A Physicochemical Study of Isocoumarin, 3,4-Dihydroisocoumarin, and Bis-3,4-dihydroisocoumarin by Dipole Moment, Infrared, Ultraviolet, and Polarographic Measurements

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Hydrogen abstraction, by t-butoxyl radicals, from 3,4-dihydroisocoumarin, produces radicals which dimerize to give bis-3,4-dihydroisocoumarin in one of two possible diastereoisomeric forms. This is shown by dipole moment measurements to be the *meso* form. I.r. measurements support this assignment. The dipole moments of the related compounds isocoumarin and 3,4-dihydroisocoumarin are reported. The results of a polarographic and u.v. spectral study of isocoumarin are also discussed.

3,4-Dihydroisocoumarin (I) may be expected to lose a benzylic α-hydrogen from attack by t-butoxyl radicals [1] to produce the radical (II) which, being stabilized by resonance hybrids such as (IIa), should then be capable of dimerizing to give bis-3,4-dihydroisocoumarin (III) in the normal and iso-forms.

When 3,4-dihydroisocoumarin was heated with di-t-butyl peroxide as the source of t-butoxyl radicals, a rather insoluble solid product having m.p. 310 °C was obtained. This proved to be a diastereoisomer of bis-3,4-dihydroisocoumarin and was designated the normal form.

The electric dipole moment and i.r. spectra of this diastereoisomer were measured and are analysed in this paper from a stereochemical point of view. Complementary dielectric and i.r. spectroscopic data on isocoumarin and 3,4-dihydroisocoumarin are also reported together with a polarographic and u.v. spectral study of isocoumarin.

Experimental

Preparation of Compounds.—Isocoumarin. The method of Johnston *et al.* [2] was followed with a modification to one of the stages of their synthetic route. Homophthalic acid was used as the starting material in our preparation instead of phthalide.

3,4-Dihydroisocoumarin. This compound was prepared by oxidation of isochroman according to the method of Colonge and Boisde. [3]

Bis-3,4-dihydroisocoumarin. 3,4-Dihydroisocoumarin (30 g) and t-butyl peroxide (25 g) and dry chlorobenzene (20 ml) were sealed under nitrogen and heated at 130 °C for 48 h. On cooling, a solid product (*ca.* 1 g) was obtained. This was filtered off and the filtrate was distilled under reduced pressure, when a resinous material and a further small crop of crystals were obtained. The combined solid product was recrystallized from benzene to give normal *bis-3,4-dihydroisocoumarin* (0.7 g), m.p. 310 °C (Found: C, 73.5; H, 4.9. $C_{18}H_{14}O_4$ requires C, 73.4; H, 4.8%).

*Polarization Measurements.—*Dielectric constants of solutions of isocoumarin, 3,4-dihydroisocoumarin, and bis-3,4-dihydroisocoumarin were determined with apparatus previously described, [4] densities and refractive indices being obtained by standard procedures. [5] The dielectric results are summarized in Table 1 using notation explained in ref 5. The i.r. spectra were recorded with a Perkin-Elmer 337 spectrometer and are listed in Table 2.

Discussion

Dipole Moments.—Isocoumarin and 3,4-dihydroisocoumarin. The dipole moments of isocoumarin (IV) and 3,4-dihydro-

