

Enol-Keto Tautomerism of Alkyl 2-Picolyl Ketones

Karl R. Wursthorn and Eldon H. Sund

Department of Chemistry, Midwestern University,
Wichita Falls, Texas 76308

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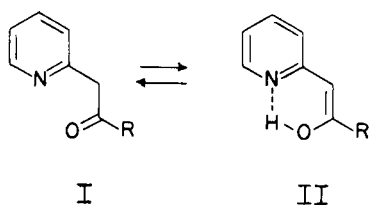
An analysis of the ir and nmr spectra taken on a series of nine different alkyl 2-picolyl ketones clearly indicates that there is an enol-keto tautomerism. The enol:keto ratio exhibits a marked dependence on both solvent polarity and the nature of the alkyl group. The equilibrium values correlate with the Taft steric substituent constants.

Introduction.

Preliminary results indicated that the equilibrium constants of the enol-keto tautomerism of alkyl 2-picolyl ketones exhibit a marked dependence on the structure of the alkyl group. Similar effects have been reported for the analogous tautomerism of β -dicarbonyls leading to a Hammett correlation of the acyl groups with the equilibrium constants and a Taft correlation with the α substituents (1). R. F. Branch noted that a Hammett correlation of the para substituent with enol:keto ratio existed for a series of *p*-phenyl 2-picolyl ketones (2-phenacyl pyridines) (2). We felt that it would be of interest to determine whether an equilibrium-structure correlation existed for the series, (I) and (II), of alkyl 2-picolyl ketones. The established method of nmr integration of the vinyl and methylene proton signals was used (3). The results were checked by a comparison of the ir double bond and carbonyl absorbancies.

Results.

The ir spectrum of *t*-butyl 2-picolyl ketone in Figure 1 is representative of the series. The significant absorptions are: a weak, broad band at 2600 cm^{-1} , chelated hydroxyl (4); a strong absorption at 1710 cm^{-1} , the carbonyl of the keto isomer; and a strong absorption at 1645 cm^{-1} , the carbon double bond of the enol isomer. The assignments are comparable to those of 2-phenacyl pyridine (2).



R = (Me, Et, *n*-Pr, *i*-Pr, *n*-Bu, *t*-Bu,
s-Bu, *t*-Bu, *n*-Pe)

The ratio of the absorbancies of the carbon double bond to the carbonyl is taken as an estimate of the equilibrium constants. It is understood that these values will differ from the true value by approximately some constant factor for the homologous series. Recorded in Table I are the frequencies and absorbancy ratios.

The nmr spectrum of *t*-butyl 2-picolyl ketone in Figure 2 illustrates the general features of the whole series. The chemical shift assignments based on those of known compounds and integrated areas are: δ 1.11 ppm (9H singlet, keto); δ 1.21 ppm (9H singlet, enol); δ 3.98 ppm (2H singlet, keto); δ 5.43 ppm (1H singlet, enol); δ 6.7-7.7 ppm (3H multiplet of the enol superimposed on a 3H multiplet of the keto); δ 8.16 ppm (1H multiplet, enol); δ 8.48 ppm (1H multiplet, keto) and δ 15.0 ppm (1H broad singlet, enol chelated hydroxyl). The large change in the chemical shift for the alpha ring proton (δ 8.48 ppm to δ 8.16 ppm) is to be expected since the polarizability of the nitrogen (5) has been greatly altered due to hydro-

TABLE I

Alkyl Group	$K_{\text{rel}} = (\text{Enol/Keto})$ (a)
methyl	.36
ethyl	.31
<i>n</i> -propyl	.51
<i>n</i> -butyl	.54
<i>n</i> -pentyl	.59
isopropyl	.63
isobutyl	.67
<i>sec</i> -butyl	.91
<i>t</i> -butyl	.93

