

Aldehyde and Enol Contents of 9-Formylfluorene

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In aqueous solution at 25 °C 9-formylfluorene is present mainly as its enol (72%, $K_E = 17$) and hydrate (24%, $K_h = 5.6$); the unstable aldehyde (4%) may be generated for kinetic and equilibrium measurements by reaction of its ethanethiol hemithioacetal with iodine.

The enol content of most simple aldehydes and ketones is small:^{1,2} e.g. for acetone and acetophenone in aqueous solution it is one part in 10^8 . Keto-enol equilibrium constants are then best determined kinetically by combining rate constants for the forward and reverse reactions. Rate constants for enolisation may be measured by trapping the enol with halogen, and those for ketonisation by generating the unstable enol in a reaction which is sufficiently fast for the subsequent tautomerisation to be rate determining,^{2,3} for example by acidification of the enolate anion.⁴

For 9-formylfluorene⁵ the n.m.r. and u.v. spectra show that, in contrast to most simple aldehydes, the dominant tautomer is the enol (**1**) [e.g. ^1H n.m.r.: δ (CDCl_3) 6.40 (1H, s, OH); δ (CD_3OD) 7.90 (1H, s, =CH-O)]. The enol content in aqueous solution may be determined as 71% from the ratio of initial to final absorbances at 315 nm (λ_{max} of the enol) following neutralisation of the enolate anion in 0.1 M HCl. However, this does not yield the keto-enol equilibrium constant because what remains is not only the aldehyde (**2**) but also, predominantly, the hydrate. The equilibrium constant may be determined kinetically, but since the stable tautomer is now the enol, means of trapping and rapidly generating the aldehyde (**2**) are required.

A suitable trapping reaction for the aldehyde was found to be addition of bisulphite ion. First order rate constants for reaction of the enol with bisulphite in acetic acid buffers were measured spectrophotometrically and are plotted against $[\text{HSO}_3^-]$ in Figure 1. Buffer dependent kinetic saturation is observed, consistent with a change in the rate-determining step from bisulphite attack on the aldehyde at low concentrations of bisulphite to formation of the aldehyde as the concentration of bisulphite increases (equation 1). The measurements give a rate constant k 0.88 $\text{l mol}^{-1} \text{s}^{-1}$ for catalysis of the ketonisation by acetate ion and show no catalysis by acetic acid.

In studying the reverse reaction, the possibilities of generating the aldehyde from its addition complexes with bisulphite, amines, hydrazine, hydroxylamine, and thiols were considered. In acetate buffers, formation of the aldehyde was rate determining in all cases and the subsequent enolisation too fast to measure. However, rapid generation of the aldehyde can be achieved by reaction of a thiol adduct with iodine.

The hemithioacetal of 9-formylfluorene with ethanethiol was prepared by reaction of a cooled solution of the liquid enol in ethanethiol. A granular white solid formed which could be filtered below 0 °C. The spectral data [^1H n.m.r.: δ (CD_3CN) 1.11 (3H, t, Me), 2.5 (2H, m, $\text{CH}_2\text{-S}$), 3.5 (1H, br., OH), 4.33 (1H, d, O-CH-S), 5.57 (1H, d, 9-fluorenyl CH), 7.2–8.0 (m, Ar); ^{13}C n.m.r. includes δ 80.0 (d, S-C-O); m/z 231 ($M^+ -$

H_2O), 194 ($M^+ - \text{EtSH}$)] were consistent with the hemithioacetal structure as was the spectrum of the corresponding dithioacetal prepared for comparison.

