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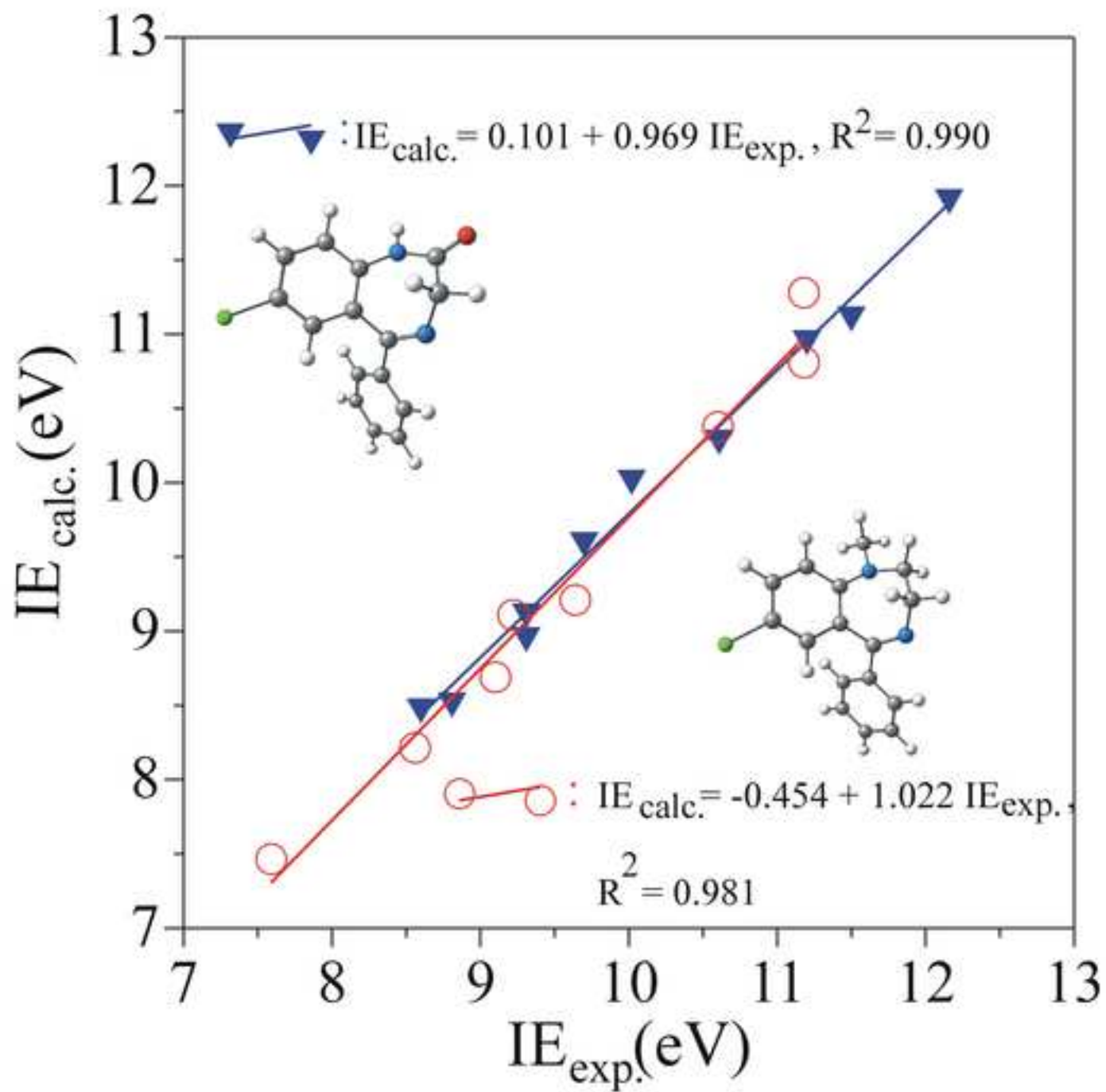
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Abstract: Abstract. Vertical ionization energies (VIEs) of medazepam and nordazepam and of their molecular subunits have been calculated with the electron propagator method in the P3/CEP-31G* approximation. Vertical electron affinities (VEAs) have been obtained with a Δ SCF procedure at the DFT-B3LYP/6-31+G* level of theory. Excellent correlations have been achieved between IE_{calc} and IE_{exp} allowing reliable assignment of the ionization processes. Our proposed assignment differs in many instances from the previously reported one in the literature. The electronic structure of the frontier Dyson orbitals shows that IE and EA values of the benzodiazepines can be modulated essentially by substitution at the benzene rings. Hardness values, evaluated as $(IE-EA)/2$, follow the trend of the experimental singlet transition energies. Medazepam is a less hard, i.e. less stable, compound than nordazepam.

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Electronic properties of neuroleptics: ionization energies of benzodiazepines

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Abstract

Vertical ionization energies (VIEs) of medazepam and nordazepam and of their molecular subunits have been calculated with the electron propagator method in the P3/CEP-31G* approximation. Vertical electron affinities (VEAs) have been obtained with a Δ SCF procedure at the DFT-B3LYP/6-31+G* level of theory. Excellent correlations have been achieved between IE_{calc} and IE_{exp} allowing reliable assignment of the ionization processes. Our proposed assignment differs in many instances from the previously reported one in the literature. The electronic structure of the frontier Dyson orbitals shows that IE and EA values of the benzodiazepines can be modulated essentially by substitution at the benzene rings. Hardness values, evaluated as $(IE-EA)/2$, follow the trend of the experimental singlet transition energies. Medazepam is a less hard, *i.e.* less stable, compound than nordazepam.

Keywords Benzodiazepines · Vertical ionization energies · Vertical electron affinities · DFT calculations · Electron propagator theory calculations

Introduction

Benzodiazepines are well known drugs of wide importance in medicinal chemistry, possessing a broad spectrum of pharmacological activity [1]. The heart of a benzodiazepine is constituted by a seven-membered partially saturated ring with nitrogen atoms at position 1 and 4, fused with a benzene ring. Substitution at the various positions of the two rings gives rise to a wide number of benzodiazepines derivatives. An accurate description of the electronic and molecular structure of representative compounds is of intrinsic value. In this respect, ultraviolet photoelectron spectroscopy (UV-PES), supported by reliable theoretical calculations, may provide precious information on the outer valence molecular orbital shapes and energies [2]. In this report we are dealing with the electronic structure of 7-chloro-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **6** (nordazepam) and molecular subunits **4** (ring D) and **5** (rings B and D) and with 7-chloro-5-phenyl-2,3-dihydro-1-H-1,4-benzodiazepin **3** (medazepam) and molecular subunits **1** (ring A) and **2** (rings B and A), Fig. 1. These compounds exhibit structural units present in several derivatives of the same family. The experimental UV-PES of compounds **3**, **5** and **6** have been reported [3, 4]. The suggested assignments of the photoionization processes are, however, very different to each other. We aim to give an accurate description of the electronic structure of medazepam and nordazepam through the computation and the analysis of the outermost Dyson orbitals and the associated vertical ionization energies (VIEs) and vertical electron affinities (VEAs). To this end we employ the *ab initio* electron propagator theory in the partial third order approximation (P3) [5]. P3 has been widely proved to give reliable interpretation of the ionization processes of a number of organic systems [6-8].

Computational details

P3 theory has been recently reviewed [9]. Briefly we recall that in the theory to every IE, there corresponds a Dyson orbital (DO) defined by

$$\phi^{Dyson}(x_1) = N^{-1/2} \int \Psi_{cation}^*(x_2, x_3, x_4, \dots, x_N) \times \Psi_{molecule}(x_1, x_2, x_3, \dots, x_N) dx_2 dx_3 dx_4 \dots dx_N$$

where N is the number of electrons in the molecule and x_i is the space-spin coordinate of electron i. To a DO is associated a so called pole strength, which indexes the validity of the perturbative treatment. Pole strength values between 0.85 and 1 indicate that the one-electron

description of the ionization process is valid. In the P3 approximation DOs are proportional to Hartree-Fock orbitals. The P3 approximation includes orbital electron correlation and relaxation effects associated to the ionization. The active space included all valence occupied and all unoccupied molecular orbitals in P3 calculations of **1**, **2**, **4** and **5**. In medazepam and nordazepam we considered all valence occupied molecular orbitals and 85% of the virtual molecular orbitals.

All calculations were performed with the Gaussian/03 program [10]. Molecular structures were fully optimized at the Density Functional Theory level (DFT) using the B3LYP functional [11, 12] and the 6-31G* basis set. Due to the size of the investigated compounds, P3 calculations were carried out with the pseudo potential (PP) CEP-31G* basis set [13]. The PP/P3 approach has been proved to be adequate in predicting VIEs [14]. Owing to the molecular size and the need of more extended basis set including diffuse functions, VEAs were computed by the widely used Δ SCF procedure [15, 16] by comparing *ab initio* B3LYP/6-31+G* total energies of the anion and neutral molecules on the geometry of the neutral compound.

