Tetrahedron. Vol. 24, pp. 923 to 932 Pergamon Press 1968. Printed in Great Britain

ON THE AROMATIC CHARACTER OF 4-PYRONES[1]

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(*Received in USA* 13 *April* 1967; *accepted for publication* 1 *June* 1967)

Abstract—NMR spectra reveal a ring current in substituted 4-pyrones which is not substantiated by magnetic susceptibility data. IR, polarographic, and hydrogen bonding data on 2,6-diaryl-4-pyrones are correlated with Hammett substituent constants.

INTRODUCTION

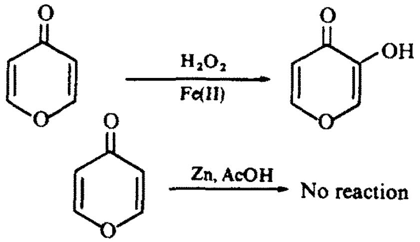
Two definitions have been used in recent years for aromaticity.[4] The *classical* definition has been in terms of chemical properties, namely, that an unsaturated ring system, in contrast to a typical olefin, is not easily oxidized, does not polymerize in acid, and undergoes substitution reactions rather than additions. Thus, aromatic systems give very little Diels–Alder reaction product, if any, and resist catalytic hydrogenation. The modern definition has been in terms of a *ring current*[4c] which is detectable by magnetic susceptibility or NMR measurements. The delocalization of π electrons, which produces this ring current, simultaneously provides an unusual stability, i.e. a large resonance energy, and requires near coplanarity of the atoms forming the aromatic ring. It is well-known that benzene is aromatic according to both definitions, and it has been shown that [18]annulene is aromatic in terms of the modern definition but not according to the classical definition. For instance, the ring sustains a ring current but it is inert under typical aromatic substitution reaction conditions and undergoes addition of bromine and maleic anhydride.[5] In this paper, it is shown that 4-pyrones, opposite to [18]annulene, are fully aromatic by the classical definition but less definitely so according to the modern definition.

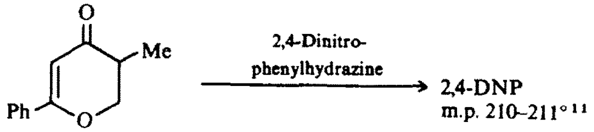
DISCUSSION

The classical or chemical aromaticity of the 4-pyrone ring is shown by the following considerations.

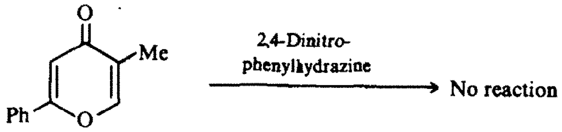
(1) *4-Pyrones undergo substitution reactions.*[6,7] Thus, 4-pyrones can be nitrated with the usual HNO_3–H_2SO_4 mixture,[8] yield aromatic bromination and Friedel–Crafts reaction products, but do not undergo a Diels–Alder reaction with maleic anhydride. In contrast, 2-pyrone polymerizes at room temperature and reacts with maleic anhydride.[9] On the other hand, 4-pyrones suffer ring opening in base to form enolate salts of the corresponding 1,3,5-triketones.

(2) *4-Pyrone reactions are not typical for its constituent functional groups.* The 4-pyrone ring may be regarded as an α-β-enone, a divinyl ether, or a vinylog of an acid lactone. However, unlike an α,β-enone, 4-pyrones do not undergo the Michael condensation,[16] resist oxidation and reduction,[7] and do not form Schiff bases in any practical yield.[10]

