*Tetrahedron* Vol 25, pp. 5839 to 5851. Pergamon Press 1969. Printed in Great Britain

# INFRARED STUDIES OF CHROMONES—II
## ISOTOPICALLY SUBSTITUTED 5-HYDROXYCHROMONES[1]

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(*Received in the UK* 14 *July* 1969; *Accepted for publication* 15 *August* 1969)

**Abstract**—By deuteration of the OH group, it has been shown that two bands, at ~ 1665 and ~ 1630 $cm^{-1}$ ($CCl_4$), in the IR spectra of 5-hydroxychromones are associated with the H-bonded CO stretching vibration. Nuclear deuteration of 5-hydroxy-2-methylchromone (**1**) under acidic conditions gave a tri- and a hexadeutero derivative; the latter, isotopically substituted at C-3, shows a single CO band at 1649 $cm^{-1}$. Hydrolysis of 3-acetyl-5-hydroxy-2-methylchromone with sodium carbonate in deuterium oxide furnished 5-hydroxy-2-trideuteromethylchromone-3-d which also exhibits a single CO absorption. Partial incorporation of $O^{18}$ into the CO group of **1** results in a single $\nu_{C=O}{}^{18}$ at 1593 $cm^{-1}$. It is suggested that the doublet CO absorption of 5-hydroxychromones arises from a Fermi resonance involving a low-energy vibrational mode of the vinyl proton on the nuclear C-3 position.

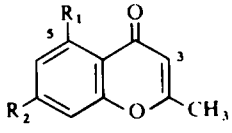
THE CO region of the IR solution spectra of 5-hydroxychromones has been shown[1] to be complex. Three relatively intense absorption maxima appear at ~1665, ~1630 and ~1600 $cm^{-1}$ and it has been inferred[1] that the two higher frequency absorptions may be in some way associated with the CO stretching vibration although neither of these bands shows appreciable solvent dependence. Again it is surprising that the most intense absorption in the CO region of the strongly chelated 5-hydroxy-2-methylchromone appears at 1659 $cm^{-1}$ in chloroform, a value 9 $cm^{-1}$ *higher* than the frequency of the single CO stretching band of 2-methylchromone (**2**) in the same solvent.

Doublet CO absorption has not been observed[2–4] for the closely related 5-hydroxyflavones but has been noted[5–7] in the spectra of the structurally simpler 4-pyrone. In the latter case, this has been found[5,6] to arise from a slightly anharmonic Fermi resonance involving the out-of-plane deformation mode of the C–H bonds adjacent to the CO group. Fermi resonance has also been suggested[5] as the explanation for the doublet CO absorption exhibited by a number of unsaturated lactones. A characteristic of the spectra of these lactones is the dependence of the positions and relative intensities of the individual components of the doublet upon solvent polarity and temperature. Even in 4-pyrone, where only a small change in position of the two CO bands is observed[5] when the spectrum is recorded in carbon tetrachloride [1678 ($\varepsilon$ 1270) and 1657 ($\varepsilon$ 320) $cm^{-1}$] and in chloroform [1674 ($\varepsilon$ 980) and 1661 ($\varepsilon$ 1210) $cm^{-1}$] there is a marked inversion in the relative intensities of the components.

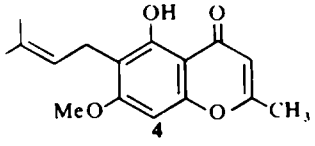
The data acquired[1] for the 5-hydroxychromones does not immediately[1] demonstrate that a Fermi resonance phenomenon is operative although the wavenumber separation, 34 ± 5 $cm^{-1}$, for the two most intense bands is within the range, 11–43 $cm^{-1}$, found for the lactones.[5] Only a small though consistent frequency shift was observed for each of the two principal absorptions of the 5-hydroxychromones when the

spectra were recorded in carbon tetrachloride and chloroform but no marked inversion of relative intensity occurred; the intensity of the highest frequency component was generally slightly less in chloroform but this may be associated with the broadening of the absorption bands found with this solvent. The apparent insensitivity to solvent polarity may be due to the strong intramolecular H-bonding which exists[1,8,9] between the 5-OH and the CO group. Chelation of this type would be expected to reduce the ability of the CO group to solvate with a polar solvent; if this were so, Fermi coupling would be to a considerable degree independent of the nature of the solvent.

The relative intensities of the two CO bands in the spectra of 4-pyrone and the unsaturated lactones have been found[5] to vary reversibly with temperature. Conversely for *p*-benzoquinone[10] which also exhibits Fermi resonance; the temperature dependence of the split CO absorption (1668 and 1656 $cm^{-1}$ in $CCl_4$) is not ascribed directly to the effect of vibrational coupling. By comparison the CO region of the IR spectra of 5-hydroxy-2-methyl-chromone (1) and 5-hydroxy-7-methoxy-2-methyl-chromone (3) shows no change of contour when recorded in tetrachloroethylene at temperatures between 20° and 100°. Since the perturbation responsible for the resonance interaction should not be temperature dependent,[5,11] the components of a Fermi resonance doublet will change in relative intensities only if one of the energy levels involved, e.g. that of the CO fundamental, varies with temperature. The data presented[10] for *p*-benzoquinone and its deuterated derivatives indicate that the quinone CO stretching frequency is in fact independent of temperature and thus it is reasonable to expect that this might also be so for the strongly H-bonded CO group of the 5-hydroxychromones.



