The Electronic Structure of Chromones, Studied by Low-energy Photoelectron Spectroscopy and *ab initio* Molecular Orbital Calculations

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The electronic structures of eleven molecules related to chromone have been studied by recording their He^{I} photoelectron spectra and interpreting these data with the aid of *ab initio* molecular orbital calculations. An assignment of the spectra is presented which is consistent with the changes in the measured ionization energies of this series of molecules, particularly those due to substituent effects.

The wide occurrence of molecules related to chromone in the field of natural products has prompted studies of it, and of its derivatives,[1] particularly the flavones and isoflavones. More recently, attention has been focused on the pharmacological activity of chromone-related molecules, particularly their 'anti-allergy' properties, this group of compounds being the first observed to display such activity.[2]

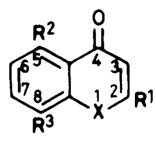
An understanding of the chemistry of such compounds and, more ambitiously, of their pharmacological activity, might be achieved through a knowledge of their electronic structure. Indeed, we have recently discussed features of their reactivity with the aid of molecular orbital (MO) calculations of their ground-state wavefunctions.[3] Furthermore, Cheney *et al.*[4] have investigated the antiallergic properties of alkoxycarbonylchromones and related molecules using fragment SCF calculations, and Kador and Sharpless have attempted to correlate the inhibition of the enzyme aldose reductase by such molecules with the results of Huckel and CNDO/2 calculations.[5,6]

In this paper we report an experimental and theoretical study of the electronic structure of a series of chromones, using photoelectron spectroscopy and *ab initio* MO calculations.

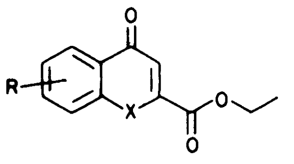
For molecules of this size accurate calculations of molecular ionization energies (IEs) are time consuming, as they require the consideration of relaxation and correlation effects. Rather than attempt a quantitative calculation of the IEs of the molecules under study, we use *ab initio* calculations at the SCF level, with quite modest basis sets, on a series of related molecules to provide insight into the expected changes in the photoelectron spectra *via* the application of Koopmans' theorem. The series we have examined includes chromone (**1**) itself, and, because of the biological importance of the 2-carboxy group, 2-ethoxycarbonylchromone (**5**), together with a number of methoxy-substituted derivatives of these molecules. In addition, we have studied 1-thiochromone (**4**), oxanilic acid (**11**), and methyl 1-ethyl-1,4-dihydro-4-oxoquinoline-2-carboxylate (**9**); the latter two compounds show similar antiallergic activity to the chromone derivatives.[7]

Experimental Methods and Results

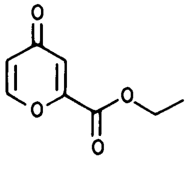
All samples were donated by Fisons plc, Pharmaceutical Division. Photoelectron spectra were run with a Vacuum Science Workshop spectrometer, with 65 mm mean radius hemispherical analyser operated with a retarding voltage scan. The spectra were obtained at the minimum temperatures (60—140 °C) needed to achieve sufficient sample pressures, giving count rates of the order of 1 000 counts s^{-1}, using He^{I} exciting radiation. All the spectra were internally calibrated with argon. Representative spectra are shown in Figure 1. The measured IEs are listed in the Table: the values quoted are for the band maxima and are to be interpreted as vertical ionization energies.



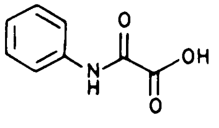
(**1**) $R^1 = R^2 = R^3 = H, X = O$
(**2**) $R^1 = Me, R^2 = R^3 = H, X = O$
(**3**) $R^1 = Me, R^2 = R^3 = OMe, X = O$
(**4**) $R^1 = R^2 = R^3 = H, X = S$



(**5**) $R = H, X = O$
(**6**) $R = 6\text{-OMe}, X = O$
(**7**) $R = 8\text{-OMe}, X = O$
(**8**) $R = 3\text{-OMe}, X = O$
(**9**) $R = H, X = NEt$



(**10**)



(**11**)

Theoretical Methods and Results

Computational Details.—To allow a comparison of the 11 molecules studied herein, restricted Hartree-Fock calculations were performed in an STO-3G minimal basis.[8] To examine the effect of basis-set extension, calculations for chromone (**1**), 1-thiochromone (**4**), oxanilic acid (**11**), and 2-ethoxycarbonyl-4-pyrone (**10**) were also performed in a 3-21G split-valence basis.[9]

