Photoelectron spectra, electronic structure and long-range electronic interaction in some steroids

T. Cvitaš, B. Kovač, Lj. Paša-Tolić, B. Ruščić, and L. Klasinc
The Ruđer Bošković Institute, University of Zagreb, YU-41001 Zagreb, Yugoslavia
J.V. Knop
Rechenzentrum der Universität Düsseldorf, Düsseldorf, FR Germany
*N.S. Bhacca and S.P. McGlynn*
Department of Chemistry, Louisiana State University, Baton Rouge, La. 70803, USA

ABSTRACT - Alicyclic molecular frameworks are useful for the study of electronic through-bond (TB) and through space (TS) interactions of functional groups over fixed distances and/or a specified number of C-C bonds. Steroids, being readily available, stable and stereochemically well-defined, are especially suited for such investigations. Indeed, their use in the study of the stereochemical aspects and the long-range effects of groups situated at specified distances from chemically reactive centers has been well documented over the last 20 years. Since steroids are compounds of considerable biological importance, their activity being dramatically dependent on construction, conformation and electronic structure, it is surprising that our knowledge of their electronic structure, whether by quantum chemistry or photoelectron (PE) spectroscopy, is so sparse. Having recorded the first PE spectra of steroids (refs. 1,2) we believe that such studies may resolve many problems concerning long-range intramolecular interaction since (i) PE spectroscopy is a gas phase method and its results pertain to the free molecule and (ii) steroids by virtue of their fixed geometry are unable to form intramolecular (head-to-tail) adducts in which both TB and TS effects might separately propagate. Indeed, one should expect the presence of TB interactions only. We report the PE spectra of several androstane derivatives and derive their electronic structure using empirical arguments and of quantum chemical, MNDO calculations. Emphasis is placed on the long range effects of a carbonyl group located at the biologically important 3-, 11- and 17- positions and the enhancement of these effects by interpolated, localized double bonds.The position and fine structure of the lowest energy PE bands and the shift of the σ-onsets are the gauges used to estimate these effects. These long range effects seem to exert considerable influence on conformation, activity and, particularly , on fast intramolecular electron transfer (ET) such as has been observed recently in steroid solutions.

INTRODUCTION

Steroids are fascinating compounds, their biological activity being the most outstanding characteristic. They are classified as hormones, substances produced at one site in the organism but acting at another, different site. Unlike other hormones, which usually affect the cell membrane by an interaction with cyclic-AMP and , thereby, increase the supply of energy to the cell, the steroids, in some of their actions at least, bind to proteins, pass through the membrane and initiate an RNA synthesis which may substantially change the biological processes at both the cellular and organismal levels. Unfortunatelly, despite much ignorance about their actions, steroids are widely used, and misused, because many desirable effects are manifested rapidly whereas the deleterious side effects may remain latent for considerable periods.

The biological activity of steroids (refs. 3-5) is so varied that one must be surprised that such diversity is achieved by a relatively simple basic molecular structure which , by a negligible change of composition and/or conformation, yields dramatic changes of intensity and modes of action. Thus, the female and male hormones, progesterone and testosterone, differ in only one functional group (i.e. , OH vs. acetyl, respectively) in the 17-position. This basic skeleton,
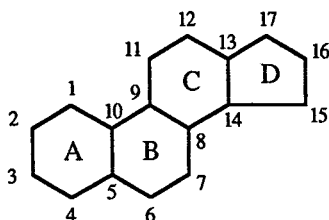
which is a perhydrogenated cyclopentanophenanthrene (also known as "sterane " or "gonane"), can be supposed to consist of two saturated bicyclic hydrocarbons
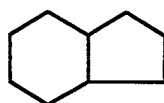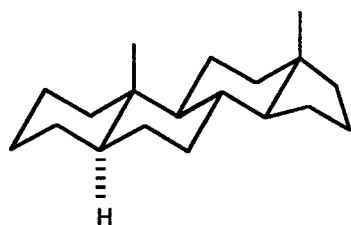
and   hydrindane
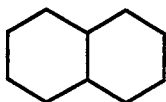
decaline

the derivatives of each of which also exhibit biological activity. Once fused into the basic steroid structure , only two possible conformations are feasible, namely

5α-androstane   5β-androstane

A "5α–steroid" contains a trans- fused A/B junction, while a "5β–steroid" contains a cis-fused junction. The designations α and β are commonly used in ring system nomenclature, particularly in steroids and sugars, to indicate substituents that lie below and above the ring, respectively. The biologically-important substitution positions are 3- and 17- , and sometimes 11-. The orientation and position of the groups attached to the steroid ring system are important indicators of biological activity. For example, a ketone at C3, when associated with a double bond at C4, is an important structural feature of the biologically active corticosteroids. Reduction of the ketone at C3 leads to the formation of two isomers: one, 3β-hydroxy; the other, 3α-hydroxy. Saturation of the double bond also leads to the formation of two isomers: 5α and 5β. In formal chemical nomenclature, the adrenocortical hormones are described as derivatives of androstane or of pregnane.

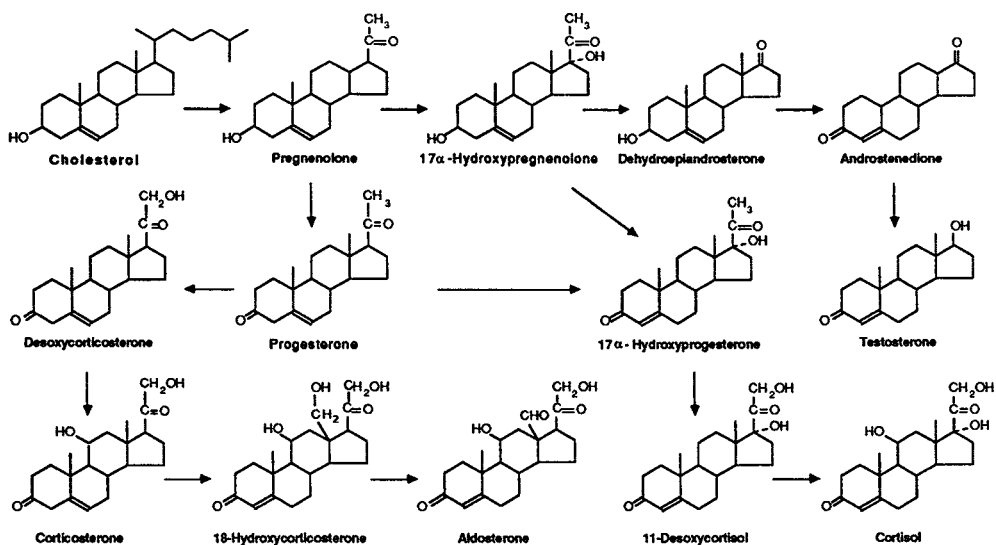The human sexual hormones and the pathways for their biotransformation are shown in Fig 1.

Figure 1.   The human sexual hormones and the pathways for their biotransformation

Biological activity is a consequence of the geometrical (i.e.,composition, configuration , conformation) and electronic (i.e.,energy, electron distribution: static-"charge" and dynamic-"reactivity") structure of a molecule. Very little information about the electronic structure of steroids is available, perhaps because the quantum chemist is somewhat inhibited by the size of these molecules or by a dearth of experience with them. Indeed, most chemical research on

steroids has been concerned with synthesis, analysis and transformations, and most chemists assumed that the basic steroid skeleton was merely an inert framework for functional groups which could be used advantagously to study cooperative substituent effects at distances fixed by that framework (i.e., chemical properties such as nmr shifts, fragmentation patterns following electron bombardment, reaction mechanisms , etc). However, recent investigations of steroids and other saturated polycyclic hydrocarbons question the assumed inertness of the framework. For example, it has been shown that the interaction of substituents separated by as many as ten bonds is quite feasible. Indeed, such findings suggest that organic superconductivity might even occur in these compounds, leading to the supposition that "ribbon-like" MO's once constituted from C2p-orbitals aligned along the molecular axes, might produce electron transmitting properties. Certainly, such orbitals appear to be the HOMO's of many large polycyclics.