1: $R_1$ = OH, $R_2$ = H
2: $R_1$ = $R_2$ = H
3: $R_1$ = OH, $R_2$ = OMe



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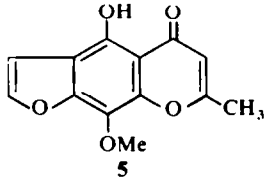

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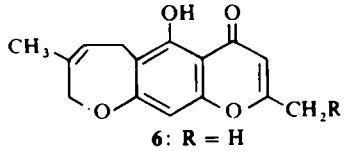
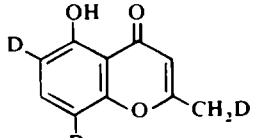


6: R = H
7: R = OH



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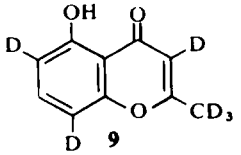

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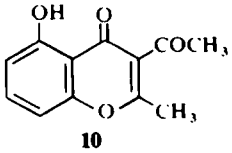

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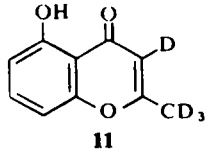

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5-O-*Deuteration*

Replacement of the hydroxylic hydrogen by deuterium in alcohols and phenols results in a considerable shift of the OH stretching frequency.[11] The appearance[1] of the OH stretching vibration of 5-hydroxychromones as a broad absorption envelope centred at $\sim 2970\ cm^{-1}$ is in accord with strong intramolecular chelation between the 5-OH and the CO group. It would be expected that deuteration of the 5-OH group, with the concomitant appearance[1] of a deuteroxyl stretching envelope centred at $\sim 2220\ cm^{-1}$, should have a definite effect on any absorptions which are associated with the CO stretching vibration.

From the practical standpoint, the most convenient method of achieving complete incoroporation of one D atom was to shake a carbon tetrachloride solution of the chromone for 3 minutes with a few drops of deuterium oxide, the reaction being monitored by the disappearance of the low-field proton[9] in the NMR spectrum. 5-Deuteroxy-2-methylchromone prepared in this way shows no proton resonance at $\tau - 2{\cdot}27$ but the intensities and chemical shifts of the other signals correspond exactly with those of the undeuterated analogue (1). Thus, under these mild conditions, monodeuteration was complete and specific for the 5-OH group. For the recording of the IR data a portion of the solution was rapidly transferred to cells having calcium fluoride windows and the spectrum recorded. This is a modification of the method used by Fales and Robertson[12] reported to be unsuccessful for strongly intramolecularly bonded OH groups. Attempts to prepare crystalline 5-deuteroxychromones by repeated treatments of chrloroform solutions of the 5-hydroxychromone with deuterium oxide followed by evaporation to dryness with benzene were ineffective. In these experiments, even when great care was taken during the transfer of material,

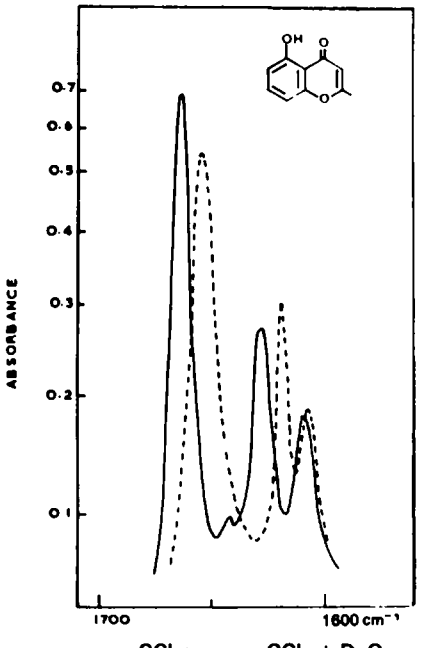



FIG. 1

the NMR spectrum indicated the presence of residual OH. This presumably arose[13] from a facile back exchange of the deuterated sample with traces of moisture in the solvents or adsorbed on the apparatus.

A significant change in the IR spectrum of 5-hydroxy-2-methyl-chromone (I) accompanies complete deuteration of the OH group (Fig. 1). The absorptions at 1661 ($\varepsilon$ 1500) and 1625 ($\varepsilon$ 585) $cm^{-1}$ ($CCl_4$) disappear and are replaced by two new sharper bands at 1652 ($\varepsilon$ 1050) and 1617 ($\varepsilon$ 550) $cm^{-1}$ (Table 1). Since it is a H-bonded CO stretching frequency which is being measured and since in effect an increase in reduced mass of the CO group accompanies the change C=O --- H to C=O --- D, the shift of the CO absorption to lower frequency is in the expected direction. Deuteration of the strongly chelated *o*-hydroxyacetophenone[14,15] under our conditions results in a similar lowering of the H-bonded CO stretching frequency from 1647 $cm^{-1}$ ($CCl_4$) to 1640 $cm^{-1}$. These observations would indicate that for 5-hydroxy-2-methylchromone, both upper peaks, 1661 and 1625 $cm^{-1}$, have high CO character.

In case the effects observed on treatment with deuterium oxide were not exclusively due to isotopic replacement of the H of the OH group, the spectrum of 5-hydroxy-2-methylchromone was recorded in carbon tetrachloride with a similar amount of added water. Although the intensity of the absorption at 1661 $cm^{-1}$ decreased slightly and that of the bands at 1625 and 1606 $cm^{-1}$ showed a slight increase, there was no frequency shift for any of these bands. With added deuterium oxide, apart from the marked frequency shift for two of the bands and a slight sharpening of the spectrum, the intensities of all three bands were of the same order as for added water.

