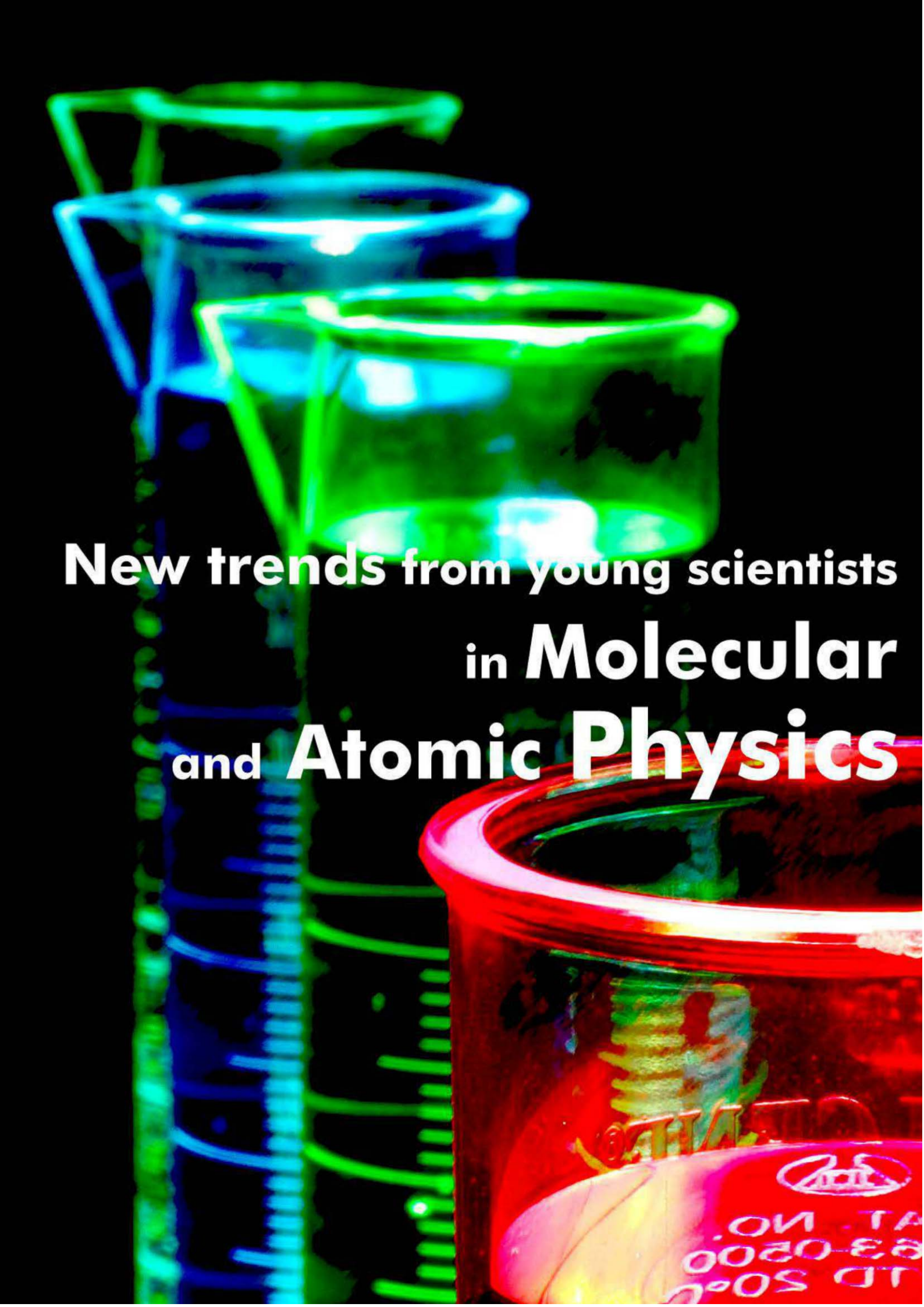

New trends from young scientists in Molecular and Atomic Physics

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Noncovalent Interactions between Cisplatin and Graphene Prototypes