The most convincing experiments concern electron transfer (ET) between a donor D and an acceptor A separated by a spacer S. The spacer S may well be the steroidal framework (ref. 6). The ET can take place either as <u>charge separation</u> in an excited molecule

$$D^* - S - A \rightarrow D^+ - S - A^-$$
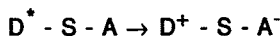
or as a <u>charge shift</u> from one end to the other

$$D^- - S - A \rightarrow D - S - A^-$$
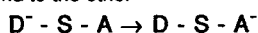
Both of these events require time and may be treated by i) 1<u>st</u> order reactions kinetics with a rate coefficient: $k \approx \exp(-E_a/k_B T)$; or ii) the reaction may be viewed as a radiationless transition with a rate coefficient given by: $k \approx |V|^2 FCWD$, where the resonance integral V in the region in which the final (b) and initial (a) states intersect is: $V \approx <a|H|b>$ and FCWD is a Franck-Condon weighted density of states; or iii) one may use the Marcus theory (refs. 7,8): $G^\dagger = (\Delta G^\circ + \lambda_s)^2/4\lambda_s)$ and $k \approx \exp[-(\Delta G^\circ + \lambda_s)^2/4\lambda_s k_B T]$, where λ_s is the free energy for solvent reorganization. Combination then yields:

$$k \approx (\lambda_s k_B T)^{-1/2} |V|^2 \exp(-G^\dagger/k_B T)$$

It is predicted that the rate will rise until such time as $\lambda_s = -\Delta G^\circ$, whereupon it will decrease and, in the process, exhibit an inverted region (refs. 7,8). This occurence has been documented for a number of acceptors in the 3-position of androstane, the 16-biphenylyl group acting as the donor (ref. 6). Several other workers have detected fast ET processes in other model systems (ref. 9). The mechanism may be supposed to be either an electron transfer from the HOMO of D through the LUMO of S to A or a hole transfer involving the intermediacy of the HOMO of S . Thus, assuming the validity of Koopmans' theorem (KT), PE spectra could provide important information, as also could quantum chemical calculations. Indeed, given the validity of KT , the two approaches are complementary , and one could be used to verify the other.

However, quantum chemical calculations for molecules as large as the steroids are scarce and their predictive power is questionable. With this in mind, we have tried to interpret the PE spectra in a correlative format that starts with molecules and molecular building blocks whose electronic structure and behavior to substitution is known (see, e.g., the composite molecule method; ref. 10). A combination of these three approaches, namely PE spectra, quantum chemical computations and correlative studies, should provide a reliable picture of the electronic structure of the steroids and the susceptibility of this electronic structure to substitution and conformational changes . As the MO method of choice, we have used the semiempirical MNDO method with geometry optimization, since it represents the limit of a computing effort which can be invested in the problem. (Quantum chemical calculations for such large molecules require enormous computer time and are subject to severe convergence problems).

EXPERIMENTAL

The Hel PE spectra of 5α−androstane (1), 5α−androstan-3-one (2), 5α−androstan-17-one (3), 5α−androstane-3,17-dione (4), 5α−androstane-3,11,17-trione (5), androst-5-en-17-one (6), androst-5-ene-3,17-dione (7), androst-4-ene-3,17-dione (8) and androsta-1,4-diene-3,17-dione (9) were recorded on a Vacuum Generators UV-G3 spectrometer (ref. 11) at 80, 130, 140, 170, 180, 160, 180, 180 and 180 °C, respectively.The energy scale was calibrated by admitting Mel and/or Ar and Xe to the sample flow. Some spectra also contained residual amounts of nitrogen.

All compounds were of commercial origin (Sigma Chemical Company), and of high purity. They were used without further purification.

CALCULATIONS

MNDO SCF MO were performed using the QCPE 464 (IBM MOPAC) program (ref. 12) adapted for the Siemens 7.580 S (turbo version) at the Computing Center of the University of Düsseldorf.

Full geometry optimization was obtained for 5α−androstane-3,11,17-trione and for all unsaturated ketones. Single geometry calculations were performed for all other compounds. The starting geometry in all cases was assumed to consist of standard bond lengths and angles (r_{CC}=154 pm, r_{CH}=108 pm, r_{CO}=122.5 pm; <CCC=109.5°, and 120.0°, <CCH=109.5°, <COC=120.0°), and crystalographic dihedral angles (ref. 13). The atomic coordinates, optimum geometries, obtained for 1 and for the carbon and oxygen atoms of 5 and 8 are given in Table 1. The net atomic charges and dipole moments are also given in Table 1 for these same molecules.

Table 1. Atomic coordinates (in Å) and dipole moments (μ/D) for 5α-androstane (1), 5α-androstane-3,11,17-trione (5) and 5α-androst-4-ene-3,17-dione (8):

1	Atom	X	Y	Z	Charge
1	C	0.0000	0.0000	0.0000	0.0068
2	C	1.5426	0.0000	0.0000	-0.0127
3	C	2.1514	1.4100	0.0000	-0.0104
4	C	1.4916	2.3434	-1.0344	-0.0004
5	C	-0.0594	2.3165	-1.0059	-0.0287
6	C	-0.7197	3.3151	-1.9799	0.0004
7	C	-2.2417	3.3800	-1.7521	-0.0018
8	C	-2.9031	1.9907	-1.9119	-0.0168
9	C	-2.2280	0.9573	-0.9283	-0.0093
10	C	-0.6530	0.8484	-1.1456	-0.0551
11	C	-2.9921	-0.4007	-0.8452	-0.0016
12	C	-4.5421	-0.3299	-0.8275	0.0153
13	C	-5.1088	0.5951	-1.9401	-0.0896
14	C	-4.4398	2.0169	-1.7213	-0.0257
15	C	-5.3515	2.9836	-2.5147	0.0004
16	C	-6.7761	2.4224	-2.2875	-0.0212
17	C	-6.6335	0.9627	-1.7944	0.0047
18	C	-4.9071	-0.0619	-3.3333	0.0566
19	C	-0.3122	0.1962	-2.5918	0.0499
20	H	-0.3387	0.3903	0.9872	0.0026
21	H	1.9187	-0.5586	-0.8862	0.0045
22	H	2.0430	1.8636	1.0130	0.0053
23	H	1.8776	2.1011	-2.0483	0.0059
24	H	-0.3314	2.6714	0.0240	0.0094
25	H	-0.4957	3.0731	-3.0412	0.0097
26	H	-2.4608	3.8140	-0.7508	0.0088
27	H	-2.7308	1.6658	-2.9632	0.0152
28	H	-2.3775	1.3894	0.0984	0.0052
29	H	-2.6893	-1.0825	-1.6691	0.0047
30	H	-4.8785	0.0175	0.1758	0.0042
31	H	-4.6038	2.2922	-0.6440	0.0090
32	H	-5.1052	3.0220	-3.5951	0.0112
33	H	-7.3213	3.0316	-1.5346	0.0082
34	H	-7.2931	0.2807	-2.3698	0.0085
35	H	-5.2710	4.0261	-2.1435	0.0091
36	H	-7.3779	2.4763	-3.2187	0.0095
37	H	-6.9805	0.8814	-0.7422	0.0074
38	H	-0.3482	-1.0551	-0.0301	0.0068
39	H	1.9143	-0.5680	0.8832	0.0068
40	H	3.2428	1.3479	-0.2041	0.0079
41	H	1.8454	3.3817	-0.8339	0.0031
42	H	-0.2981	4.3341	-1.8182	0.0042
43	H	-2.6689	4.0964	-2.4905	0.0044
44	H	-2.7043	-0.9295	0.0953	0.0015
45	H	-4.9458	-1.3628	-0.9222	0.0051
46	H	-0.5231	-0.8936	-2.5156	0.0048
47	H	0.7559	0.2968	-2.7964	-0.0062
48	H	-0.8845	0.6298	-3.3625	-0.0050
49	H	-5.4155	-1.0479	-3.3766	-0.0076
50	H	-3.8475	-0.2619	-3.5849	-0.0063
51	H	-5.3183	0.5571	-4.1574	-0.0063
μ/D:		0.027	0.039	-0.050	tot. 0.069