As with 5-hydroxy-2-methylchromone, consistent shifts to lower frequencies of $\sim 10$ $cm^{-1}$ on deuteration were found for the two most intense bands in the CO region of the substituted 5-hydroxychromones, peucenin 7-methyl ether (**4**)[16] and khellinol (**5**).[17] It is evident (Table 1) that replacement of OH by OD in **4** results in a shift of the absorption at 1662 ($\varepsilon$ 1450) to 1653 ($\varepsilon$ 1140) $cm^{-1}$ with that at 1629 ($\varepsilon$ 490) moving to 1618 ($\varepsilon$ 740) $cm^{-1}$. Careful examination of the bands at 1662 and 1629 $cm^{-1}$ in the spectrum[1] of peucenin 7-methyl ether shows them to be broad and probably composite in nature. Indeed, part of this underlying absorption is revealed at 1661 $cm^{-1}$ in the spectrum of the 5-OD analogue. It has already been noted[1] that even for the structurally simpler 5-hydroxy-7-methoxy-2-methylchromone (**3**) the absorptions are complex with those at 1666 and 1630 $cm^{-1}$ ($CCl_4$) noticeably split into doublets. The furanochromone, khellinol (**5**) shows the characteristic bathochromic shift of its two principal absorptions at 1663 and 1638 $cm^{-1}$ to 1652 and 1633 $cm^{-1}$ respectively on deuteration.

In the spectra of the 5-OD analogues of ptaeroxylin (**6**) and karenin (**7**) where only partial deuteration of the 5-OH group was achieved using the less successful technique, the two bands at $\sim 1658$ and $\sim 1630$ $cm^{-1}$ broadened on deuterium incorporation. With progressive enrichment in the isotope the bands appeared as doublets (Table 2), the components showing a wavenumber separation of 6–10 $cm^{-1}$; the lower component increased in intensity at the expense of the upper with increasing incorporation.

Although it seems likely then that the two intense absorptions at $\sim 1665$ and $\sim 1630$ $cm^{-1}$ in the carbon tetrachloride solution spectra of 5-hydroxychromones must be largely associated with the CO vibration, the reason for this absorption is not immediately clear. The closely related 5-hydroxyflavones exhibit[18] only one CO

stretching frequency at 1655 ± 2 $cm^{-1}$ in the same solvent. Consistent with our results however, 5-deuteroxyflavone has been found[19] to exhibit the CO band at 1640 $cm^{-1}$, a value which is 12 $cm^{-1}$ lower than that of 5-hydroxyflavone, and also flavone, in this solvent.

*Nuclear deuteration*

In an endeavour to rationalise the doublet CO absorption of 5-hydroxychromones and seek an explanation for the anomalously high frequency of the principal absorption, incorporation of deuterium into the chromone nucleus was undertaken. It has been shown[5,6] for 4-pyrone that Fermi resonance occurs between the CO stretching vibration and the first overtone of the absorption at 851 $cm^{-1}$ assigned to the out-of-plane bending mode of the C—H bond α to the CO group. By replacement of the C-3 and C-5 protons by deuterium,[6] the deformation overtone was moved sufficiently in energy to cause an interruption of the Fermi resonance and consequently a collapse of the CO absorptions at 1674 and 1661 $cm^{-1}$ to a singlet.

Deuteration of 5-hydroxy-2-methylchromone in an acidic medium, prepared from deuterium oxide and acetyl chloride in dioxan, gave mainly two labelled products depending on reaction time. The 5-hydroxy-2-methylchromone recovered from short-time reaction was mainly trideuterated as shown by mass spectral analysis; 53 ± 3% $C_{10}H_5D_3O_3$, 20 ± 3% $C_{10}H_4D_4O_3$ and 16 ± 3% $C_{10}H_6D_2O_3$. The fragmentation pattern[20] indicated that these three species possessed two D atoms in the benzenoid ring and differed only in incorporation into the Me group. An important fragmentation of the 4-pyrone ring of 5-hydroxy-2-methylchromone (**1**) is a retro-Diels–Alder cleavage with loss of propyne to give a quinonoid ketene ion, bearing C-4, at *m/e* 136. This ion loses carbon monoxide leading to a fragment ion at *m/e* 108. In the mass spectrum of the deuterated sample, the intensities of the ions at *m/e* 138 and 110 necessitate that they arise from more than one of several parent ions. In accord, the NMR spectrum indicated a replacement by deuterium of the higher-field protons at C-6 and C-8, the remaining aromatic proton appearing as a singlet at τ2·54 (1H). The signal at τ 7·64 assigned to the Me group, integrated for approximately two protons but the olefinic resonance[21] at τ 3·94 showed no diminution in intensity. The protons *ortho* and *para* to the OH and the vinylic methyl hydrogens would be favoured as the most reactive towards exchange from mechanistic considerations. The major component of this mixture is therefore 5-hydroxy-2-monodeuteromethylchromone-6, 8-$d_2$ (**8**). (It is expected that any deuterium incorporated into the 5-OH group would be lost on exposure to moist air during isolation).

The product of prolonged deuteration[6] contained 68 ± 3% $C_{10}H_2D_6O_3$, 22 ± 3% $C_{10}H_3D_5O_3$, and 5 ± 3% $C_{10}H_4D_4O_3$ and was mainly 5-hydroxy-2-trideuteromethylchromone-3,6,8-$d_3$ (**9**) on the following evidence. The NMR spectrum of this mixture possesses a singlet at τ 2·53, the proton resonance at C-7; the area of this signal was approximately five times greater than that of a small residual vinyl absorption at τ3·93, the only other discernible signal. The mass spectrum shows fragmentation to ions at *m/e* 138 and 110 which is also consistent with only two deuteriums in the benzenoid ring.

