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Photoelectron spectroscopy of natural products. Part 1. Polypodanes

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ABSTRACT: He I UV photoelectron spectra of four naturally occurring polyenes were measured. The spectra were interpreted on the basis of empirical arguments and semiempirical MO calculations. The results show that through-bond interactions between π-orbitals are discernible in spite of the non-rigid molecular geometry. This work shows that natural products have electronic structures which are of interest to a wider circle of chemists than just those who specialize in natural products. Copyright © 1999 John Wiley & Sons, Ltd.

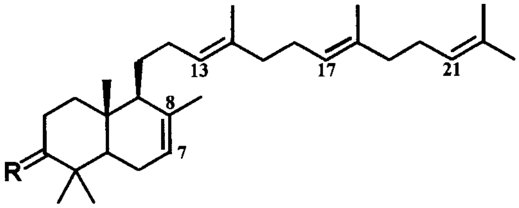
KEYWORDS: photoelectron spectra; natural products; polypodanes; polyenes

INTRODUCTION

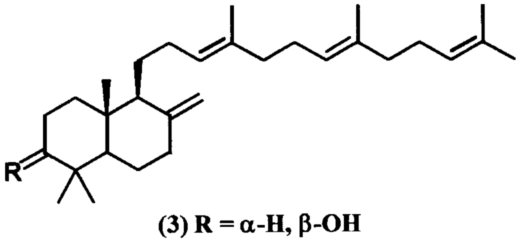
Many natural products have unusual molecular structures and, as a consequence, they may also have interesting electronic structures. The interest in the electronic structure of natural products may stem from either the relationship between the electronic structure and biological function of the compound or the uniqueness of the electronic structure from the point of view of basic research. One of the best examples is artemisinin, which contains an unusual endoperoxide functional group[1] and this group may be related to its biological (anti-malarial) function. The polypodanes discussed in this work are major components of the bark resin which is used in ethnomedicine for the treatment of skin diseases and other ailments.

The molecular structures of natural products have been extensively investigated by NMR techniques; indeed, such studies are essential for the identification of new compounds. On the other hand, very few studies of the electronic structures of natural products have been reported.[2] Several reasons can be put forward for the scarcity of electronic structure data. The standard method for electronic structure analysis (UV photoelectron spectroscopy in combination with MO calculations; UPS/MO) requires that natural product compounds be isolated in quantities (0.5–1 g) which are often unavailable. Furthermore, many natural products decompose at elevated temperatures that are required to produce sufficient vapour pressures for UPS measurements. Finally, many natural products contain numerous functional groups, which give rise to overlapping spectral bands, thus rendering such molecules unsuitable for UPS/MO analysis.

This paper is the first in a series of studies dedicated to the electronic structure of natural products. The selection of the polypodanes **1–4** originates from our interest in intramolecular, through-bond (TB) interactions and from the availability of these compounds in relatively large quantities following our work on the phytochemistry of Asian plants.[3,4] We have demonstrated previously that TB interactions in non-rigid, monocyclic, non-conjugated polyenes can be studied successfully by the UPS method.[5]



(1) R = α-H, β-OH
(2) R = O



(3) R = α-H, β-OH
(4) R = O

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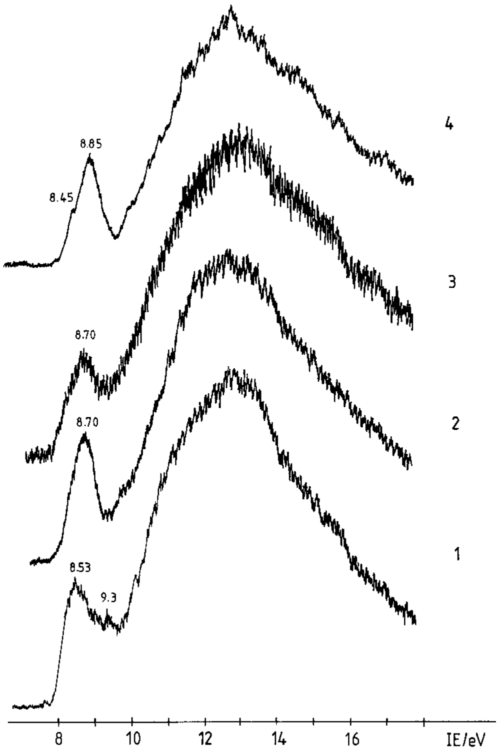

Figure 1. He I photoelectron spectra of polypodanes **1–4**

EXPERIMENTAL

Spectra were recorded using a modified Perkin-Elmer PS16 UV photoelectron spectrometer using the He I line. The plates of the 127° cylindrical analyser were scanned, producing a resolution as indicated by the FWHM of the Ar^+ $^2P_{3/2}$ peak of about 25 meV. Spectra were calibrated using N_2O assuming the sharp features[6] at 12.89, 16.39 and 20.11 eV, and were recorded at (**1**) 143, (**2**) 115, (**3**) 135 and (**4**) 74 °C. AM1 calculations were performed with the HyperChem 5 program package[7] and included full geometry optimization. The conformer space search was achieved using the Spartan program.[8]