isocoumarin (I) have not been reported before. Their moment values (14.18 and 15.25×10^{-30} Cm respectively) may be compared with those of coumarin [6] (V) (14.95×10^{-30} Cm) and 3,4-dihydrocoumarin [7] (VI) (12.68×10^{-30} Cm). The dipole moments of these four compounds arise essentially from the presence of the lactone group. The moments expected for the localized covalent structures (I), (IV), (V), and (VI) can be computed by vector summations of the C=O and C–O bond moments whose values [8] may be taken as 2.72 D or 9.08×10^{-30} Cm and 1.66 D or 5.54×10^{-30} Cm, respectively. Assuming oxygen and ketonic valency angles of 120°, the resultant moment is 3.83 D or 12.77×10^{-30} Cm. This is the dipole moment value the four compounds would have if we ignore resonance effects and intramolecular electrostatic induction. [9] Coumarin (V) and isocoumarin (IV) can be considered to be derivatives of α-pyrone in which the pyrone moiety has been fused to a phenyl ring. Unfortunately, α-pyrone itself is difficult to obtain and its moment apparently has never been measured. A value for its dipole moment however can be estimated from the measured moments [10] of 4,6-dimethyl-2*H*-pyran-2-one (X) (18.68×10^{-30} Cm), 2,6-dimethyl-4*H*-pyran-4-one (IX) (16.35×10^{-30} Cm), and 4*H*-pyran-4-one (VIII) (12.34×10^{-30} Cm). Comparing the moments of (IX) and (VIII) we note a difference of 1.2 D (4.0×10^{-30} Cm) which must be caused by the presence of the two methyl groups in (IX). Assuming a hexagonal ring structure with intervalency angles of 120°, vectorial analysis shows that the methyl groups in (IX) each contributes a group moment of 1.2 D (4.0×10^{-30} Cm) acting at an angle of 120°. If we further assume that the methyl groups also contribute the same moment values in (X) then vectorial analysis again shows that the moment of (VII) should be 4.4 D or 14.68×10^{-30} Cm if the resultant of the two methyl groups acting along the C=O axis coincides with the moment of (VII); and should be 4.43 D or 14.78×10^{-30} Cm if an angle of 15° separates them.

For practical purposes it seems reasonable to assume that the moment of (VII) is *ca.* 4.4 D or 14.68×10^{-30} Cm. Thus we may expect the moments of coumarin and isocoumarin to have values close to this. This has indeed been found to be the case: 14.95×10^{-30} Cm for coumarin [6] and 14.18×10^{-30} Cm for isocoumarin (Table 1). The slightly higher dipole moment of coumarin could be due to conjugation of the C=O group with the ethylenic side chain double bond resulting in additional stabilization from structures such as (Va and b). In the case of isocoumarin the C=O bond is in the α-position to the phenyl ring and so the ethylenic double bond has much less effect on it. From the observed moment values it appears that fusion of the phenyl ring to the α-pyrone moiety does not confer additional stability.

Table 1. Polarisation, refractions, and dipole moments at infinite dilution at 25 °C

Solute	Solvent	Conc. range $(10^5 w_2)$	αE_1	β	$\gamma n_1{}^2$	P_2/cm^3	R_D/cm^3	$R_D(calc)/cm^3$	$10^{30}\mu\,{}^a/Cm$
Isocoumarin	Benzene	579—2 131	13.81	0.346	0.313	411.8	40.71	39.65	14.18 ± 0.03
3,4-Dihydroisocoumarin	Benzene	2 111—5 422	15.61	0.285	0.177	470.6	40.43	40.13	15.25 ± 0.10
3,4-Dihydroisocoumarin	Dioxane	1 709—4 829	18.02	0.132	0.300	476.3	39.64	40.13	15.38 ± 0.10
Bis-3,4-dihydroisocoumarin	Dioxane	158—374	2.56	0.219	0.402	187.8	77.32	76.92	7.61 ± 0.30

^{a} μ Is calculated assuming that $_DP = 1.05\ R_D$.

Table 2. a, I.r. spectra listings of the isomer of bis-3,4-dihydroisocoumarin obtained (cm^{-1})

KBr Disc

3 420(7)	1 475(47)	1 170(34)	760(50)
3 030(15)	1 465(55)	1 130(64)	720(34)
2 975(13)	1 390(62)	1 090(46)	705(36)
2 920(12)	1 330 (58)	1 040(46)	700(47)
1 990(4)	1 315(28)	1 030(9)	595(27)
1 955(8)	1 290(17)	1 020(43)	560(63)
1 840(16)	1 275(50)	995(18)	530(19)
1 730(82)	1 260(6)	958(12)	498(62)
1 720(82)	1 245(50)	950(40)	448(21)
1 680(24)	1 215(26)	885(20)	420(17)
1 610(30)	1 198(16)	802(35)	

b, I.r. spectral listings of 3,4-dihydroisocoumarin (cm^{-1}) (as a neat liquid)

