Edward J. Drexler and Kurt W. Field University of Wisconsin-Whitewater Whitewater, 53190

# An NMR Study of Keto-Enol Tautomerism in $\beta$ -Dicarbonyl Compounds

Ketones readily undergo acid or base catalyzed  $\alpha$ -hydrogen substitution reactions in which the rate determining step is the formation of the enol or enolate anion



Compared to the acid catalyzed process, the self enolization (tautomerization) of most ketones is negligible;<sup>1</sup> the keto form is favored almost exclusively (1).  $\beta$ -Dicarbonyl compounds also undergo tautomerization; however, the enol tautomer may predominate at equilibrium. The enol isomer is stablized relative to the keto form via resonance through the conjugated  $\pi$ -system and by intramolecular hydrogen bonding.





An investigation of the keto-enol tautomerization of  $\beta$ dicarbonyl compounds provides an excellent undergraduate physical organic or instrumental analysis experiment. The effects of solvent, concentration (2, 3), and temperature (4) on the equilibrium constant can be shown and the thermodynamic functions for enolization (4) obtained.

A procedure for the quantitative determination of the equilibrium constant  $(K_{eq})$  for the tautomerization of  $\beta$ -dicarbonyl compounds was developed by Kurt Meyer (5); the method involves the direct titration of the enol with bromine. The equilibrium constants have also been ascertained by infrared (4, 6), ultraviolet (7), and nuclear magnetic resonance techniques (8–11), and by refractive index measurements (4, 12). The volumetric method may, in

<sup>1</sup> Acetone exists as 0.00025% enol; see Ref. (1).

<sup>2</sup> With  $\beta$ -dicarbonyl compounds in which R' and R" (eqn. (2)) are not identical, two different enols may be possible, (I) and (II). Due to differences in R and R" (steric and electronic) the two enols should have different equilibrium constants. The determination of these rate constants is usually not possible by proton nmr techniques because the proton and electronic shifts are faster than the proton nmr time scale. The  $K_{eq}$ 's can be obtained for these substrates via oxygen-17 nmr (14), infrared (15), and ultraviolet (16) spectroscopy.

for β-Dicarbonyl Compounds					
Compound			20% in CCl <sub>4</sub>		
	Ne Enol, %	at K <sub>eq</sub> a	Enol, %	K <sub>eq</sub> a	Signals Integrated <sup>b</sup>
Acetylacetone	74.7	2.95	90.3	9.33	CH3K/CH3e
acetate	6.44	0.0690	19.4	0.240	CH3K/CH3e
zoylacetate -Benzoylace-	18.6	0.229	36.7	0.584	CH3t/CHe
tone Diethyl 1,3- Acetone- dicarboxyl-			86.6	7.00	CH3 <sup>t</sup> /CH <sup>e</sup>

37.6

0.606

CH3t/CH2k

Percent Enol Tautomers and Equilibrium Constants

 ${}^{a} \kappa_{eq}$  = (enol)/(keto); spectra recorded at 37 ± 2° C. b e = enol; k = keto; t = total.

0.263

20.7

ate



Figure 1. Proton nmr spectra of acetylacetone and ethyl acetoacetate as neat liquids at 37  $\pm$  2°C.

some instances, give erroneous results due to the chemical disturbance of the equilibrium. A quantitative determination of  $K_{eq}$  by absorption methods may be complicated by deviations from Beer's Law and possible differences in the absorptivities of the keto and enol carbonyl bands. Nmr appears to be the method of choice because under normal

operating conditions, the conversion rate between the two tautomers is sufficiently slow so that a combined spectrum of each tautomer is obtained.<sup>2</sup> In addition to providing information about  $K_{eq}$  the nmr method can be used to determine the thermodynamic parameters for tautomerization by measuring the temperature dependence of  $K_{eq}$ .

We offer herein experiments designed to use the nmr spectrometer as an analytical instrument from which an understanding of a number of the factors involved in the keto-enol tautomerism is obtained.

## **Determination of Enol Content**

In the initial portion of the experiment, the enol content of several  $\beta$ -dicarbonyl compounds and their equilibrium constants are determined (see the table). The spectra of acetylacetone and ethyl acetoacetate and their interpretations are reproduced in Figure 1.

## **Solvent Effects**

The second portion of the experiment involves the determination of the equilibrium constants in several solvents at various concentrations (9, 10) and constant temperature. Figure 2 reveals that both solvent and concentration have a pronounced effect on  $K_{eq}$ . The enol form of a  $\beta$ -diketone or  $\beta$ -keto ester is the least polar of the two tautomers because the intramolecular hydrogen bonding in the enol helps reduce the dipole-dipole repulsion of the carbonyl groups which occurs in the keto form (1). Consequently, as the polar carbonyl compounds are progressively diluted with non-polar solvents the enol content of the system increases. Likewise, at constant concentrations, the differences in polarity between these "inert" solvents also produces predictable shifts in the equilibrium. Conversely, progressive dilution of the  $\beta$ -dicarbonyl with a more polar solvent than the solute increases the stability of the keto form relative to the enol.

