

Clay promoted oligomerisation of benzylic alcohols via EAS pathway: a theoretical study

R. Salcedo^{a,*}, M. Salmón^b, A. Cabrera^b, L.E. Sansores^a

^aInstituto de Investigaciones en Materiales, UNAM, Circuito Exterior s/n, C.U., P.O. Box 70-360, Coyoacán 04510 D.F., Mexico

^bInstituto de Química, UNAM, Circuito Exterior, C.U., Coyoacán 04510 D.F., Mexico

Received 12 May 1999; accepted 31 May 1999

Abstract

The selectivity of trimers of benzylic alcohols in order to join a fourth aromatic ring is a known fact but there are few arguments to explain this phenomenon from experimental evidences. Here, we present some theoretical results at GAUSSIAN 94 and MOPAC level that may help to give a reasonable explanation to this feature. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Clay promoted benzylic alcohols; Inductive effect; Wheland intermediates

1. Introduction

Bentonitic clay promotes cyclooligomerization of [3,4,5]-trimethoxybenzyl alcohol, yielding tricycloveratrylene **1** (Fig. 1) and other interesting linear oligomers [1]. An electrophilic aromatic substitution pathway has been suggested for this reaction [2,3]. However, there are doubts concerning this reaction because of the apparent absence of some possible and expected compounds.

Compounds **5** and **6** (see Fig. 1) would be the products of an electrophilic aromatic substitution carried out on **4**. However, only **5** is found in an appreciable quantity. Compound **6** has neither been isolated, nor detected in the same preparation environment. This is a strange aspect, because it is possible to consider compound **5** as a more stable isomer, but

the presence of **6** would be expected, however it would be considered that this last compound would be only present in traces in the subproduct set.

It has been suggested [1] that this strong selectivity could be due to some interaction between the oxygen atom of the ether group and the catalyst, or may be that there is some effect on the pathway of the reaction that precludes the formation of isomer **6**.

There are many features to consider when an aromatic electrophilic substitution reaction is involved [4,5]; inductive effects, presence of charge densities on the ring, formation of Wheland intermediates, etc. Furthermore, the phenomena might be controlled in a thermodynamic or a kinetic fashion.

In view of these arguments, ab initio calculations were carried out in order to look for an explanation of the peculiar behaviour of these ethers with respect to the ring reactions. Therefore, molecules **1–6** were modelled (see Fig. 1) in the ground state, as well as the corresponding Wheland intermediates and transition states (**7**, **8** and **9**, respectively) (Fig. 2).

* Corresponding author. Fax: + 52-5-616-1201.

E-mail address: salcedo@servidor.unam.mx (R. Salcedo).