Results and discussion

The molecular structures of compounds **1-6** are shown in Fig. 1. Starting geometries were taken, when available from X-ray data in the solid [17, 18]. To find minimum energy conformations we performed molecular dynamics (MD) simulation with AMBER force field for 1 ns at 600 K and a time step of 1 fs. The obtained conformations were optimized by AM1 calculations. The most stable structures were further fully optimized at B3LYP/6-31G* level. Theoretical geometries are in very good agreement with experimental data [17, 18]. Minimum energy conformations were confirmed by vibrational analysis. The seven-membered ring adopts a boat structure in **3**, **4**, **5** and **6** and a twisted-boat structure in **1** and **2**. Benzene ring B is planar. Benzene ring C can rotate around the single C-C bond by producing in **3** two isoenergetic conformations with dihedral angles between the two benzene rings of -157.3° and 24.8° , respectively, separated by an energy barrier of $6.31 \text{ kcal mol}^{-1}$ with a maximum at 114.8° . The corresponding figures in **6** are: -136.5° , 27.7° , $5.98 \text{ kcal mol}^{-1}$, 123.4° (Fig. S1 of the supplementary material). Cartesian coordinates of the minimum energy conformations are reported in Tables S1-S6 of the supplementary material.

In the extensive work of Ortiz and co-workers P3 calculations were widely and successfully carried out with the 6-311G** basis set [19]. In the present work, owing to the size of the molecules we are dealing with, we used the smaller CEP-31G* basis set. The comparison of the CEP-31G* results with the 6-311G** ones and the experimental data for compound **5**, as a test case, relative to the first five ionization energies, is given in Fig. 2. It can be seen that IE_{calc} vs. IE_{exp} correlation is similar for the two levels of theory and that experimental numerical data are well reproduced. In view of applying this methodology to larger related molecular systems we also tested the use of the even smaller CEP-31G basis set. The result, reported in Fig. 2 indicates a possible use also of this unpolarized double-zeta basis, although some energy shift is to be expected for orbitals with large nitrogen lone pair amplitude (third point in the correlation line of Fig. 2). Pole strength values of all the investigated compounds are between 0.87 and 1, indicating that one-electron description of the final state is qualitatively valid.

Our theoretical electronic structure analysis starts from the isolated diazepine rings A and D followed by the more complex systems **2**, **5** and **3**, **6**.

Vertical ionization energies

Compounds 1 and 4

Dyson orbitals and energy levels of diazepine rings A and D are presented in Fig. 3. The first cationic final state of compound **1** is described by a rather high-energy $\pi_{\text{C=C}}$ orbital with contributions from $n\text{N}$ lone pairs. The methyl group gives a small contribution through hyperconjugative interaction. Next two IEs at 9.10 and 10.00 eV pertain to $n\text{N}$ orbitals mainly localized on N_4 atom. An in-phase $\pi \text{C=N}^4$ and C=C-C-N^1 combination characterizes the fourth ionization at 11.62 eV. Almost the same sequence of DOs characterizes the electronic structure of the diazepine ring D bearing the C=O group but lacking the CH_3 group. This substitution produces important changes in the orbital composition and IE values of the outermost final states, which all show contributions from the $n\text{O}$ lone pairs and are stabilized owing to the strong electron withdrawing power of the C=O group. Of particular significance is the 1.33 eV stabilization of the lowest-energy DO.

Compounds 2 and 5

Dyson orbital structures of compounds **2** and **5** are shown in Fig. 4 and the correlation diagram of the corresponding IEs in Fig. 5. The fusion of ring A and D with a benzene ring to give **2** and **5** introduces the b_{1-} and a_{2-} -like benzene orbitals, which give the major contribution to the first two energy levels in both compounds. They are followed by a cationic state essentially localized on an N^4 lone pair, which in **5** has also some nO amplitude. The last two DOs in Fig. 4 have π symmetry and are mainly localized on the benzene ring and on N^1 the former orbital and on the C=N bond the latter one. Both compounds show the same succession of cationic states with IE values which are about 1 eV higher in **5** than in **2**. Experimental IEs of **5** are known from photoelectron spectroscopy measurements [4] and are reported in Fig. 5 for comparison. On the basis of our calculations, the characterization of the electronic nature of the outermost cationic states differs in some instances from that proposed by Khvostenko *et al.* [4]. The most remarkable discrepancy lies in the assignment of the structured band at 9.4-9.6 eV which we assign to the ionization from the $\pi_B(a_2)$ level at 9.17 eV, while Khvostenko *et al.* associate this band to two ionizations of $\pi_A(a_2)$ and nN^4 symmetry, respectively. Our assignment is supported by the observation that P3 calculations uniformly somewhat underestimate the experimental IE and by the fact that it produces, as previously seen, an excellent IE_{calc} vs. IE_{exp} correlation (Fig. 2). A second main discrepancy refers to the assignment of the $\pi_{C=N}$ ionization, which Khvostenko *et al.* associate to the IE_5 at 11.42 eV in the photoelectron spectrum, while, on the contrary, we assign to the 5th ionization with nO and nN^1 character calculated at 11.21 eV. Our calculations predict the $\pi_{C=N}$ at 11.76 eV, which on the basis of the correlation line in Fig. 2 should be found at the beginning of the broad band envelope centred at 13.32 eV in the photoelectron spectrum [4].

The electronic structure of the frontier DOs suggests that the redox properties of compounds **2** and **5** can be varied essentially by substitution at the benzene ring.

Compounds 3 (medazepam) and 6 (nordazepam)

Outermost DOs of medazepam and nordazepam are shown in Fig. 6. The corresponding ionization energies are assigned and correlated in Fig. 7 where available experimental data are also reported for comparison. As observed in the previous compounds, **3** and **6** show the same succession of cationic states with IE values of the carbonilic compound **6** higher than in **3** by

0.2-1 eV. The first four ionizations are of π type localized in the benzene rings. A nN^4 ionization interposes between the third and fourth π levels. The ionization with high $\pi_{C=N}$ character is calculated at 10.38 eV in **3** and at 10.97 eV in **6**. The latter value is in agreement with the experimental IE at 11.2 eV in the PE spectrum [4], while we associate the former value to the experimental band at 10.49-10.6 eV [3, 4] in agreement with the Andreocci *et al.* assignment [3] but in disagreement with the Khvostenko *et al.* assignment [4] (Fig. 7). To compare theoretical and experimental data we look at an one to one correlation between theoretical and experimental values. The very good correlations obtained, Fig. 8, give valuable support to our assignment of the ionization processes of both benzodiazepines. The PE spectrum of medazepam was reported by Khvostenko *et al.* [4] and by Andreocci *et al.* [3]. The assignment of the ionization bands proposed by the two research groups differs noticeably with each other. The first ionization energy at 7.7 eV in [3] and 7.59 eV in [4] was assigned to a nN^1 lone pair ionization by Andreocci *et al.* and to a $\pi_A(b_1)$ ionization by Khvostenko *et al.*. Our P3 results assign the first calculated ionization at 7.46 eV to a $\pi_B(b_1)$ level, in agreement with Khvostenko *et al.*. The band in the 8.2-10.2 eV range in the PE spectrum of **3** was associated to four ionizations by Khvostenko *et al.*, with energy level succession $\pi_C(b_1) < \pi_C(a_2) < \pi_A(a_2) < nN^4$, on the basis of the ratio area of this band envelope and the first one-electron band. On the contrary, Andreocci *et al.* [3] associate this multi-processes band to five final states, in the order: $nN_4 < \pi_B < \pi_B < \pi_C < \pi_C$. P3 calculations associate the band to five ionizations with succession $\pi_C(b_1) < \pi_C(a_2) < nN^4 < \pi_B(a_2) < \pi$, on the basis of the same previous area ratio approach. This is in agreement with the results of the deconvolution of the first two ionization bands in the PE spectrum of **3** (Fig. 9), which gives an area ratio of 5.07.

In the case of compound **6** we notice only one discrepancy with the assignment proposed by Khvostenko *et al.*. These authors assign the third band in the spectrum at 9.7 eV to a nN^4 ionization, while we assign it to a π_B ionization calculated at 9.61 eV and put the nN^4 ionization ($IE_{\text{calc}}=9.12$ eV) in the experimental band centred at 9.31 eV. Our assignment of the ionization processes for nordazepam does not confirm the one reported by Andreocci *et al.* for diazepam (N^1 -methylnordazepam) [3], which associate the first two IEs to nN^1 and nN^4 ionizations, respectively.