5	Atom	X	Y	Z	Charge
1	C	0.0000	0.0000	0.0000	0.0007
2	C	1.5435	0.0000	0.0000	-0.0470
3	C	2.1087	1.4200	0.0000	0.2156
4	C	1.5085	2.3441	-1.0618	-0.0331
5	C	-0.0392	2.3141	-1.0275	-0.0318
6	C	-0.6786	3.3456	-1.9926	-0.0005
7	C	-2.1844	3.4543	-1.7097	-0.0047
8	C	-2.9132	2.0915	-1.8023	-0.0127
9	C	-2.2476	1.0306	-0.8433	-0.0347
10	C	-0.6837	0.8704	-1.1266	-0.0433
11	C	-3.1122	-0.2552	-0.7430	0.2186
12	C	-4.6514	-0.1235	-0.6333	-0.0086
13	C	-5.2163	0.8698	-1.6762	-0.1176
14	C	-4.4294	2.2215	-1.5035	-0.0313
15	C	-5.3145	3.2803	-2.2080	-0.0006
16	C	-6.7646	2.8442	-1.8918	-0.0521
17	C	-6.6787	1.3650	-1.4709	0.2328
18	C	-5.1723	0.2205	-3.0918	0.0505
19	C	-0.4235	0.1932	-2.5048	0.0427
20	O	2.9793	1.7858	0.7791	-0.2783
21	O	-7.6133	0.7022	-1.0557	-0.2659
22	O	-2.6371	-1.3822	-0.6833	-0.2836
μ/D:		-0.953	2.687	-2.668	tot. 3.905

8	Atom	X	Y	Z	Charge
1	C	0.0000	0.0000	0.0000	0.0051
2	C	1.5374	0.0000	0.0000	-0.0470
3	C	2.1199	1.4134	0.0000	0.2539
4	C	1.2992	2.4547	-0.6844	-0.1304
5	C	0.0405	2.2682	-1.1543	-0.0528
6	C	-0.6640	3.4201	-1.8453	0.0254
7	C	-2.1228	3.6128	-1.4058	-0.0008
8	C	-2.9372	2.2989	-1.4166	-0.0147
9	C	-2.2021	1.1729	-0.6003	-0.0103
10	C	-0.7026	0.9177	-1.0675	-0.0282
11	C	-3.0655	-0.1183	-0.4668	-0.0037
12	C	-4.5614	0.0785	-0.1232	0.0219
13	C	-5.2467	1.1638	-0.9936	-0.1178
14	C	-4.3742	2.4698	-0.8545	-0.0272
15	C	-5.3037	3.6253	-1.3060	-0.0014
16	C	-6.7143	3.2014	-0.8351	-0.0517
17	C	-6.6258	1.6995	-0.5070	0.2327
18	C	-5.4819	0.6321	-2.4370	0.0544
19	C	-0.6050	0.2331	-2.4651	0.0477
20	O	3.2018	1.6733	0.5166	-0.2856
21	O	-7.5004	1.0485	0.0382	-0.2711
μ/D:		-1.065	0.696	-2.453	tot. 2.764

RESULTS AND DISCUSSION

Here we report, assign and compare the HeI PE spectra of 1 - 5 (Fig. 2) as well as those of 6, 8 and 9 (Fig. 4). The expanded low-energy parts of the PE spectra for the three saturated ketones are given in Fig. 3, those for the four unsaturated ketones are given in Fig. 5. Both the full PE spectrum and the expanded low energy part of it for 7 are shown in Fig.6. The numbers atop the observed band maxima represent vertical ionization energies $E_{i,v}$ /eV.

Androstane is a 51 atom system with 108 valence electrons. Koopmans' theorem suggests that their HeI PE signals correspond to the ionizations from at least 25 different MO's. A similar conclusion pertains to the androstane derivatives. The questions now become: 1) What may one expect a PE spectrum of a saturated polycyclic hydrocarbon to look like? and 2) What should be the effect of replacing one (or several) of the CH_2-groups by carbonyl-group(s)?

In searching for answers to those two questions, we are forced to constrain attention to the characteristics of a very few of the lowest energy bands (i.e., to the effect of removal of the very outer valence electrons). Some clues, fortunately, may be obtained by inspection of the spectra of the cyclic hydrocarbons, cyclohexane and adamantane, and their ketones (ref. 14; Fig. 7). These spectra indicate that the lowest-energy σ-ionization, I(σ), of the hydrocarbon, which usually exhibits some fine structure, is shifted to higher energy and is "replaced" by a structured band system arising from the in-plane lone pair ionization, I(n_O), of the carbonyl oxygen. The shift of I(σ) to higher energy is greater than 1.2 eV for the C_6 and approximately 0.9 eV per carbonyl group for the C_{10} compounds, indicating that it could well be ~0.2-0.3 eV per carbonyl in a C_{19}-compound. The reason for the shift lies primarily in the greater electronegativity of oxygen compared to carbon as can be demonstrated using, as an example, the ionization events of ethene, methanimine and formaldehyde (ref.15; Fig. 8). Inspection of Fig. 8 indicates that the effect of nitrogen (-2eV) is just one half that of oxygen (-4eV) and that methyl substitution destabilizies I(σ) more than I(π_{CO}). Thus, one may assume that, in large cyclic ketones, the I(σ) band will lie next to I(n_O).
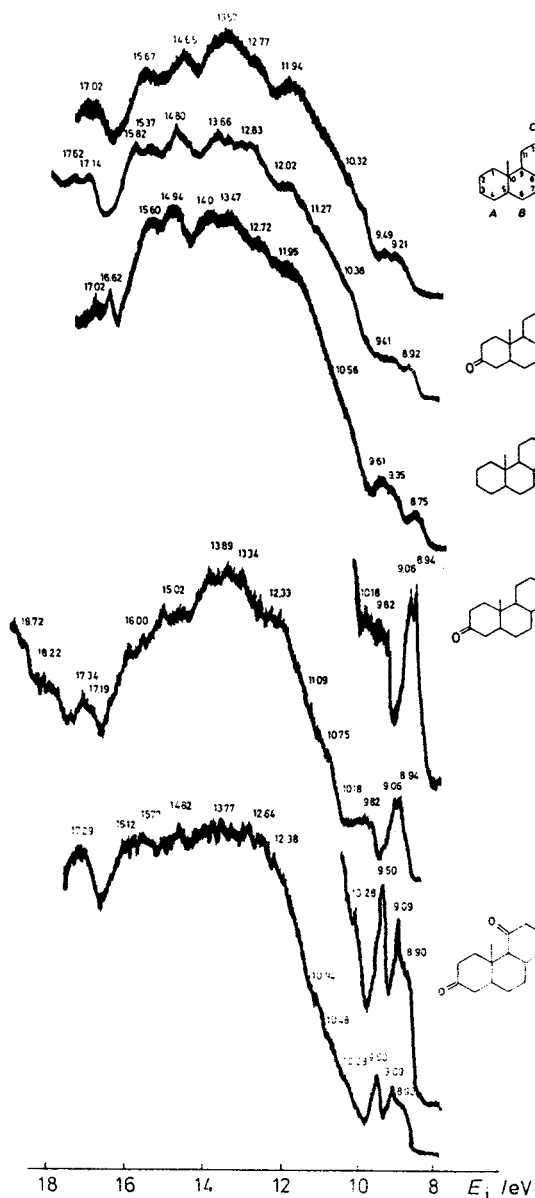
Fig. 2. Low resolution HeI PE spectra of 1 - 5
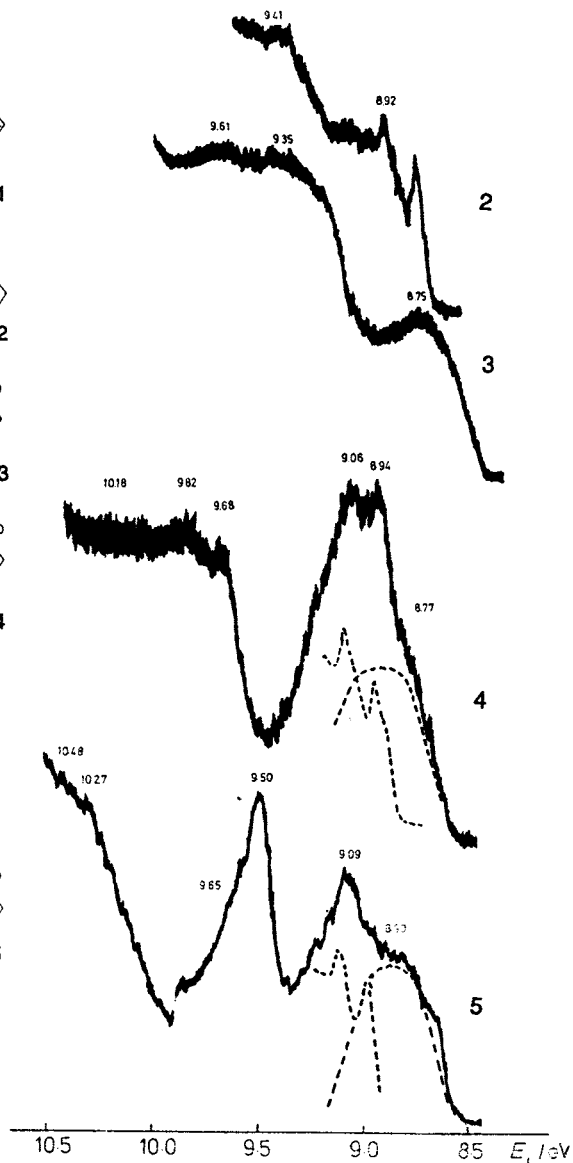(from top to bottom)

