Phenylacetaldehyde and its *cis*- and *trans*-Enols and Enolate Ions. Determination of the *cis* : *trans* Ratio under Equilibrium and Kinetic Control

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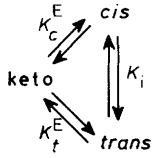
A method of determining individual keto–enol equilibrium and acid dissociation constants for systems in which unstable enols can exist in *cis* and *trans* isomeric forms is developed and is applied to phenylacetaldehyde in aqueous solution; the results give equilibrium *cis* : *trans* ratios of 35 : 65 in acidic and neutral solutions and 20 : 80 in a basic solution (where the enols are converted to enolate ions), but show considerably less *cis* : *trans* differentiation for enols formed under kinetic control.

The chemistry of simple enols is currrently undergoing vigorous exploration due in large part to the development of methods for generating these unstable substances in solution at greater than equilibrium concentrations under conditions where their rates of reaction can be measured directly.[1] This has allowed determination of specific rates of enol ketonisation, k^K, which has led to the evaluation of keto–enol equilibrium constants, K^E, as ratios of enolisation to ketonisation rate constants, $K^E = k^E/k^K$.[2—5] This method encounters difficulty, however, when the enol can exist in *cis* and *trans* isomeric forms. In such cases there are two separate enol-forming equilibria (equation 1) governed by two separate



(1)

relationships, $K_c^E = k_c^E/k_c^K$ and $K_t^E = k_t^E/k_t^K$, and, whereas k_c^K and k_t^K may be measured independently if the two isomeric enols can be prepared, conventional methods of determining enolisation rate constants, *e.g.* halogen scavenging, give only a single, global specific rate of enolisation, k^E, which is the sum of the two individual rate constants, $k^E = k_c^E + k_t^E$. This global rate constant cannot be separated into its components without knowledge of the *cis* : *trans* product ratio, which is difficult to determine for unstable enols that revert back to their keto isomers faster than they are formed. We report that we have devised a method of solving this problem and have applied it to the determination of *cis* : *trans* enol and enolate ion ratios in the phenylacetaldehyde system.

Our method is based upon the fact that individual *cis* and *trans* keto–enol equilibrium constants can be expressed as functions of the three directly measurable rate constants and a *cis-trans* isomerisation constant K_i (= [*cis*]/[*trans*]): K_c^E, $K_t^E = f$ (k^E, k_c^K, k_t^K, K_i). This isomerisation constant can sometimes be measured directly, *e.g.* when the enol content of the system is sufficiently high to allow direct observation by a spectroscopic method. That unfortunately was not the case here, but K_i is also a function of the three rate constants plus the acidity constants of the *cis* and *trans* enols ionising as oxygen acids $(K_a^E)_c$ and $(K_a^E)_t$ and the global acidity constant of the keto isomer, ionising as a carbon acid, K_a^K: $K_i = f$ [k^E, k_c^K, k_t^K, $(K_a^E)_c$, $(K_a^E)_t$, K_a^K].

The equilibrium constant K_i can be formulated as a function of rate constants for interconversion of the *cis–trans* isomers *via* the keto form, equation (2) [*cf.* equation (1)]. Use of the definition of k_E ($= k_c^E + k_t^E$) to eliminate first k_t^E and then k_c^E from this expression leads to the relationships of equation (3). These in turn provide the expressions of equation (4). The global acidity constant K_a^K is equal to the sum of the acidity constants for ionization of the keto isomer to individual *cis* and *trans* enolate ions, equation (5), each of which may be expressed as the product of a keto–enol equilibrium constant and an enol ionization constant, equation (6). Combination of equations (4), (5) and (6) then leads to equation (7).

$$K_i = k_t^K k_c^E / k_c^K k_t^E \quad (2)$$

$$k_c^E = k^E k_c^K K_i/(k_c^K K_i + k_t^K); k_t^E = k^E k_t^K/(k_c^K K_i + k_t^K) \quad (3)$$

$$K_c^E = k_c^E/k_c^K = k^E K_i/(k_c^K K_i + k_t^K); \quad K_t^E = k_t^E/k_t^K = k^E/(k_c^K K_i + k_t^K) \quad (4)$$