Vertical electron affinities

B3LYP/6-31+G* VEA values are reported in Table 1 and the electronic structure of the lowest unoccupied molecular orbitals (LUMO) of the fully optimized neutral initial state, the extra electron site, in Fig. 10. It can be seen that the extra charge in **3** is localized in both the benzene rings, while in **6** essentially in the B ring. Therefore the VEA of nordazepam can be mainly varied by substitution in the benzene B ring, and by substitution at both rings in medazepam. Data in Table 1 indicate that IEs of the diazepine seven-membered rings are predicted to be negative; the fusion of a benzene ring and the C=O group, however, produces a significant EA increase, so both benzodiazepine show positive VEA values. IE and EA values determine the redox properties of a molecule. The obtained values indicate that medazepam is more easily oxidized (lower IE) and less easily reduced (lower EA) than nordazepam. The IE-EA energy gap, which determines the hardness value of a molecule expressed as $\eta = (IE-EA)/2$, decreases along the series as: $\eta(\mathbf{1}) > \eta(\mathbf{2}) > \eta(\mathbf{3})$ and $\eta(\mathbf{4}) > \eta(\mathbf{5}) > \eta(\mathbf{6})$, with medazepam less hard, *i.e.* less stable than nordazepam. Interestingly, computed hardness values of **3**, **5** and **6** follow well the trend of the available experimental singlet UV transition energies [4], which seems to indicate that in the present compounds the hardness value follows the HOMO and LUMO position and that configuration interaction effects in the excitation process are comparatively similar.

Summary and conclusions

The *ab initio* electron propagator theory in the P3/CEP-31G* approximation has been used to calculate vertical ionization energies of medazepam and nordazepam and of their molecular subunits. Vertical electron affinities were obtained by a Δ SCF procedure from the total energies of the anions and neutral compounds using the B3LYP/6-31+G* method. The electronic character of the ionization processes has been established through the analysis of the Dyson orbitals and compared with available experimental and theoretical data. The comparison with previous estimates shows significant divergences in many cases. Our assignment is supported by the very good correlation we obtain between theoretical and experimental IE values. The outermost cationic states and the lowest anionic state of the investigated compounds have π character. The electron affinity of the medazepam and the ionization potential of nordazepam can be varied essentially by substitution at both the

benzene rings, while the EA of nordazepam and the IE of medazepam can be varied by substitution at the benzene B ring. Owing to the strong electron withdrawing power of the C=O group, nordazepam has higher EA and IE than medazepam; as a result medazepam is a less hard, *i.e.* less stable, compound than nordazepam. Interestingly hardness values of the investigated compounds follow the trend of the experimental singlet UV transition energies.

Supplementary material available

Supplementary material contain Cartesian coordinates of compounds **1-6** (Tables S1-S6) and torsional potential energy curve relative to the rotation of the benzene C ring for compounds **3** and **6** (Fig. S1).

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Tables

Table 1 Vertical electron affinity VEA, vertical ionization energy VIE, hardness $\eta=(\text{VIE}-\text{VEA})/2$, and experimental first singlet transition energy S_1 of diazepines. Values in eV

Compound	1	2	3	4	5	6
VIE	7.48	7.35	8.22	8.81	8.46	8.49
VEA	-0.78	-0.38	0.23	-0.14	0.13	0.60
η	4.13	3.86	3.99	4.48	4.16	3.94
S_1 ^a			3.47		4.14	3.92

^a Ref. [4].

Figure captions

Fig. 1 Molecular structures of the investigated compounds determined by B3LYP/6-31G* calculations

Fig. 2 IE_{calc} vs. IE_{exp} correlations for 1,3-dihydro-2H-1,4-benzodiazepin-2-one (**4**)

Fig. 3 Dyson orbitals and ionization energies of compounds **1** and **4**

Fig. 4 Dyson orbitals of compounds **2** and **5**

Fig. 5 Correlation diagram for compound **2** and **5** and comparison with experimental data

Fig. 6 Dyson orbitals for compounds **3** and **6**

Fig. 7 Correlation diagram for compounds **3** and **6** and comparison with experimental data

Fig. 8 IE_{calc} vs. IE_{exp} for medazepam and nordazepam

Fig. 9 Deconvolution of the 8.2-10.2 eV experimental ionization energies envelope of medazepam (Ref. [4])

Fig. 10 Lowest unoccupied molecular orbitals of the investigated compounds

Figure 1
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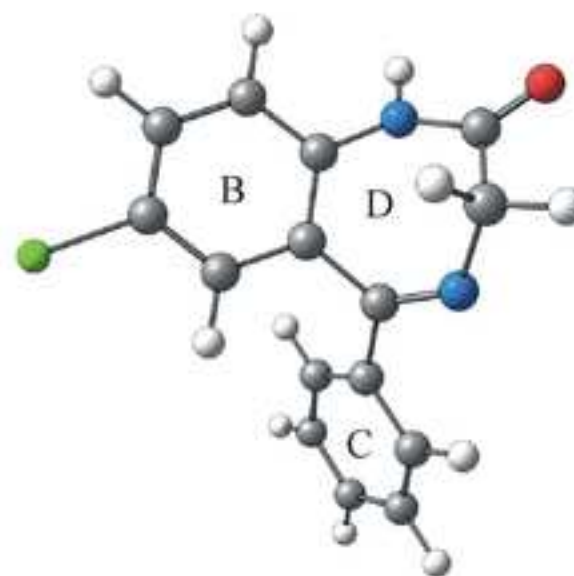
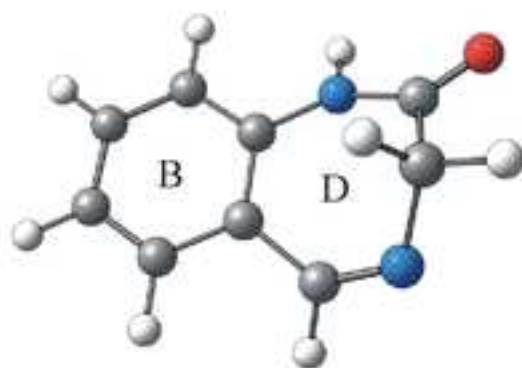


Figure 2
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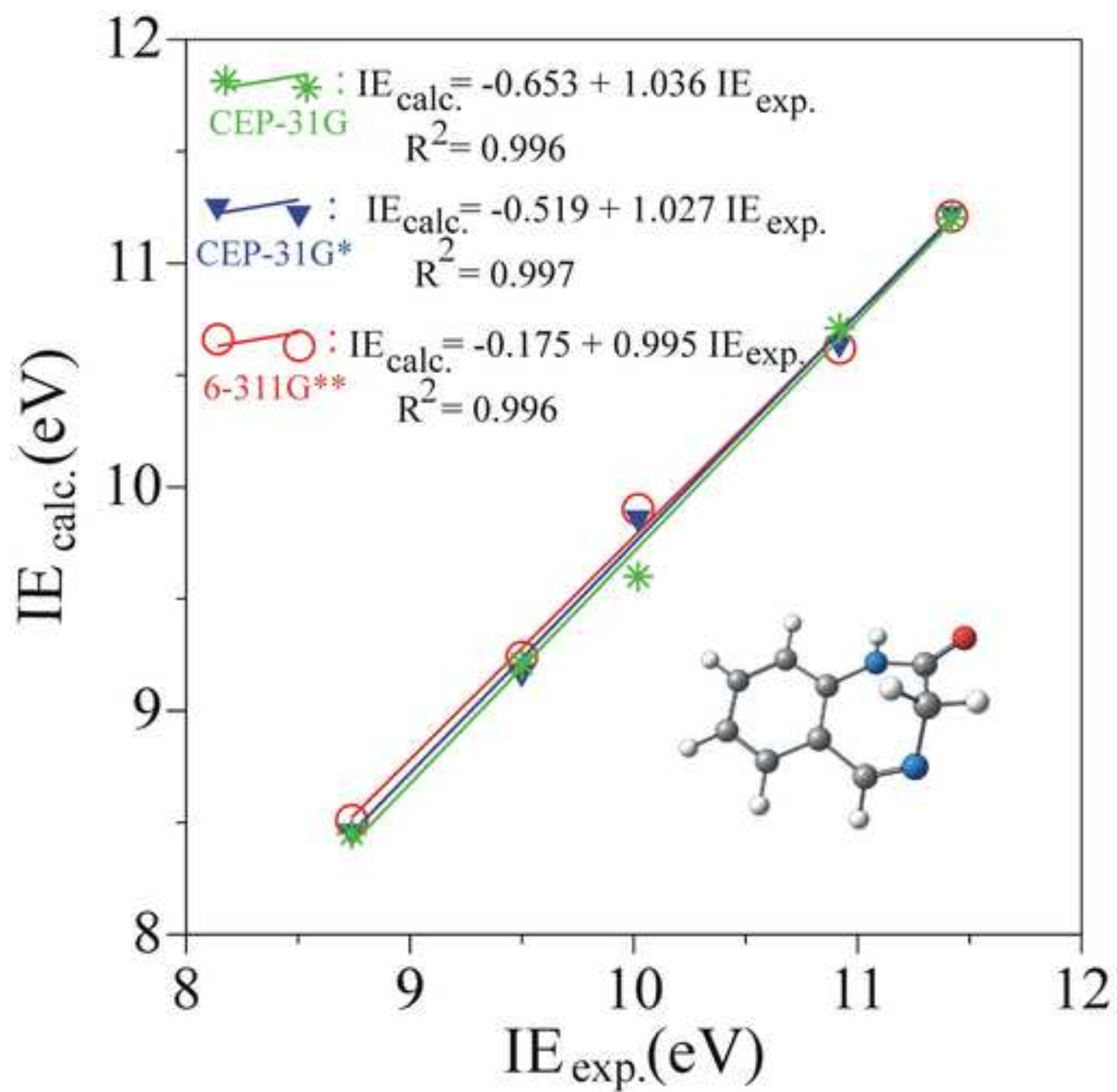