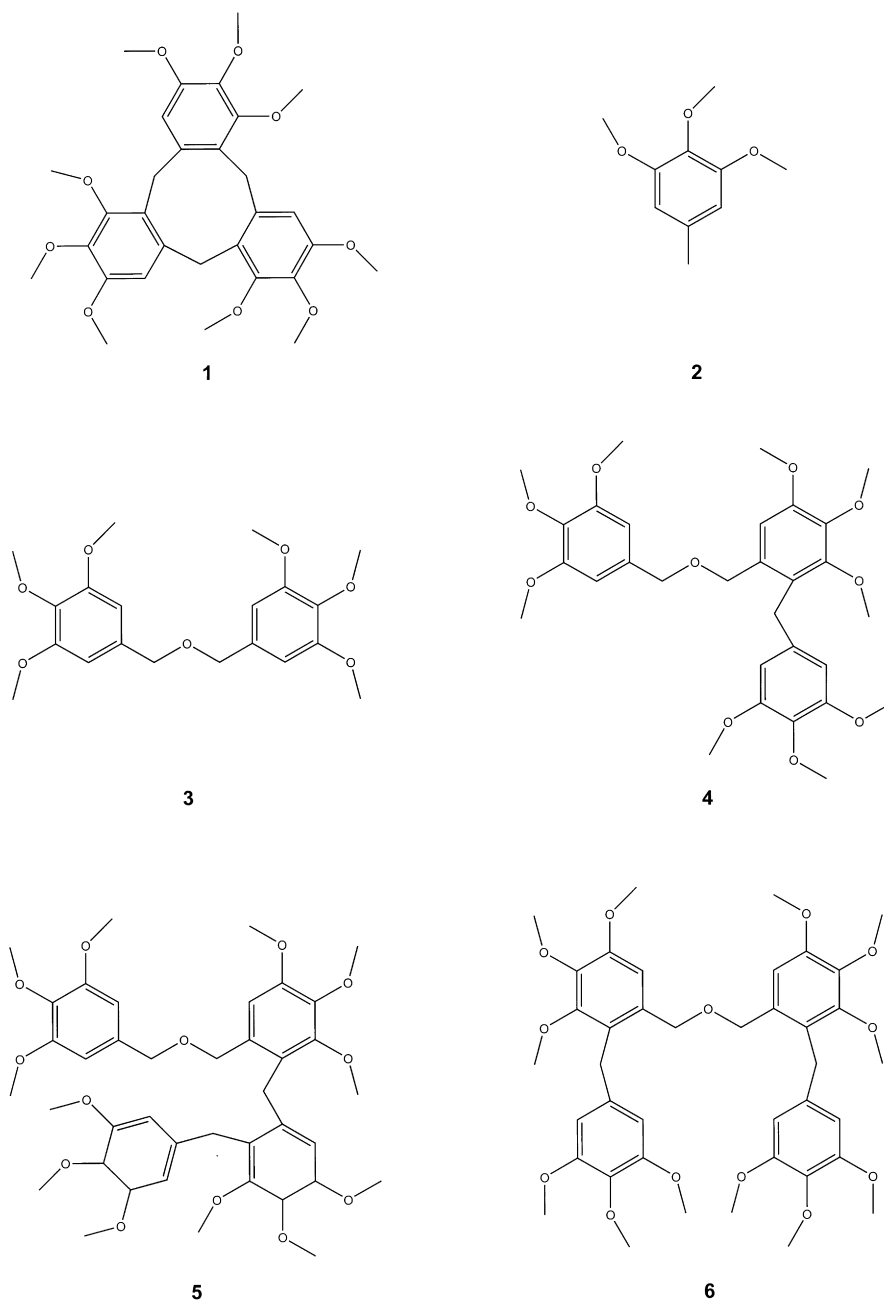


Fig. 1. The compounds under study.

2. Computational methods

All calculations were carried out at the HF/3-21G level using the GAUSSIAN 94 code [6] with total opti-

misation of geometry including the Wheland intermediates of each isomer. The magnetic susceptibilities were calculated using the continuous set of the gauge transformation method [7,8]. Initial

geometries were obtained by the Universal 1.01 molecular mechanics method [9] included in the CERIUSt² package¹. The calculations of the transition states were carried out using the AM1 program [10] included in the Mopac package [11] starting from the optimised geometries obtained by GAUSSIAN 94.

3. Results and discussion

It has been reported that an electrophilic aromatic substitution is possible for compounds such as **4**, but this reaction can only happen in one of the aromatic rings, and not in both [3], and indeed compound **6** does exist. Several propositions based on our theoretical results can be made to explain these facts. The first one arises from the analysis of the frontier orbitals of the calculated molecules.

The shape of the frontier orbitals can be seen in Fig. 3. Molecule **3** has some degree of symmetry and can even be considered to belong to the C_{2v} point group, if the lateral ether groups are frozen in fixed positions as shown in the figure. Then the HOMO of this molecule belongs to an A₂ irreducible representation of these conditions. It is possible to consider that electrophilic aromatic reactions could occur in both rings of the molecule, however this is not possible, as we will see from the following. The symmetrical situation is broken when molecule **4** is formed from **3** and **2**, and therefore the HOMO is a function, totally concentrated, on the terminal ring of the molecule. The same ring was substituted in the first electrophilic reaction. However, at the same time the other terminal ring gives no participation to the HOMO function; under these conditions it is very difficult for it to receive another substituent. A similar calculation for the four ring molecules **5** and **6**, indicates that they present similar behaviour in that all of the HOMO function is concentrated on one of the terminal rings with little participation from its neighbour.

In Fig. 3, the functions that correspond to the LUMOs are also shown, the behaviour of **3** is again that of a symmetrical species, but now in the case of **4** the function is concentrated on the central ring as in

the case of **5**. This effect is interesting but not relevant for an electrophilic attack.

One explanation for the initially mentioned unusual behaviour is related to the oxygen atom that joins both units as a bridge in molecule **3**. Mulliken analysis shows that this atom has a large charge of -0.72 in molecule **3** and -0.73 in molecule **4**. Thus, this is an electronegative centre as can be seen in the total electron density maps shown in Fig. 4. In this sense, this electronegative centre can be considered as an electronic withdrawal group, and therefore is a substituent that deactivates the ring.