(a) $K_{\text{rel}} = \text{C=C Absorbance/C=O Absorbance}$

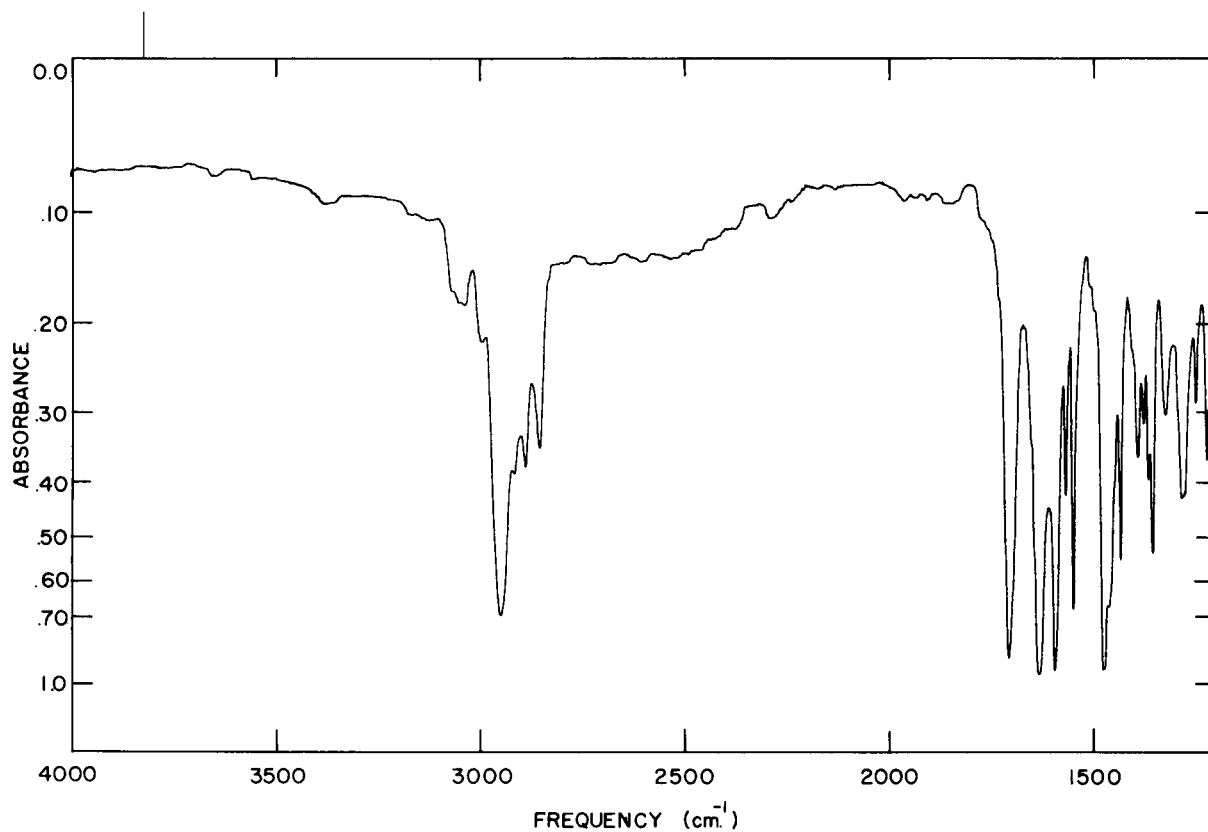


Figure 1. The ir spectrum of *t*-butyl 2-picolyyl ketone, thin film.