3 080(2)	1 480(42)	1 210(2)	955(20)
3 000(4)	1 463(18)	1 200(11)	910(8)
2 960(4)	1 448(43)	1 163(3)	800(12)
2 900(11)	1 425(2)	1 130(50)	750(48)
1 940(2)	1 400(80)	1 120(16)	733(4)
1 830(2)	1 370(71)	1 098(38)	715(10)
1 720(70)	1 363(22)	1 068(22)	695(31)
1 680(11)	1 303(62)	1 040(33)	665(3)
1 608(32)	1 250(46)	1 035(40)	640(16)
1 485(21)	1 238(22)		

c, I.r. spectral listings of isocoumarin (cm^{-1})

Nujol mull

3 080(6)	1 570(3)	1 165(4)	958(10)
1 970(2)	1 490(25)	1 155(11)	930(17)
1 945(3)	1 410(18)	1 132(1)	900(9)
1 860(5)	1 333(22)	1 120(25)	880(16)
1 840(2)	1 313(20)	1 100(6)	803(47)
1 730(30)	1 280(24)	1 055(33)	795(41)
1 710(30)	1 253(25)	1 048(37)	782(24)
1 695(17)	1 245(23)	1 038(27)	752(24)
1 640(18)	1 230(9)	1 017(25)	722(8)
1 620(6)	1 205(5)	1 004(26)	690(52)
1 603(6)	1 195(13)	980(2)	660(38)
1 595(5)			

The numbers in parentheses indicate relative intensities.

The structures of 3,4-dihydrocoumarin (VI) and 3,4-dihydroisocoumarin (I) lack a side chain ethylenic double bond and so we may generally expect the moments of these two compounds to be lower than that of α-pyrone. This has been found to be true in the former case (VI) but not in the latter (I). It appears that the location of the C=O group in the structure makes a significant difference. In (I) it conjugates easily with the phenyl ring thus acquiring an enhanced moment from excited states such as (IIb—e) whereas in (VI) there does not appear to be additional excited states other than (VIa) to augment the dipole moment.
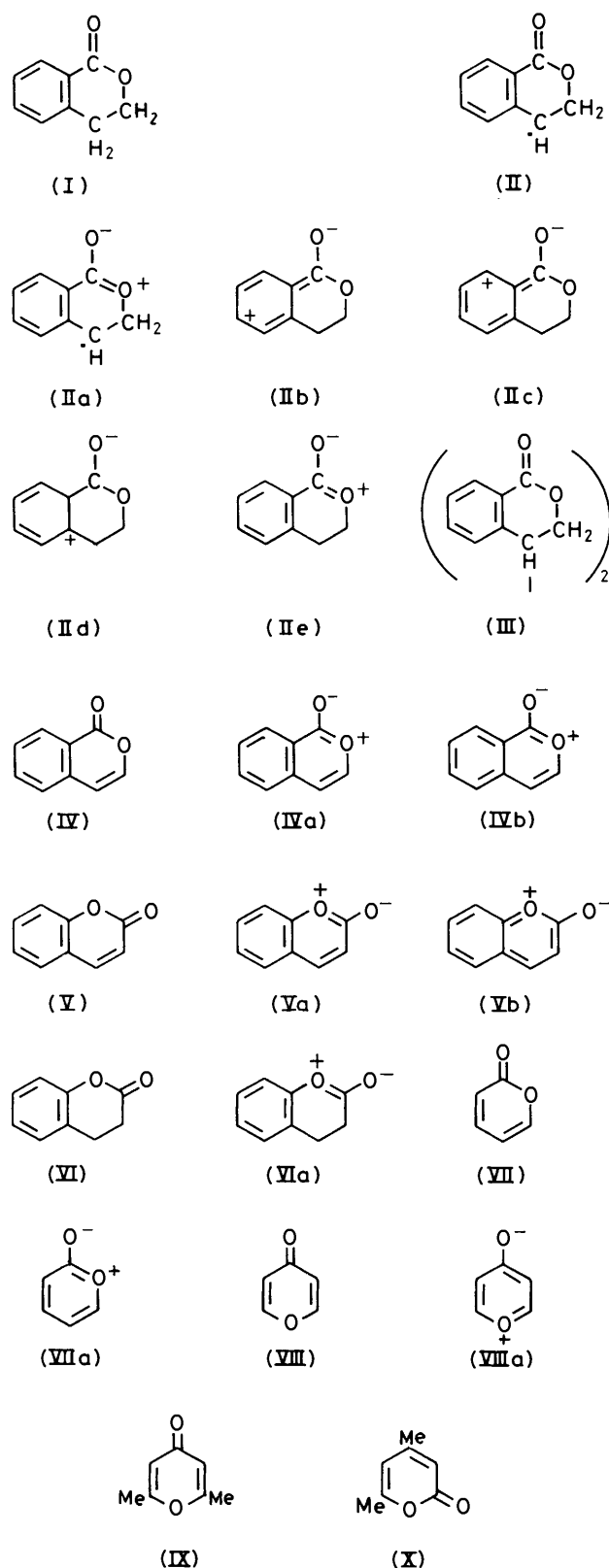
Bis-3,4-*dihydroisocoumarin.* Our sample of bis-3,4-dihydroisocoumarin has a dipole moment of 7.61×10^{-30} Cm, which is identical with that of *meso*-bis-3,4-dihydrocoumarin[7] [*cf.* moment of (±)-bis-3,4-dihydrocoumarin:[7] 14.28×10^{-30} Cm]. Since the distribution of rotational isomers in the *meso* and racemic diastereoisomers of both compounds may be expected to be very similar because they differ only in the relative positions of the C=O and C–O–C groups, it seems reasonable to infer that the sample isolated by us corresponds to *meso*-bis-3,4-dihydroisocoumarin.