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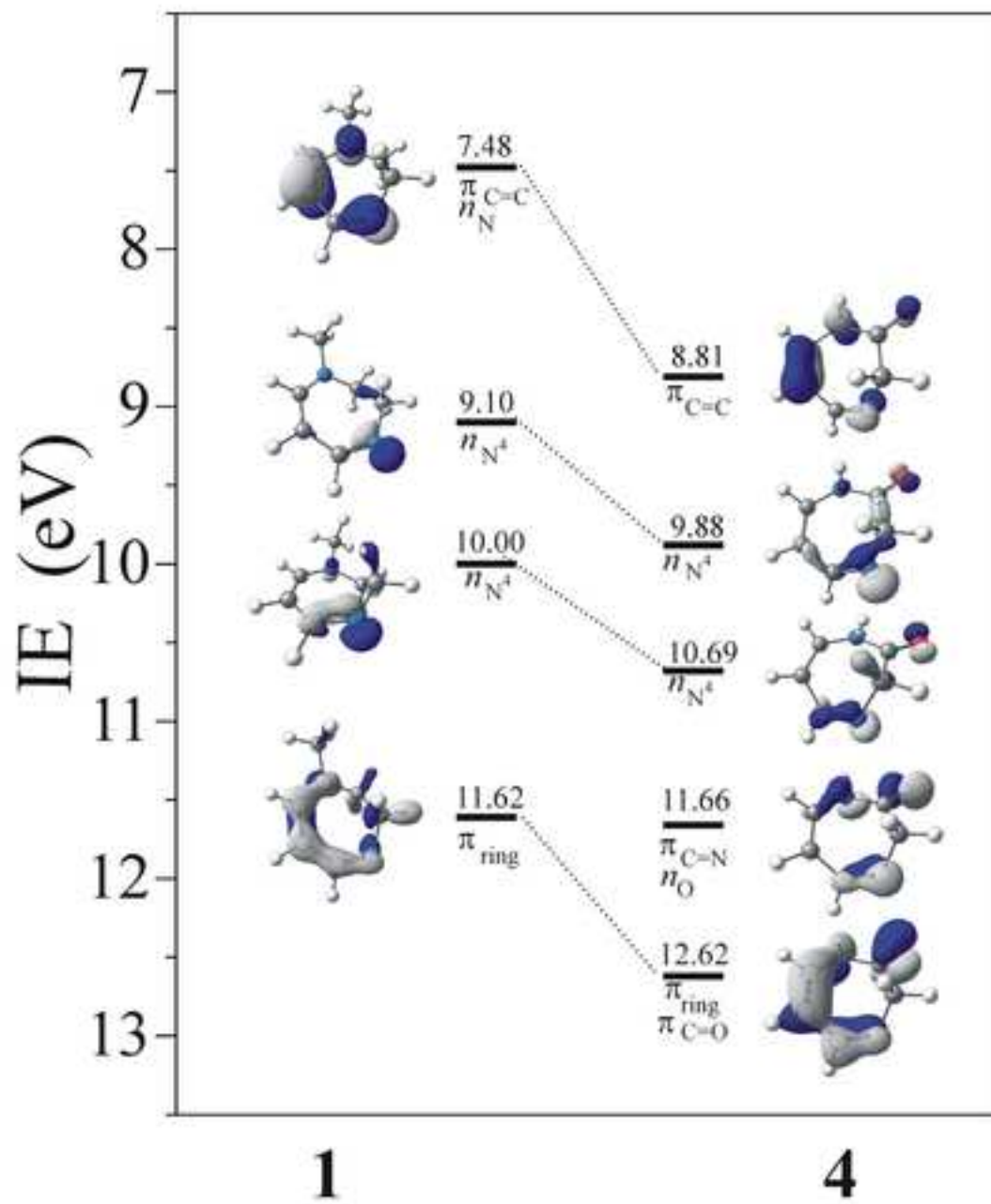