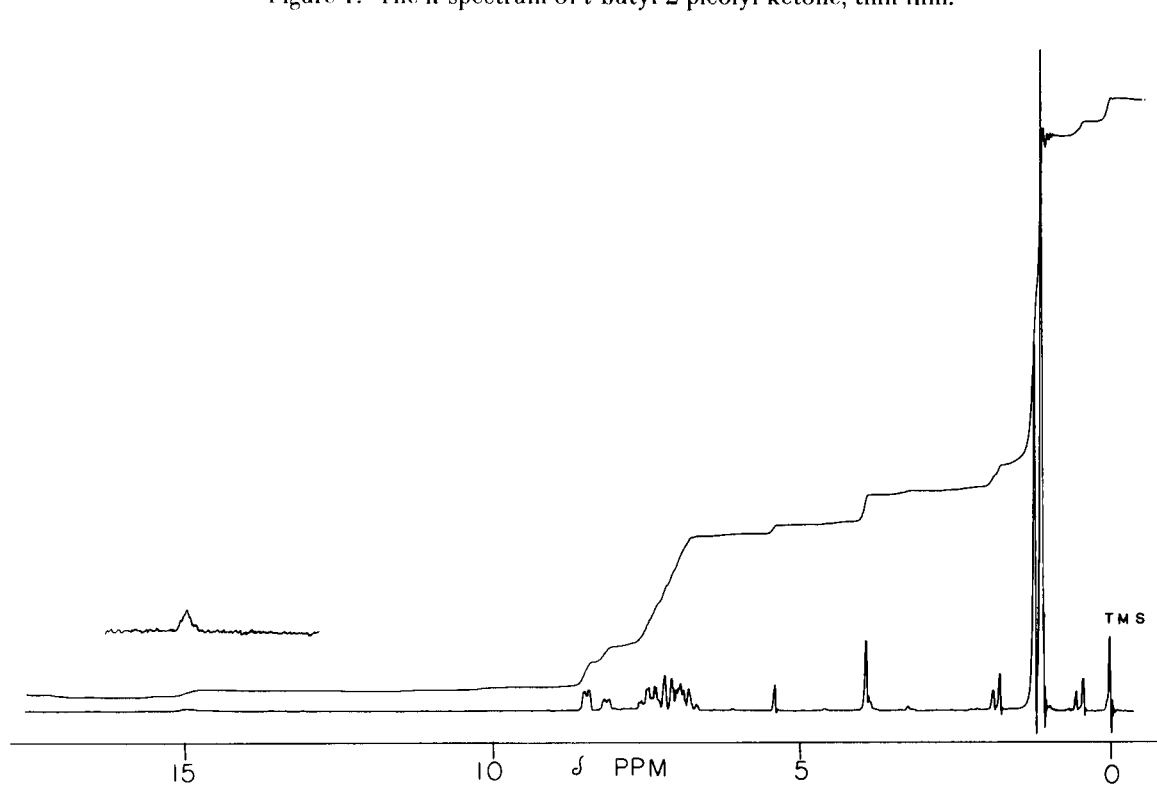


Figure 2. The nmr spectrum of *t*-butyl 2-picolyyl ketone, neat sample with TMS as internal standard. Sweep width 1200 cps.