In this way, the process can be envisioned in a different sense; molecule **3** is symmetrical and can receive a new ring by the electrophilic aromatic substitution, it has a deactivant group but the reaction can be achieved using a catalyst, and in this way it is possible to prepare compound **4**. In order to prepare **5** and **6**, the reaction can be carried out at this point, but now there is a competition between the deactivant ring joined to the original ring, and the new ring that does not have a similar oxygen atom but a methylene group joined to another aromatic ring. Thus here, this is a more activating group, which controls the orientation yielding compound **5**. This is a rationalisation taking into account only the inductive effects.

From this model, it is reasonable to assume that small quantities of **6** should be formed. However, the experimental work has demonstrated [3] that it is very difficult to find this substance, therefore we proceed to analyse the mechanism of the formation of the Wheland intermediates for both cases and the corresponding transition states, and the results are as follows.

First, we calculate the structure corresponding to both Wheland intermediates (Fig. 2). In this figure, **7** corresponds to the Wheland intermediates of **5** and **8** to the same intermediate for **6**.

As was established, the pathway for an aromatic electrophilic substitution is a second-order process. The first step is characterised as a slow step with the formation of the Wheland intermediate. The second one, the fast step, consists of the elimination of the leaving group and regeneration of the aromaticity. Thus, the most significant point in the reaction coordinate is the curve for the first step i.e. the formation of the Wheland intermediate and the corresponding activated complex or transition state.

¹ CERIUSt²™ was developed by Molecular Simulations Incorporated.

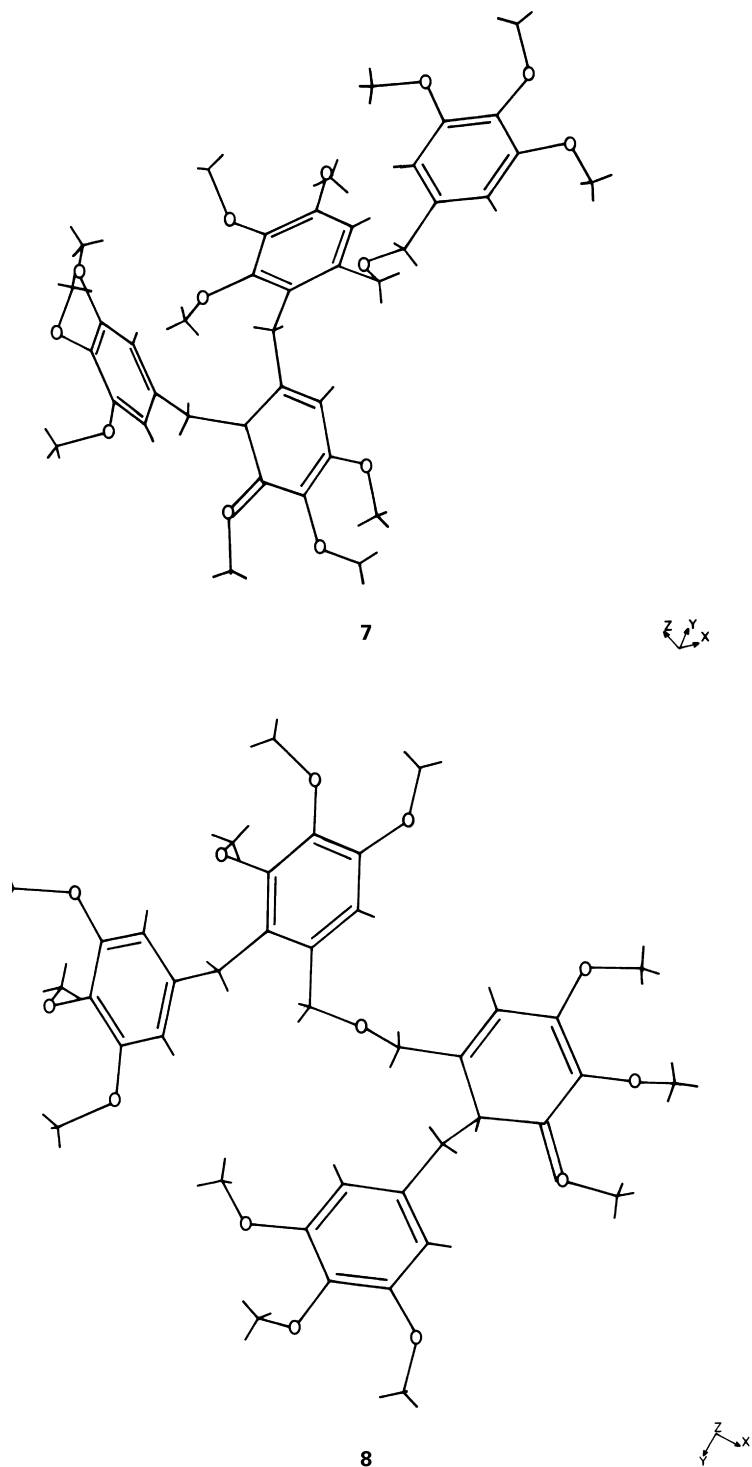


Fig. 2. Wheland intermediates and transition states.

