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Electronic Structure of Terpenoids

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Introduction

Terpenoids with the general formula $C_{15}H_{24}$ and their oxy derivatives are an interesting class of natural products, which occur in many plant species. The structural formulas of the compounds studied are shown in Figures 1−3. Most of them are used as fragrance ingredients, while some (e.g., **9**) are plant growth regulators. The current knowledge of the mechanism of olfaction and the structure of odorant receptors is limited, and the olfactophore models had been proposed as heuristic aids in computer design of new fragrances.[1] Besides relevance for the mechanism of olfaction, the electronic structure of terpenoids makes an interesting case study of substituent effects. The reports of nonbonding interactions between several functional groups within the molecule, obtained by UV photoelectron spectroscopy (UPS), have been reviewed previously at considerable length.[2,3] Here we are interested in the single functional group and how its (de)stabilization can be used as an indicator of substituent effects within the isomeric series.

UV photoelectron spectroscopy (UPS) combined with MO calculations was shown to be a good method for studying the electronic structure of natural products.[4]

Experimental Section

The sample compounds 4-aromadendrene (**1**), 5,11-guaiadiene (**2**), 10(14)-aromadendrene (**3**), β-cedrene (**4**), α-cedrene (**5**), β-caryophyllene (**6**), epoxycaryophyllene (**7**), alloisolongifolene (**8**), longifolene (**9**), α-humulene (**10**), and germacrone (**11**) were obtained from Fluka AG, and their identity was checked by melting point determination. He I photoelectron spectra were recorded on a Vacuum Generators UV-G3 spectrometer (at "R.Boskovic" Institute) and calibrated with small amounts of Xe gas which was added to the sample flow. The spectral resolution was 25 meV when measured as fwhm of $^2P_{3/2}$ Ar^+ line. For compounds **1**−**11** elevated sample temperatures of 30, 200, 170, 150−160, 160−180, 185, 40−60, 160, 170, 180, and 180 °C, respectively, were required in order to achieve sufficient vapor pressures in the sample flows. UV spectra were recorded in hexane on a Philips PU 8730 UV/VIS spectrometer.

The molecular mechanics (MM) and quantum mechanical (QM) HF/6-31G* MO calculations were performed with the Titan set of programs.[5] The QM/MM approach consisted of an initial MM conformational search in order to identify the most stable conformer, followed by subsequent full geometry optimization at the ab initio level. Some of the compounds (e.g., **6**) are known to populate several conformer forms at room temperature.[6] To establish how such conformer distribution may affect the appearance of spectra, we used the QM/MM method to calculate orbital energies for various conformers of each compound. The variations were <0.1 eV, which suggests that although the recorded spectra may in some cases correspond to a superposition of conformer spectra (and lead to band broadening), the deductions about the electronic structure are still valid since the accuracy of ionization energy measurements was ±0.05 eV. The atom numbering and stereochemical representations of the title compounds as depicted in Figures 1−3 were taken from the standard reference source.[7]