#### **Thermodynamic Functions**

The final portion of the experiment involves the determination of the thermodynamic parameters for enolization by measuring  $K_{eq}$  as a function of temperature (4, 10). Figure 3 represents a plot of log  $K_{\rm eq}$  versus 1/T for the tautomerization of acetylacetone. The thermodynamic data for acetylacetone determined by this method is:  $\Delta H(-2.7)$ kcal/mole),  $\Delta S(-6.3 \text{ cal/mole deg})$ , and  $\Delta G_{298}(-776 \text{ cal})$ .

#### **Experimental Section**

The nmr spectra were recorded on a Varian A-60 instrument equipped with a variable temperature probe. The probe temperatures were determined by using an ethylene glycol reference. The spectra in Figure 2 were obtained using tetramethylsilane (sealed capillary) as an internal reference. The solvents (spectro grade) and  $\beta$ -dicarbonyl compounds were used as received except for acetylacetone and ethyl acetoacetate which were distilled prior to use. For the solvent studies, weight percent solutions of the solutes (2, 5, 10, 20, 40, 60, and 80%) were prepared.

The equilibrium constants3 (the table), solvent data (Fig. 2), and thermodynamic parameters (Fig. 3) were obtained by integrating (10 determinations) the appropriate enol and keto signals. The standard deviation in the determination of percent enol was less than  $\pm 4\%$ .<sup>3</sup> The slope of the line from a plot of log  $K_{eq}$  versus 1/T afforded  $-\Delta H/R$ . The free energy changes at the various temperatures were calculated using  $\Delta G = -2.303 RT \log K_{eq}$ .

#### **Proton Assignments**

The proton assignments for the resonances of the compounds listed in the table are based on relative signal intensities, chemical shifts, and peak multiplicities. In many



Figure 2. Effect of solvent and concentration on the keto-enol equilibrium of acetylacetone at 37 ± 2°C. (O) CCl<sub>4</sub>; (△) CHCl<sub>3</sub>; (●) CH<sub>2</sub>Cl<sub>2</sub>; (▲) HCON(CH<sub>3</sub>)<sub>2</sub>.



Figure 3. The temperature dependence of  $K_{eq}$  for the tautomerization of acetylacetone.

cases the assignments may be confirmed by diluting the  $\beta$ dicarbonyl with a non-polar solvent which increases the enol content, or by measuring  $K_{eq}$  at two temperatures, the higher temperature favoring the keto form.

#### **Additional Experiments**

The literature abounds with other keto-enol systems amenable to nmr study. The method has been used to examine a homologous series of  $\beta$ -diketones in which the structures of R' and R" (eqn. (2)) are varied. Such studies revealed that the enol content increases as the steric requirements of the substituents increase (13). In addition to variations in  $K_{eq}$ , solvent effects are also responsible for predictable chemical shifts of the —OH proton in the  $\beta$ dicarbonyl relative to the neat material (9).

### Literature Cited

- (1) Gould, E. S., "Mechanism and Structure in Organic Chemistry," Holt, Rinehart, and Winston, New York, 1959, p. 376f. Ward, C. H., J. CHEM. EDUC., 39, 95 (1962). Lockwood, K. L., J. CHEM. EDUC., 42, 481 (1965)
- (2)
- (3)
- (4) Dawber, J. G., and Crane, M. M., J. CHEM. EDUC., 44, 150 (1967).
- (5) Meyer, K. H., Ann., 380, 212 (1911).
  (6) Powling, J., and Bernstein, H., J. Amer. Chem. Soc., 73, 4353 (1951).
- (b) Townig, S., and Denseen, H., G. Matter, Creen Soc., 19, 400 (1977).
   (7) Briegleb, G., and Strohmeier, W., Z. Naturforsch., 6b, 6 (1951).
   (8) Jarrett, H. S., Sadler, M. S., and Shoolery, J. N., J. Chem. Phys., 21, 2092 (1953).
   (9) Rogers, M. T., and Burdett, J. L., Can. J. Chem., 43, 1516 (1965).
- Allen, G., and Dwek, R. A., J. Chem. Soc., B, 161 (1966).
   Schweitzer, G. K., and Benson, E. W., J. Chem. Eng. Data, 13, 452 (1968).
   Meyer, K. H., and Wilson, F. G., Chem. Ber., 47, 837 (1914).

- (13) Koshimura, H., Saito, J., and Okubo, T., Bull. Chem. Soc. Jap., 46, 632 (1973).
- (14) Gorodetsky, M., Luz, Z., and Mazur, Y., J. Amer. Chem. Soc., 89, 1183 (1967) (15) Forsen, S., Merenyi, F., and Nilsson, M., Acta Chem. Scand., 18, 1208, (1964).
- (16) Barnum, D. W., J. Inorg. Nucl. Chem., 21, 221 (1961).

<sup>3</sup> Computer programs are available from the authors to calculate the  $K_{eq}$ , % enol and standard deviations, and to determine the thermodynamic quantities. They are written in PL1 language.