The stem bark of *Cratoxylum cochinchinense* (Lour.) B1. was collected in South Vietnam and Singapore. In each case, the ground plant material was continuously extracted by percolation with hot hexane. Column chromatography of the crude extracts (silica gel, ethyl acetate–hexane step gradient) followed by gel permeation chromatography [Sephadex LH-20, $CHCl_3$–MeOH (1:1)] and reversed-phase column chromatography (C_{18}, acetone–acetonitrile gradient) gave polypoda-7,13,17,21-tetraen-3β-o1 (**1**) from the Vietnamese material and polypoda-8(26),13,17,21-tetraen-3β-o1 (**3**) from the Singapore material. Oxidation of **1** and **3** with Jones reagent afforded the ketones **2** and **4**, respectively.[3,4]

Table 1. Ionization energies (*IE*) and AM1 orbital energies (ε) for compounds **1–4**

Compound	*IE* (eV)	ε (eV)	MO character[a]
1	8.53	9.13	$\pi_{13}-\pi_{17}+\pi_{21}$
		9.20	π_7
		9.26	$\pi_7-\pi_{13}+\pi_{21}$
	9.30	9.27	$\pi_{13}+\pi_{17}+\pi_{21}$
2	8.70	9.16	$\pi_{13}-\pi_{17}+\pi_{21}$
		9.33	$\pi_7+\pi_{21}$
		9.48	$\pi_7-\pi_{13}+\pi_{21}$
		9.74	$\pi_{13}+\pi_{17}+\pi_{21}$
		10.06	n_O
3	8.70	9.05	$\pi_{13}-\pi_{17}+\pi_{21}$
		9.31	$\pi_{13}-\pi_{21}$
		9.55	π_8
		9.65	$\pi_{13}+\pi_{17}+\pi_{21}$
4	8.45	9.14	$\pi_{13}-\pi_{17}+\pi_{21}$
	8.85	9.40	$\pi_{13}-\pi_{21}$
		9.71	$\pi_{17}+\pi_{21}$
		9.76	π_8
		10.06	n_O

[a] The π_n labels designate C=C bonds originating at C_n carbons.

RESULTS AND DISCUSSION

The UPS spectra of **1**–**4** are shown in Fig. 1. The most interesting part of the spectra comprises bands with ionization energy (*IE*) <10 eV. These bands correspond to ionizations from π-orbitals and oxygen lone pairs (n_O) of the keto group. The hydroxyl group oxygen lone pair n_{OH} appears above 10 eV. The rest of the bands are poorly resolved; they belong to ionizations from σ-orbitals and are of minor interest. The assignment of spectra is usually achieved with the aid of MO calculations. We selected the AM1 method as the best compromise between computational cost and accuracy. However, AM1 results (Table 1) are not very useful in the present study because of the high density of π-ionizations. It is well known that in such cases MO results are generally unreliable. The only useful prediction from AM1 calculations concerns the n_O energy, which is suggested to be higher than that of π-orbitals. The π and n_O orbitals can interact via a TB mechanism.

Such intramolecular interactions are the main interest in this work and will be discussed in some detail. The interactions in our molecules can be classified as being of 1,4-π,π, 1,5-π,π and 1,6-n,π type. The larger the energy separation between non-conjugated orbitals, the weaker their interaction becomes unless there is an efficient 'relay' in the form of intervening σ-orbitals. Inspection of the number of resolvable π bands can reveal such interactions; the more bands there are, the stronger are the orbital interactions. Taking this argument into consideration, we can conclude that π,π interactions are stronger in **1** than in its $\Delta^{8(26)}$ isomer (**3**), as evidenced by the appearance of a single π band for **3** (at 8.7 eV) vs two π

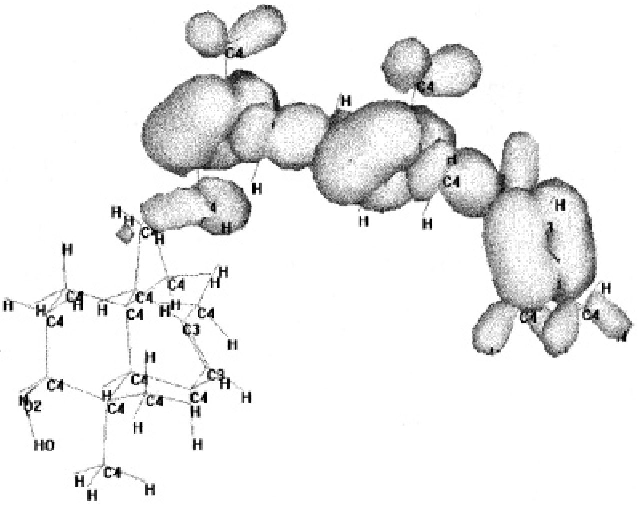

Figure 2. HOMO electron density in **1** indicating TB interactions

bands (at 8.53 and 9.3 eV) for **1**. Furthermore, the average *IE* of the π-manifold is lower in **1** than **3**, which also suggests enhanced TB interactions. The destabilization of the manifold is caused by π, σ interactions between double bonds and the σ skeleton. Long-range TB interactions have been studied and discussed in great detail[2,9] but usually on examples of rigid bicyclic or monocyclic systems. The interesting point is that we can distinguish TB interactions even in non-rigid molecules. Why are interactions more pronounced in **1** than in **3**? The explanation can be sought in the 'all-*trans*' effect[10] which favours interactions in molecules with a greater number of *trans* C═C configurations (**1**). The through space (TS) and TB interactions are competitive and often occur simultaneously in a particular molecule.[10] They can, however, be distinguished on the basis of their spatial range; TB interactions can have long ranges whereas TS interactions rely on direct overlap and are often short range.[10] In the polypodanes, TS interactions are unlikely owing to the molecular structure, which has spatially well separated double bonds.