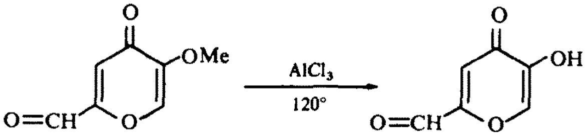


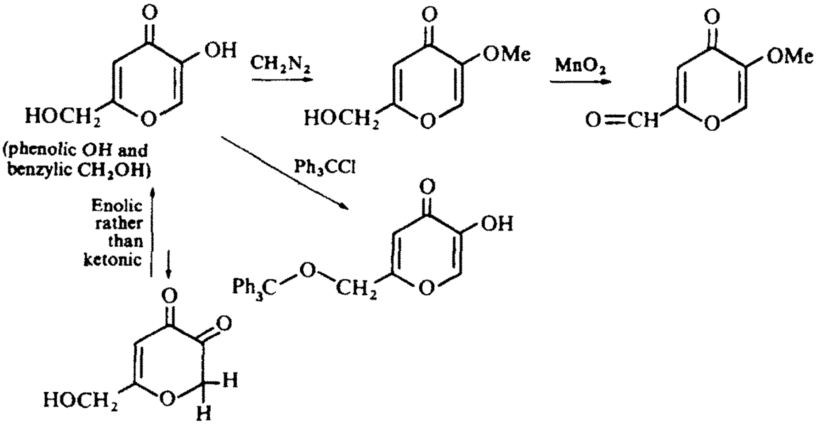


whereas



The carbonyl group in 4-pyrone is unusually basic, $pK_a \sim 0{\cdot}3$ in contrast to $-6{\cdot}0$ for acetophenone.[7] For example, 4-pyrones form stable salts with Lewis acids,[12] which is similar to tropone in this respect. Unlike vinyl ethers, 4-pyrones are stable in acid. For instance, an alkoxy-4-pyrone does not suffer ring cleavage under conditions which hydrolyze ethers.[12]

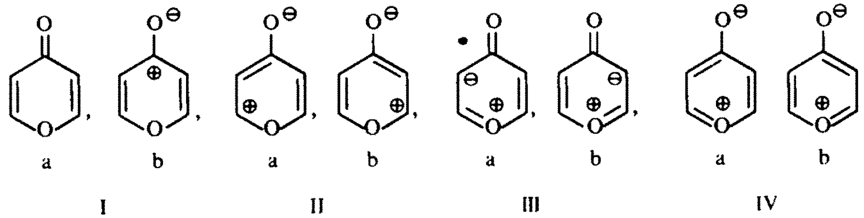




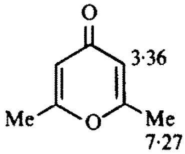
(3) Substituents react as when attached to the benzene ring:[12,13]

Semi-theoretical MO calculations on 4-pyrones[4,14] indicate a large delocalization energy (ca. $-2{\cdot}9\beta$), and that there is a higher electron density at C_3, C_5 than at C_2, C_6. This charge density is consistent with the fact that the 4-pyrone ring undergoes electrophilic substitution at the 3- and 5-positions,[7,*] and the chemical shifts for the C_3—H and C_5—H protons occur at higher fields in the NMR. Although the resonance energy (33 kcal)[16] of 2,6-dimethyl-4-thiopyrone may be slightly larger than that of the corresponding pyrone, this large value indicates that the 4-pyrone ring also has a rather large resonance energy.

All of the properties described above are understood in terms of 4-pyrone being a resonance hybrid of structures I–IV. Structures I and II are characteristic of an α,β-enone, III of a divinyl ether, and IV is the complementary extension of II and III, which implies a Kekulé-type resonance for the ring. It should be pointed out that 4-pyrones are more polar than their dipole moments (ca. 3·7 D) imply. The pyrone ring has two opposing electronegative oxygen atoms at opposite ends of the molecule which decreases the observed moment. However, the solubility characteristics of 4-pyrones (sol. H_2O, alcohol; sl. sol. C_6H_6), the m.p. of 4-pyrones compared with their hydrogenated products (pyrones have higher m.ps), and the greater adsorption of 2,6-dimethyl-4-pyrone on alumina than its reduction products (Experimental) all confirm a very polar character of 4-pyrones. This would be expected for a substantial contribution from structures of type IV.