I.r. Data.—Isocoumarin and 3,4-*dihydroisocoumarin.* The main difference in the i.r. spectra of isocoumarin and 3,4-dihydroisocoumarin consists of the fact that in 3,4-dihydroisocoumarin the carbonyl absorption occurs as a singlet at 1 720 cm^{-1} (which is somewhat lower than the frequency at which the band appears in Δ^5-lactones) whereas isocoumarin exhibits two bands in the C=O region at 1 730 and 1 710 cm^{-1} of about equal intensity. This splitting of the C=O band is characteristic of most unsaturated five- and six-membered-ring lactones in which the double bond is conjugated with the carbonyl group.[11] It also occurs in coumarin,[11] but not in 3,4-dihydrocoumarin.[7] The splitting of the C=O stretching band has been attributed to an intramolecular vibrational effect possibly depending on Fermi resonance with the overtone of a lower lying fundamental vibration.[11]

Bis-3,4-*dihydroisocoumarin.* The i.r. spectra of bis-3,4-dihydroisocoumarin show extra lines in polar solvents which are absent in the solid-state spectra (KBr, Nujol, and hexachlorobutadiene): 976 and 660 in CHCl$_3$ and 900, 830, 670, and 620 cm^{-1} in CH$_3$CN. The presence of these extra lines provide strong evidence that only one rotamer (probably the *trans*) exists in the solid state but that both *gauche* and *trans* rotamers are present in solution.[7] As the racemic diastereoisomer of bis-3,4-dihydroisocoumarin is not likely to show extra lines in solution when compared with the solid state,[7] we conclude that our sample of bis-3,4-dihydroisocoumarin corresponds to the *meso*-diastereoisomer as inferred earlier from dipole moment data.

Many of the absorptions in 3,4-dihydroisocoumarin are also found in the spectra of the dimer. However, whereas 3,4-dihydroisocoumarin exhibits only a 'singlet carbonyl' absorption at 1 720 cm^{-1}, the dimer exhibits a 'doublet carbonyl' absorption of equal intensity at 1 720 and 1 730 cm^{-1}. This is rather surprising as we should expect the dimer to follow the behaviour of 3,4-dihydroisocoumarin from which it is derived.

Carbonyl-band splitting in some cases has been associated with equilibria between conformational isomers[11] but this explanation is unlikely to be applicable here because it would require *meso*-bis-3,4-dihydroisocoumarin to exist as a mixture of *gauche–trans* rotamers not only in solution but also in the solid state, contrary to the evidence of the additional lines in solution indicating the presence of only one rotamer in the solid state. We are thus unable to offer an explanation as to why *meso*-bis-3,4-dihydroisocoumarin should have a 'doublet carbonyl' absorption whereas 3,4-dihydroisocoumarin does not.