Fig. 3. High resolution HeI PE spectra of the low-energy
ionizations of 2 - 5 (from top to bottom)

We now discuss the consequences that arise from the presence of double bonds in the molecule. From the behavior of unsaturated cyclic ketones, it can be expected that the $I(\pi_{CC})$ event will lie next to $I(n_O)$, and that $I(\pi_{CC})$ will become of even lower energy if these double bonds are "aromatic" (ref. 16). None of the carbonyl compounds reported here contain any aromatic ring , and it is expected that the lowest energy ionization(s) in them should correspond to $I(n_O)$ events. However, so far little or no PE results have been available for such big unsaturated ketones.

Another question concerns the degree to which aliphatic and/or alicyclic substituents might lower $I(\pi_{CC})$, more than $I(n_O)$ in any of the monosubstituted compound. The lowest measured I_p for a noncyclic alkene is 8.04 eV (ref. 17) and 7.84 eV for a cyclic one (ref. 18). Octahydronaphthalene (ref. 19) has an I_p of 8.3 eV. Steroids with a single keto group have I_p's > 8.5eV. Thus, even if a "noninteracting" keto group increases the lowest ionization event in hydrocarbons by ~0.3 eV, this would still imply that, in very big unsaturated ketones, $I(\pi_{CC}) < I(n_O)$ or , at least, that both ionization events are of very similar energy.

The extent to which calculations confirm the above qualitative reasoning, and to which they provide additional information on MO symmetries and on the type and extent of interactions as a function of substitution site is of considerable interest. The canonical orbital energies, ε^{MNDO}/eV, for the ten highest occupied MO's of the steroids are given in Table 2. Consider, first, the saturated compounds. The energies, relative to experimental, are systematically off
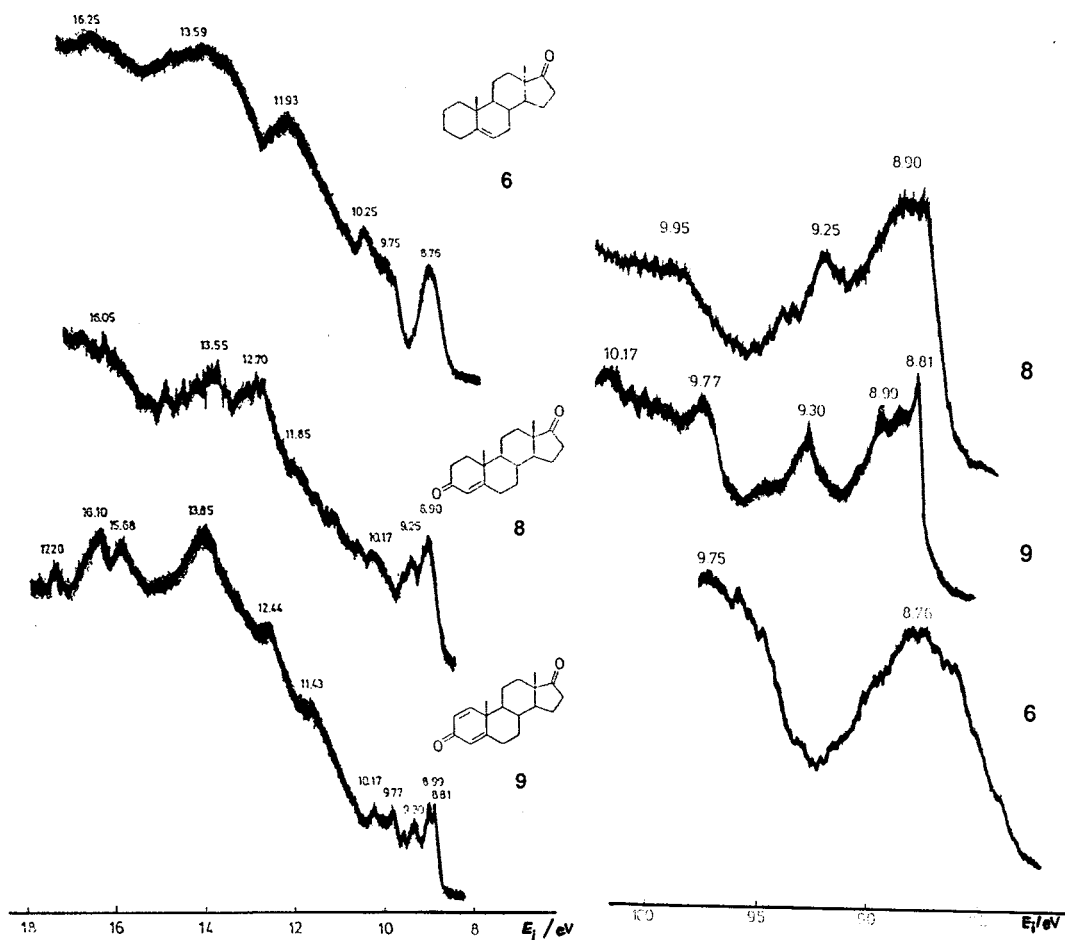
Fig. 4.   Low resolution HeI PE spectra of 6,8 and 9
(from top to bottom)