NMR data. Although NMR spectra of 4-pyrones have been reported,[16–18] suitable models have not been chosen for comparison in order to substantiate the presence of a ring current in the 4-pyrone nucleus. From an inspection of the chemical shifts for the C_3, C_5 protons of compound **8** and **12** compared to those in **9** and **11**, it appears that the former values are smaller than can be attributed to an electronegative



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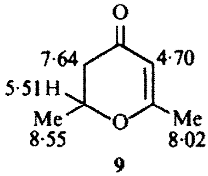

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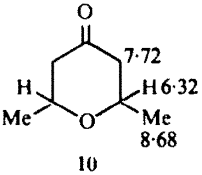

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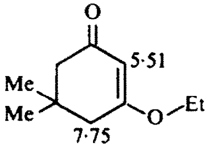

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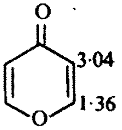

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[*] Deuterium exchanges with the 2- and 6-position hydrogens but by an addition-elimination mechanism.[15]

effect of the second double bond in the ring. Two types of comparisons support this view. One is the semi-quantitative approach of Abraham *et al.*[19]

Abraham and Thomas[19] have shown, in rebuttal to former criticism,[20] that when one double bond is removed from an aromatic ring, the resulting compound serves as a good model for estimating the diamagnetic anisotropic effect of the ring current in the aromatic compound. Thus, the cyclohexadiene ring can be used as a model for the benzene nucleus and 2,3-dihydrofurans for the furan ring.

Following the suggestion of Pople,[21] wide use has been made of the ring current concept to account for the downfield shift of aromatic protons in the NMR relative to olefinic protons.[22,*] It has been shown, however, that part of this shift is due to local atomic diamagnetic anisotropy resulting from the change in orbital hybridization.[23] Based on a comparison of calculated with observed diamagnetic susceptibilities, Pople has estimated that the atomic diamagnetic effect accounts for about a third of the observed diamagnetic exaltation of aromatic rings. Furthermore, the observed difference between the chemical shift of protons or groups when attached to an aromatic ring and when attached to a nonaromatic model ring should be reduced by an amount attributable to the presence of the additional double bond in the aromatic ring. Finally, when comparing ring-current effects for different nuclei, consideration must be given to the area of the ring current, since the diamagnetism increases with the radius of the ring. This adjustment can be made by use of the equivalent dipole approximation expressed by the equation:

$$\frac{i_B}{i_X} = \frac{\Delta_X}{\Delta_B} \cdot \frac{A_B}{A_X} \cdot \left(\frac{R_X}{R_B}\right)^3 \tag{1}$$

where i is the ring current, Δ is the NMR chemical shift, A is the area of the ring, R is the distance of the proton or group from the center of the ring, and the subscripts B and X refer to benzene and the other compound.

The ratio of ring currents in the 4-pyrone and benzene nuclei can be compared using this technique, similarly as Abraham and Thomas did for the furan and thiophene nuclei.[19] The pertinent data are given in Table 1. The A and R values of the two rings for Eq. (1) are essentially the same within the precision of the method, therefore the corrected chemical shifts Δ may be compared directly. The effect of the third double bond in the benzene ring is assumed to be the same as the difference between the first and second double bond in the cyclohexane ring, i.e. the C-1 proton in cyclohexene (4·33) less the C-2 proton in 1,3-cyclohexadiene (4·14) equal to 0·19 ppm. The effect on the methyl protons is expected to be much less than this, and a value of 0·05 is used.[19] The effect of the second double bond in the 4-pyrone ring is taken as the difference between the chemical shifts of the C-3 proton in **10** (7·72) and the C-3 proton of **9** (7·64) equal to 0·08 ppm. The effect on the 2-Me group is taken as the difference between the chemical shift of the Me in **10** (8·68) and the 2-Me in **9** (8·55) equal to 0·13 ppm.