The IR spectrum of this hexadeutero compound possesses *two* significant absorptions at 1649 and 1610 $cm^{-1}$ ($CCl_4$) (Fig. 2). Deuteration of the OH group results in a bathocromic shift to 1639 $cm^{-1}$ of the sharp intense maximum at 1649 $cm^{-1}$. This

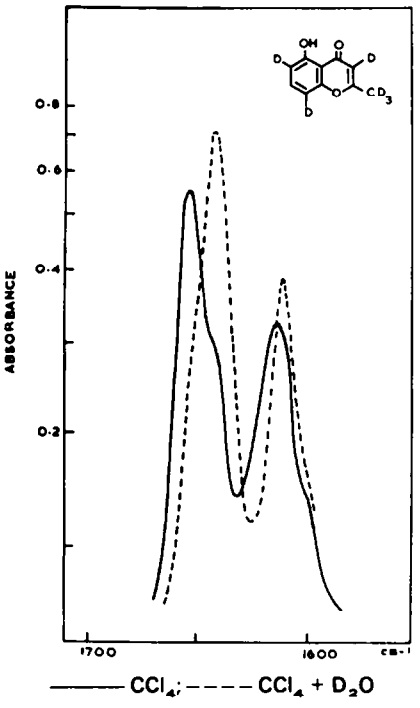



FIG. 2

requires that the 1649 $cm^{-1}$ band represents the H-bonded CO stretching frequency, a value which is close to the 1652 $cm^{-1}$ absorption of 5-hydroxyflavone. The inference of these observations is that the bands at 1661 and 1625 $cm^{-1}$ ($CCl_4$) in the spectrum of 5-hydroxy-2-methylchromone arise by a Fermi resonance interaction between the H-bonded CO stretching vibration (presumably at approximately 1650 $cm^{-1}$) and an almost degenerate overtone or combination involving a low-energy vibrational mode of the vinyl proton on C-3. Since a sharp, moderately intense maximum in the spectrum of 5-hydroxy-2-methylchromone (**1**) at 837 $cm^{-1}$ (KBr), possibly due to the CO group is absent in the hexadeuterated sample (but present in the trideuterated compound **8**), it is very probably the first overtone of this bending mode which is involved in Fermi resonance with the CO fundamental. Replacement of this hydrogen by deuterium lowers the energy of the deformation such that Fermi coupling is no longer possible, which results in collapse of the CO doublet to the singlet at 1649 $cm^{-1}$. Similar results have been found[10] for *p*-benzoquinone: incorporation of deuterium into position 2 results in a single CO absorption at 1664 $cm^{-1}$ intermediate in frequency between the Fermi resonance components at 1668 and 1656 $cm^{-1}$.

Analysis of the data for the nuclearly deuterated chromones is not however straightforward. The spectrum of 5-hydroxy-2-mondeuteromethylchromone-6, 8-$d_2$ (**8**) shows that deuteration of two positions of the benzenoid ring and replacement of effectively one H atom in the Me group has only a slight lowering effect on the 1661 $cm^{-1}$ band which moves to 1656 $cm^{-1}$ but has a greater effect on the 1625 $cm^{-1}$ absorptions which shifts to 1616 $cm^{-1}$ (Fig. 3). Only with further incorporation of D into the Me group and isotopic replacement of the hydrogen at C-3 is the major

absorption lowered to 1649 $cm^{-1}$. It would appear too that the bands at 1625 and 1606 $cm^{-1}$ in 5-hydroxy-2-methylchromone are coalescing on successive incorporation of D. It seems likely then that the 1606 $cm^{-1}$ absorption, is an aromatic ring stretching mode and that the 1625 $cm^{-1}$ absorption, although predominantly a CO absorption, possesses some aromatic ring stretching character, the energy of the ring stretching modes being affected by the increase in the mass of the substituents on deuteration. It should be noted here that all the chromone spectra are complex and almost all maxima in the CO region unsymmetrical.

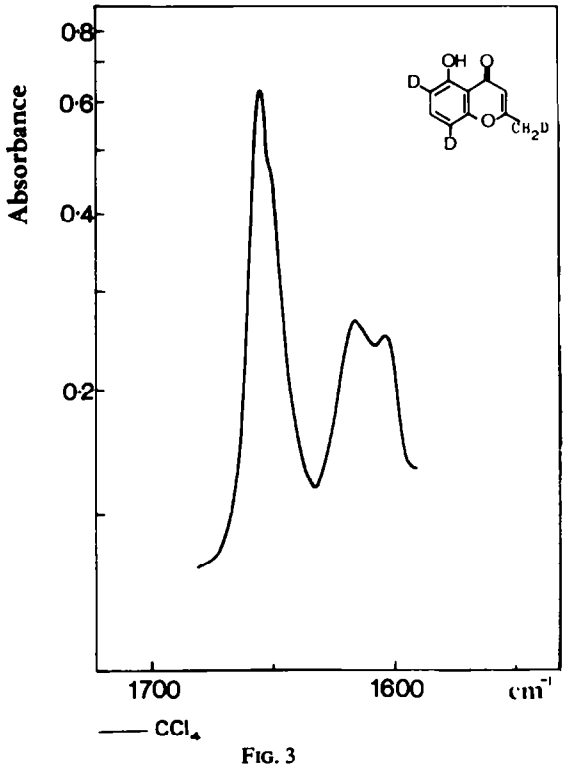



FIG. 3

To circumvent the difficulties incurred by multiple D incorporation, a more specifically labelled sample of 5-hydroxy-2-methyl-chromone was prepared by hydrolysis of 3-acetyl-5-hydroxy-2-methylchromone (**10**) with sodium carbonate in deuterium oxide. The 5-hydroxy-2-methylchromone isolated was completely deuterated at position 3 as shown by the absence of proton resonance at $\tau$ 4·04 and the Me group had also suffered almost complete isotopic replacement. The three aromatic protons however were in this case intact. Mass spectral analysis confirmed that the main product was 5-hydroxy-2-trideuteromethylchromone-3-d (**11**). Again, the CO spectrum of this product displays only two peaks at 1655 and 1616 $cm^{-1}$ ($CCl_4$). The upper band, which is close to the single CO absorption of **9**, undergoes a bathochromic shift to 1643 $cm^{-1}$ on deuteration of the 5-OH group (Fig. 4).

