrahedron Lett.*, 1967, 2951.  
16 R. L. DeKock and C. P. Jasperse, *Inorg. Chem.*, 1983, **22**, 3839.

*Received 22nd April 1985; Paper 5/660*