The correction for atomic anisotropic effects on the protons is taken to be a third of the observed chemical shift of the protons. Since the magnetic field due to the

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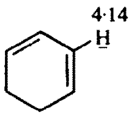
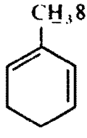
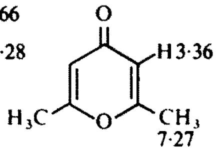
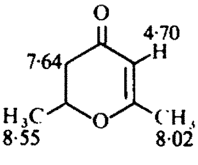
[*] Two alternative criteria for aromaticity have been suggested to replace chemical shifts. One is the magnitude of vicinal olefinic coupling constants (smaller for aromatic protons than for olefinic protons.[22] and the second is an empirical relationship between chemical shifts and J(C^{13}-H) coupling constants.[22b]

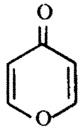
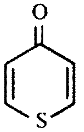
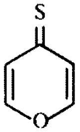
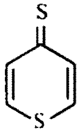
TABLE 1. CHEMICAL SHIFTS OF BENZENE AND 4-PYRONE DERIVATIVES

	Aromatic ring			
	Benzene		4-Pyrone	
Models used	C_6H_5—$\underline{H}$ 2·66 	C_6H_5—$C\underline{H}_3$ 7·66 		
	H-3	CH_3	H-3	2-CH_3
Observed chemical shift	1·48	0·62	1·34	0·75
Correction for additional C═C	−0·19	−0·05	−0·08	−0·13
Difference	1·29	0·57	1·26	0·62
Correction for atomic diamagnetism	−0·43	−0·05	−0·42	−0·05
Δ	0·86	0·52	0·84	0·57

atomic currents is proportional to R^{-3} and the Me groups are about twice as far from the center of the ring as are the protons, the atomic anisotropic effects on the Me group are taken as $(1/2)^3$ or 1/8th of the effect on the protons.

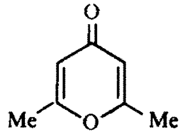
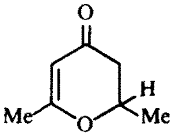
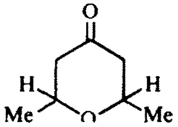
When these corrections are made on the observed chemical shifts of the H-3 and 2-CH_3 groups of the two rings, and since $[A_B/A_P \times (R_P/R_B)^3] = 1$ for both rings, it is found that the ring current in the 4-pyrone ring is approximately the same as it is in benzene, i.e. $\Delta_P \simeq \Delta_B$ based on either H-3 or 2-CH_3 chemical shifts, and therefore, $i_P = i_B$.

A second sort of comparison of chemical shifts of aromatic nuclei was made by Gutowsky *et al.*[24]