That the presence of hydrogen on C-3 of the 5-hydroxychromone nucleus is a prerequisite for a splitting of the CO stretching frequency is conclusively demonstrated

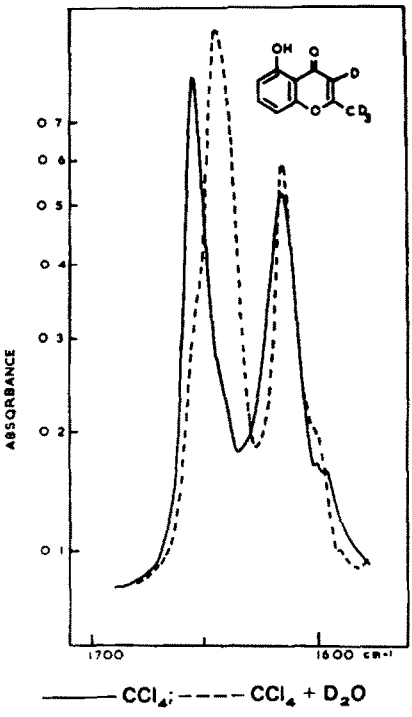
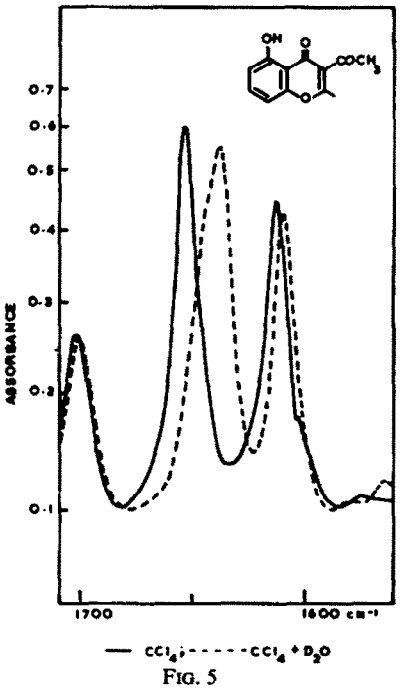

OH
O
D
CD3
0·7
0·6
0·5
0·4
0·3
0·2
0·1
ABSORBANCE
1700
1600 cm⁻¹
CCl4; ---- CCl4 + D2O

FIG. 4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0·6
0·5
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0·3
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0·1
ABSORBANCE
1700
1600 cm⁻¹
CCl4; ---- CCl4 + D2O

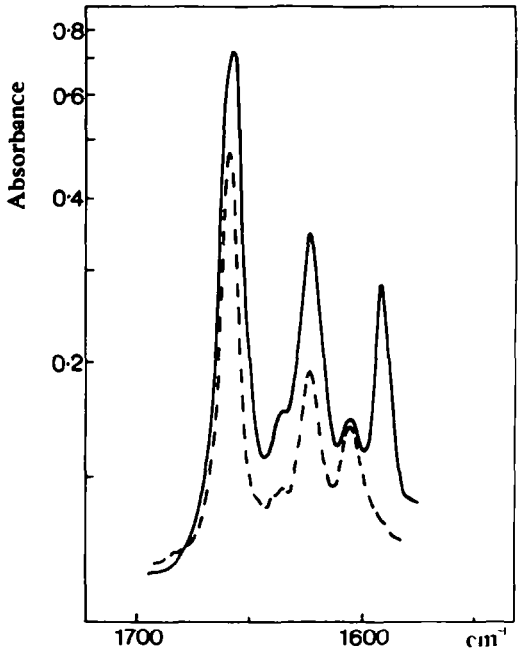
FIG. 5

in the spectrum (Fig. 5) of 3-acetyl-5-hydroxy-2-methylchromone (**10**). This 3-substituted compound possesses a sharp symmetrical singlet at 1650 $cm^{-1}$ ($CCl_4$) which shifts to 1636 $cm^{-1}$ when the 5-OH group is deuterated; the other two absorptions in this region, 1698 $cm^{-1}$ (methyl ketone) and 1610 $cm^{-1}$ remain unchanged in the 5-OD analogue.

These experiments verify that 5-hydroxychromones exhibit two CO absorptions caused by Fermi resonance, the operation of which depends on the presence of a proton on the C-3 position.

*Oxygen-18 incorporation*

A further parallel can be drawn between the spectra of 5-hydroxychromones and *p*-benzoquinone.[10] Incorporation, albeit incomplete, of $O^{18}$ into the *p*-benzoquinone CO groups results[10] in the appearance of a single CO band at 1634 $cm^{-1}$, 30 $cm^{-1}$ lower than the unsplit CO frequency of quinone-2d. A similar situation obtains for $O^{18}$ enriched 5-hydroxy-2-methylchromone. Mass spectral assay of a sample, prepared by exchange with $O^{18}$ enriched water in an acidic medium, indicated that




Oxygen-18 enriched 5-hydroxy-2-methylchromone (———) 5-Hydroxy-2-methylchromone (– – – –). Solutions in $CCl_4$.