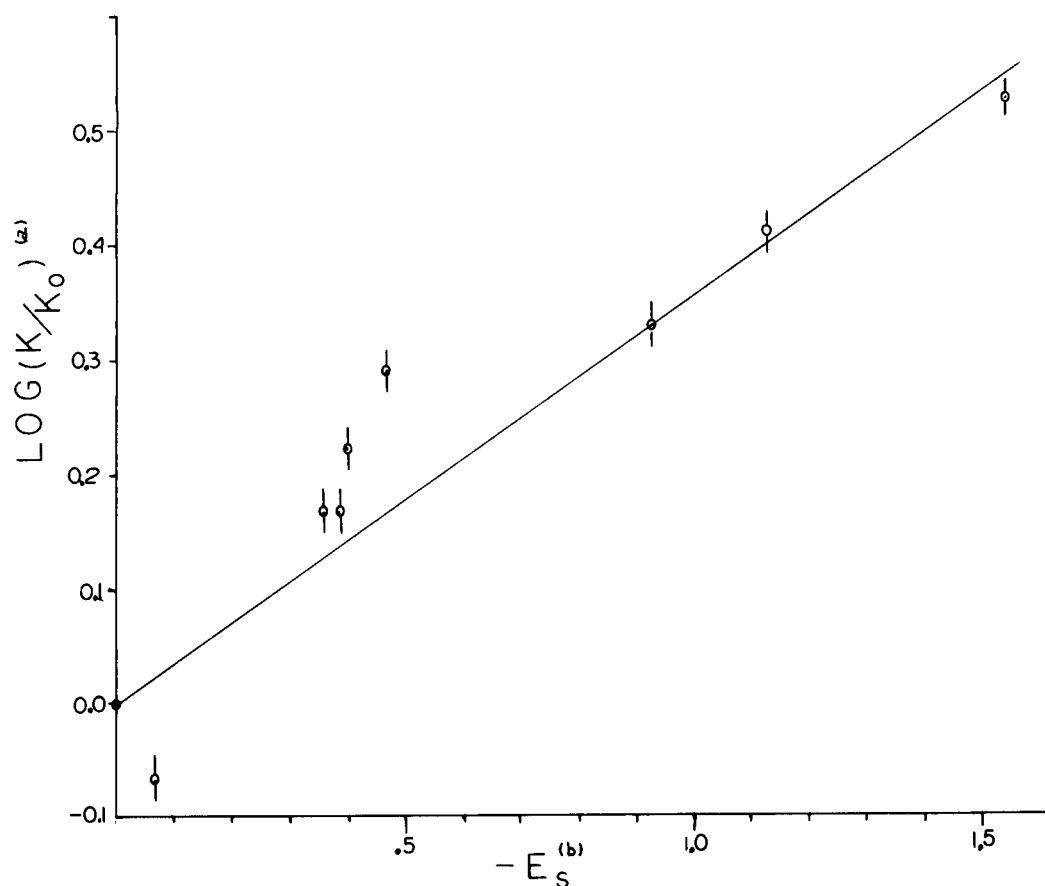


Figure 3. Taft correlation of steric substituent constants vs. $\text{Log}(K/K_0)$. (a) $K = (\text{enol})/(\text{keto})$, K_0 is the equilibrium constant of methyl 2-picolyl ketone. (b) E_s are the steric substituent constants (9).

TABLE II

R	CH_2 ppm	Neat Sample C=C-H ppm	Enol/Keto	Enol/Keto in Various Solvents		
				CCl_4	CDCl_3	DMSO
methyl	3.93	5.35	.21	.27	.15	.17
ethyl	3.94	5.40	.18	.24	.07	.13
<i>n</i> -propyl	3.88	5.35	.31	.31	.18	.19
<i>n</i> -butyl	3.89	5.36	.31	.43	.16	.20
<i>n</i> -pentyl	3.88	5.35	.35	.26	.15	.21
isopropyl	3.96	5.37	.41	.47	.25	.16
isobutyl	3.86	5.34	.45	.49	.19	.28
<i>sec</i> -butyl	3.90	5.33	.54	.52	.32	.41
<i>t</i> -butyl	3.97	5.43	.71	.70	.35	.40

gen bonding of the enol isomer. Integrated areas were used to make the assignment of the alpha ring proton and the *t*-butyl group; the validity depends on the proper assignment of the methylene (δ 3.98 ppm) and the vinyl (δ 5.43 ppm) protons. Although the spectra of other compounds of the series were more complicated (6), all

had the same features in the portion of the spectrum from δ 3.5 ppm to δ 15.0 ppm, thus, integration to obtain equilibrium constants was possible in all cases. Table II gives the data for the series of compounds neat and in solution.

Further confirmation of the assignments was made

possible by deuterium exchange. An equimolar mixture of deuterium oxide with *t*-butyl 2-picoyl ketone caused exchange of the methylene, vinyl and enol protons with deuterium in nearly theoretical amount after 24 hours in acetone solution.

Discussion.