(I)   (II)

(IIa)   (IIb)   (IIc)

(IId)   (IIe)   (III)

(IV)   (IVa)   (IVb)

(V)   (Va)   (Vb)

(VI)   (VIa)   (VII)

(VIIa)   (VIII)   (VIIIa)

(IX)   (X)

Figure 1. Plot of i_d versus pH

(IV)   (XI)   (XII)

Scheme 1.

Polarogarphic Measurements.—Here we present a polarographic study of the hydrolysis of isocoumarin in aqueous ethanol. The pH-dependent equilibria are expected to involve the species in Scheme 1.
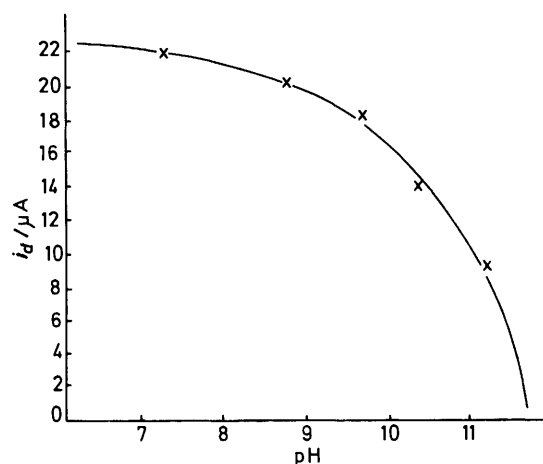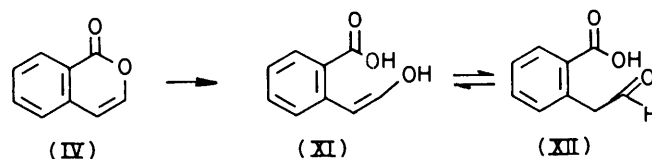
Polarographic analysis of isocoumarin. The polarographic

analysis of isocoumarin was carried out in solutions of 0.028M-isocoumarin in 10% ethanol using Britton–Robinson buffers[12] in the pH range 6—12. A polarographic reduction was carried out on a synthetic scale[13] to determine the product of formation.

The polarographic waves of isocoumarin were obtained using a standard EIL model 8410 polarograph.

For the synthetic experiment, an H-type polarographic cell with a saturated calomel working electrode and a dropping electrode assembly similar to that described by Lingane and Laitinen[14] was used.

A Hitachi 124 u.v.–visible spectrophotometer was used for recording the u.v. spectra of isocoumarin in the various buffers.

Isocoumarin (I) is stable in acidic conditions. However, hydrolysis takes place under alkaline conditions to give the tautomeric products (XI) and (XII).

A plot of i_d, the limiting current, *versus* pH indicates a marked change in the character of the polarographic wave height for the pH range 9.62—10.38 (Figure 1). Since isocoumarin is stable in acidic conditions our results show that this form is reducible over the pH range studied but that the formyl form of the hydrolysis product of isocoumarin is not. The formyl form (XII) is also present only in negligible proportions for pH <9.62 and isocoumarin is present in negligible proportions for pH >9.62. Decomposition of the formyl form takes place at pH >11.2 as evidenced by the fact that no polarographic wave of isocoumarin was obtained for this pH.

Variation of the concentration of isocoumarin present in the polarographic solution for a constant pH at 7.62 showed that the i_d is proportional to the concentration of the solute. The current at the top of the wave at pH 7.62 is therefore diffusion controlled. A qualitative determination of isocoumarin is therefore possible, except for solutions containing a great excess of more readily reducible substances.

Plots of $\ln i/(i_d - i)$ *versus* E gave slopes which average 0.030. Equating this to $2.303RT/nF$, n being the number of electrons transferred, a value of $n = 2$ is obtained.