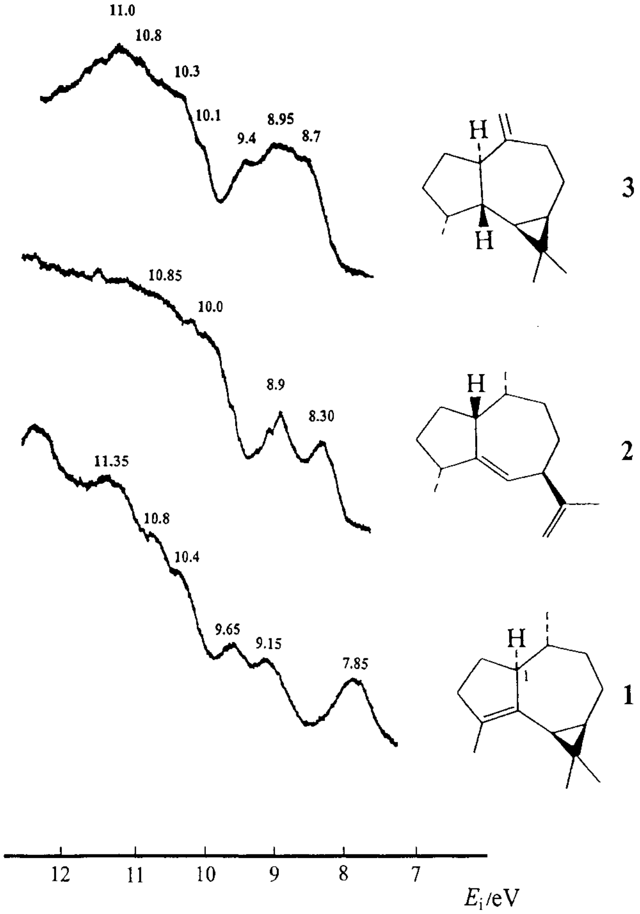

Figure 1. He I photoelectron spectra of terpenoids **1**−**3**.

Results and Discussion

The He I photoelectron spectra of **1**−**11** are shown in Figures 1−3. The assignments shown in Table 1 are based on comparison with the spectra of related alkenes and cycloalkenes[8,9] and ab initio HF-SCF-MO calculations via Koopmans approximation. The comparison indicates that the lowest energy bands, which are usually well separated from the rest, originate from the ionization of

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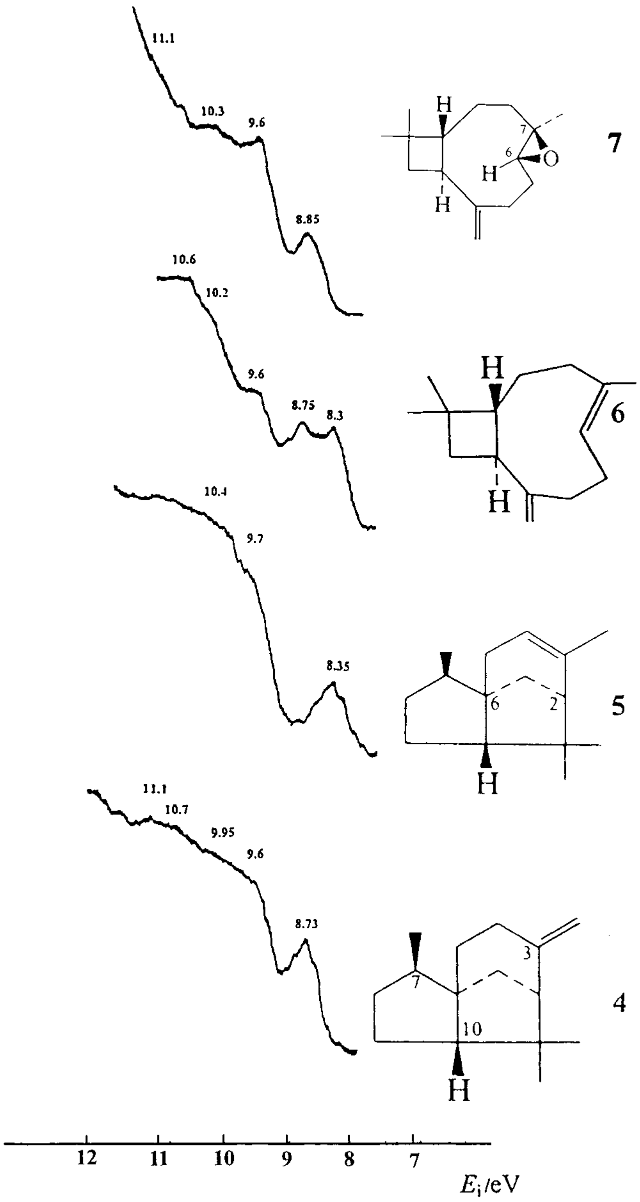

Figure 2. He I photoelectron spectra of terpenoids **4**−**7**.

