ab initio Molecular Orbital Study of the Effects of α-Substitution on Keto–Enol Tautomerism

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Summary The effects of α-substitution on the keto–enol equilibrium in acetaldehyde are investigated by *ab initio* molecular orbital theory; for all substituents considered, the enol structure is stabilized preferentially to the keto.

Although the enolization of acetaldehyde is the classical example of a molecular tautomerization,[1] few details about the manner in which variations in molecular structure alter the equilibrium are available. Here we apply simple theoretical techniques to probe the role of a single α-substituent in altering the relative stabilities of the keto and enol forms of acetaldehyde.

We have used single determinant LCAO *ab initio* molecular orbital theory throughout, employing an extended basis of Gaussian type functions. This basis set, termed 4-31G,[2] consists of a single inner shell function, written as a linear combination of 4 Gaussians, and a valence shell split into inner and outer parts represented by 3 and 1 Gaussian functions, respectively. Such a level of theory has already met with considerable success in describing the relative stabilities of small polyatomic molecules.[3-5] We have employed standard model bond-lengths and bond-angles,[6] while single bond conformations have been selected as optimum within the limited number of choices open to us.[3]

Energy data for the keto and enol forms of acetaldehyde and a variety of its α-substituted derivatives are presented in Table 1. Of some importance is the observation that all substituents considered lower the energy of the enol structure in preference to that of the keto. Indeed, the effect is such that an α-amino- or hydroxy-group causes a 50% decrease in the keto–enol difference in stabilities. The keto forms are, however, still favoured in all cases. These observations may be rationalized by considering the energies of the isodesmic† reactions (1 and 2) which provide

$$CH_2XCHO + CH_4 \rightarrow CH_3CHO + CH_3X \quad (1)$$

$$CHX{=}CH(OH) + CH_4 \rightarrow CH_2{=}CH(OH) + CH_3X \quad (2)$$

some measure of the degree of interaction between the substituent X and the keto and enol forms of acetaldehyde, respectively.‡ These quantities are given in Table 2. Thus, with the exception of the keto form of α-fluoroacetaldehyde, all substituents stabilize the parent molecules. This stabilization is significantly greater for the enol forms than for the keto (except for α-methyl substitution). More simply stated, substituents interact to a greater extent with double bonds than they do with single linkages.

Table 1. *Energy data for molecules* $CH_2X{-}CH{=}O \longleftrightarrow CHX{=}CH(OH)$

	Keto form		Enol form		
X	Single bond conformations[a]	*E*(hartrees)	Single bond conformations[a]	*E*(hartrees)	*E*(enol)−*E*(keto) (kcal mol^{-1})
H		−152·68475	CCOH *cis*	−152·66422	12·9
CH_3	CCCO *cis*	−191·66266	CCCO *cis*, CCOH *trans*	−191·64463	11·3
NH_2	NCCO *cis*, CCN:[b] *trans*	−207·61945	NCCO *cis*, CCOH *trans*	−207·61100	5·3
OH	OCCO *cis*, CCOH *gauche*	−227·41757	OCCO *cis*, CCOH *cis*, CCOH *trans*	−227·40813	5·9
F	FCCO *gauche*	−251·39979	FCCO *cis*, CCOH *cis*	−251·38699	8·0

[a] Chosen as optimum within the limited range of specific conformations allowed by the model described in ref. 3. [b] N: refers to the fourth tetrahedral direction for pyramidal nitrogen.

Table 2. *Stabilization energies*[a] (*kcal* mol^{-1})

X	Keto form	Enol form
CH_3	1·6 (3·5)[b]	3·2
NH_2	3·9	11·5
OH	1·4	8·3
F	−1·2	3·7

[a] Calculated from the 4-31G total energies given in Table 1 and the following theoretical energies for CH_4 and the CH_3X molecules: CH_4, −40·13955; CH_3CH_3, −79·11484; CH_3NH_2, −95·06803; CH_3OH, −114·87020; CH_3F, −138·85648.

[b] Experimental determination. Heats of formation (at 298 K) taken from ref. 3.

One might expect even further relative stabilization of the enol by formally unsaturated substituent groups (vinyl and cyano, for example) where extended conjugation becomes possible. Although none of the α-substituents we have dealt with actually lowers the energy of the enol below that of the corresponding keto form, continued substitution should provide an accessible route to stable enols.

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† Isodesmic reactions, those in which equal numbers of each type of bond are present on both sides of the arrow, are well described by simple levels of *ab initio* molecular orbital theory. Although experimental thermochemical data on most of the molecules considered here are unavailable, previous studies indicate a mean deviation of theory from experiment of 3·0 kcal mol^{-1} in the description of the heats of isodesmic reactions. (Ref. 3 and references therein.)

‡ A positive energy for reactions (1) and (2) indicates a stabilizing interaction; a negative value, a destabilizing interaction.

[1] For a recent complete review see: S. Forsen and M. Nilsson, in "The Chemistry of the Carbonyl Group," part 2, ed. S. Patai, Interscience, New York, 1970.
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