In the absence of experimental geometries for these species, and in view of the semiquantitative nature of the results of these calculations, we estimated the geometries from those of similar compounds for which crystallographic data have been obtained.[10—13] Deviations from planarity for some of these molecules have been suggested. Thus, Cheney *et al.*[14] have reported that in the solid state the side-chain in some oxanilic acid derivatives may not be coplanar with the aniline fragment, though their calculations suggest that the acid itself will be planar in the gas phase. A PCILO calculation suggested that the carboxylate group in 2-methoxycarbonylchromone was coplanar with the chromone nucleus.[15] STO-3G calculations which we have carried out suggest that the planar conformation is preferred in both oxanilic acid (**11**) and 2-ethoxycarbonylchromone (**5**), but the calculated energy differences (less than 3 kcal mol^{-1}) are too small to be conclusive. The side-chain in (**9**) was calculated to prefer a perpendicular conformation, presumably owing to the steric repulsion of the ethyl group bonded to the nitrogen atom. To turn now to the other substituents, Anderson *et al.*[16] have discussed the non-coplanarity of methoxy groups in some polysubstituted benzenes. Our calculations indicate that the most stable conformation is for

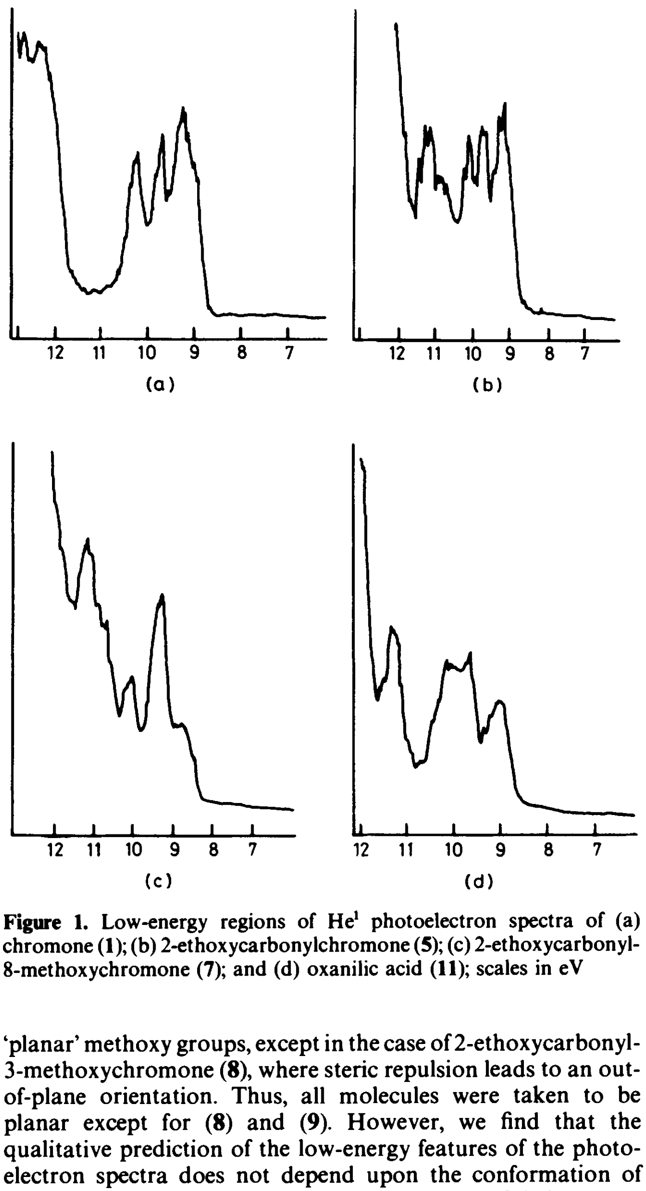


Figure 1. Low-energy regions of He^{I} photoelectron spectra of (a) chromone (**1**); (b) 2-ethoxycarbonylchromone (**5**); (c) 2-ethoxycarbonyl-8-methoxychromone (**7**); and (d) oxanilic acid (**11**); scales in eV

'planar' methoxy groups, except in the case of 2-ethoxycarbonyl-3-methoxychromone (**8**), where steric repulsion leads to an out-of-plane orientation. Thus, all molecules were taken to be planar except for (**8**) and (**9**). However, we find that the qualitative prediction of the low-energy features of the photoelectron spectra does not depend upon the conformation of these two molecules, so that our measurements of their spectra do not provide any evidence as to the preferred conformations.