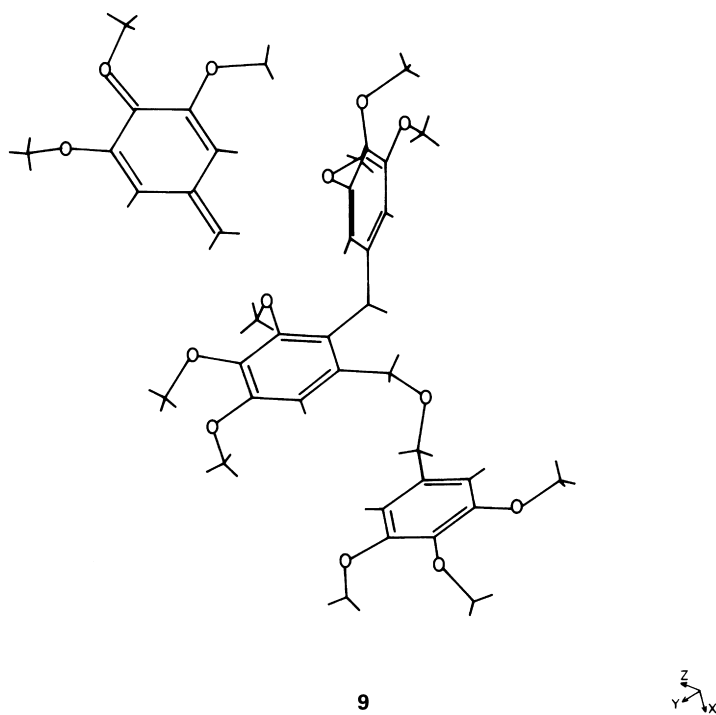


Fig. 2. (continued)

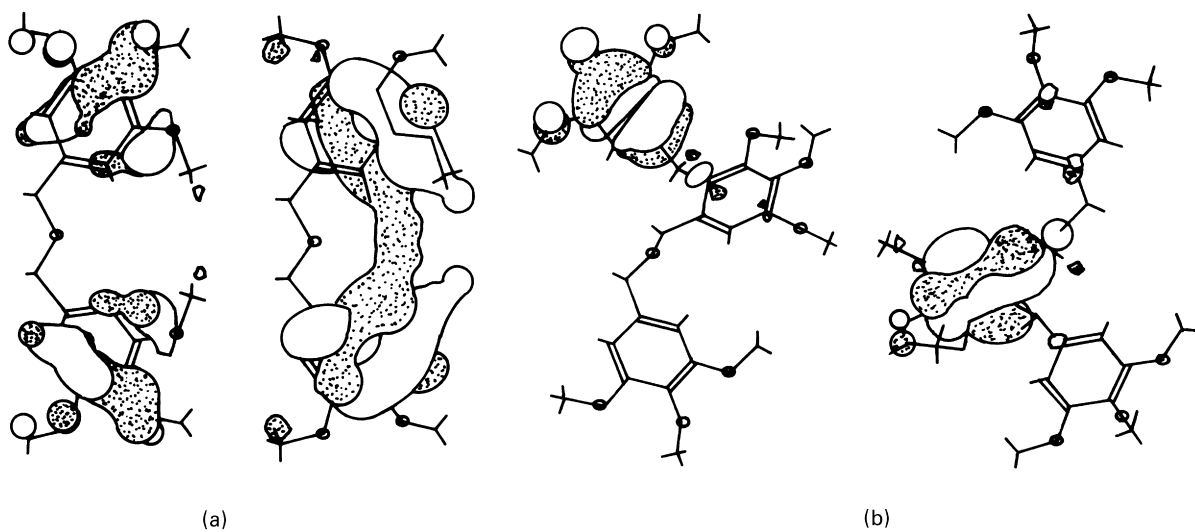


Fig. 3. (a) HOMO and LUMO of molecule 3. (b) HOMO and LUMO of molecule 4.