Fig. 5.   High resolution HeI PE spectra of the low-energy
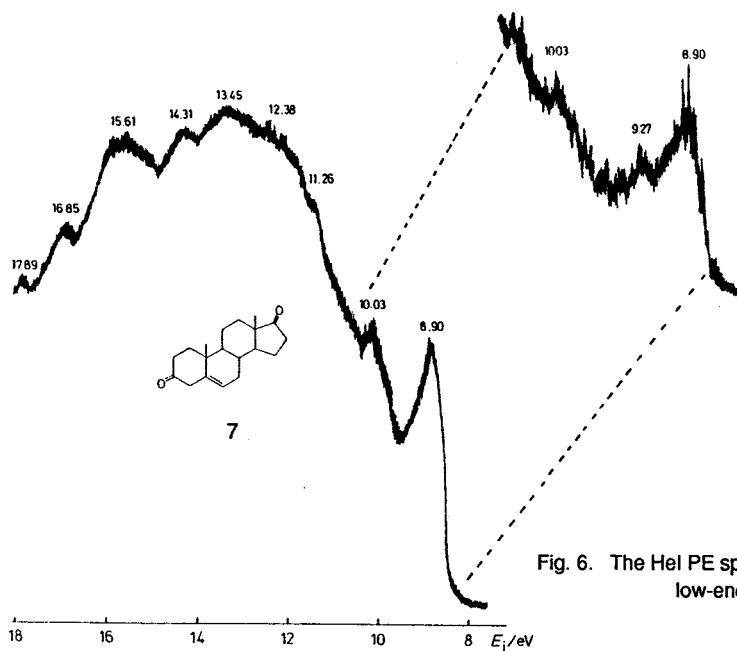ionizations of 8,9 and 6 (from top to bottom)

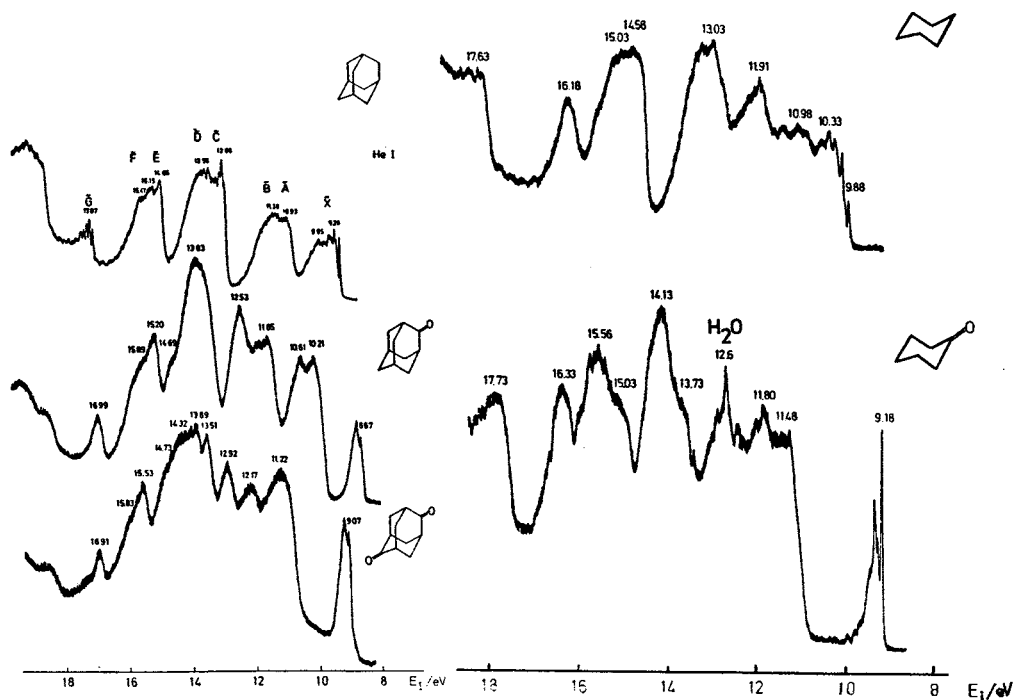Fig. 6.   The HeI PE spectra of 7 with the expanded
low-energy part (top)

Fig. 7. The HeI PE spectra of adamantane, adamantanone, 2,6-adamantandione, cyclohexane and cyclohexanone (from top to bottom and left to right)
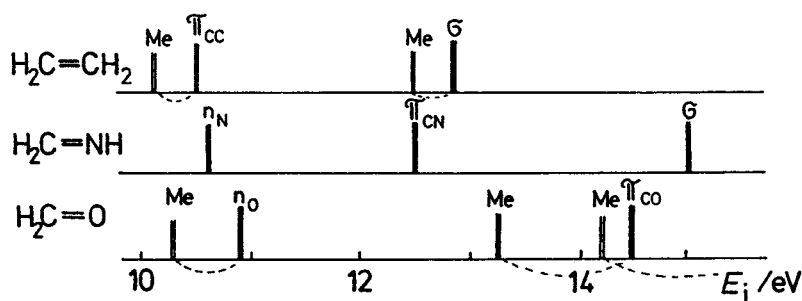

Fig. 8. Correlation of observed ionization energies I(π), I(n) and I(σ) in ethene, methanimine and formaldehyde and their shift on methyl substitution

by about -1.5-2 eV (Fig. 9). However, relative to the lowest energy events, there is both agreement and disagreement with the qualitative predictions. On the positive side, one finds :

- The two lowest I_p's of 1 are correctly predicted to be close in energy and well separated from ta cluster of events that follows at higher energy.
- The I(σ) shift for the ketones amounts to -0.2 to -0.3 eV per carbonyl group.
- The I(n_O) event for 3 is correctly predicted to be of lower energy than I(n_O) for 2.
- In saturated ketones, the lowest energy ionizations are always I(n_O).

On the negative side, one finds:

- All I(n_O) events are calculated to be of too low energy, as shown by the dotted line in Fig. 9.
- The location of I(π_{CO}) is calculated to be much too high in energy (~20th MO).
- PE spectra indicate that the introduction of a double bond (especially in the 5-position) produces a large increase of I(σ), a result that is contrary to calculation.

In sum, a comparison of the PE spectra of unsaturated and saturated derivatives leads one to conclude that the introduction of a double bond has but little effect on the value of $I(n_O)$. However, it is not possible to say which of $I(\pi_{CC})$ or $I(n_O)$ is the lower energy. Calculations always predict that $I(\pi_{CC}) < I(n_O)$. However, since examples are known (e.g., the quinonoids; ref. 20) for which the calculation is wrong, this last conclusion must be viewed with caution.