The Ilkovic equation ($i_d = 607\ nD^{\frac{1}{2}}m^{\frac{2}{3}}t^{\frac{1}{6}}C$) was also used

$$+ 2e^- \longrightarrow R^{--} \ (\text{slow - step}) \ (\text{RDS})$$

$$R^{--} + 2H^+ \longrightarrow R' \ (\text{fast - step})$$
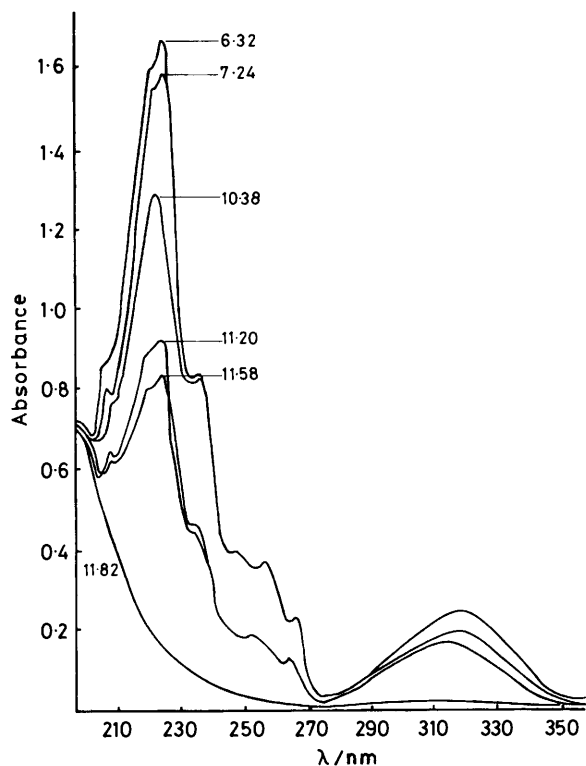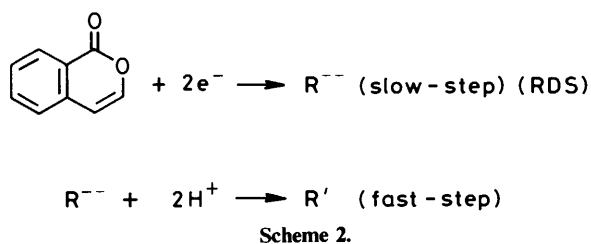
Scheme 2.

Figure 2. U.v. spectra of isocoumarin in 10% ethanol (aqueous) for pH 6—12

to calculate n, the number of electrons transferred, based on $m = 1.67 \times 10^{-3}$ g s^{-1}, $t = 2.5$ s, $D = 0.8 \times 10^{-5}$ C m^2 s^{-1} and the limiting current (i_d) value at pH 7.62. This also gives $n = 2$.

$E_\frac{1}{2}$, The half-wave potential, was independent of pH. The reduction step therefore does not involve H$^+$ participation.

It is interesting to note that the $E_\frac{1}{2}$ for coumarin[15] under similar conditions of observation was -1.53 V, a value significantly smaller than that of -1.78 V recorded for isocoumarin in this work. A likely reason for this is that the ethylenic linkage in coumarin is conjugated with the carbonyl bond whereas such conjugation is absent in isocoumarin. Conjugated systems are known to lower the reduction potential of ethylenic linkages significantly.[16]

Harle and Lyons[15] reported that electron reduction of coumarin yields the dimeric tetrahydrobicoumarin-4-yls involving a one-electron transfer. In the case of isocoumarin, electrolytic reduction at a measured and sustained voltage of -1.9 V versus saturated calomel electrode gave no precipitate. Extraction of the electrolytic solution with chloroform (500 ml) gave a product (yellow oil) that from its refractive index (1.5700 at 25 °C) and i.r. spectrum (Table 2b) can be concluded to be 3,4-dihydroisocoumarin.

The ethylenic linkage in isocoumarin is conjugated only with the aromatic ring and would be expected to resemble styrene
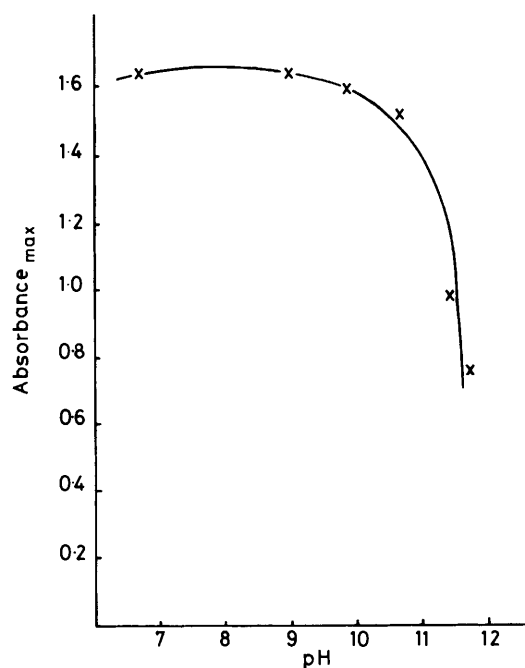