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IE

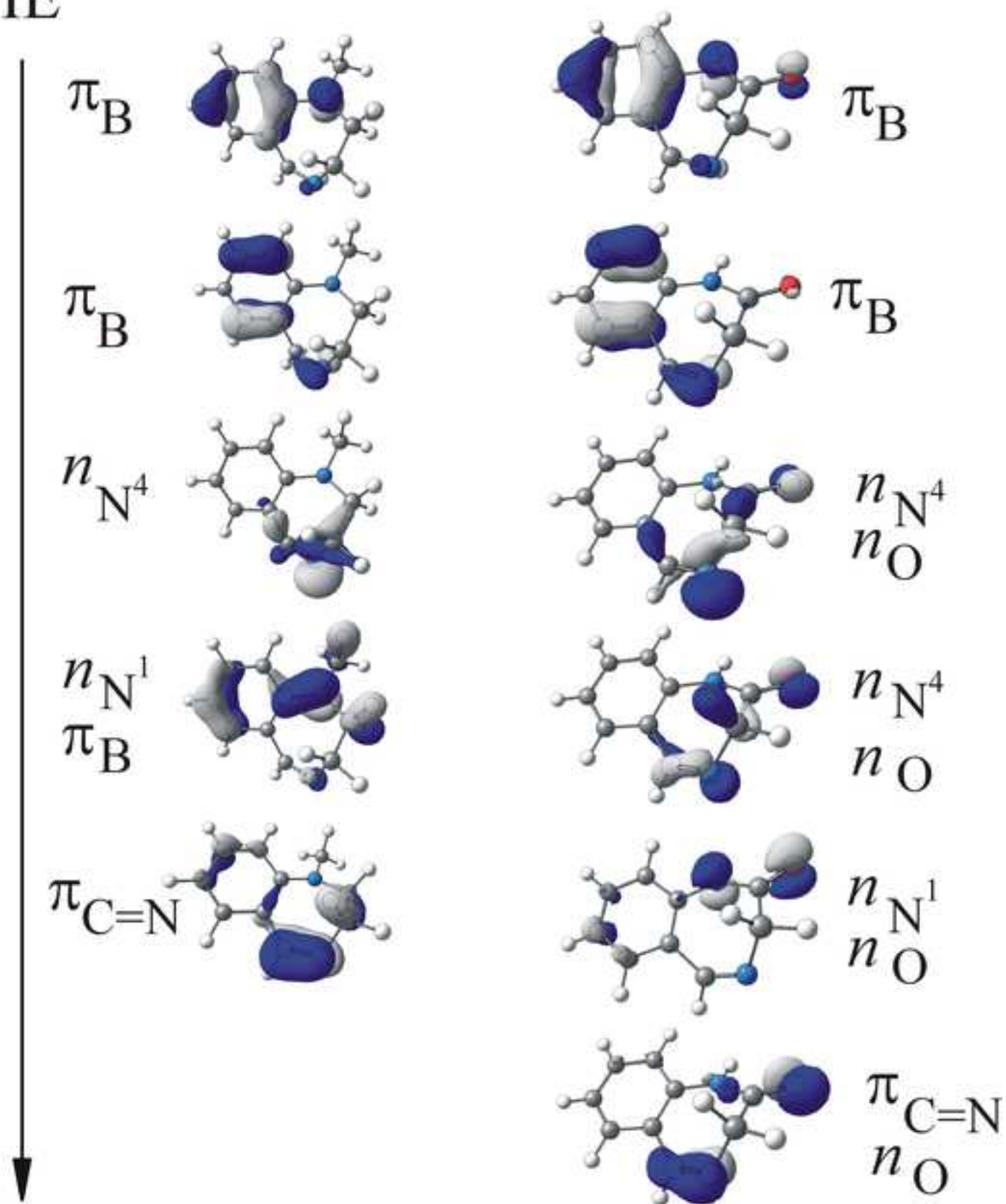


Figure 5

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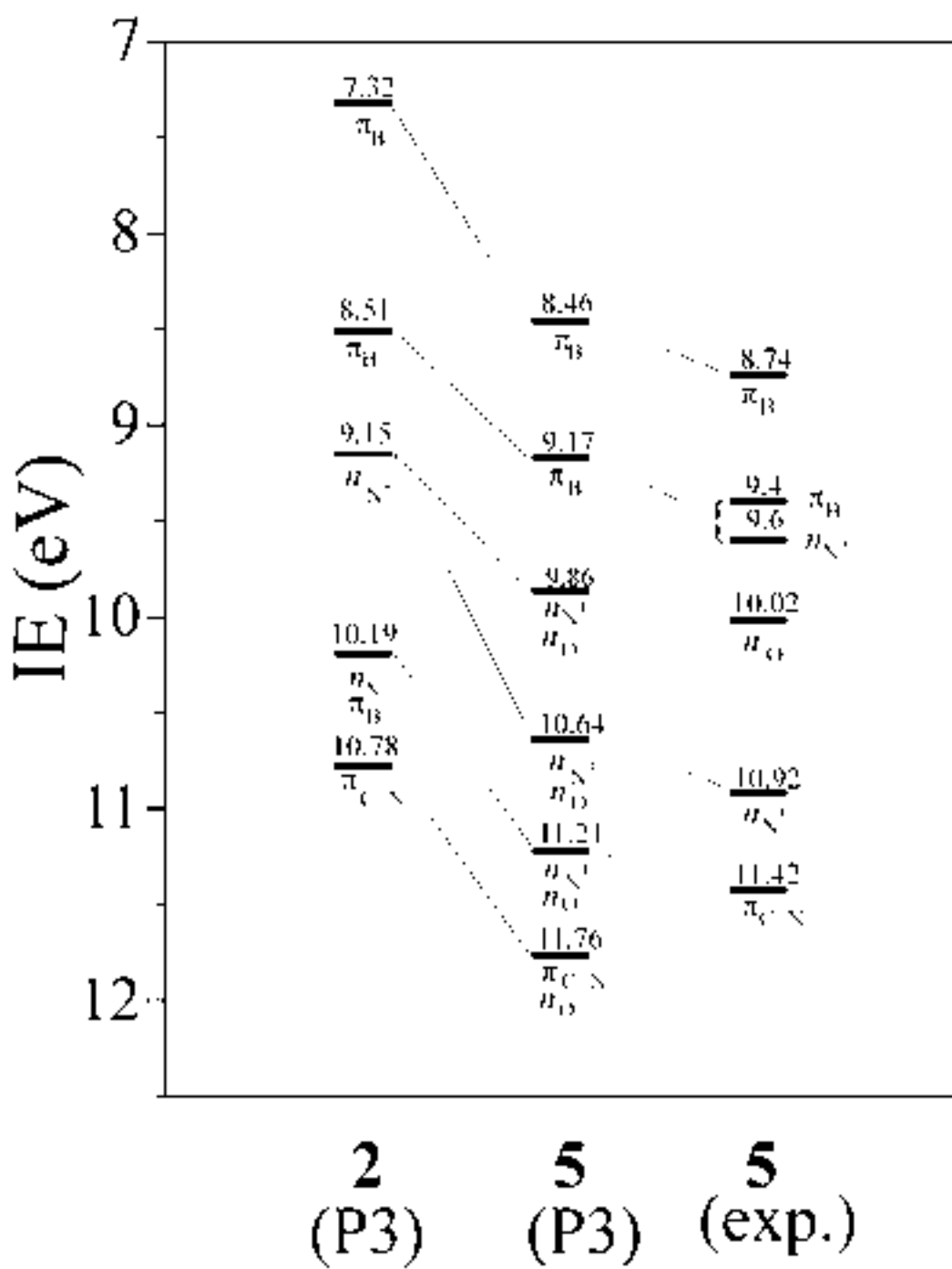


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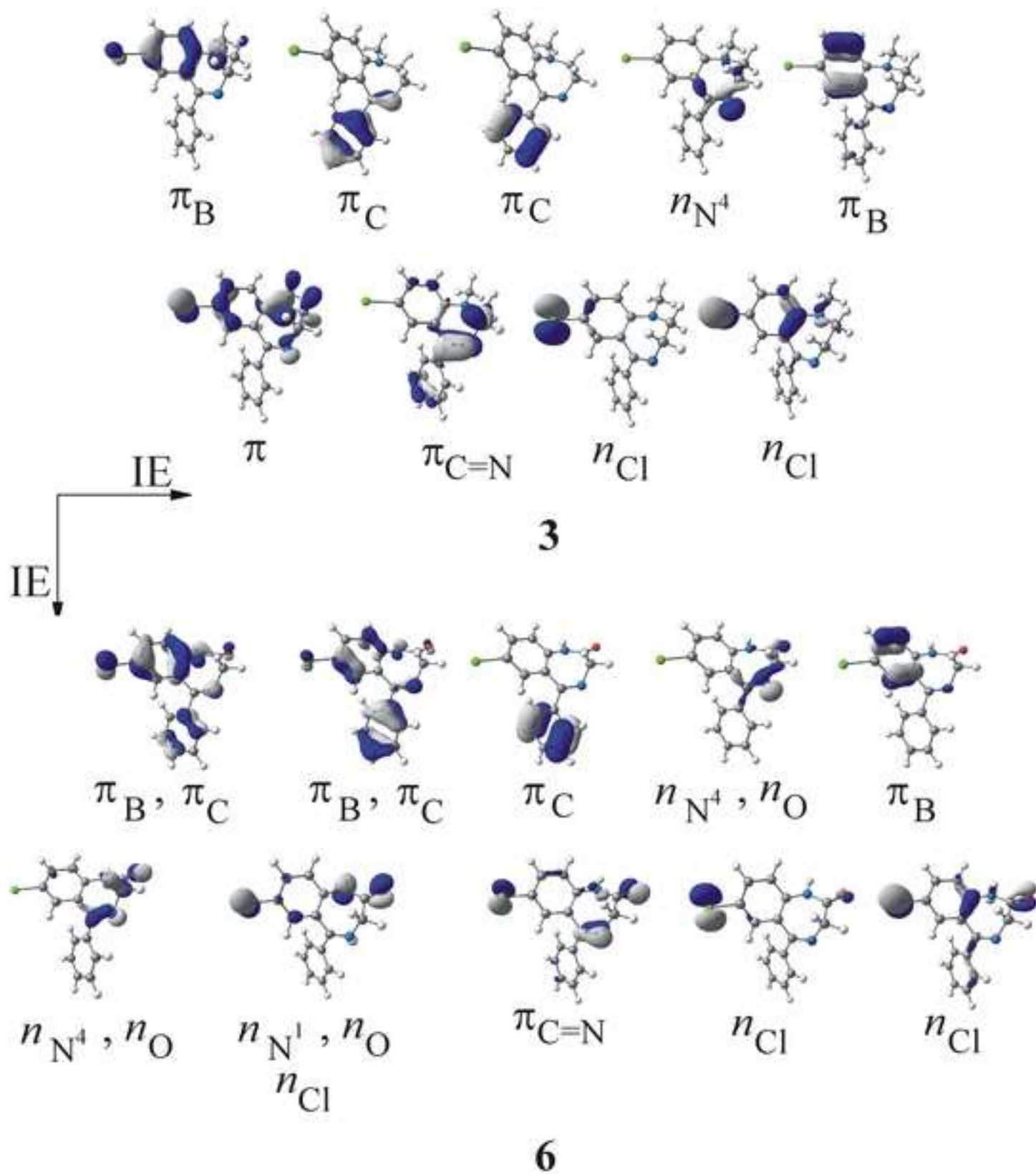