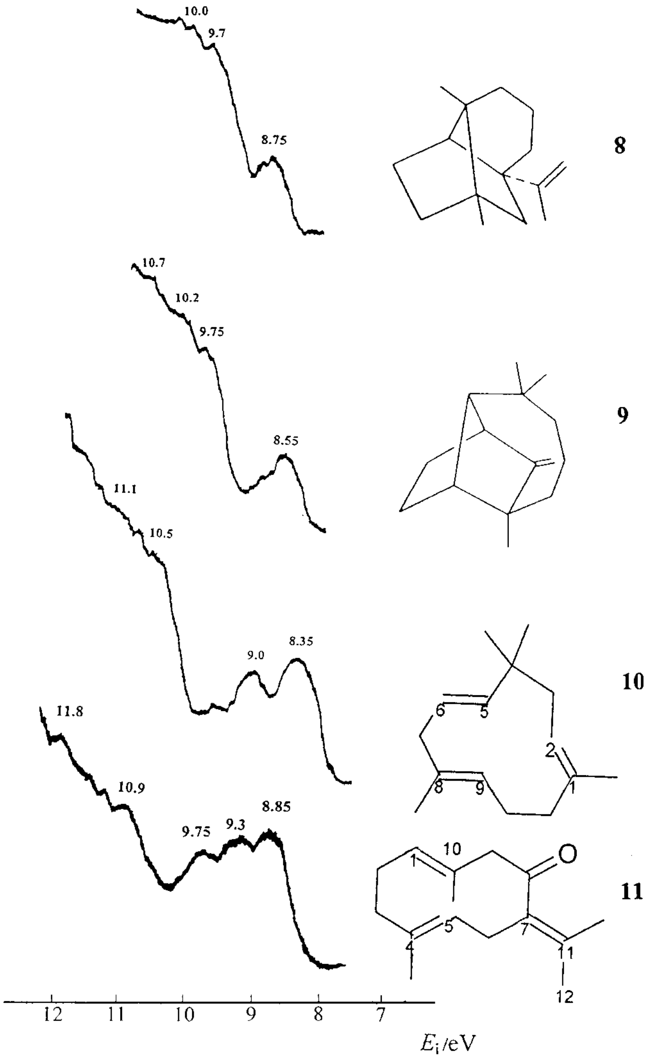

Figure 3. He I photoelectron spectra of terpenoids **8**−**11**.

π-orbitals. In the spectra of **7** and **11**, in addition, the oxygen lone pair bands are expected to appear. However, the oxygen lone pair of epoxide ring has an ionization energy >10 eV,[8] and the relevant band is expected to occur within the dense σ-manifold. The UPS/UV assignments are summarized in Table 1. In all the molecules, the LUMO can be described as an out-of -phase counterpart of HOMO, which is localized primarily along a particular double bond. The assignments of UV spectra, based on measured molar absorption coefficients showed that the transitions were of π-π* type. We have used vertical ionization energies to estimate the HOMO energy, and the energies of strong UV transitions to estimate the HOMO−LUMO energy gap. Such orbital energies are listed in Table 1. UV transition energies vary little among different compounds, which is an indication that both HOMO and LUMO are similarly affected by substituent effects.

Compounds with a Single C=C Bond. In the spectra of **1**, **3**, **4**, **5**, **7**, **8**, and **9**, the lowest energy band can be assigned to π-ionization. All the compounds are isomers with the same number of valence electrons and the same number of particular bond types. The observed π-ionization energy shifts can be attributed to variations in the number of alkyl substituents on each C=C bond. The study of methyl-substituted ethenes[8] revealed that π-ionization energy is reduced upon increasing the degree of methylation of the double bond. *Exo* C=C bonds have lower degree of alkylation than *endo* C=C bonds, and thus the inductive destabilization of π-orbital energies is greater in the latter. The inductive destabilization seems to be the strongest in **1** (where the first ionization energy is the lowest of all $C_{15}H_{24}$ isomers) and weakest in **4** and **8**. The π-orbital energy in **7** is even lower, but this can be due to the presence of oxygen atom. The unusually low value of π-ionization energy in **1** can then be attributed mainly to the presence of four alkyl substituents at the double bond. However, additional lowering of π-ionization energy may be due to hyperconjugation of C=C group with the σ-orbitals of cyclopropane ring. Further evidence in support of the alkylation as the source of π-orbital destabilization can be found in the