M. Refugio Cuevas, Massimiliano Bartolomei and Marco A. García-Revilla

1. Introduction

Cisplatin (CP) belongs to the most widely used anticancer drugs; it is the basis of a family of derivatives displaying a large anticancer activity, for example carboplatin and oxaliplatin. Nevertheless, CP displays a low bioavailability and for this reason the design of effective ways to reach the biological target is paramount and also very challenging[1]. In recent years, the use of nanomaterials as drug delivery systems has become important[2,3] and among them graphene (G), a two-dimensional material formed by a single layer of repeated hexagonal lattice of six atoms of carbon[4], represents an ideal adsorbing platform. The physicochemical properties of G are related to its ¶-electrons conjugated system, which confers the capability of adsorbing different substances such as anti-cancer drugs, antibodies, peptides, DNA, RNA, genes[5-8], etc. Recent reports have discussed the favourable physisorption of CP on carbon nanomaterials, like carbon nanotubes[9] and nanohorns[10]. Also, the study of the non-covalent interactions of G and Graphene Oxides with adsorbed molecules holding a ¶-character, has been recently addressed[11].

In the present contribution Pyrene (P) was selected as the minimum prototype of G and its non-covalent interaction with CP was characterized by using a variety of electronic structure methodologies.

2. Results

The Coupled Second-order Moller-Plesset Perturbation Theory (MP2C)[12] was used as the reference method to obtain benchmark values of the interaction energies: the

used basis sets were the aug-cc-pVTZ-PP[13] for Pt and the aug-cc-pVTZ[14] for the rest of atoms. MP2C results were compared with standard MP2 interaction energies as well as with DFT estimations. For the latter the PBE[15], B3LYP[16] and M062X[17] functionals were exploited together with the basis set 6-311+(2d,2p)[18] for all atoms except Pt, for which the Stuttgart-Dresden pseudopotential[19] was used. In the case of the PBE and B3LYP functionals, the latest dispersion correction ((D3)-BJ)[22] contribution of Grimme, which includes the "damped dispersion" approach of Johnson-Becke (BJ)[23], was also taken into account. For all cases, rigid configurations of both monomers were used for the calculation of the interaction corresponding to their relative approach. All computed interaction energies were corrected for the Basis Set Superposition Error (BSSE)[20] by using the Counterpoise method[21].

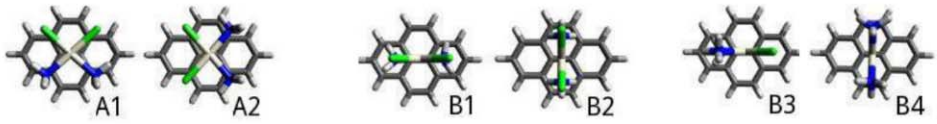

Figure 1. Main limiting configurations of the pyrene-cisplatin complex.

The six configurations of the P-CP complex that were selected are presented in Fig. 1. Moreover, the corresponding MP2C energy profiles are displayed in Fig. 2 as a function of the intermolecular distance joining the mass-centre of pyrene and the Pt atom and ranging from 8 to 2 Å. In the first panel of Fig. 2, almost equivalent energy profiles for the A1 and A2 configurations can be observed: the minimum of both configurations is located at about 3.5Å, but A2 displays a slightly larger interaction energy of about 10.3 meV. In the second panel, the profiles of the B1 and B2 configurations are compared: the minimum of both configurations is found at larger distances and located around 4.75Å; it can be also observed that the B1 well is deeper than that of B2 of about 38.4 meV. The results for the B3 and B4 perpendicular configurations are presented in the third and fourth panels, respectively: the minimum

of their energy profiles is located at even larger distances (around 5Å) being the corresponding wells quite shallower (-279.1 meV for B3 and -111.7 meV for B4) with respect to those for the other configurations.

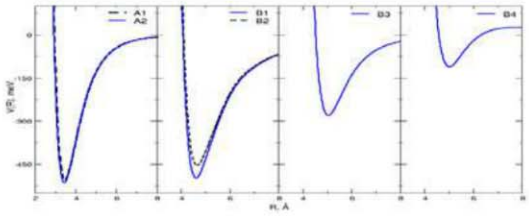

Figura 2. Interaction energies at the MP2C level for the A1, A2, B1 to B4 configurations of the pyrene-cisplatin complex.