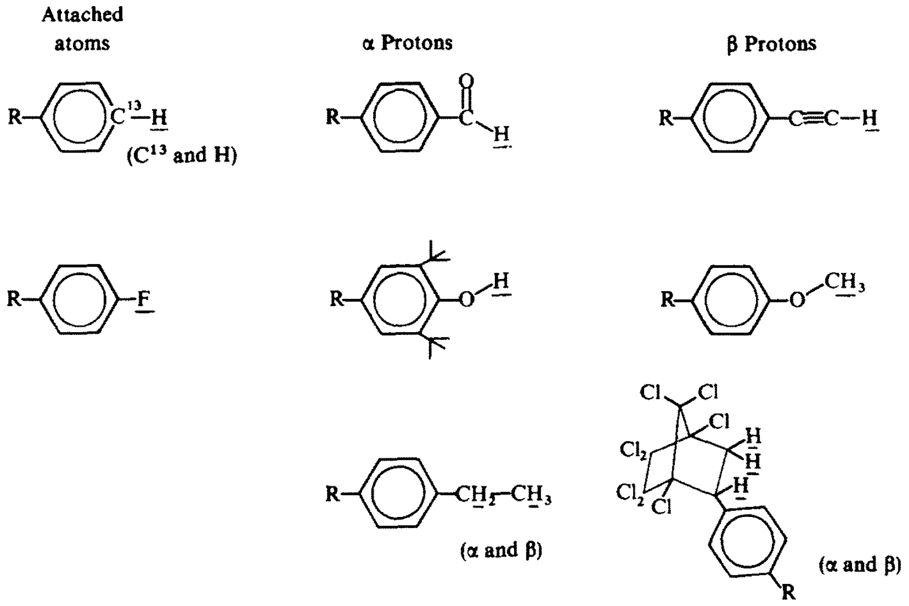
				
Ave. τ for H-2 and H-3	2·75	2·75	2·62	2·3

One would expect the average chemical shift to move upfield as oxygen is replaced by sulfur since sulfur has the smaller electronegativity. The opposite trend could be attributed to the presence of an increased ring-current in the sulfur compounds.

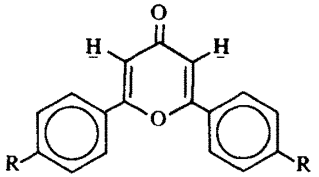
Now, although the NMR properties of 4-pyrones support the presence of a ring current, the magnetic susceptibility of 2,6-dimethyl-4-pyrone does not. These exaltations (page 928) are small compared with the values for benzene (18·7), tropolone (15·2), or furan (14·3). It is realized that the ring currents of benzene and 2,6-dimethyl-4-pyrone as calculated here involve quite a number of assumptions, and when more is known about diamagnetic effects, it may turn out that the magnetic susceptibility and NMR data are not as incompatible as indicated here.

	$-10^6\,\chi_{obs.}$	$-10^6\,\chi_{calc'd}$	$\Delta\chi\,(\times 10^6)$
	59·52	57·33	2·19
	70·94	68·69	2·25
	88·90	92·20	−3·30

Some correlations. Reasonably good correlations of Hammett substituent constants have been made with chemical shifts for atoms attached directly to a benzene ring as well as with α and β protons.



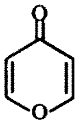
Chemical shifts for the C_3—H protons of 2,6-diaryl-4-pyrones, which are β to a phenyl ring, also correlate fairly well with Hammett constants:

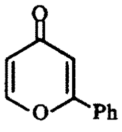


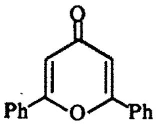
$\delta = 6{\cdot}83 + 0{\cdot}083\rho_p$, ppm

R = Me, H, OMe, Cl, CF_3

When Ph groups are successively introduced into the 2,6 positions of 4-pyrone, the carbonyl IR frequencies decrease.







$\nu_{C=O}$ = 1680 1658 1653 cm^{-1}

This is attributed to an increase in the contribution of structures II to the resonance hybrid at the expense of structures III and IV, since the positive charge on C_2 and C_6 can be delocalized into the benzene ring. This lowers the bond order of the carbonyl group and also of the ring C—O bond. (Structures IV increases the *endo* C—O bond order). Hence, this trend can be expected to continue with an increase in the electron-donating character of Ph substituents. That is, $\nu_{C=O}$ and ν_{C-O} should decrease in the order

$$p\text{-R} = CF_3 > Cl > H > Me > OMe.$$

This is indeed the order observed (Table 2) with $\nu_{C=O} = 1649 + 15\rho_p$ cm^{-1}.

The 2,6-diaryl-4-pyrones exhibit a doublet in the 1600–1700 cm^{-1} range and as a means of selecting the carbonyl band(s), the effect of solvent on this doublet was compared with the effect on the 1715-cm^{-1} band of acetone. The respective frequencies of 2,6-diphenyl-4-pyrone and of acetone were determined in cyclohexane, isooctane, carbon tetrachloride, tetrachloroethylene, acetonitrile, methylene chloride, and chloroform. The $\Delta\nu/\nu$ values for the carbonyl band of acetone were plotted against the corresponding values for the two strong bands in the 1600–1680 cm^{-1} region of the pyrones.