Injection of a stock solution of the hemithioacetal in acetonitrile into 10^{-3} M aqueous HCl gave solutions sufficiently stable for stopped flow measurements of its reaction with iodine in acetic acid buffers. Rapid disappearance of the u.v. spectrum of iodine was followed by a slower appearance of the spectrum of the enol. The expected reaction of the hemithioacetal with iodine is the formation of an iodosulphonium ion in a rapid pre-equilibrium⁶ followed by elimination of ethanesulphenyl iodide (Scheme 1). Qualitative investigation confirmed that the disappearance of iodine was, as expected, inversely dependent on $[\text{H}^+]$ and $[\text{I}^-]$.²

The appearance of the enol was catalysed by acetate ion with a rate constant of $14.9 \text{ l mol}^{-1} \text{ s}^{-1}$.[†] Combining this rate constant with that for ketonisation yields a keto-enol tautomerisation constant K_E 17 ($\text{p}K_E = -1.23$). Combining K_E with the enol content determined by titration gives an equilibrium constant for hydration of the aldehyde, K_h 5.6. In aqueous solution, therefore, 9-formylfluorene is 72% enol, 24% hydrate, and 4% aldehyde.

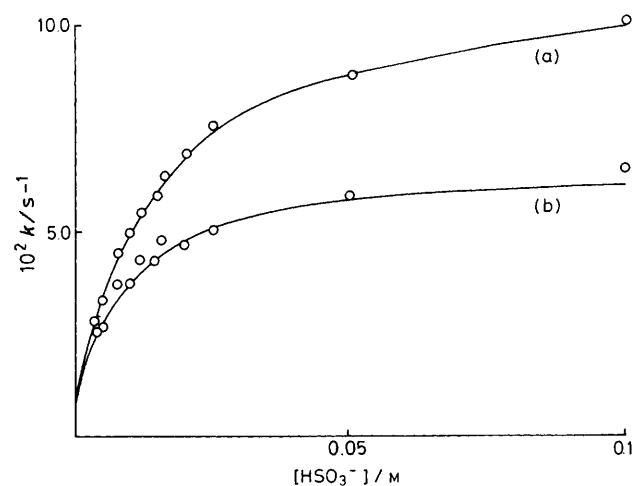
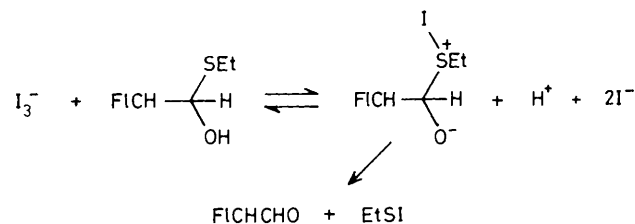
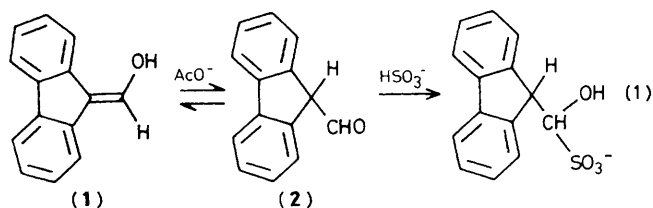


Figure 1. Plot of first order rate constants for the reaction of 9-formylfluorene enol with bisulphite against $[\text{HSO}_3^-]$ in 1:1 acetic acid buffers: (a) 0.1 M buffer; (b) 0.05 M buffer; $T = 25^\circ\text{C}$.



[†] Corrected for reverse and competing hydration reactions.

Above pH 6 ionisation of 9-formylfluorene to its enolate anion occurred, and measurement of an apparent pK_a in lutidine buffers gave pK_a values of 7.4 and 6.2 for the enol and aldehyde, respectively. As expected, 9-formylfluorene has a higher enol content and higher acidity than the corresponding 9-acetylfluorene⁷ which exists predominantly in the keto form with $K_E 5.0 \times 10^{-3}$ ($pK_E 2.3$) and $pK_a 9.5$. The fluorene substituent has a large stabilising effect on both enol and enolate anion. Compared with acetaldehyde ($pK_E 6.23$, $pK_a 16.73$) the enol and enolate anion are stabilised relative to the keto tautomer by factors of nearly 10^8 and 10^{10} , respectively.

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