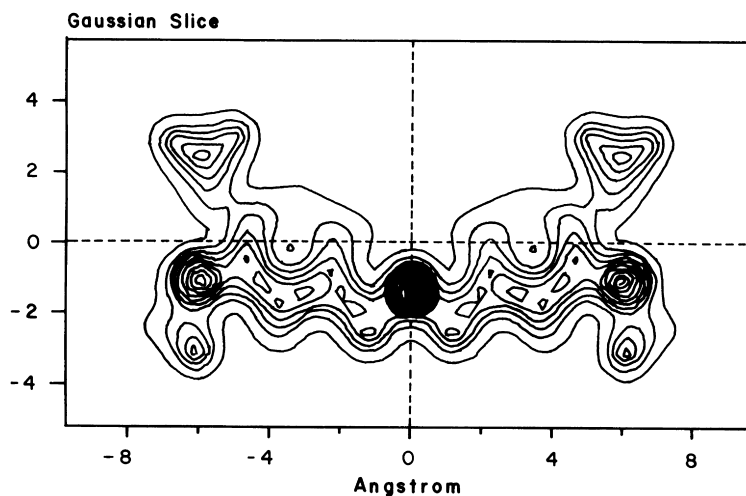


Fig. 4. Total electron density map for molecule 3.

In Fig. 5, we can analyse the shape of the curve for the process and the corresponding energy values for reactivities, transition state and the intermediate. We have found that the lowest energy condition for the transition state **9** is where the entering group is separate from the receiving molecule as is shown in Fig. 2. The interesting feature is that there is an energy difference between **7** and **8** of 1.6 kcal/mol, favouring the formation of **7** (and consequently the route for the formation of **5**). Considering the Boltzmann distribu-

tion for both intermediates, we obtain 6.7% for **6** and 93.3% for **5**. Later, experimentally it would be difficult to detect **6**.

From the shape of molecule **5** as shown in Fig. 1 it can be observed that the molecule has a tendency to fold its chain, this being a consequence of the presence of aliphatic groups and it is expected that it can take a ladder or spiral conformation if the chain grows. This idea is in agreement with the X-ray analysis [12].

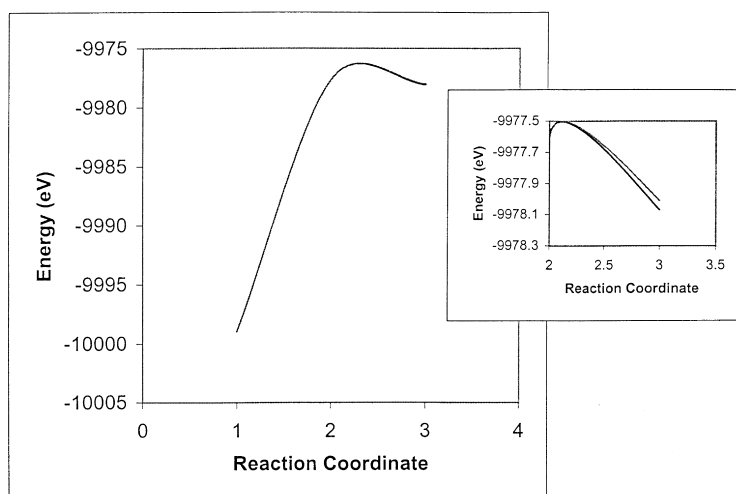


Fig. 5. Reaction co-ordinate for the formation of Wheland intermediates.

Table 1
Magnetic susceptibilities

Compound	χ_m (ppm)	Δ
2	-73.9216	0
3	-174.8311	-3.78
4	-251.7082	-26.908
5	-322.8881	-27.2016
6	-319.4801	-23.7936

The isotropic magnetic susceptibility values of compounds **2–6** are shown in Table 1, the high negative values suggest the aromatic character is not decreased, and therefore there is no possibility of other resonant forms but for aromatics. For example, no quinoid structures are expected which is a consequence of the rupture of delocalisation between two contiguous rings due to the presence of aliphatic bridges and in one case the ether group. The value of the diamagnetic exaltation (Δ) was computed taking as a reference the magnetic susceptibility of the quinoid form of **2** that is considered as not aromatic.

This result is very interesting because **5** displays more aromatic behaviour than **6** and this feature accounts for the larger thermodynamic stabilisation for **5**; another argument in favour of the presence of this isomer.

Table 2 shows the dipole moment values obtained for molecules **4–8**. These results can be used to predict some of the reactive behaviour of the involved molecules.