Globally, the A2 (-511.73 meV) and B1 (-487.84) configurations are those showing the largest interaction energies, being A2 the more attractive profile. In order to make a simple comparison of methods, we have just selected the A2, B1, B3 and B4 configurations, and an analysis of the reliability of the related interaction energies at the MP2 and DFT and levels was performed, Figs. 3 and 4.

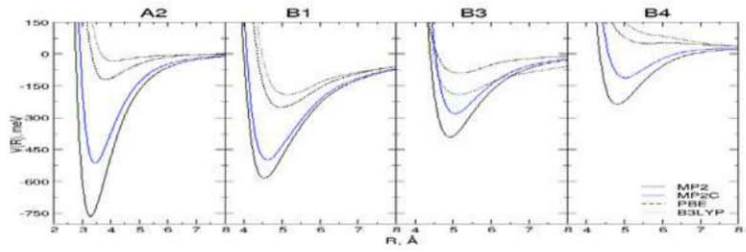

Figure 3. Interaction energies for the A2, B1, B3 and B4 configurations at the MP2C, MP2 and DFT levels.

In Fig. 3 the B3LYP and PBE results underestimate the reference MP2C interaction energies for all considered configurations, while MP2 energy overestimates such energy. The underestimation provided by the DFT results can be explained by considering that in general DFT fail to properly describe systems where the London

dispersion contribution to the interaction energy is relevant. To correct this deficiency, we also include the (D3)-BJ dispersion contribution to the PBE and B3LYP results. Such results are reported in Fig. 4 together with those carried out with the M062X functional, which indeed is in general a good option to describe van der Waals systems. It is clearly shown that the inclusion of the dispersion correction lead to a better agreement with the reference MP2C profiles. The B3LYP (D3)-BJ approach now provides an overestimation of the reference profiles, being such overestimation more significant for the A2 configuration. The M062X results are in general closer to the MP2C references in the well region; however, it must be noticed that the agreement get worse in the dissociation limit, where the M062X interaction energies draws away from the MP2C curve, especially for the perpendicular configurations.

The PBE (D3)-BJ results are indeed those providing the best agreement with the MP2C reference in the whole range of intermolecular distances for all selected configurations, being the energy difference around the minimum of 2.0%, 3.0%, 0.03% and 0.11% for A2, B1, B3 and B4, respectively. On top of that, the PBE (D3)-BJ approach has the advantage of being the most affordable method, among those considered, from the computational cost point of view.

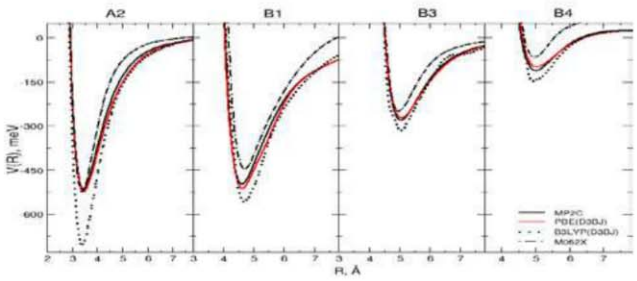

Figure 4. Interaction energies for the A2, B1, B3 and B4 configurations at the MP2C and DFT levels.

4. Conclusions

Accurate interaction energy profiles related to the main limiting configurations of the P-CP complex were obtained at the MP2C level of theory. The A1 and A2 parallel approaches provide the most attractive profiles with favourable binding energies (around 500 meV) suggesting that the CP physisorption on G sheets is in principle possible. Interestingly, the minimum for the B1 perpendicular configuration is close in energy but displaced at larger intermolecular distances. This behaviour suggests that, even if the various interaction contributions are likely different for the parallel and perpendicular approaches, their combined effect leads to similar total interaction energies.

The reference MP2C results also served to test and validate several functionals within the DFT ansatz: the PBE(D3)-BJ method was that providing the best agreement together with an affordable computational and it is recommended for the description of the non-covalent interactions in G-CP complexes.

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