$$K_a^K = (K_a^K)_c + (K_a^K)_t \quad (5)$$

$$(K_a^K)_c = K_c^E (K_a^E)_c; (K_a^K)_t = K_t^E (K_a^E)_t \quad (6)$$

$$K_i = [k^E (K_a^E)_t - K_a^K k_t^K]/[K_a^K k_c^K - k^E (K_a^E)_c] \quad (7)$$

The various quantities needed to determine K_i in this way were obtained using methods we have developed for other keto–enol systems which are not complicated by *cis–trans* isomerism.[2] Global rates of enolisation of phenylacetaldehyde were determined by halogen scavenging. Measurements in dilute mineral acid solutions gave $k_{H+}^E = (1.53 \pm 0.04) \times 10^{-4}$ dm^3 mol^{-1} s^{-1},†‡ and those in dilute sodium hydroxide solutions gave $k_{HO-}^E = 42.4 \pm 1.3$ dm^3 mol^{-1} s^{-1}.†‡§ Individual rates of ketonisation were determined using *cis* and *trans* enols generated separately *in situ* by hydrolysis of the corresponding trimethylsilyl enol ethers.[6] Measurements in dilute mineral acid solutions gave $(k_{H+}^K)_c = 0.190 \pm 0.010$ and $(k_{H+}^K)_t = 0.0745 \pm 0.0042$ dm^3 mol^{-1}, and those in dilute sodium hydroxide and hydrogen carbonate buffer solutions gave $(k_{HO-}^K)_c = (4.48 \pm 0.37) \times 10^4$ and $(k_{HO-}^K)_t = (2.91 \pm 0.10) \times 10^4$ dm^3 mol^{-1} s^{-1}.† The measurements in hydrogencarbonate buffer solutions also led to the individual enol acidity constants $p(K_a^E)_c = 9.76 \pm 0.03$ and $p(K_a^E)_t = 9.46 \pm 0.01$,†¶ and a spectrophotometric titration curve determined in dilute sodium hydroxide solutions gave the global keto acidity constant $pK_a^K = 12.43 \pm 0.08$.†‡§¶

These data provide two semi-independent values of K_i, one using the rate constants measured in acid solution and the other using the rate constants measured in basic solution, but both employing the single set of acidity constants. The acid data give $K_i = 0.57 \pm 0.21$ and the base data give $K_i = 0.41 \pm 0.26$; their weighted average is $K_i = 0.51 \pm 0.16$. An equilibrium constant for the corresponding interconversion of *cis* and *trans* enolate ions, K_i^- (= [*cis*$^-$][*trans*$^-$]), may also be obtained from the relationship $K_i^-/K_i = (K_a^E)_c/(K_a^E)_t$, giving $K_i^- = 0.25 \pm 0.08$. These isomerisation equilibrium constants make the *trans* enol more stable than the *cis* by 0.4 kcal mol^{-1} (cal = 4.184 J) and the *trans* enolate ion more stable than the *cis* ion by 0.8 kcal mol^{-1}. This is consistent with a similar small difference in the stabilities of the corresponding *cis* and *trans* enol ethers.[7]

These results lead to the individual keto–enol equilibrium constants $pK_c^E = 3.35 \pm 0.09$ and $pK_t^E = 3.07 \pm 0.10$, and an overall keto–enol equilibrium constant $pK^E = 2.88 \pm 0.08$.‖ The enol content of phenylacetaldehyde is thus quite high, three orders of magnitude greater than that of acetaldehyde itself for which $pK^E = 6.23$.[2b] This is as expected from the well-known carbon–carbon double bond stabilising effect of a phenyl substituent,[8] and is consistent with observations for other enols.[1,2d,9] These results also show that, at equilibrium in acidic and neutral solutions, where K_i governs the *cis–trans* isomerisation, some 35% of the enol exists as the *cis* isomer and 65% as the *trans*, whereas in basic solution, where the enols are converted to enolate ions and K_i^- applies, the difference rises to 20% *cis* and 80% *trans*. Under kinetic control, on the other hand, there is much less differentiation. In this case the isomer distributions are governed by the relative values of the rate constants for the *cis*- and *trans*-enol-forming reactions, and the data obtained here indicate that these are not very different. For acidic solutions, $(k_{H+}^E)_c = (8.6 \pm 1.9)\ 10^{-5}$ and $(k_{H+}^E)_t = (6.4 \pm 1.6)\ 10^{-5}$ dm^3 mol^{-1} s^{-1},†‡ and for basic solutions, $(k_{HO-}^E)_c = 20 \pm 5$ and $(k_{HO-}^E)_t = 25 \pm 6$ dm^3 mol^{-1} s^{-1}.†‡§ Maximum differentiation between *cis* and *trans* isomers can thus be achieved in basic solution under equilibrium control.

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† Aqueous solution, ionic strength = 0.10 M.

‡ Corrected for hydration of the aldehyde using the hydration equilibrium constant $K^h = 2.93 \pm 0.04$ determined here.

§ Corrected for acid ionization of the aldehyde hydrate using the acidity constant $pK_a^h = 13.28 \pm 0.08$¶ determined here.

¶ Concentration equilibrium constant appropriate to aqueous solution at 0.10 M ionic strength.

‖ K^E = ([*cis*] + [*trans*])/[keto].

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