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Table 1. Vertical Ionization Energies (E_i), HF-SCF-MO Energies (ϵ), Assignments, UV Absorption Maxima (λ, ϵ), and HOMO−LUMO Gap (ΔE) for 1−11[a]

compd	$E_i \approx -\epsilon_{HOMO}$/eV	ϵ/eV	assignment	λ/nm; ϵ/cm^{-1} mol^{-1} dm^3; (ΔE/eV)
1	7.85	−8.37	π_{en}	211; 7530; (5.89)
2	8.30	−8.77	π_{en}	210; 4950; (5.90)
	8.90	−9.38	π_{ex}	249; 730; ($S_0 \rightarrow T_1$ transition?)
3	8.7	−9.09	π_{ex}	207; 2310; (5.99)
4	8.73	−9.14	π_{ex}	207; 2080; (5.99)
5	8.35	−9.28	π_{en}	209; 2460; (5.96)
6	8.3	−8.86	π_{en}	210; 7670; (5.90)
	8.75	−9.09	π_{ex}	
7	8.85	−9.27	π_{ex}	210; 3970; (5.92)
8	8.75	−9.17	π_{ex}	208; 1480; (5.98)
9	8.55	−9.05	π_{ex}	210; 3880; (5.92)
10	8.35	−8.55	π_{8-9}	210; 6100; (5.91)
	8.35	−8.74	π_{1-2}	
	9.0	−9.53	π_{5-6}	
11	8.85	−8.70	π_{4-5}	213;[b] 12570; (5.85)
	(8.85)[d]	−9.14	π_{1-10}	
	9.3	−9.46	π_{7-11}	
	9.75	−10.95	n_o	237;[c] 3190

[a] Subscripts *en* and *ex* refer to *endo* and *exo* C═C bonds, respectively. [b,c] Bands were assigned to $\pi-\pi^*$ transitions within diene[a] and unsaturated carbonyl[b] chromophores, respectively, on the basis of comparison with the standard spectra.[13] [d] Band at 8.85 eV appears to contain two unresolved ionizations.

spectrum of **10**. The π-orbital (π_{5-6}) has higher ionization energy than π_{1-2} or π_{8-9}. This is because the *endo* $(C{=}C)_{5-6}$ bond has only two alkyl substituents compared with three substituents in each one of *endo* $(C{=}C)_{1-2}$ and $(C{=}C)_{8-9}$ bonds.

The observation that compounds containing a single *exocyclic* C═C bond have higher π-ionization energy than those with a single *endocyclic* bond was made by Asmus and Klessinger.[10] However, they did not compare spectra of isomers and they observed only small (<0.05 eV) *endo*−*exo* differences in five- and six-member rings.

The π- and σ-bands in the spectrum of **3** show considerable overlap so an additional evidence (besides MO result), is desirable in order to confirm the HOMO assignment. The comparison of **3** with UPS of *cis*-7,7-dimethylbicyclo[4.1.0]hept-3-ene[9] suggests that in **3** the HOMO ionization is of π- rather than σ-type.

Compound **9** has lower π-ionization energy than **8** although both C═C bonds contain the same number of alkyl substituents. The difference can be attributed to the smaller CCC bond angle at the *exo*-bond in **9**.

Compounds with Two C═C Bonds. In the spectra of **2** and **6** two double bonds exist, and they can be expected to give rise to two π-ionization bands as was in fact observed. The nature of the π-ionizations, i.e., whether they are related to the *endo* or *exo* C═C group, can be deduced from calculations and empirical arguments. The calculated energy differences between the two types of MO are <0.5 eV (Table 1) and hence can be deemed unreliable. A comparison with the spectra of related compounds leads to a more reliable assignment. The spectrum of **2** is compared with **1** and **3**. Since **1** has only the *endo* C═C group and **3** only the *exo* C═C group, the comparison unambiguously attributes the 8.30 eV band in **2** to MO localized on *endo* and the 8.9 eV band to MO localized on the *exo* C═C group. Analogously, the spectrum of **6** can be compared with its epoxide derivative **7** where the *endo* C═C group had been lost thorough oxidation. The comparison suggests that in **6**, the 8.3 eV band belongs to π-ionization of the *endo* and 8.75 eV band to π-ionization of the *exo* C═C group. This is consistent with both the MO calculations (Table 1) and the previous deduction that *endo* π-ionizations have lower ionization energies.