FIG. 6

~40% of the product was unlabelled and in all but ~1% only one atom of $O^{18}$ had replaced the normal isotope. From the relative abundance of the benzofuran fragment ions at *m/e* 148 and 150, which arise by loss of carbon monoxide from the CO group,[20] it could be deduced that ~23% of the recovered material contains $O^{18}$ in the CO

group and ~30% in the OH and ether oxygens.[22] The infrared hydroxyl region of this sample is closely similar to that of 5-hydroxy-2-methylchromone but possesses a small, ill-defined maximum at 2350 $cm^{-1}$, possibly associated with the $O^{18}$—H stretching vibration.

The carbonyl region (Fig. 6) is identical to that of unlabelled compound with respect to the position of absorption of the original bands of the unlabelled compound present but, significantly, a sharp new absorption appears at 1593 $cm^{-1}$ the intensity of which suggests that it may be the CO stretching frequency of the $O^{18}$ enriched CO group. The single new CO frequency is 49 $cm^{-1}$ lower than the mean (1642 $cm^{-1}$) of the CO doublet of 5-hydroxy-2-methylchromone (**1**). Although this separation, which represents the expected approximate difference between the $O^{16}$ and $O^{18}$ CO stretching frequencies, is somewhat greater than those previously observed[23] for other CO compounds, it is nevertheless of the correct magnitude (~40 $cm^{-1}$) as predicted by the classical Hooke's Law equation[23b] which relates the stretching frequency with the stretching-force constant of the bond and the reduced mass of the atoms containing the bond.* As for *p*-benzoquinone, the $O^{18}$ CO group of labelled 5-hydroxy-2-methylchromone appears as a singlet because by insertion of the heavy O atom the CO stretching fundamental vibration has been changed sufficiently in energy to render Fermi resonance impossible.

## CONCLUSION

The apparent diminution in intensity of the 1606 $cm^{-1}$ band of $O^{18}$ enriched 5-hydroxy-2-methylchromone could be associated with incorporation of $O^{18}$ into the ether oxygen position.[6, 22] Increase in the mass of this atom might be expected to have a small effect on the ring stretching mode to which the 1606 $cm^{-1}$ band has already been assigned. One disturbing feature, however, is that deuteration of the OH group of the $O^{18}$ enriched sample (Fig 6) has apparently no effect on the new absorption at 1593 $cm^{-1}$ which might suggest that this absorption is not a CO stretching frequency.

The results of isotope incorporation into 5-hydroxy-2-methylchromone would suggest that, but for the intervention of Fermi resonance the CO stretching frequency would have a value of ~1650 $cm^{-1}$ in carbon tetrachloride. In this position, the chelated CO absorption is situated 15 $cm^{-1}$ lower than the single free CO band of 2-methylchromone (**2**), a relationship which would be expected by comparison with other chelated CO systems.[11, 24]

2-Methylchromone displays absorption characteristic of an enone system perturbed by the effects of the pyrone ether O atom and the benzene ring; thus, the CO stretching frequency at 1665 $cm^{-1}$ ($CCl_4$) appear 10–20 $cm^{-1}$ lower than the normal position of absorption of unsaturated or aromatic ketones. When an OH group is present in the 5-position of the nucleus, the enone system can suffer three further

* It must be emphasised that this calculation is only very approximate since it presupposes that the stretching motion is simple harmonic and that the CO group can be treated as though it were a simple diatomic molecule. Another model for calculation, in which the reduced mass contains terms representing the O atom as the mass on one side of the stretching bond and the rest of the molecule as the mass on the other, gives the ratio $\nu_{CO_{16}}/\nu_{CO_{18}}$ as 1·06. This value predicts that the separation between $\nu_{CO_{18}}$ and $\nu_{CO_{16}}$ should be ~ 90 $cm^{-1}$, which is approximately three times as large as experimentally determined separations.[23]

TABLE 1. CO ABSORPTIONS OF 5-HYDROXY- AND 5-DEUTEROXYCHROMONES (METHOD A) IN $CCl_4$ (s = shoulder, v.b. = very broad)

| | 5-OH | | | 5-OD | | |
|---|---|---|---|---|---|---|
| | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ |
| 5-Hydroxy-2-methylchromone (1) | 1661 | 9 | 1450 | 1652 | 11 | 1050 |
| | 1625 | 11 | 560 | 1617 | 7 | 550 |
| | 1606 | 11 | 360 | 1605 | 8 | 350 |
| 5-Hydroxy-2-methylchromone (1) + water | 1660 | 9 | 1010 | | | |
| | 1624 | 15 | 580 | | | |
| | 1605 | 16 | 390 | | | |
| Peucenin 7-methyl ether (4) | 1662 | 10 | 1450 | 1653 | 10 | 1140 |
| | 1629 | 30 | 490 | 1618 | 13 | 740 |
| | 1599 | 24 | 450 | 1599 | 15 | 660 |
| Khellinol (5) | 1663 | 15 | 700 | 1652 | | |
| | 1638 | 25 | 335 | 1633 | | |
| | 1595 | 15 | 550 | 1596 s | | |
| | | | | 1591 | | |
| 5-Hydroxy-2-monodeutero-methylchromone-6,8-$d_2$ (8) | 1656 | | | | | |
| | 1616 | | | | | |
| | 1603 | | | | | |
| 5-Hydroxy-2-trideuteromethyl-chromone-3,6,8-$d_3$ (9) | 1649 | 13 | 1020 | 1649 s | | |
| | 1642 s | | | 1639 | 13 | 1320 |
| | 1610 | 21 | 570 | 1608 | 14 | 700 |
| 5-Hydroxy-2-trideuteromethyl-chromone-3-d (11) | 1655 | 9 | | 1643 | 12 | |
| | 1616 | 14 | | 1614 | 10 | |
| 3-Acetyl-5-hydroxy-2-methyl-chromone (10) | 1698 | 15 | 365 | 1698 | 15 | 365 |
| | 1650 | 10 | 995 | 1637 | 17 | 920 |
| | 1610 | 12 | 725 | 1608 | 11 | 705 |
| Oxygen-18 enriched 5-hydroxy-2-methylchromone | 1659 | 10 | ~1300 | 1653 | 9 | ~1350 |
| | 1637 s | | | 1616 | | ~ 750 |
| | 1624 | 15 | ~ 580 | 1605 | 8 | ~ 230 |
| | 1606 | | ~ 210 | 1593 | | ~ 570 |
| | 1593 | 15 | ~ 370 | 1560 | v.b. | ~ 50 |