Figure 7

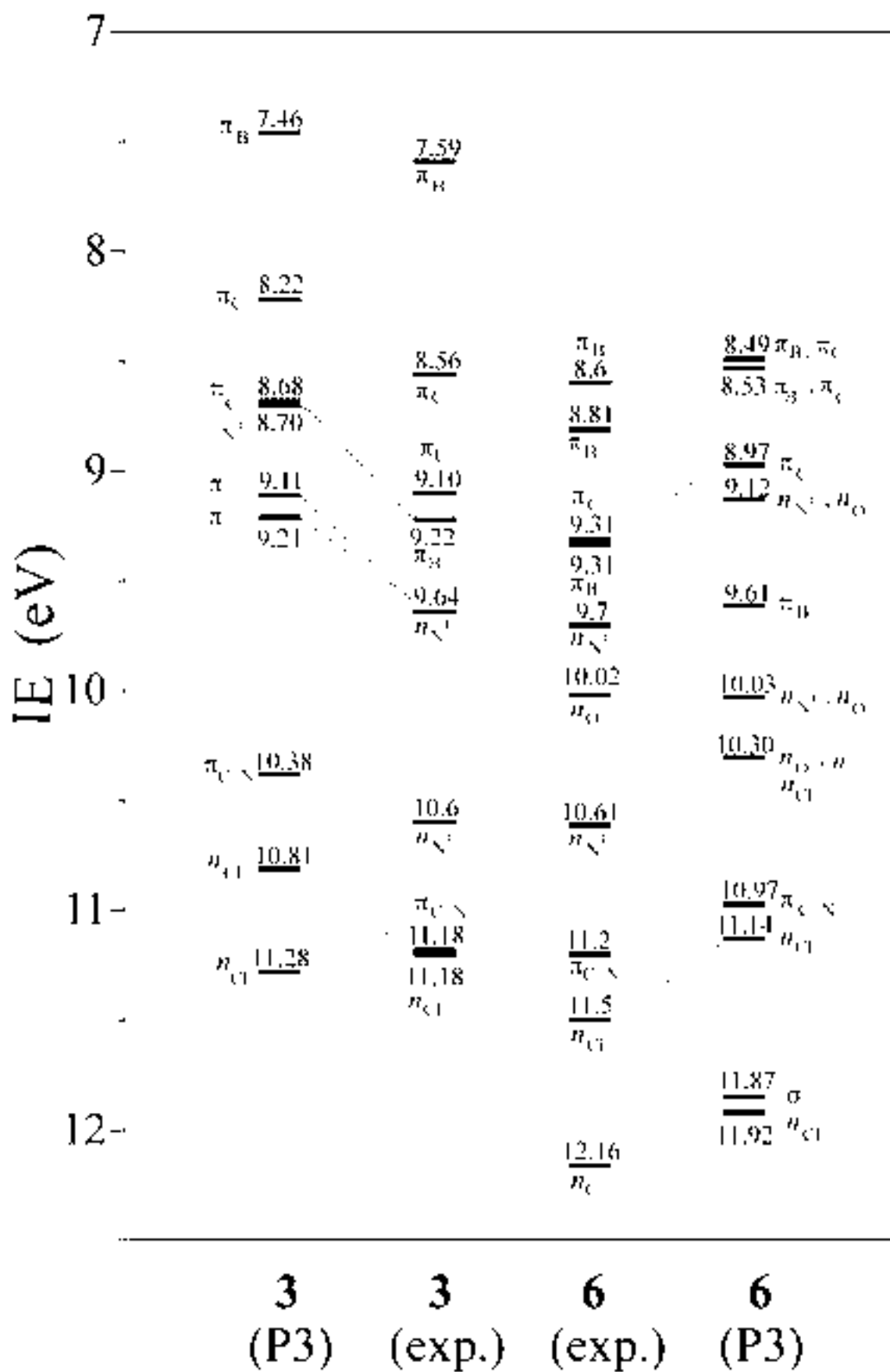
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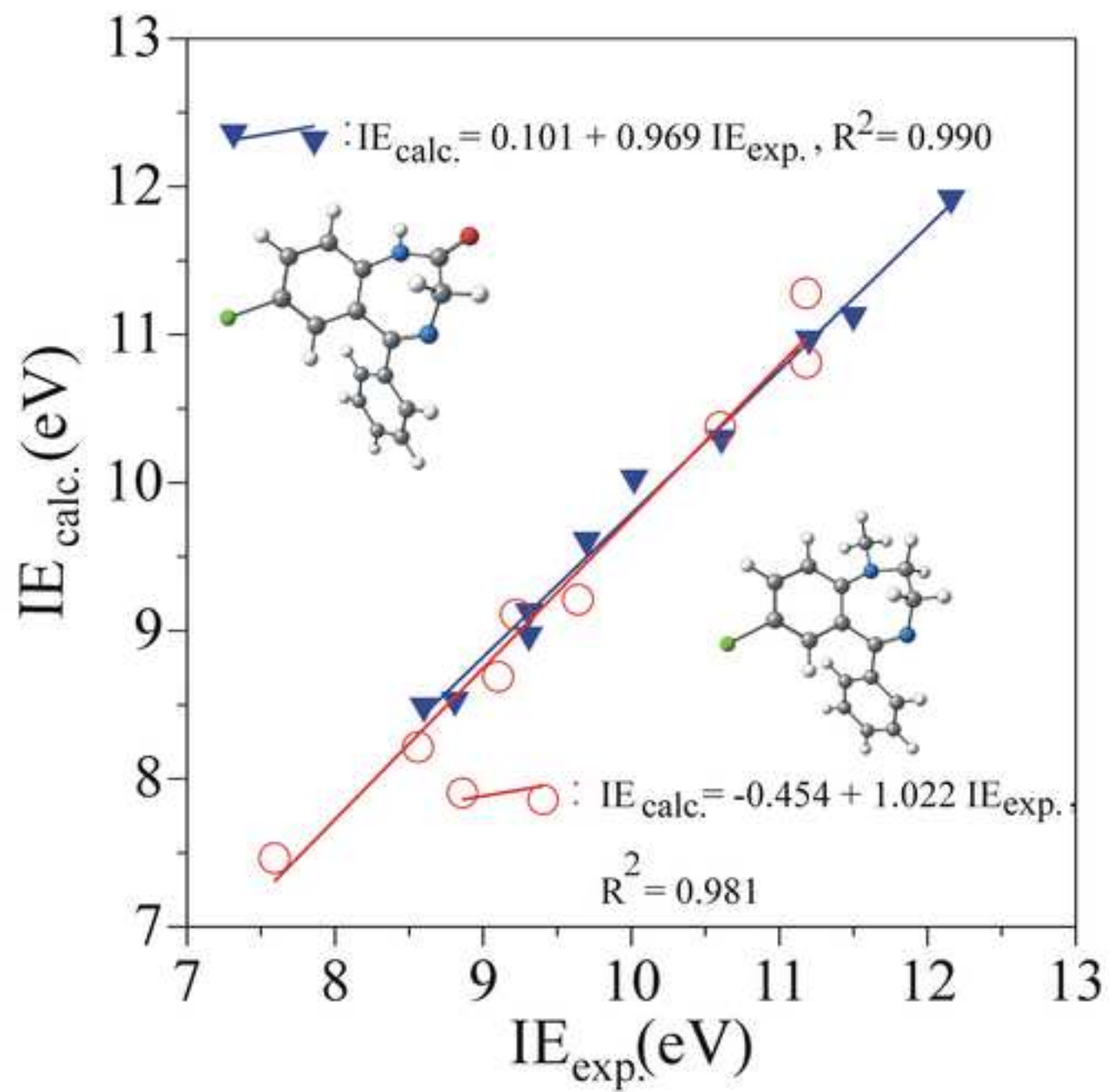


Figure 9
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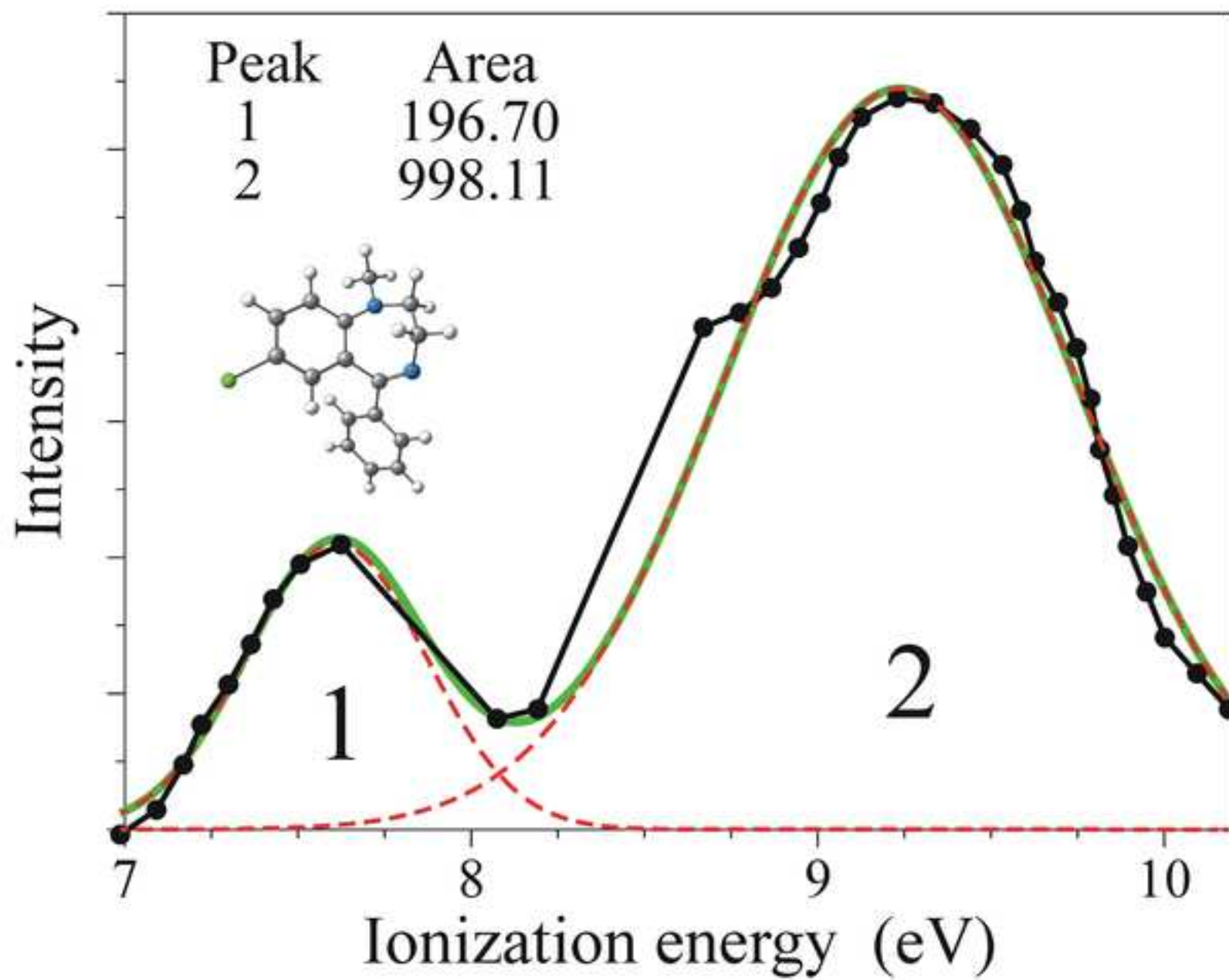
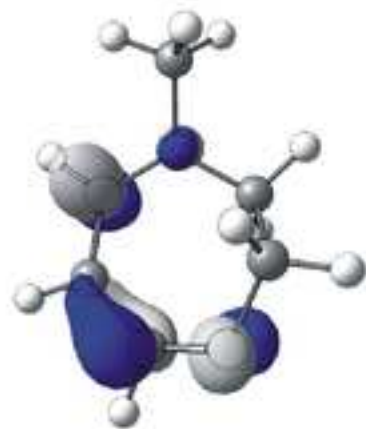