General Features of the Valence MOs.—Before discussing the general aspects of the SCF results we note first that for those molecules for which calculations were carried out in both the STO-3G and 3-21G bases, the resulting sets of valence orbitals were qualitatively similar. We now discuss the characters of the less tightly bound valence orbitals, which will determine how the orbital energies, and associated bands in the photoelectron spectra, will change through the series of molecules studied. We shall discuss only the low-energy region of the He^{I} photoelectron spectra, since only here are well resolved bands present. Chromone itself has four orbitals in this region of interest: addition of a carboxylate group introduces a further two. This set of six MOs will be used to interpret the photoelectron spectra, the essential features of which are found to be preserved in spite of substitution.

The four highest occupied MOs of chromone are shown in Figure 2. If we consider phenol and acrylaldehyde as sub-units of chromone, π_1 may be regarded as arising from the out-of-phase combination of the highest occupied π orbitals of these two species which have IEs of 8.37[17] and 10.95 eV,[18] respectively. The orbital π_2 may be similarly correlated with the second occupied MO of phenol, of a_2 symmetry in C_{2v} (IE 9.28 eV[17]). The nodal structure of these two orbitals are retained throughout the series, with π_1 always predicted as the highest occupied π orbital. The third π MO, π_3, sometimes has significant density on the carboxylate carbonyl oxygen atom, but may still be classified as essentially a chromone MO. Depending upon the substitution pattern, π_2 and π_3 may be predicted in either order. In chromone itself, π_3 is the more tightly bound.

The σ non-bonding p 'lone pair' of the chromone carbonyl oxygen atom is denoted n_1 in Figure 2, and the corresponding lone pair on the carboxylate group n_2. Some mixing of these two orbitals occurs, but this is slight, and the characters of the MOs are clear in all cases. Orbital π_4 is localized on the carboxylate group and correlates with the highest occupied π-orbital of formic acid, which has an IE of 12.51 eV.[19] We note from the calculation that there is little conjugation between the carboxylate group and the π-system of the chromone, leading to the prediction that the photoelectron spectra are relatively insensitive to side-chain conformation.

The orbitals of 2-ethoxycarbonyl-4-pyrone (**10**) are closely related to those of (**5**). Their nodal structures may be simply obtained from those of Figure 2 by ignoring the appropriate part of the benzene ring, there being no MO in (**10**) corresponding to π_2.

The orbitals of oxanilic acid must be discussed separately. The highest filled MO (π_1) is the antibonding combination of the benzene b_1 (one component of the e_{1g} in D_{6h}) and –N–C=O π orbitals, with π_3 the corresponding bonding combination. The orbital π_2 is localized on the benzene ring and correlates with the a_2 MO of benzene. The oxygen lone pair combination, n_+, is largely as found in oxamic acid,[20] and π_4 is the carboxy π orbital.

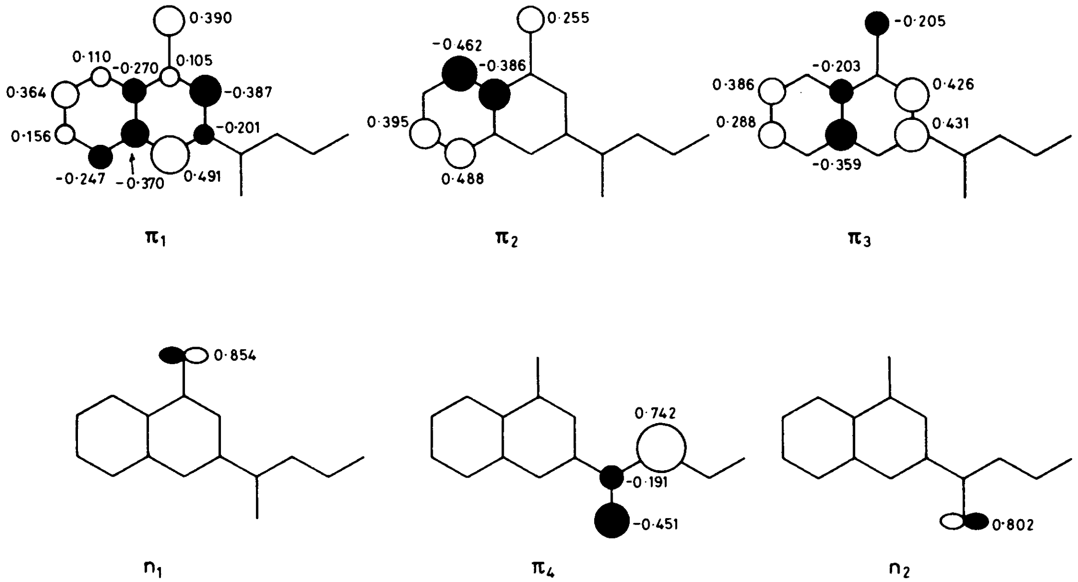
As to the orbital ordering, π_1 is always predicted to be the least stable of the π orbitals, whilst π_3 is usually more tightly bound than π_2. However, in (**6**) and (**8**), with methoxy substituents at the 6- and 3-positions, this latter order is reversed, since π_3 has large coefficients at these positions, in contrast to π_2 (Figure 2). The carboxylate MOs, where present, have considerably higher IEs than the chromone orbitals.