TABLE 2. CO ABSORPTIONS OF 5-DEUTEROXY ENRICHED CHROMONES (METHOD B) IN $CCl_3^{b}$ OR $CHCl_3^{c}$ (d = doublet, s = shoulder. Figures in parenthesis are the absorptions shown by undeuterated samples).

| | | | | | |
|---|---|---|---|---|---|
| 5-Hydroxy-7-methoxy-2-methylchromone[b] (3) | (1666 d), | 1656, | (1630), | 1621, | (1601) |
| Ptaeroxylin[b] (6) | (1658), | 1648, | (1628 s), | 1619, | (1598) |
| Karenin[c] (7) | (1656), | 1650, | (1627), | 1621 | |

perturbing effects—extended mesomerism involving the 5-OH group, strong H-bonding between the OH and the CO group, and a Fermi resonance interaction between the carbonyl stretching fundamental and the overtone of the C—H deformation of the C-3 proton. The combination of these effects is a doublet CO absorption ~1665 and ~1630 $cm^{-1}$, the contour of which is independent of both solvent polarity and temperature.

## EXPERIMENTAL

For general experimental details see the preceding paper.

*5-O-Deuteration Method A.* 5 Hydroxy-2-methylchromone (15 mg) in $CCl_4$ (1 ml) was shaken for 3 min with $D_2O$ (99·8 atom %, 3 drops), the soln transferred, with minimum exposure to the atmosphere, to IR cells (0·05 mm) having $CaF_2$ windows and the spectrum recorded.

The procedure was repeated with the chromones listed in Table 1. In each case, the spectra of the 5-hydroxy and 5-deuteroxychromones were recorded at the same concentrations under identical conditions, and the disappearance of the signals at ~ − 3 τ noted in the NMR spectra of the deuterated samples.

*Method B.* Samples (8–10 mg) of all the chromones listed in Tables 1 and 2 (apart from those with nuclear isotope incorporation) in anhydrous AnalaR chloroform or $CCl_4$ (1–2 ml), dried over silica gel, were shaken with $D_2O$ (5 drops) for 3 min. With minimum exposures to moist air, the mixtures were evaporated to dryness under reduced press, the process repeated 4 times and residual $D_2O$ removed in anhyd benzene vapour under vacuum. Immediately, IR and NMR spectra were recorded simultaneously in $CCl_4$, but in each case, both spectra indicated the presence of residual 5-hydroxychromone. The integrated intensity of the peak at τ − 2. 3 increased with time in the NMR spectrum of deuterated 5-hydroxy-2-methylchromone kept in a sample tube exposed to the atmosphere.

*5-Hydroxy-2-monodeuteromethylchromone-6,8-$d_2$.* 5-Hydroxy-2-methylchromone (14 mg) in dioxan (0·1 ml), $D_2O$ (0·6 ml) and acetyl chloride (0·2 ml) was heated at 96 ± 3° (oil bath temp) for 70 hr in a sealed tube. The cooled reaction soln was diluted with $CHCl_3$ and dried. Evaporation furnished 5-hydroxy-2-monodeuteromethylchromone-6,8-$d_2$ as a pale yellow solid, m.p. 86–89°, mass spectral peaks at *m/e* 181 (31), 180 (82), 179 (100), 178 (54), 153 (11), 152 (32), 151 (48), 150 (40), 149 (16), 139 (10), 138 (55), 111 (10), 110 (100), 109 (19%). This sample was used directly for IR measurements without purification. Alternative conditions in which 5-hydroxy-2-methylchromone (12 mg) was heated in a sealed tube in presence of $D_2O$ (0·4 ml) and 12 N HCl (0·06 ml), with and without added dioxan, were ineffective in promoting deuteration.

*5-Hydroxy-2-trideuteromethylchromone-3,6,8-$d_3$.* 5-Hydroxy-2-methylchromone (14 mg) in dioxan (0·1 ml), $D_2O$ (1·2 ml), and acetyl chloride (0·8 ml) was heated at 90 ± 3° in a sealed tube for 116 hr. Isolated as above, 5-hydroxy-2-trideuteromethyl-3,6,8-$d_2$ sublimed at 76°/0·04 mm as a colourless solid, m.p. 87–89°, mass spectral peaks at *m/e* 182 (100), 181 (49), 180 (12), 154 (35), 153 (20), 152 (20), 138 (33), 110 (56), 109 (11%).