TABLE 2. O—H FREQUENCY-SHIFTS OF PHENOL MIXED WITH 4-PYRONES, AND CARBONYL FREQUENCIES OF 2,6-DIARYL-4-PYRONES.[a]

Compound	H-bonded phenol ν_{OH} cm^{-1}	$\Delta\nu_{O-H}$ (monomeric phenol = 3597 cm^{-1}) cm^{-1}	$\nu_{C=O}$ cm^{-1}
1	3268	329	1649·4
2	3185	412	1646
3	3215	382	1648·5
4	3322	275	1653·7
5	3333	264	1654·5
6[b]	3356	241	
7[c]	3247	350	1665

[a] Solvent = carbon tetrachloride.

[b] 3,5-Diphenyl-4-pyrone.

[c] 2,6-Dimethyl-4-pyrone.

The slopes indicate that both bands are largely carbonyl in character. The band at the higher frequency shows the smaller deviations, so the corresponding band of the 2,6-diaryl-4-pyrones is used for correlations.

The basicity of the carbonyl oxygen should parallel the single-bond character of the carbonyl group. This was examined by measuring the change in the O—H IR frequencies of phenol when mixed with the series of 2,6-diaryl-4-pyrones and by measuring their polarographic reduction half-wave potentials (Table 3). Intermolecular hydrogen bonding lowers the O—H stretching frequency proportionately to the strength of the hydrogen bonds, which in turn is a reflection of the basicity of the doner atom. Phenol has been shown to be a good probe for this technique.[25] Also, increasing the charge-density on the oxygen atom should make it more difficult to reduce the group. Again, these two properties correlate fairly well with Hammett substituent constants and, hence, with each other:

TABLE 3. POLAROGRAPHIC HALF-WAY REDUCTION POTENTIALS OF 2,6-DIARYL-4-PYRONES

Compound	$E_{\frac{1}{2}}^{a}$ volts
1	−1·896
2	−2·040
3	−1·980
4	−1·800
5	−1·740

[a] All values include DMF aqueous junction potential

$$\Delta\nu_{OH} = 329 - 1{\cdot}85\rho_p\,\mathrm{cm}^{-1}$$

$$-E_{1/2} = -1{\cdot}896 - 0{\cdot}44\rho_p \text{ volts}$$

EXPERIMENTAL

(a) *Preparation of compounds.* The 2,6-diaryl-4-pyrones were prepared by dissolving the respective triketones in conc H_2SO_4 and pouring the acid solns over crushed ice.[26] The triketones were synthesized by a double condensation of substituted methyl benzoates with acetone.[27] 2,6-*Diphenyl-4-pyrone* (**1**) m.p. 138·5–139·5° (lit.[28] 139–140°). 2,6-*Di-*p-*anisyl-4-pyrone* (**2**) m.p. 193–194° (lit.[27] 194–195°). 2,6-*Di-*p-*tolyl-4-pyrone* (**3**) m.p. 178–180°. (Found: C, 82·79; H, 5·78. Calc: C, 82·59; H, 51·83%). 2,6-*Di-*(p-*chlorophenyl*)4-*pyrone* (**4**) m.p. 234–235° (lit.[27] 236–237°). 2,6-*Di-*(p-*trifluoromethylphenyl*)4-*pyrone* (**5**) m.p. 228–229°. (Found: C, 59·49; H, 2·65. Calc.: C, 59·37; H, 2·60%). 3.5-*Diphenyl-4-pyrone* (**6**) was prepared by condensing dibenzyl ketone with ethyl formate in the presence of MeONa in ether; m.p. 186–187° from benzene, then alcohol (lit.[29] 186–187°). NMR in $CDCl_3$: τ 2·33 (10H); τ 1·80 (2H) singlet. A crude sample of 2,6-*dimethyl-4-pyrone*[30] (**7**) was recrystallized twice from n-heptane and sublimed to give needles. m.p. 132° (lit.[31] 132°). *Dimedone ethyl ether* was prepared from dimedone and abs EtOH, b.p. 95°/14 mm; NMR ($CDCl_3$): C═CH, τ 4·51 (1H), singlet; EtO, τ 5·98 (2H) quartet; τ 8·62 (3H) triplet; CH_2—C═C, τ 7·75 (2H) singlet; CH_2—CO, τ 7·67 (2H) singlet; Me_2C, τ 8·90 (6H) singlet.