Table 2.   Canonical orbital energies, ε_i^{MNDO}/eV, for the ten highest occupied levels in 5α-androstane derivatives

ε^{MNDO}	1	2	3	4	5	6	7	8	9
HOMO	-10.975	-10.532 n_O	-10.367 n_O	-10.453 n_O	-10.474 n_O	-9.718π_{CC}	-9.804π_{CC}	-10.255π_{CC}	-10.216π_{CC}
2nd	-11.127	-11.191	-11.209	-10.601 n_O	-10.618 n_O	-10.382n_O	-10.204 n_O	-10.516 n_O	-10.506π_{CC}
3rd	-11.515	-11.447	-11.313	-11.511	-11.059 n_O	-11.346	-10.515 n_O	-10.610 n_O	-10.536 n_O
4th	-11.552	-11.698	-11.698	-11.721	-11.919	-11.428	-11.532	-11.648	-10.639 n_O
5th	-11.756	-11.908	-11.819	-11-906	-12.085	-11.799	-11.681	-11.882	-11.700
6th	-11.819	-12.034	-11.948	-12.188	-12.243	-11.946	-11.959	-12.119	-11.997
7th	-12.006	-12.060	-12.243	-12.233	-12.381	-12.176	-12.298	-12.384	-12.261
8th	-12.143	-12.196	-12.374	-12.429	-12.472	-12.289	-12.390	-12.417	-12.489
9th	-12.187	-12.346	-12.449	-12.718	-12.813	-12.455	-12.569	-12.679	-12.577
10th	-12.336	-12.470	-12.552	-12.787	-12.905	-12.699	-12.709	-12.764	-12.734

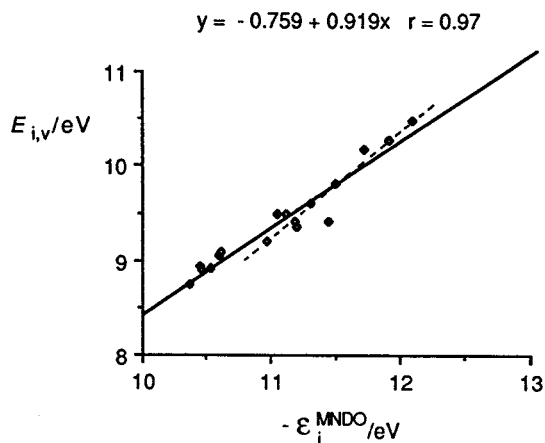$$y = -0.759 + 0.919x \quad r = 0.97$$

Fig. 9.   The correlation diagram of ionization potentials vs. calculated energies of 1 and saturated keto-steroids (2-5)
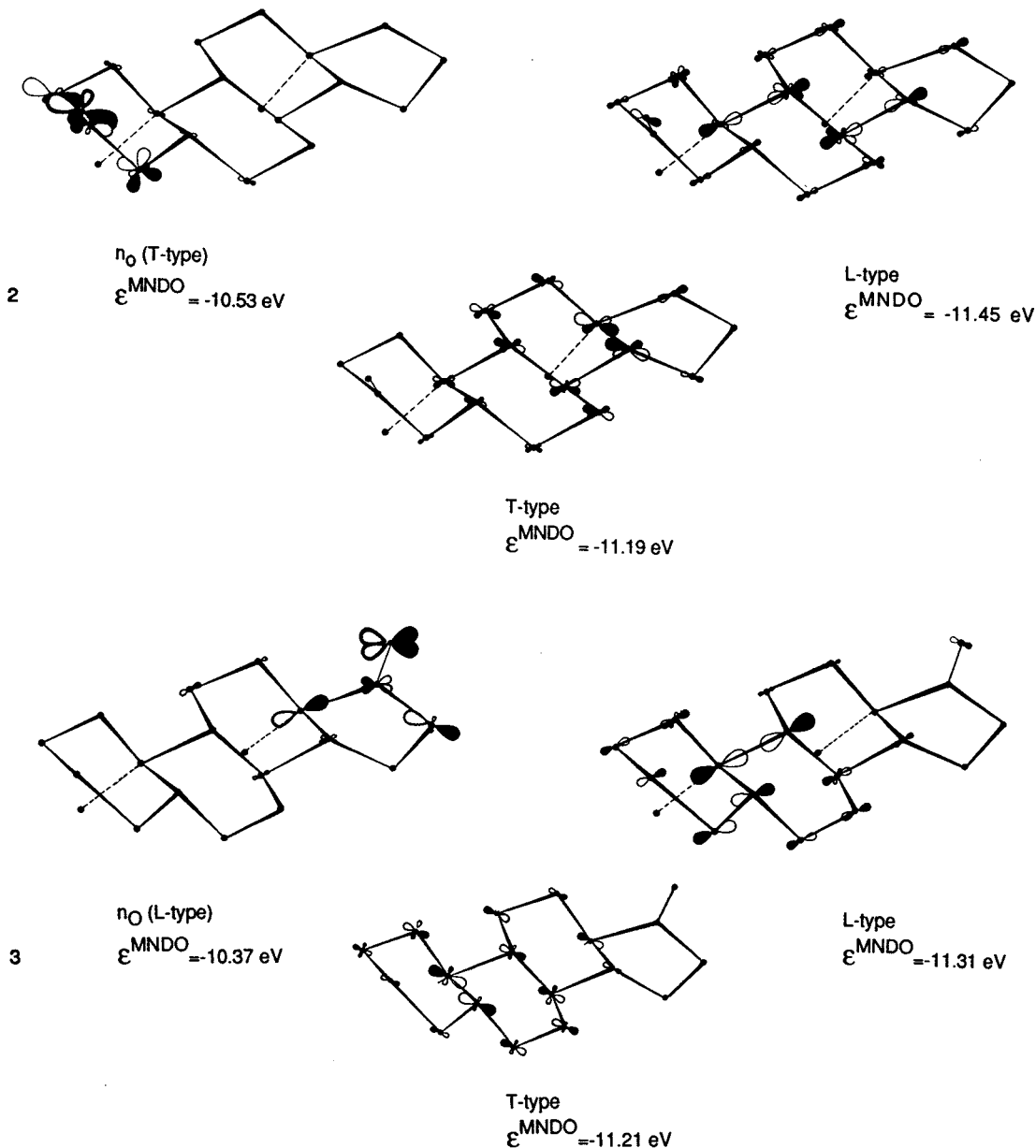
We now turn to the symmetry properties and the types of interaction between atomic centres they permit. For this purpose, we choose such an orientation of the basic steroidal skeleton that is optimal for the display of the alignment of C2p and/or O2p orbitals relative to the molecular plane. Thus, the two HOMO's of 1

T-type
$\varepsilon^{MNDO} = -10.98$ eV
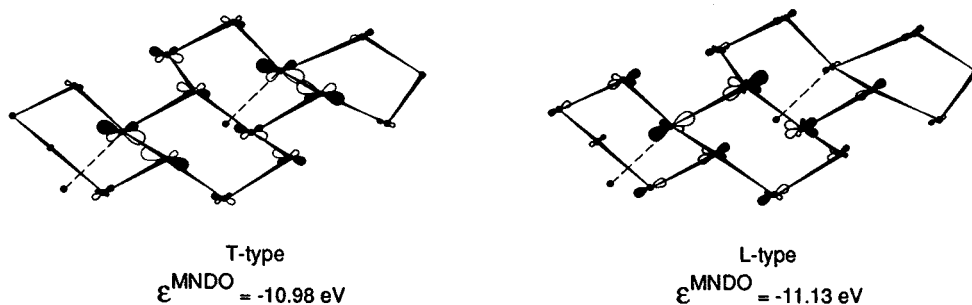
L-type
$\varepsilon^{MNDO} = -11.13$ eV

correspond, according to MNDO results, to transversal (i.e. along the short axis, T-type) and longitudinal (along the long axis, L-type) ribbon-like MO's, respectively. Calculations predict that the highest electron population will occur on