Compounds with More than Two C═C Bonds. Compounds **10** and **11** contain several functional groups and the assignment must attribute specific bands to specific π-ionizations for each functional group. MO calculations (Table 1) suggest possible energy level patterns, but the closeness of orbital eigenvalues makes an independent confirmation of assignment desirable. In the spectrum of **10**, the 8.35 eV band has twice the intensity of 9.0 eV band. We can compare the spectrum of **10** with *all-trans*-1,5,9-cyclododecatriene.[11] The π-ionizations bands in the latter are quasi-degenerate corresponding to a single band at 8.89 eV. In **10**, two of the double bonds are methylated, which lowers their ionization energies. The energy lowering occurs due to hyperconjugative stabilization of the ionic state in which electron had been ejected from an orbital localized on methylated C═C group. This accounts for 2:1 intensity ratio and allows the assignment of 8.35 eV band to π-ionizations from 1−2 and 8−9 double bonds. Thus, the 9.0 eV band belongs to ionization of π-orbital localized along 5−6 double bond.

The assignment of **11** is more difficult due to the presence of carbonyl group which is conjugated to the *exocyclic* C═C bond. For assignment purposes, one may consider the molecule as comprising two moieties (chromophores): the diene moiety containing two nonconjugated *endocyclic* C═C bonds and the α,β-unsaturated ketone. The diene and ketone moieties are nonconjugated and thus interact only weakly. Diene fragment can be compared with 1,5-cyclooctadiene[11] where quasi-degenerate π-ionizations were observed at 8.7 and 9.0 eV. The ketone fragment can be related to 2-cyclooctenone where it was established that the ionization energies of the oxygen lone pair and the π_{CC} orbital are 9.18 and 9.80 eV, respectively.[12] The bands at 8.85, 9.3, and 9.75 eV can then be assigned to the total of four ionizations: [π_{4-5}, π_{1-10}], π_{7-11}, and n_O (Table 1). However, in view of the unreliability of Koopmans approximation when bands are 0.5 eV apart, the proposed ordering of ionizations is tentative.

Our final comment is concerned with the comparison of UV band intensities (Table 1) between pairs of isomers: {**1**,**3**}, {**4**,**5**}, {**8**,**9**}, and {**2**,**6**}. We suggest that a tentative explanation for different intensities may be sought in the relative rigidity of ring systems. In **4** and **5**, the ring systems are rigid which implies that geometries of ground and excited states will be similar and hence (according to Franck−Condon principle) the π-π^* transition intensities will be of comparable magnitude.[13] In **1**, the C═C group is in a more rigid ring environment than **3**. This implies that the UV transition in the former should be more intense than in the latter as was indeed

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observed (Table 1). Similar arguments can then be extended to isomeric pairs {**8**,**9**} and {**2**,**6**}.

Conclusion

UPS has provided direct estimates of substituent effects in several isomeric terpenoids. This was possible due to the analysis of isovalent isomers (same number of bond types) which makes such estimates more reliable than those obtained via the homologous series of nonisomeric compounds. Terpenoids are a very diverse family of molecules, both in terms of molecular structure and reaction pathways/mechanisms, which they participate in. The details of their electronic structure, revealed in this work, may be useful in the understanding of their properties. One such property concerns their interactions with olfactory receptors (see Introduction). While olfactophore models are mainly concerned with the stereochemistry of odorants, we have obtained information about their electronic structure, which may shed light on the binding between odorant and its receptor. The binding is likely to occur via weak charge-transfer (CT) or van der Waals type interactions between the terpenoid molecule and flat, hydrophobic part of the olfactory receptor.[14] Of course the higher the π-energy, the stronger the binding can be expected. Such predictions are possible, because the only functional groups present in the terpenoids are C═C groups. The inclusion of compounds **7** and **11** (even though they are not isomers of the rest) was prompted exactly because of their importance in flavor and odorant chemistry.

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