Ionization Constants of Some Hydroxy-pyrones at 25 °C

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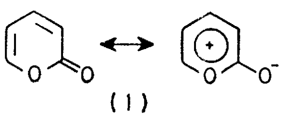
The ionization constants of some hydroxy-pyrones have been measured in aqueous solutions by a spectrophotometric method and compared with those of analogous phenols. The strikingly high acidity of 3,5-diacetyl-4,6-dihydroxy-2-pyrone has been explained by the formation of a symmetrical and extensively resonance-stabilized monoanion through ionization of the C-6 hydroxy-group.

THAT 2- and 4-pyrones (1) and (2) are resonance hybrids of covalent and dipolar structures has important manifestations in their physical properties. The significant contributions of the dipolar structures are reflected, for instance, by their large dipole moments.[1,2] Another consequence of the positively charged character of the pyrone rings should be the enhancement of the acidity of their hydroxy-derivatives over that of the corresponding phenols.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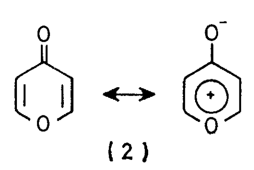
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RESULTS AND DISCUSSION

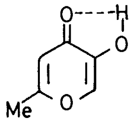
The pK values of five hydroxy-pyrones and the three hydroxy-acetophenones have been determined in aqueous solutions by a spectrophotometric method[3,4] and are summarized in the Table; the detailed results are given in Supplementary Publication No. SUP 22584 (10 pp.).†

Summary of pK values

Hydroxypyrone	pK	Phenol	pK
(3)	8.21	p-Cresol[5]	10.26
(4)	8.68	o-Cresol[5]	10.29
(5)	4.94	m-Cresol[5]	10.09
(6)	5.26	o-Hydroxyacetophenone	10.30
		m-Hydroxyacetophenone	9.17
		p-Hydroxyacetophenone	8.09
(7)	pK_1 1.25		
	pK_2 9.21		

As expected, 3-hydroxy-6-methyl-4-pyrone (3) and 3-hydroxy-2-methyl-4-pyrone (4) have been found to be substantially more acidic than p- and o-cresol[5] respectively. The differences in acidity could have been larger but for the acid-weakening effect of possible intramolecular hydrogen-bonding between the hydroxy and the pyrone carbonyl groups. Steric crowding in compound (4) may cause closer approach of these two groups, with consequential increase in the strength of the hydrogen bond, thus accounting for the slightly lower acidity of (4) compared to (3).

4-Hydroxy-6-methyl-2-pyrone (5) is tautomeric with 2-hydroxy-6-methyl-4-pyrone. That it is much more acidic than m-cresol[5] as well as compounds (3) and (4) is largely attributable to the stabilization of its anion (5a) through delocalization of the negative charge; the anions of (3) and (4) cannot be similarly stabilized.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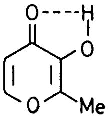
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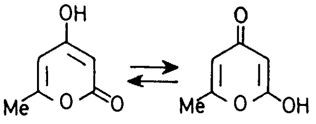
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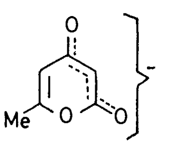
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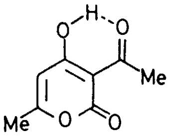
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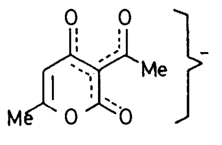
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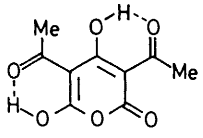
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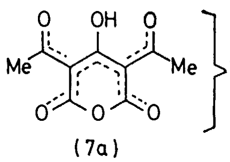
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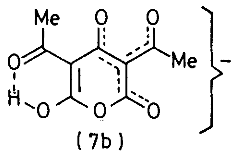
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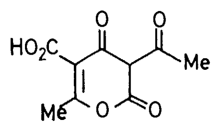
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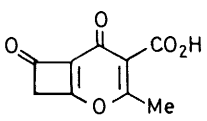
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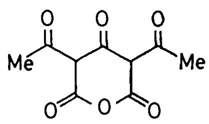
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3-Acetyl-4-hydroxy-6-methyl-2-pyrone (6), on the other hand, is a slightly weaker acid than (5), their pK values differing by 0.32 unit. The expected acid-strengthening effects due to electron-withdrawal by the acetyl substituent and the increased delocalization of the negative charge in the anion (6a) appear to be off-set by the relative stabilization of the un-ionized molecule through intramolecular hydrogen-bonding. A similar interplay of electron-withdrawing effect and intramolecular hydrogen-bonding is evident in the hydroxyacetophenones. The pK of o-hydroxyacetophenone has been found to be 0.30 unit higher than that of phenol,[5]

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† For details of obtaining this material, see Notice to Authors, No. 7, *J.C.S. Perkin II*, 1978, Index issue.