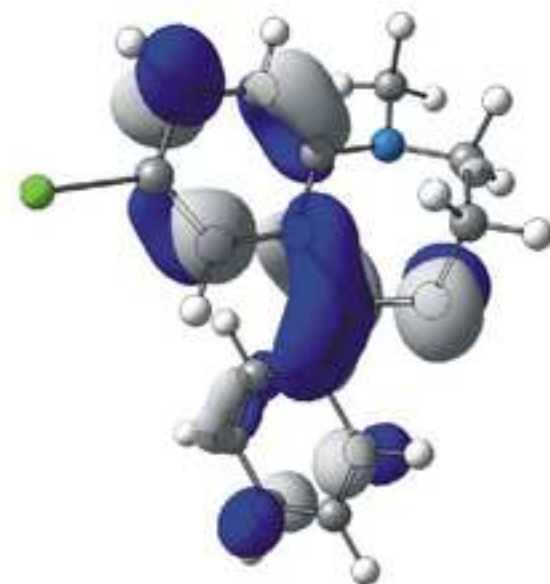
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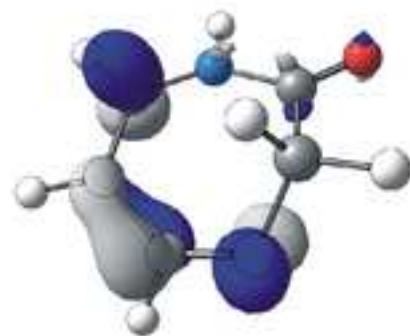
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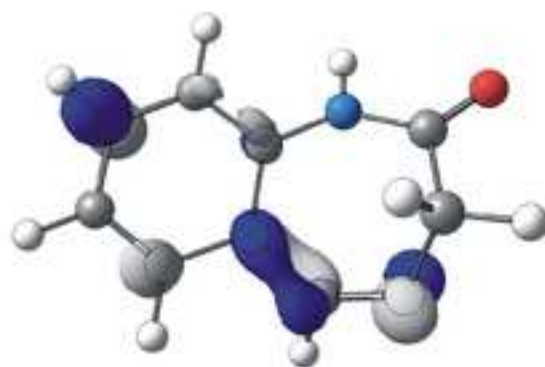
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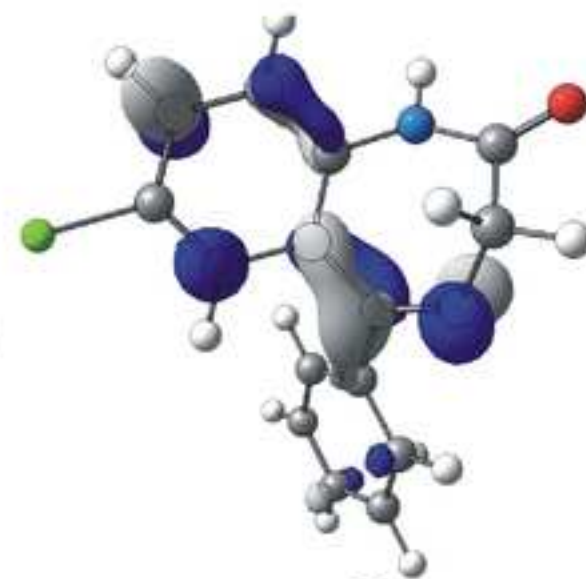
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4



5



6

SUPPLEMENTARY MATERIAL

**Electronic properties of neuroleptics:
ionization energies of benzodiazepines**

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The data here reported are:

Fig. S1	Torsional potential energy curve relative to the benzene ring C rotation for compounds 3 and 6 . B3LYP/6-31G* results
Table S1	Cartesian coordinates of 1
Table S2	Cartesian coordinates of 2
Table S3	Cartesian coordinates of 3
Table S4	Cartesian coordinates of 4
Table S5	Cartesian coordinates of 5
Table S6	Cartesian coordinates of 6

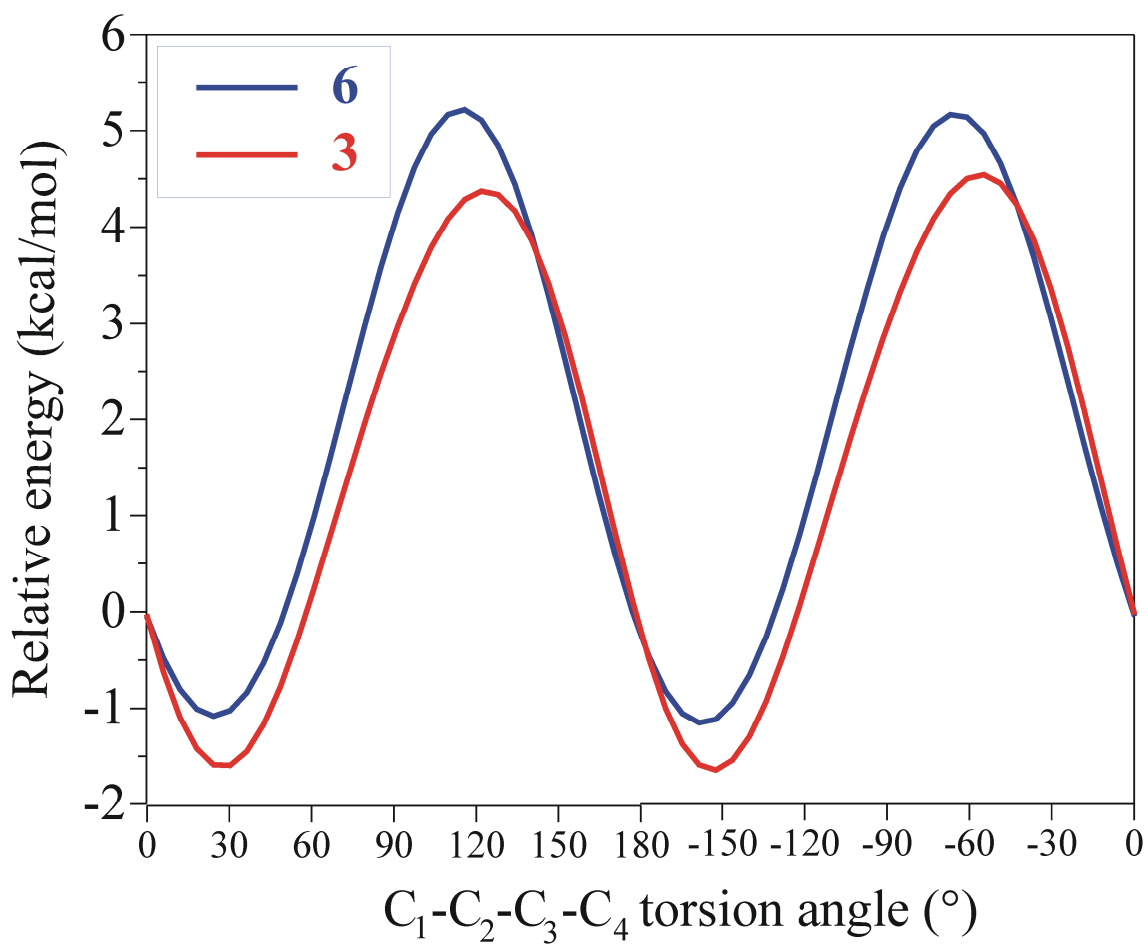
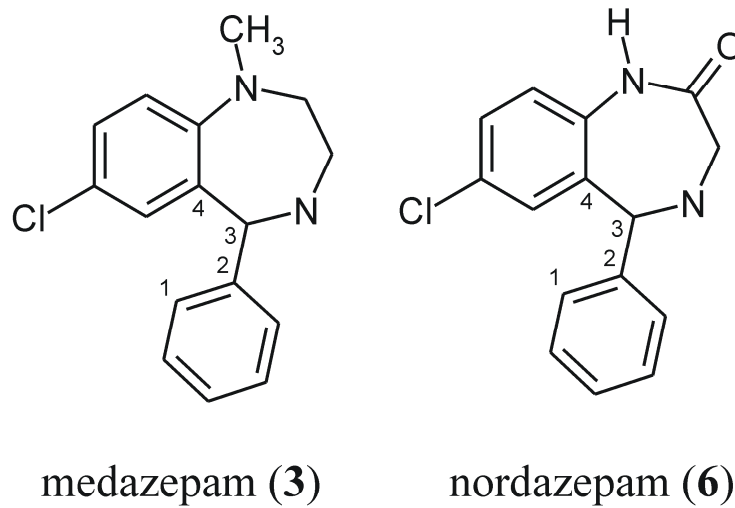