Assignment of the Photoelectron Spectra.—We first discuss the photoelectron spectra of compounds (**1**)—(**4**), in which a carboxylate side-chain is absent. We begin with the simplest molecule, chromone itself (**1**). The spectrum (Figure 1a) has three low-energy features, at 9.13, 9.67, and 10.2 eV, the first of which is the most intense and possibly shows a low-energy shoulder. It thus probably contains two ionization bands. Orbitals π_1 and π_2 arise from the e_{1g} orbitals of benzene, which have an IE of 9.24 eV. The involvement of O(2p) in π_1 will lower the IE from the value in benzene, so we assign an IE of 9.13 eV to π_1 and 9.67 eV to π_2. The oxygen lone pair IE is at 9.37 eV in acetophenone,[21] and is likely to be lower in (**1**), because of increased conjugation. We thus assign n_1 to the band at 9.13 eV, along with π_1. We assign the remaining low-energy band at 10.20 eV to π_3, which may be compared with the first π ionization of acrylaldehyde, occurring at 10.95 eV. In the case of 2-methylchromone (**2**), there are only two distinct bands. The major effect of methyl substitution at the 2-position will be to raise the energy of π_3 so that its energy is now close to that of π_2, π_1 and π_2 being little affected since there is little involvement of C-2 in these MOs. Compare, for example, the raising of the highest occupied π orbital of acrylaldehyde by 0.8 eV upon substitution of a methyl group at the γ-position.[22] The first band of (**2**) is thus assigned to π_1 and n_1 [as in (**1**)], whilst the second band contains π_2 and π_3, implying a raising of π_3 by about 0.5 eV. Further confirmation of our assignment of

Table. Experimental vertical ionization energies (eV) and spectral assignments[a]

Ionization	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
π_1	9.13	8.95	8.08	8.50	9.10	8.47	8.6	9.06	7.88	9.5	9.08
n_1	9.13	8.95	8.85	9.16	9.10	9.1	9.2	8.65	8.60	9.5	10.17(n_+)
π_2	9.67	9.67	8.85	9.53	9.62	9.62	9.2	9.62	9.37		9.70
π_3	10.20	9.67	9.61	10.07	10.0	9.62	10.05	9.62	9.37	11.0	11.32
n_2					10.9	10.7	10.7	10.9	10.7	11.0	
π_4					11.21	11.24	11.14	10.9		11.0	

[a] Values quoted are for the band maxima; estimated accuracy ±0.05 eV where two decimal places are quoted, otherwise ±0.1 eV.



π_1 π_2 π_3

n_1 π_4 n_2

Figure 2. Coefficients of p orbitals in π_1, π_2, π_3, and n_1 MOs of chromone (**1**) and in π_4 and n_2 of 2-ethoxycarbonylchromone (**5**) obtained from STO-3G calculations

chromone comes from the spectrum of 1-thiochromone (**4**). Here, four bands are observed, with an additional low-energy feature now apparent at 8.50 eV, the remaining three bands being at energies close to the three bands of chromone (**1**). Substitution of sulphur for oxygen in (**1**) will leave π_2 and π_3 largely unchanged in energy, but will raise the energy of π_1, which has a large oxygen component. Hence in (**4**), the first band of (**1**) is split into two components, the low-energy peak being due to π_1.

The effect of the methoxy substituents at the 5- and 8-position in (**3**) will be to raise the energy of those MOs which have substantial contributions from C-5 and C-8. Thus, the energies of π_3 and n_1 are close to those in (**2**), whilst both π_1 and π_2 are raised in energy as compared with (**2**), giving the spectral assignment in the Table.