The presence of a keto group in **2** and **4** significantly modifies the appearance of the π-manifold. Compound **4** now has observable splitting whereas **2** does not. The n_O orbital energy is lower (more negative) than the π-manifold which (in the simple perturbation theory picture) leads to selective destabilization of π-orbitals. The extent of destabilization will depend on the proximity (on the energy scale) of n_O to each π orbital. The destabilisation is reflected in the changes of π band contours: the band which is split in **1** ceases to be so in **2**, while the compact band in **3** exhibits a small splitting (at 8.45 eV) in **4**.

The possibility that the measured spectrum refers to the superposition of conformer spectra should also be considered. The presence of a conformer mixture would be significant only if conformers have noticeably different electronic structures. One can calculate MO levels for each conformer and compare the levels with band shapes. However, in view of the unreliability of the AM1 method in predicting closely spaced orbital ionizations, we instead performed a conformational space search in order to establish what would be the population of higher energy conformers (assuming a Boltzmann distribution). The population of higher energy conformers at the temperature of the experiment turned out to be less than 17% (for **1** and **4**) and thus cannot influence band shapes appreciably. The partially resolved features in the lowest *IE* bands of **1** and **4** can hence be attributed to orbital interactions rather than to the superposition of conformer spectra.

Finally, it is interesting to compare the spectra of the polyenes **1–4** with that of all-*cis*-1,4,7,10-cyclododecatetraene.[11] The dodecatetraene (which also contains four unconjugated π-bonds) can serve as a reference for the analysis of various intramolecular interactions. The first interesting observation is that π ionization energies are higher in dodecatetraene (8.9 and 9.3 eV) than in the polypodanes, in spite of the presence of formally electron-withdrawing hydroxyl or keto groups in the latter. This is to be expected because of the larger density of σ-orbitals in the polypodanes and subsequent strong TB interactions between π- and σ-orbitals. The second notable observation concerns splitting of π bands. In dodecatetraene the splitting is approximately 0.4 eV, which is similar to **4** but smaller than in **1**. The change in π bond splitting on going from **3** to **4** and from **1** to **2** has already been rationalized by the of the keto groups. Similarity of π bond splitting is an indication that TB interactions have similar effectiveness.

CONCLUSION

We have demonstrated two important points, first that natural products often have interesting electronic structures which can be studied by the UPS/MO method and second that TB interactions can be observed in non-rigid polyene compounds. Both conclusions should encourage further studies of such compounds. An example intended to give a clearer picture of TB interactions is shown in Fig. 2, which displays the HOMO electron density of **1**. The orbital has most of its electron density localized along the side-chain. One can see three double bond (π-orbital) moieties which are linked via 'bridges' composed of σ-electron densities. The MO densities in other compounds exhibit very similar types of interactions.

Acknowledgements

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REFERENCES

1. A. Robert and B. Meunier, *Chem. Soc. Rev.* **27**, 273–279 (1998).
2. I. Novak and B. Kovač, *J. Electron Spectrosc. Relat. Phenom.* **70**, 259–261 (1995).
3. G. J. Bennett, L. J. Harrison, G.-L. Sia and K.-Y. Sim, *Phytochemistry* **32**, 1245–1251 (1993).
4. L. H. D. Nguyen and L. J. Harrison, *Phytochemistry* **50**, 471–476 (1999).
5. I. Novak and A. W. Potts, *Tetrahedron* **53**, 14713–14718 (1997).
6. D. W. Turner, A. D. Baker, C. Baker and C. R. Brundle, *Molecular Photoelectron Spectroscopy*. Wiley, New York (1970).
7. *HyperChem 5*. Hypercube, Gainesville, FL (1997).
8. *PC Spartan Pro.* Wavefunction, Irvine, CA (1999).
9. T. Bally and E. Heilbronner, in *The Chemistry of Dienes and Polyenes*, edited by Z. Rappoport, **Vol. 1**, pp. 173–261. Wiley, Chichester (1997).
10. M. Eckert-Maksic, in *Molecular Spectroscopy, Electronic Structure and Intramolecular Interactions*, edited by Z. B. Maksic, pp. 153–198. Springer, Berlin (1991).
11. A. Krause, H. Musso, W. Boland, R. Ahlrichs, R. Gleiter, R. Boese and M. Bär, *Angew. Chem., Int. Ed. Engl.* **28**, 1379–1380 (1989).