while those of the *meta*- and *para*-isomers are significantly lower

A particularly interesting compound is 3,5-diacetyl-4,6-dihydroxy-2-pyrone (7), which was first prepared by von Pechmann and Neger [6] and was previously assigned various structures such as (8),[6] (9),[7] and (10).[8] Structure (7),[9] which is tautomeric with (10), is preferred on the grounds of stabilization by resonance in the pyrone ring and by favourable intramolecular hydrogen-bonding between the acetyl and hydroxy-groups, as shown by the absence of anhydride and free hydroxy-absorptions in the i.r. spectrum. This structure is also consistent with its behaviour as a strikingly strong dibasic acid. Its very low pK_1 value may, at first sight, appear unexpected in view of the acid-weakening effect of chelation as observed above in compound (6) and in *o*-hydroxyacetophenone. Thus, the exceptionally strong acidity of (7) must be due to some other over-riding factor. Ionization of the C-6 hydroxy-group would yield a monoanion (7a) which should be highly stabilized by very extensive delocalization of the negative charge over the pyrone ring and all four carbonyl oxygen atoms, resulting in a completely symmetrical structure. On the other hand, ionization of the C-4 hydroxy-group would give a less symmetrical and less stable monoanion (7b) as delocalization of the negative charge is much less extensive, being comparable to that in the anion (6a). Hence pK_1 is likely to be a measure of the ionization of the C-6 hydroxy-group. pK_2 is much higher since the C-4 hydroxy-group in the monoanion (7a) can now form a hydrogen-bond with either of the two acetyl oxygen atoms which carry part of the anionic charge.

EXPERIMENTAL

Compounds (3), (5), and (7) were prepared according to reported methods.[9-11] Compounds (4), (6), and the hydroxy-acetophenones were obtained commercially. All compounds were purified by repeated recrystallization and their purity checked by microanalyses.

AnalaR grade chemicals were used for preparing the buffers.

Determination of p*K Values*.—The spectrophotometric method is essentially the same as that used by Robinson and Ang [3] and Robinson.[4] The two pK values of compound (7) are well separated permitting their individual determination directly. All spectral measurements were made in triplicate on solutions thermostatted at 25 °C; matched 1-cm silica cells were used with a Beckman DU-2 spectrophotometer coupled to a Hewlett–Packard 3465A multimeter for digital readout of the percentage transmission. The cell compartment was maintained at 25 °C and the temperature of the air-conditioned room in which measurements were made was also kept close to this value. Appropriate blanks were used throughout.

For compounds (3) and (4) the pK was calculated from equation (1),[4] where the last term is assumed to be negligible, and for compounds (5) and (6) from equation (2),[3]

$$\mathrm{p}K = \mathrm{p}(a_{\mathrm{H}^+}\gamma_{\mathrm{Cl}^-}) - \log[(D_1 - D)/(D - D_2)] + \log(\gamma_{\mathrm{HR}}\gamma_{\mathrm{Cl}^-}/\gamma_{\mathrm{R}^-}) \quad (1)$$

$$\mathrm{p}K = \mathrm{p}K_{\mathrm{R}} + \log(\text{salt/acid}) - \log[(D_1 - D)/(D - D_2)] \quad (2)$$

where the symbols have their usual meaning as given in refs. 3 and 4.

For compound (7) the ionization may be represented as taking place in two stages, where in the 1st stage D_1, D_2,

1st stage: $\mathrm{H_2R} \rightleftharpoons \mathrm{HR^-} + \mathrm{H^+}$

$$\text{and } \mathrm{p}K_1 = \mathrm{pH} - \log[(D_1 - D)/(D - D_2)] - \log\gamma$$

2nd stage: $\mathrm{HR^-} \rightleftharpoons \mathrm{R^{2-}} + \mathrm{H^+}$

$$\text{and } \mathrm{p}K_2 = \mathrm{p}(a_{\mathrm{H}^+}\gamma_{\mathrm{Cl}^-}) - \log[(D_2 - D)/(D - D_3)] - \log(\gamma_{\mathrm{HR}^-}\gamma_{\mathrm{Cl}^-}/\gamma_{\mathrm{R}^{2-}})$$

and D are the absorbance of the $\mathrm{H_2R}$, $\mathrm{HR^-}$, and partially transformed form of the pyrone, respectively, the stoicheiometric concentrations of the pyrone in all three solutions being the same and measurements being made with the same or identical cells and at the same wavelength. In the 2nd stage, D_3 represents the completely ionized form of pyrone, $\mathrm{R^{2-}}$; the other symbols are the same as those in the 1st stage. The activity coefficients are calculated by means of the Davis equation (ref 12, p. 146).

Each pK value is corrected for the influence of the ionization of the pyrone on the pH or $\mathrm{p}(a_{\mathrm{H}^+} + \gamma_{\mathrm{Cl}^-})$ value of the buffer.[13]

The precision of the pK values for compounds (3)—(6) and the three hydroxyacetophenones is better than 0.01 pK units in each case; for compound (7), pK_1 = 1.25 ± 0.03 and pK_2 = 9.21 ± 0.01.

[9/065 *Received*, 15*th January*, 1979]

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