Fig. S1

Table S1
B3LYP/6-31G* Cartesian coordinates (Å) of **1**

N	1.966137000	-0.713838000	-0.112221000
C	-0.513137000	1.292903000	0.006634000
C	0.835390000	1.515175000	-0.007548000
C	1.934067000	0.566775000	0.035841000
C	0.726295000	-1.406771000	-0.385755000
C	-0.432183000	-1.069094000	0.597263000
N	-1.181223000	0.128019000	0.246121000
C	-2.526609000	-0.043813000	-0.279710000
H	-2.526539000	-0.527319000	-1.269700000
H	-3.126028000	-0.655021000	0.403292000
H	-3.007591000	0.933263000	-0.380395000
H	-1.140485000	-1.901581000	0.644055000
H	-0.003027000	-0.940202000	1.597802000
H	0.375593000	-1.192504000	-1.408096000
H	0.922230000	-2.485221000	-0.336435000
H	2.911527000	1.031982000	0.203700000
H	-1.174049000	2.145872000	-0.139912000
H	1.131029000	2.560408000	-0.051956000

Table S2
B3LYP/6-31G* Cartesian coordinates (Å) of 2

N	1.865077000	-1.891510000	-0.211799000
C	-0.360914000	0.508996000	-0.024779000
C	-0.488859000	-0.914528000	-0.001743000
C	0.589953000	-1.923358000	-0.123096000
C	2.632588000	-0.668291000	-0.132731000
C	1.997900000	0.492875000	0.638892000
C	-1.542320000	1.284263000	-0.022952000
H	-1.473100000	2.365307000	-0.025512000
C	-2.802351000	0.698663000	0.016098000
H	-3.682449000	1.336815000	0.021372000
C	-2.937046000	-0.689883000	0.066805000
C	-1.785099000	-1.464307000	0.056314000
H	-1.873036000	-2.548231000	0.072960000
N	0.882256000	1.126245000	-0.059363000
C	0.967507000	2.562735000	-0.263130000
H	0.646047000	3.152833000	0.611913000
H	2.004652000	2.825597000	-0.487729000
H	0.356593000	2.861224000	-1.120593000
H	1.674614000	0.131169000	1.626317000
H	2.761660000	1.256771000	0.813808000
H	0.173483000	-2.936499000	-0.170514000
H	-3.916907000	-1.155980000	0.102259000
H	2.878468000	-0.336227000	-1.150644000
H	3.590490000	-0.918916000	0.346435000

Table S3
B3LYP/6-31G* Cartesian coordinates (Å) of **3**

N	0.794580000	-1.948238000	-1.103965000
C	-1.652100000	-0.740284000	0.316314000
C	-0.513379000	-0.073079000	-0.220135000
C	0.756008000	-0.814913000	-0.498420000
C	-0.466582000	-2.509539000	-1.560367000
C	-1.278086000	-3.091837000	-0.407850000
C	-2.797888000	0.028329000	0.595939000
H	-3.679560000	-0.451566000	1.005656000
C	-2.845892000	1.395969000	0.337088000
H	-3.745217000	1.963411000	0.553093000
C	-1.736653000	2.024222000	-0.222442000
C	-0.579892000	1.299529000	-0.492295000
H	0.287591000	1.803743000	-0.903741000
Cl	-1.789743000	3.747547000	-0.574598000
N	-1.590407000	-2.106400000	0.638867000
C	2.055358000	-0.220224000	-0.061815000
C	2.139750000	0.679181000	1.012971000
C	3.239590000	-0.603311000	-0.715290000
H	1.239500000	0.973444000	1.542757000
H	3.169613000	-1.306641000	-1.538056000
C	3.375194000	1.184982000	1.421130000
C	4.469731000	-0.092694000	-0.311764000
H	3.422979000	1.874623000	2.259634000
H	5.375115000	-0.391764000	-0.833498000
C	4.542537000	0.805043000	0.758242000
H	5.503467000	1.204428000	1.071869000
C	-2.538326000	-2.627696000	1.608411000
H	-3.553847000	-2.778214000	1.199077000
H	-2.176901000	-3.600744000	1.959001000
H	-2.604015000	-1.959057000	2.471052000
H	-2.210909000	-3.521305000	-0.819428000
H	-0.719186000	-3.913425000	0.057642000
H	-1.075272000	-1.763783000	-2.094547000
H	-0.253167000	-3.321046000	-2.264956000

Table S4
B3LYP/6-31G* Cartesian coordinates (Å) of **4**

O	2.433977000	-0.066657000	-0.306542000
N	0.576555000	1.221908000	-0.102366000
N	-0.667373000	-1.562313000	-0.238059000
C	1.263283000	0.008547000	0.011841000
C	0.447124000	-1.135956000	0.604541000
C	-1.666015000	-0.763792000	-0.354209000
C	-1.785329000	0.615947000	0.097052000
C	-0.754823000	1.493445000	0.155618000
H	1.185322000	2.000448000	-0.327085000
H	0.081751000	-0.812948000	1.593249000
H	-2.531918000	-1.160224000	-0.893844000
H	1.135641000	-1.971847000	0.737520000
H	-0.948762000	2.539942000	0.376243000
H	-2.783559000	1.011570000	0.260178000

Table S5
B3LYP/6-31G* Cartesian coordinates (Å) of **5**

O	-3.117235000	-1.272728000	-0.167126000
N	-0.861965000	-1.140062000	-0.337160000
N	-1.559151000	1.799539000	-0.084751000
C	-2.100026000	-0.637760000	0.042292000
C	-2.070118000	0.714097000	0.747602000
C	-0.324641000	1.786218000	-0.415278000
C	2.042381000	1.181076000	-0.034873000
C	3.078974000	0.276008000	0.148766000
C	2.789428000	-1.093177000	0.184485000
C	1.479558000	-1.535242000	0.049489000
C	0.703902000	0.763619000	-0.156883000
C	0.422948000	-0.622859000	-0.119253000
H	-0.918349000	-2.095652000	-0.671436000
H	-1.464022000	0.611362000	1.662281000
H	2.254072000	2.246350000	-0.088997000
H	3.587747000	-1.818220000	0.315423000
H	1.257205000	-2.599325000	0.071909000
H	4.101575000	0.625775000	0.251635000
H	0.031161000	2.664735000	-0.963514000
H	-3.098128000	0.938582000	1.035004000

Table S6
B3LYP/6-31G* Cartesian coordinates (Å) of **6**

N	-0.741219000	2.009970000	-0.808877000
C	1.732155000	0.701967000	0.477415000
C	0.606879000	0.073403000	-0.106046000
C	-0.668591000	0.810945000	-0.347929000
C	0.476434000	2.713902000	-1.172930000
C	1.268110000	3.128091000	0.065719000
C	2.879398000	-0.058252000	0.762771000
H	3.734933000	0.428898000	1.223300000
C	2.945678000	-1.408559000	0.449075000
H	3.839638000	-1.982945000	0.666624000
C	1.850550000	-2.015035000	-0.171642000
C	0.696058000	-1.291459000	-0.435978000
H	-0.153815000	-1.782956000	-0.895186000
Cl	1.934171000	-3.713408000	-0.610032000
N	1.728923000	2.060832000	0.830940000
C	-1.961326000	0.125399000	-0.040876000
C	-2.070865000	-0.840304000	0.972824000
C	-3.116890000	0.492541000	-0.751565000
H	-1.195425000	-1.122330000	1.549282000
H	-3.031057000	1.248821000	-1.524264000
C	-3.303028000	-1.427243000	1.264379000
C	-4.343340000	-0.100291000	-0.465282000
H	-3.371823000	-2.166260000	2.057973000
H	-5.225807000	0.187449000	-1.030430000
C	-4.441047000	-1.063551000	0.543563000
H	-5.398993000	-1.525847000	0.766191000
H	1.131565000	2.101575000	-1.814973000
H	0.217661000	3.629314000	-1.706894000
O	1.498736000	4.277159000	0.387442000
H	2.367358000	2.350014000	1.563945000