*3-Acetyl-5-hydroxy-2-methylchromone* (**10**), m.p. 119–122° (lit.[25] 122°) was prepared from 2,6-dihydroxyacetophenone by the method of Limaye and Kelkar,[25] isolated by preparative TLC ($CHCl_3$) from the least polar band, and crystallized from MeOH; mass spectral peaks at *m/e* 218 (76), 203 (100), 200 (31), 176 (14), 137 (58), 136 (18), 108 (22), 67 (45%); τ 7·47 and 7·37, 2 × 3 H, s, 2-C$\underline{H}_3$ and 3-COC$\underline{H}_3$; −2·3, 1H, s, 5-O-$\underline{H}$.

*5-Hydroxy-2-trideuteromethylchromone-3-d* (**11**). Crude 3-acetyl-5-hydroxy-2-methylchromone (1·5 g) was refluxed gently for ½ hr with $Na_2CO_3$ (0·95 g), $D_2O$ (4 ml). The cooled mixture was extracted with ether; work up gave a brown gum (1·2 g) which was separated on TLC ($CHCl_3$). The TLC pure 5-hydroxy-2-trideuteromethylchromone-3-d sublimed at 80°/0·02 mm as an oily solid, which contained some 5-hydroxy-2-dideuteromethylchromone-3-d (NMR signal at τ 7·60), mass spectral peaks at *m/e* 181 (40), 180 (100), 179 (30), 153 (15), 152 (35), 151 (15), 150 (15), 136 (31), 108 (46%).

*$O^{18}$ Enriched 5-hydroxy-2-methylchromone.* A suspension of 5-hydroxy-2-methylchromone (12 mg) in $O^{18}$ enriched water (0·2 ml) was treated with dry HCl (~ 100 mg). The pyrylium chloride soln was heated in a sealed apparatus at 96 ± 3° for 95 hr and, after cooling, extracted with anhyd $CHCl_3$. Removal of solvent under vacuum and sublimation of the residue at 75°/0·01 mm furnished a crystalline product (10 mg), m.p. 88–90°, mass spectral peaks at *m/e* 178 (100), 176 (68), 150 (19), 148 (27), 147 (19), 138 (23), 136 (18), 110 (27), 108 (16%).

## REFERENCES


[1] R. D. H. Murray and P. H. McCabe, *Tetrahedron* **25**, 5819 (1969).
[2] J. H. Looker and W. W. Hanneman, *J. Org. Chem.* **27**, 381 (1962).
[3] H. L. Hergert and E. F. Kurth, *J. Am. Chem. Soc.* **75**, 1622 (1953); B. L. Shaw and T. H. Simpson, *J. Chem. Soc.* 655 (1955); P. Lebreton and J. Chopin, *Spectrochim. Acta* **19**, 2099 (1963).
[4] L. H. Briggs and L. D. Colebrook, *Ibid.* **18**, 1939 (1962).
[5] R. N. Jones, C. L. Angell, T. Ito and R. J. D. Smith, *Canad. J. Chem.* **37**, 2007 (1959).
[6] P. Beak and G. A. Carls, *J. Org. Chem.* **29**, 2678 (1964).
[7] A. R. Katritzky and R. A. Jones, *Spectrochim. Acta* **17**, 64 (1961).
[8] F. M. Dean, *Naturally occurring Oxygen Ring Compounds*, p. 252. Butterworths, London (1963).
[9] G. Govil and C. L. Khetrapal, *Curr. Sci.* **34**, 116 (1965).
[10] E. D. Becker, H. Ziffer and E. Charney, *Spectrochim. Acta* **19**, 1871 (1963).
[11] L. J. Bellamy, *Advances in Infrared Group Frequencies*. Methuen, London (1968).
[12] H. M. Fales and A. V. Robertson, *Tetrahedron Letters* 111 (1962).
[13] H. M. Randall, R. C. Fowler, M. Fuson and J. R. Dangyl, *Infrared Determination of Organic Structures*. Van Nostrand, N.Y. (1949).
[14] R. A. Nyquist, *Spectrochim. Acta* **19**, 1655 (1963).
[15] Z. Yoshida and M. Haruta, *Tetrahedron Letters* 2631 (1964); 3745 (1965).
[16] E. Späth and K. Eiter, *Ber. Dtsch. Chem. Ges.* **74B**, 1851 (1941).
[17] W. Bencze, J. Eisenbeiss and H. Schmid, *Helv. Chim. Acta* **39**, 923 (1956).
[18] J. H. Looker, W. W. Hanneman, S. A. Kagal, J. I. Dappen and J. R. Edman, *J. Heterocyclic Chem.* **3**, 55 (1966).
[19] J. H. Looker, S. A. Kagal and J. R. Edman, *Ibid.* **3**, 61 (1966).
[20] M. M. Badawi, M. B. E. Fayez, T. A. Bryce and R. I. Reed, *Chem. Ind.* 498 (1966).
[21] [a] P. H. McCabe, R. McCrindle and R. D. H. Murray, *J. Chem. Soc.* (C), 145 (1967); [b] M. M. Badawi and M. B. E. Fayez, *Indian J. Chem.* **5**, 93 (1967).
[22] G. Aksnes, D. Aksnes and P. Albriktsen, *Acta Chem. Scand.* **20**, 1325 (1966).
[23] [a] G. J. Karabatsos, *J. Org. Chem.* **25**, 315 (1960); [b] M. Halmann and S. Pinchas, *J. Chem. Soc.* 1702 (1958); [c] M. Byrn and M. Calvin, *J. Am. Chem. Soc.* **88**, 1916 (1966).
[24] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Methuen, London (1958).
[25] D. B. Limaye and G. R. Kelkar, *J. Indian Chem. Soc.* **12**, 788 (1935).