Obviously the corresponding values of the Wheland intermediates are very high because they are charged and unstable molecules. Furthermore, these values suggest that the charge interaction inside this molecule is very strong and should produce vibrations that lead to the stabilisation of the molecule and inducing the formation of the products. However, the most interesting feature to point out in the table is the larger value of the neutral molecule **5** and a moderately large one of **4**. Furthermore, the resultant vector in the case of **4** is directed towards the solitary ring joined to the ether group, whereas the corresponding vector for **5** is directed towards the set of three rings on the other side of the ether group which means that the electronegative centres change from **4** to **5**, with the negative one preferred to be in the electrophilic

Table 2
Dipole moments

Molecule	μ
4	3.436
5	6.905
6	1.690
7	19.670
8	20.567

attack zone, as happens in **4** but with completely inverse behaviour for **5**. The dipole moment of **6** is almost negligible and is localised perpendicularly to the oxygen atom of the ether group with a direction towards the outside of the molecule.

The result indicated above for the dipole moment of molecule **4** reinforces the concept that an electrophilic group attacks in a region far from the ring joined to the ether group, and this is in good agreement with the experimental results.

4. Conclusion

The reaction of benzylic alcohols via electrophilic aromatic substitution can take several pathways when the molecule has two or more aromatic rings. However, in the case of the ether compound **4** with three aromatic rings, the reaction to join a fourth ring is very selective, yielding a main compound (molecule **5**) up to 90%. The explanation for this behaviour is found in our theoretical study by two routes. First, the inductive effect caused by the aromatic ring joined to an oxygen atom from an ether group and the corresponding aromatic ring joined to a methylene group is different and the former is a better activant group. Second, there is a significant energy difference between the Wheland intermediates that favour the formation of the asymmetric compound **5**.

Acknowledgements

We thank the Dirección General de Asuntos del Personal Académico, UNAM (grant IN101597) for financial support. We would like to acknowledge the Dirección General de Computo Académico, UNAM for providing computer time and Dr S. Muhl for useful discussions.

References

- [1] M. Salmón, N. Zavala, M. Martínez, R. Miranda, R. Cruz-Almanza, J. Cárdenas, R. Gaviño, A. Cabrera, *Tetrahedron Lett.* 35 (1994) 5977.
- [2] M. Salmón, N. Zavala, J. Cárdenas, R. Gaviño, R. Miranda, M. Martínez, *J. Mol. Catal. A Chemical* 104 (1995) L127.
- [3] R. Cruz-Almanza, I. Shiba-Matzumoto, A. Fuentes, M. Martínez, A. Cabrera, J. Cárdenas, M. Salmón, *J. Mol. Catal. A Chemical* 126 (1997) 161.
- [4] H. Perkampus, E. Baumgarten, *Angew. Chem. Int. Ed. Engl.* 3 (1964) 776.
- [5] H. Perkampus, *Adv. Phys. Org. Chem.* 4 (1966) 195.
- [6] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.A. Robb, J.R. Cheeseman, T.A. Keith, G.A. Petersson, J.A. Montgomery, K. Raghavachari, M.A. Al-Laham, V.G. Zakrzewski, J.V. Ortiz, J.B. Foresman, J. Cioslowski, B.B. Stefanov, A. Nanayakkara, M. Challacombe, C.Y. Peng, P.Y. Ayala, W. Chen, M.W. Wong, J.L. Andres, E.S. Replogl, R. Gomperts, R.L. Martin, D.J. Fox, J.S. Binkley, D.J. Defrees, J. Baker, J.P. Stewart, M. Head-Gordon, C. Gonzalez, J.A. People, GAUSSIAN 94 (Revision B.1), Gaussian Inc., Pittsburgh, PA, 1995.
- [7] T.A. Keith, R.F.W. Bader, *Chem. Phys. Lett.* 210 (1993) 223.
- [8] T.A. Keith, R.F.W. Bader, *Chem. Phys. Lett.* 194 (1992) 1.
- [9] A.K. Rappé, K. Casewit, K.S. Colwell, W.A. Goddard, W.M. Skiff, *J. Am. Chem. Soc.* 114 (1992) 10 024.
- [10] M.J.S. Dewar, E.G. Zoebisch, E.F. Healy, J.J.P. Stewart, *J. Am. Chem. Soc.* 104 (1985) 3902.
- [11] J.J.P. Stewart, *J. Comput. Aided Mol. Design* 4 (1990) 1.
- [12] M. Martínez, unpublished results.