Figure 3. Plot of absorbance$_{max.}$ versus pH for isocoumarin in 10% ethanol

and other phenyl-substituted alkenes[17] in polarographic activity. The observation of the transfer of two electrons for isocoumarin is thus within expectations. A possible mechanism can thus be proposed (Scheme 2). The product R' could be the 3,4-dihydroisocoumarin since no solid dimer was obtained.

The u.v. absorption spectra of isocoumarin in aqueous buffers of 9×10^{-5}M are shown in Figure 2. Maxima were obtained at (a) 320 nm and (b) two poorly resolved bands at 228 and 223 nm. The molar extinction coefficients for these bands are 2 500, 18 500, and 17 700, respectively. The intensities of these absorptions decrease gradually with increasing alkalinity of the solution from pH 6.32 to 9.62, more drastically from 9.62 to 11.58, and disappear altogether at pH 11.82.

These observations are explicable from a consideration of the pH-dependent tautomeric equilibrium. Figure 3 shows a plot of $\varepsilon_{max.}$ against pH. The pH range for which the $\varepsilon_{max.}$ changes drastically ($>$pH 9.62) corresponds to that observed from polarographic analysis. The bands observed at pH up to 9.62 represent the electronic transitions of isocoumarin. The absence of additional bands at pH $>$ 9.62 indicates that electronic transitions of the aldehydic form do not occur within the range studied.

In alkaline solutions, however, the acid group would be ionized to give benzoate-type ions. The electrons are not localized at the C=O bond but spend part of the time on the oxygen atoms. This would cause a bathochromic shift of the wavelength of the C=O group possibly into the visible region of the spectrum.

A comparison with the u.v. spectra of coumarin in various buffers would be appropriate here. It is noted that the pH of marked change in $\varepsilon_{max.}$, i.e. pH 9.3—10.3 for coumarin, is comparable to that of 9.62—10.38 for isocoumarin. This indicates that the lactone form of coumarin and isocoumarin is stable up to the same pH range. In the case of coumarin, the hydrolysis product, coumarinic acid, which is stable for pH ranges $>$10.38, contains an ethylenic linkage which is conjugaged with the carbonyl group of the acid group. This explains the fact that although the absorption bands due to the lactone form disappear for solutions of high alkalinity they are

replaced by the $\pi \rightarrow \pi^*$ bands of the C=C double bond in coumarinic acid.

Assignment of the Bands.—The band at 320 nm may be attributed to $n \rightarrow \pi^*$ electronic transitions of the C=O bond. The bands at 228 and 223 nm might be due to the $\pi \rightarrow \pi^*$ transition of the C=C bond, which is conjugated only with the aromatic ring. Upon raising the pH of the solution to > 10.38, the molar extinction coefficient decreases drastically. The aldehydic group in (XII) is not conjugated with an ethylenic linkage, in other words it is isolated. The $n \rightarrow \pi^*$ transition of this C=O bond is forbidden and should resemble those for simple aldehydes. The molar extinction coefficient of these is of the order of 10—10^2 and hence would not be observed in our spectra.[18]

The wavelength of absorption of the electronic transitions of the acid group in the *ortho* position would be expected to resemble that for benzoic acid. The K or primary band of benzoic acid occurs at 230 nm with $\varepsilon_{max.}$ 11 500; the B or secondary band at 273 nm with $\varepsilon_{max.}$ 970. The primary band at 230 nm of benzoic acid is very close to those of 223 and 228 now attributed to $\pi \rightarrow \pi^*$ transition of the C=O bond of isocoumarin. This would account for the fact that no extra absorptions were observed to replace the diminishing bands attributed to isocoumarin with increasing alkalinity.

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