We turn now to a discussion of the spectra of those species having a carboxylate side-chain, where two additional low-energy bands are expected. In the spectrum (Figure 1b) of 2-ethoxycarbonylchromone (**5**), five separate features are discerned. The first three bands are close in energy to those of (**1**) and are similarly assigned. The observed raising of the energy of π_3 (arising from the significant contribution of C-2 in this MO) by 0.2 eV is predicted by the SCF calculation. As previously discussed for (**3**), methoxy substitution in (**6**) and (**7**) raises the energy of those MOs with appreciable contributions from the carbon atom at the point of substitution. Thus, compared with the corresponding MO in (**5**), π_1 and π_3 are raised in (**6**), and π_1 and π_2 are raised in (**7**), giving the assignments in the Table. The interpretation of the spectrum of the 3-methoxy compound (**8**) is somewhat different, since the SCF calculations predict the methoxy group to be non-planar, so that the oxygen lone pair orbital does not conjugate with the π-system. The *ab initio* calculation does indicate, however, that the methoxy group perturbs π_3 significantly, raising its energy as compared with π_3 in (**5**), π_1 and π_2 being unaffected. In addition, the calculation reveals significant mixing between the methoxy lone pair and that of the carbonyl oxygen atom *via* a through-bond interaction, with a consequent decrease in the IE of n_1. Thus, in the case of (**8**) we assign the first IE at 8.65 eV to n_1, π_1 to the band at 9.06 eV, and both π_2 and π_3 to the 9.62 eV peak.

In the case of (**5**) we assign the additional features at 10.9 and 11.21 eV, absent in (**1**), to the carboxylate ionizations n_2 and π_4 respectively. This region of the spectrum closely resembles that of ethyl ethanoate,[23] and is similarly assigned, there being little conjugation with the π-system of the ring to affect their IEs. These two carboxylate ionizations are essentially unchanged by methoxy substitution in (**6**) and (**7**). In (**8**), only one band is observed in the region of the carboxylate ionizations. This clearly incorporates ionizations from n_2 and π_4, and its intensity suggests it may contain another ionization. This would be ionization from the in-phase combination of the methoxy with the carbonyl oxygen lone pair, the counterpart of the first ionization. A band due to this ionization is not observed in (**5**)—(**7**), since here conjugation with π_1 and π_3 lowers the energy of the methoxy $O(2p_\pi)$ orbital to below 11.5 eV.

The spectrum of (**9**) is somewhat different from those already discussed. The replacement of the ring oxygen by nitrogen is expected to raise the energy of the chromone π-orbitals. The carbonyl lone pair may also be indirectly affected *via* the redistribution of charge. The *ab initio* calculations indicate a marked lowering of this IE, but not as great as that for π_1. In view of this we assign the first two peaks at 7.88 and 8.60 eV to π_1 and n_1 respectively. A relatively intense band at 9.37 eV is assigned to π_2 and π_3. The carboxylate bands for this molecule are largely obscured by the low-energy onset of the σ-framework ionizations.

The spectrum of (**10**) contains only two distinct features in the low-energy region, with an intensity ratio of approximately 2:3. The low-energy band is assigned to the MO localized on the pyrone nucleus, which correlates with π_1 of the chromones, together with ionization from n_1. The second band consists of ionization from the MO correlating with π_3, together with the two carboxylate ionizations not greatly shifted from their values in (**5**).

Finally we turn to the spectrum of oxanilic acid, which is not directly related to that of chromone. We thus use the results of our *ab initio* calculations previously discussed to indicate the character, and ordering, of the MOs. Four ionizations are expected corresponding to π_1, π_2, π_3, and n_+. Three distinct bands are observed, one of which is partially split into two components (see Figure 1d). The lowest IE is associated with π_1: the antibonding combination of the benzene b_1 and amide π orbitals. The low-energy component of the second band is assigned to π_2, which correlates with the a_2 MO of benzene. The remaining component may be associated with the lone pair ionization n_+, which is slightly destabilized with respect to the corresponding ionization in oxamic acid (10.51 eV).[20] The third band arises from ionization from π_3, the corresponding bonding combination to π_1.

Conclusions

In the present study of the electronic structure of a series of chromones, an assignment of their low-energy photoelectron spectra is achieved through a study of substituent effects and is aided by *ab initio* MO calculations, the IEs being obtained *via* the use of Koopmans' theorem from these calculations. At this level of accuracy the calculations are valuable as an aid to assignment, but the absolute magnitudes of the calculated IEs are of little value. Indeed, the STO-3G values generally differ from the experimental values by more than 2 eV. As to the calculated orbital ordering, that of the π orbitals is in accord with the assignments presented herein. However, as found in other molecules, the relative ordering of the lone pair and π orbitals is incorrectly given by Koopmans' theorem. Thus, in chromone (**1**) n_1 and π_3 are predicted to be nearly degenerate by Koopmans' theorem, whereas our assignment places n_1 in the first band and π_3 in the third band separated by ~1 eV. As expected, more sophisticated calculations, using a better atomic basis, and including relaxation and correlation effects, are needed to provide quantitative theoretical estimates of the IEs.

Acknowledgements

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