atoms of the middle rings B and C, and indicate that an interaction within these MO's will be most effectivelly disturbed by insertion of double bonds into these two rings.
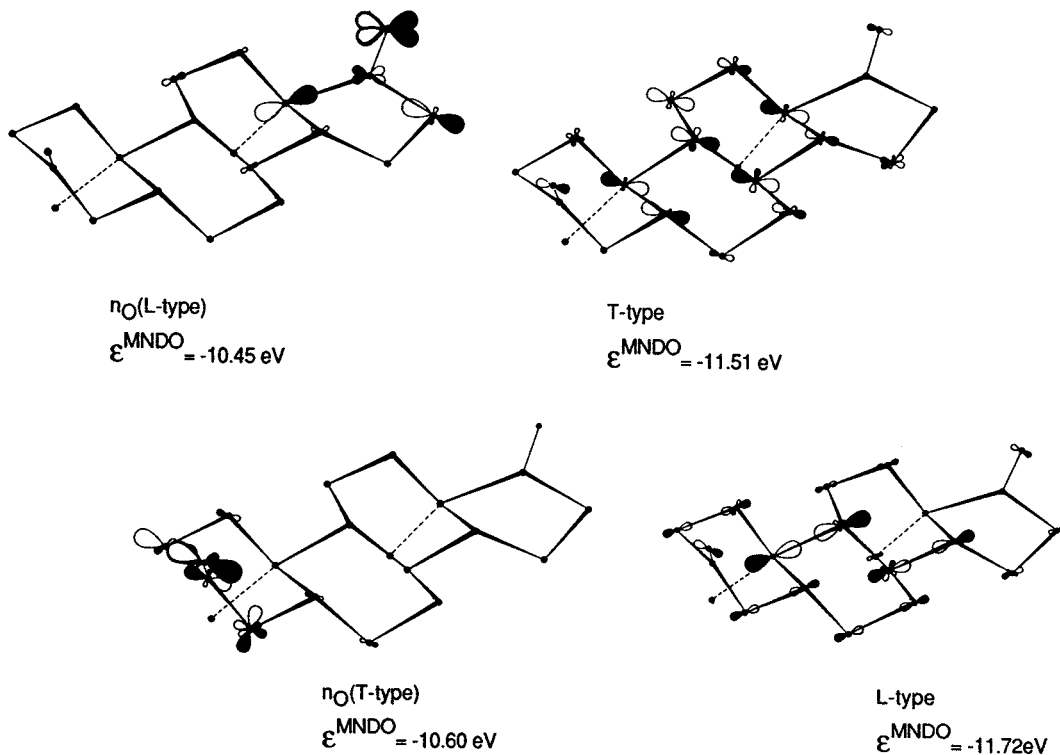
For 2 and 3, the following MO diagrams are obtained

n$_O$ (T-type)

2   ε^{MNDO} = -10.53 eV

L-type

ε^{MNDO} = -11.45 eV

T-type

ε^{MNDO} = -11.19 eV

n$_O$ (L-type)

3   ε^{MNDO}=-10.37 eV

L-type

ε^{MNDO}=-11.31 eV

T-type

ε^{MNDO}=-11.21 eV

Each of the two highest MO's in 2 seems to be T-type, the influence of the oxygen lone pair on the first being localized at the A-ring, whereas the second MO is similar to the HOMO of 1 (i.e., no contribution from O2p) but with an electron density that is shifted somewhat towards ring C. The third orbital is found to be of L-type , to have some contribution from O2p and to possess maximum electron density on carbon atoms 8,9,10 and 14.

The HOMO of 3, however, is of L-type, the dominant contributions coming from O2p and C2p AO's of atoms 13, 16 and 17 so that this MO does not extend much beyond ring C. The diagram of the next MO is very similar to the T-type MO of 1, the electron density being shifted somewhat from ring D towards rings C, B and A. The third MO is of L-type, spreading mostly over rings A and B and having a small contribution from O2p.

The above results indicate that the 3- and 17-carbonyl groups act somewhat independently, at least for the higher MO's and suggest that a 3,17-derivative should exhibit a simple additive behavior. The four highest-energy occupied MO's of 4

n_O(L-type)

$\varepsilon^{MNDO} = -10.45$ eV

T-type

$\varepsilon^{MNDO} = -11.51$ eV

n_O(T-type)

$\varepsilon^{MNDO} = -10.60$ eV

L-type

$\varepsilon^{MNDO} = -11.72$ eV

actually appear to be similar to HOMO(3), HOMO(2), 2nd(3), and 3rd(2,3), respectively. Both MO's corresponding to the -11.51 eV and -11.72 eV ionization events show simultaneous, small contributions of the O2p AO's on the 3- and 17-one. It is not surprising, then, that the overlapping low -energy band in the PES of 4 can be represented as a simple addition of 2 and 3 lowest energy bands (including a -0.2 eV inductive shift for the one additional oxygen in 4; Fig. 4). Evidently, considerable interaction occures within the σ-MO's set in this molecule: a clear gap appears in the spectrum between the I(n_O)'s and I(σ)'s subsets of ionization events.

$\varepsilon^{MNDO} = -10.47$ eV

$\varepsilon^{MNDO} = -10.62$ eV

$\varepsilon^{MNDO} = -11.06$ eV
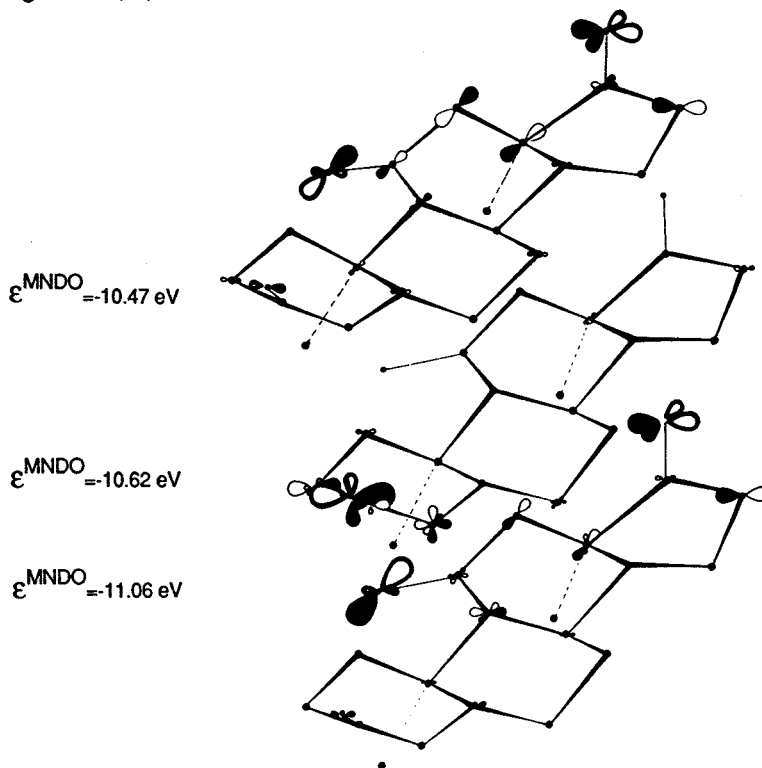
Consequently, it is relatively easy to interpret the spectrum of 5. The second of the three PES bands with maxima at 8.9, 9.09 and 9.50 eV, is a largely unperturbed $I(n_O)$ event of 3-one. The oxygen AO's at positions 11- and 17- interact significantly, and split considerably to yield the 1st and 3rd PES events of $I(n_O)$ type.

The $I(n_O)$ events in this molecule are clearly separated from the higher energy $I(\sigma)$ subset (Fig. 2 bottom).

The insertion of a double bond does not seem to influence the value of $I(n_O)$. However, it does introduce a new low-energy $I(\pi_{CC})$ event and it does shift the $I(\sigma)$ set by >0.5eV to higher energies. These findings are not confirmed by calculation. Calculations do predict that $I(\pi_{5,6}) < I(\pi_{4,5})$ and a stronger influence of the double bond in position 5(6) on $I(n_O)$-values. Such a double bond may well be an effective transmitter of effects between the 3- and 17- positions. The discrepancy of experiment and calculation results can arise for many reasons. However, a resolution of the problem requires that the PE spectra of the unsaturated hydrocarbons be accessible in order to locate the $I(\pi_{CC})$-band securely . Such work is in progress.

In conclusion, the PE spectra of steroids are a challenge to both experiment and theory. The reported long range interactions between the 3- and 17- positions (ten bonds) are not detectable in the present spectra .