The dihydro- and tetrahydro-2,6-dimethyl-4-pyrones and 2,6-dimethyltetrahydropyran-4-ol were prepared by hydrogenation of 2,6-dimethyl-4-pyrone in 95% EtOH using 10% Pd-C at 3–4 atmospheres until 0·08 moles H_2 per mole of pyrone were absorbed. After removal of the EtOH, the residue was chromatographed over neutral alumina, Activity II, with pet. ether (b.p. 30–60°) eluent, to remove the unreacted 2,6-dimethyl-4-pyrone. The pet. ether fractions were combined, the solvent removed, and the residue fractionated by GLC on a 10-ft, 15% carbowax on Chromasorb W column, He flow rate ca. 60 ml/min. Retention times: tetrahydropyrone, 6 min, tetrahydropyran-4-ol, 15 min, dihydro pyrone, 24 min.

2,6-Dimethyltetrahydropyran-4-ol was also prepared by hydrogenation of 2,6-dimethyl-4-pyrone over platinum oxide catalyst. 2,3-*Dihydro-2,6-dimethyl-4-pyrone*: n_D^{25} 1·4910 (lit. 1·4972,[32] 1·4908[33]); dinitrophenylhydrazone, m.p. 151–152° (lit.[33] 151–152°); ν 1608, 1667 cm^{-1} (lit.[33] 1608, 1665 cm^{-1}); λ_{max}^{EtOH} 263 mμ (lit.[32,33] 263 mμ). *Tetrahydro-2,6-dimethyl-4-pyrone*: b.p. 41–42°/6 mm (lit.[32] 61°/14 mm); n_D^{22} 1·4405 (lit.[32] 1·4465); λ_{max}^{EtOH} 276 mμ (lit.[32] 276 mμ); ν 1727 cm^{-1} (lit.[34] 1725 cm^{-1}); semicarbazone, m.p. 239–240°. 2,6-*dimethyltetrahydropyran-4-ol*. b.p. 45–47°/2 mm (lit.[32] 88°/14 mm); n_D^{23} 1·4534 (lit.[32] 1·4517); *p*-nitrobenzoate, m.p. 94–95° (lit.[32] 96°).

(b) *IR measurements*. All measurements were made on a Perkin–Elmer Model 21 spectrophotometer in cells of path lengths 0·1 mm, 1 mm, and 3 mm, with NaCl windows. Spectra of the 2,6-diaryl-4-pyrones were measured in CCl_4, CH_2Cl_2, and KBr discs.

For the hydrogen-bonding studies, solns of freshly distilled phenol were prepared in a dry box. Solns used were 0·003 M in pyrone and 0·01 M in phenol in the 3-mm cells, and 0·003 M in pyrone and 0·1 M in phenol in the 1-mm cells.

(c) *Polarographic measurements*. Reductions were made in dimethylformamide solvent using tetraethylammonium perchlorate as the supporting electrolyte, a standard calomel reference electrode, an agar–KCl bridge, a thermostated H cell, and a Sargent Model XV recording polarograph.

(d) *NMR measurements*. Spectra were obtained with a Varian A 60 spectrometer using 5% solns (w/v) in $CDCl_3$ and TMS internal standard.

(e) *Magnetic susceptibility measurements*. Measurements were made using the Thorpe–Senftle method and equipment.[35]

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