The data in Table II show that nonpolar solvents have little or no effect on the equilibrium, while polar solvents shift the equilibrium to the keto isomer. This indicates that intermolecular hydrogen bonding is unlikely and the enol is nonpolar relative to the keto isomer. This would be true only if an intramolecular hydrogen bond existed. The ir and nmr absorptions at 2600 cm^{-1} and $\delta\ 15.0$ ppm respectively are characteristic of cyclic hydrogen bonded enols (3,4). Alkyl 4-picoyl ketones have an enol:keto ratio that is an order of magnitude lower than the alkyl 2-picoyl series (7) demonstrating that position of the nitrogen is critical to enol stability. These results are most easily accommodated by an intramolecular hydrogen bond for the enol.

To make an equilibrium-structure correlation it was demonstrated that an equilibrium does exist. Under the condition used the nonlabile vinyl proton must exchange by equilibration with the keto isomer whose methylene protons are relatively labile.

The Taft linear free energy relationship is given by: $\text{Log}(K/K_0) = \sigma^*\rho^* + \delta E_s$, $K = [\text{enol}]/[\text{keto}]$ and K_0 refers to methyl (8). There was no correlation with the polar substituent constants alone; however, a reasonably good correlation (Figure 3) is found with the steric substituent constants (E_s). From the data presently available it seems likely that ρ^* is greater than zero (1,2). Further evidence is given by the (strongly electron withdrawing) trifluoromethyl group in trifluoromethyl 2-picoyl ketone having an enol:keto ratio greater than nine (10). An improved correlation is obtained if values of between zero and one are used; however, such an approach is purely artificial until ρ^* can be independently determined.

Fisher-Hirschfelder-Taylor space filling models suggest how steric effects could be operative without any effective change in hybridization at the carbonyl carbon. Free rotation of the keto picoline moiety is severely hindered for bulky alkyl groups. By necessity of the intramolecular hydrogen bond, all such rotations are restricted in the enol; thus, the total decrease in entropy is greater for bulky alkyl groups. Since these effects are a long range interaction between the alkyl group and the ring protons as compared with the shorter range interactions upon which the E_s values were determined, deviations are expected. It is realized that more subtle causes may be in effect but would in no way alter the fact that a correlation does exist.

These results have stimulated further research to determine the value of ρ^* . A study of the alkyl 2-picoyl thioketone tautomerism is planned to test the generality of the results.

Acknowledgments.

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EXPERIMENTAL

Preparation of Alkyl 2-Picoyl Ketones.

The preparation was done by the method of Levine (11) and the physical properties of the alkyl 2-picoyl ketones and derivatives are reported elsewhere (12). Purification was done on a Nester Faust annular teflon spinning band column and purity was checked by gas chromatography using a 5 ft. x $\frac{1}{4}$ in., 3% S. E. 30 column in a Varian 90-P Aerograph instrument.

Infrared Analyses.

A Perkin-Elmer Model 337 Grating Infrared Spectrophotometer was used for all ir analyses. Thin film samples were used, the thickness of film adjusted so that all samples exhibited approximately the same absorbance. The absorbance at 1850 cm^{-1} was adjusted to zero and used as the base line. The relative equilibrium constants were calculated as:

$$K_{\text{rel}} = \text{Absorbance C=C} / \text{Absorbance C=O}$$

Nuclear Magnetic Resonance Analyses.

A Hitachi Perkin-Elmer High Resolution Nuclear Magnetic Resonance Spectrometer Model R-20 was used. The probe temperature was 33.0° ; TMS was used as an internal standard; the chemical shifts are reported in ppm relative to it in all cases. Typical instrument settings were: sweep width 600 cps, sweep time 250 sec., time constant .1 sec., RF field $H_1\ 5 \times 10^2$ micro-volt, and sensitivity 2.5×10^1 . The equilibrium constants were obtained by integrating the vinyl and methylene protons at 5.35 ppm and 3.90 ppm respectively.

$K = 2 \times (\text{Area})$ of vinyl proton / Area of methylene proton. The neat samples were integrated three times, the average value was reported. The solution spectra were run at approximately 50 v/v % dilution.

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