Acknowledgement

REFERENCES

1.   N.S. Bhacca and L. Klasinc, Z. Naturforsch. 40A, 706 (1985)

2.   L. Klasinc, B. Ruščić, N.S. Bhacca and S.P. McGlynn, Int. J. Quantum Chem. QBS12, 161 (1986)

3.   F. Murad and R.C. Haynes, Jr.: "Hormones and Hormone Antagonists" Ch.15, in Goodman and Gilman's "The Pharmacological Basis of Therapeutics", A. Goodman Gilman, L.S. Goodman, Th. W. Rall and F. Murad (eds.), 7th Edition, Macmillan Publishing Co., New York, p.p. 1360-1517 (1985)

4.   J.E. Dumont, "Action of Hormones on Protein and Nucleic Acid Synthesis" in "Fundamentals of Biochemcal Pharmacology", Z.M. Bacq (ed.), Pergamon Press, Oxford, p.p.519-534 (1971)

5.   E. Heftmann, "Steroid Biochemistry" , Academic Press, New York, 1970.

6.   G.L. Closs and J.R. Miller, Science 240, 440 (1988) ; G.L. Closs, L. T. Calcaterra, N. J. Green, K. W. Penfield and J.R. Miller, J. Phys. Chem. 90, 3673 (1986); L. T. Calcaterra, G. L. Closs and J. R. Miller, J. Am. Chem. Soc. 105, 670 (1983); J. R. Miller, L. T. Calcaterra and G. L. Closs, ibid. 106, 3047 (1984); J. R. Miller, J. V. Beitz and R. K. Huddelston, J. Am. Chem. Soc. 106, 5057 (1984); R. K. Huddelston and J. R. Miller, J. Chem. Phys. 79, 5337 (1983); P. Pasman and J. W. Verhoeven, Th. J. de Boer, Chem. Phys. Lett. 59, 381 (1978); P. Pasman, N. W. Koper and J. W. Verhoeven, Recl. Trav. Chim. Pays-Bas 101, 363 (1982); P. Pasman, F. Rob and J. W. Verhoeven, J. Am. Chem. Soc. 104, 5127 (1982); P. Pasman, G. F. Mes, N. W. Koper and J. W. Verhoeven, ibid. 107, 5839 (1985)

7.   R.A. Marcus, J. Chem. Phys. 24 (1956) 966.; Ann. Rev. Phys. Chem. 15, 155 (1964)

8.   V.O. Levich, Adv. Electrochem. Electrochem. Eng. 4, 249 (1966); N. S. Hush, Trans. Faraday Soc. 57, 577 (1961); N. R. Kestner, J. Jortner and J. Logan, J. Phys. Chem. 78, 2148 (1974); S. F. Fischer and R. P. Van Duyne, Chem. Phys. 26, 9 (1977); R. P. Van Duyne and S. Fischer, Chem. Phys. 5, 183 (1974); J. Ulstrup and J. Jortner, J. Chem. Phys. 63, 4358 (1975); J. Jortner, ibid. 64, 4860 (1976); B. S. Brunschwig, J. Logan, M. Newton and N. Sutin, J. Am. Chem. Soc. 102, 5798 (1980); I. Webman and N. R. Kestner, J. Chem. Phys. 77, 2387 (1982); B. S. Brunschwig, S. Ehrenson and N. Sutin, J. Am. Chem. Soc. 106, 6858 (1985)

9.   N. S. Hush, M. N. Paddon-Row, E. Cotsaris, H Oevering, J. W. Verhoeven and M. Heppener, Chem. Phys. Lett. 117, 8 (1985); J. M. Warman, M. P. de Haas, M. N. Paddon-Row, E. Cotsaris and N. S. Hush, Nature (London) 320, 615 (1986); J. M. Warman, M. P. de Haas, H. Oevering, J. W. Verhoeven, M. N. Paddon-Row, A. M. Oliver and N. S. Hush, Chem. Phys. Lett. 128, 95 (1986); K. W. Penfield, J. R. Miller, M. N. Paddon-Row, E. Cotsaris, A. M. Oliver and N. S. Hush, J. Am. Chem. Soc. 109, 5061 (1987); H. Oevering, M. N. Paddon-Row, M. Heppener, A. M. Oliver, E. Cotsaris, J. W. Verhoeven and N. S. Hush, J. Am. Chem. Soc. 109, 3258 (1987); H. Oevering, J. W. Verhoeven, M. N. Paddon-Row, E. Cotsaris and N. S. Hush, Chem. Phys. Lett. 143, 488 (1988); C. A. Stein, N. A. Lewis, G. Seitz and A. D. Baker, Inorg. Chem. 22, 1124 (1983); A. D. Joran, B. A. Leland, G. G. Geller, J. J. Hopfield and P. B. Dervan, J. Am. Chem. Soc. 106, 6090 (1984); B. A. Leland, A. D. Joran, P. M. Felker, J. J. Hopfield, A. H. Zewail and P. B. Dervan, J. Phys. Chem. 89, 5571 (1985)

10.   V. Butković, B. Kovač, I. Novak, B. Ruščić, A. Sabljić, L. Klasinc and S. P. McGlynn , "Photoelectron Spectra of Some Biologically Active Molecules", Ch. 15, p.p. 251-267, in "Modelling of Structures and Properties of Molecules", Z. B. Maksić, ed., Ellis Horwood, Chichester, England 1987; S. P. McGlynn, L. Vanquickenborne,

11.   L. Klasinc , B. Kovač and B. Ruščić, <u>Kem. Ind. (Zagreb) 10</u>, 569 (1974)

12.   Quantum Chemistry Program Exchange, Indiana University, Bloomington,Ind., Program QCPE 464 (IBM MOPAC), written by J. J. P. Stewart

13.   B. A. Cooper, E. M. Gopalakrishna and D. A. Norton, <u>Acta Cryst. B25</u>, 935 (1969); E. M. Gopalakrishna, B. A. Cooper and D. A. Norton, <u>ibid. B27</u>, 1 (1971); D. A. Norton, G. Kartha and C. T. Lu, <u>ibid. 16</u>, 89 (1971)
       F. V. Brutcher, Jr. and E. J. Leopold, <u>J. Am. Chem. Soc 88</u>, 3156 (1966)

14.   B. Kovač and L. Klasinc, <u>Croat. Chem. Acta 51</u>, 55 (1978)

15.   L. Klasinc and S. P. McGlynn, "The Photoelectron Spectra of Doubly Bonded CC, CN, NN and CO Groups", in <u>"Chemistry of Functional Groups"</u>, S. Patai and Z. Rappaport, eds., Wiley, New York (in press)

16.   L. Klasinc, I. Novak, A. Sabljić and S. P. McGlynn, <u>Int. J. Quantum Chem., Quantum Biol. Symp. 15</u>, 259 (1988)

17.   P. Masclet, D. Grosjean, G. Mouvier and J. Dubois, <u>J. Electron Spectrosc. 2</u>, 225 (1973)

18.   P. D. Mollere, K. N. Houk, D. S. Bomse and H. Morton, <u>J. Am. Chem. Soc. 98</u>, 4732 (1976)

19.   P. Bischof, J. A. Hashmall, E. Heilbronner and V. Hornung, <u>Tetrahedron Lett. 1970,</u> 1033; idem, <u>Helv. Chim. Acta 52</u>, 1745 (1969)

20.   L.Klasinc and S. P. McGlynn, "Photoelectron Spectra of Quinonoid Compounds", Ch. 5, p.p. 155-201, in <u>"The Chemistry of Quinonoid Compounds"</u>, Vol. II, S. Patai and Z. Rappaport, eds., Wiley, New York, 1988.