Pergamon

Tetrahedron 55 (1999) 14931-14940

TETRAHEDRON

Complexation of Fullerenes by Calix[n]arenes: Molecular Dynamic Simulations and *Benesi-Hildebrand* Equilibrium Constants[1]

Ingo Schlachter[a)] [†], Udo Höweler[a)], Waldemar Iwanek[b)] Mariusz Urbaniak[b)] and Jochen Mattay[c)] *[††]

a) Organisch-Chemisches Institut, Universität Münster, Corrensstr. 40,
D-48149 Münster, Germany
b) Institute of Chemistry, Pedagogical University, Checinska 5, Kielce 25-369, Poland
Kielce 25-369, Poland
c) Organische Chemie I, Fakultät für Chemie, Unversität Bielefeld, Postfach 10 01 31
D-33501 Bielefeld, Germany

Received 2 April 1999; revised 26 October 1999; accepted 27 October 1999

Abstract: MD simulations using a combination of AM1 and AMBER are performed to elucidate the origin of complexation between fullerenes and calix[n]arenes (n = 4,6,8). Only calix[6]arenes and calix[8]arenes are suitable for complex formation. By introducing benzyl substitutents on the upper rim of the calixarenes the interaction energy between host and guest is even improved. Analysis of the data also reveals a strong stabilization by t-butyl or benzyl substitutents beside π-π interactions between the arene units of the calixarene and fullerenes. The calculated data perfectly correlate with the experimentally observed equilibrium constants.

Key words: Fullerene, Calix[n]arene, MD Simulations, Complexation, Benesi-Hildebrand

INTRODUCTION

Only five years after its discovery by Kroto and Smalley[2] an international group headed by Krätschmer and Huffman[3] succeeded in developing an extraordinary simple procedure to prepare fullerenes on a large scale. From the beginning chemists were fascinated not only by the unusual geometry of fullerenes but especially by their reactivity, which is mainly governed by the olefin-type double bonds and by the strain energy of ca. 8 kcal/mol per carbon.[4] Beside modifications of fullerenes from the outside (exohedral functionalizations)[4,5], from the inside (endohedrals)[4,6] and within the carbon wall (heterofullerenes)[7,8] the extraordinary spheric structure has often attracted supramolecular chemists searching for host molecules suitable to form host-guest complexes with fullerenes. These host molecules must be characterized by cavities such as γ-cyclodextrine[9,10] or calixarenes.[9,11-13]

[†] New address: Goldschmidt AG, Goldschmidt-Str. 100, D-45127 Essen, Germany

[††] E-mail: mattay@uni-bielefeld.de; Fax: +49-521-106-6417

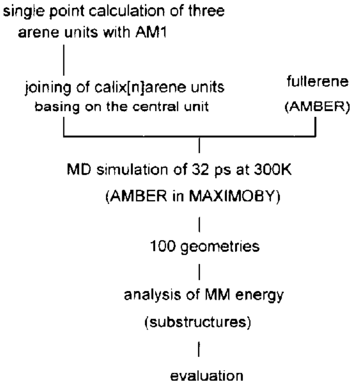
0040-4020/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0040-4020(99)00967-9

Especially the bowl-shaped calix[n]arene molecules are promising candidates for controlled complex formation because they are easily accessible in various sizes (generally n = 4, 6, 8 ; for n = 5 cf. Ref. 14) and due to their versatile modifications.[15] Depending on the monomer, these macrocycles are devided into two types, the Gutsche-type resulting from p-alkyl phenols (calix[n]arene) and the resorc[4]arene-type yielding from resorcinol.[15,16]

In case of calix[4]arene the number of conformations is quite limited. Reinhoudt *et al.* determined in their investigation with the AMBER[17] force field the 1,2 alternate conformation to be energetically preferred.[18] They showed that the stability of a conformation depends of the subtituent's number and position at the phenolic oxygen. It is predominantly controlled by the Coulomb interaction of intramolecular hydrogen bonds. Among the other conformations as 1,3 alternate and partial cone (paco) is the cone the next stable one. Since we focus on the calculation of complexes of calixarenes with fullerenes, we considered only the latter conformation.

Our goal was to calculate complexes between fullerenes (C_{60}/C_{70}) and *p*-^{t}butylcalix[n]arenes (n=4,6,8) with MM methods in order to scale their relative stabilities.[1] This knowledge may be used for designing specific host molecules for selective host-guest complex formation. Since the calculation does not refer to only one molecule but to a complex of two compounds, the optimization of a single geometry cannot account for the dynamic of the system and does not provide sufficient data. Therefore only a molecular dynamic (MD) simulation provides a satisfying solution.

Method of Calculation



Scheme 1: Procedure for the QC/MM Calculation

In a study of calix[4]arenes by Karplus *et al.*, AMBER[17] proved to be a suitable force field to determine the pathways for conformational interconversion of calix[4]arenes.[19] With the exception of the phenyl atoms as 2C (MOBY code symbol) and 3C instead of CT, we used the same center types in our calculations. Since we want to examine host-guest interactions, the choice of the center types is not a sensitive point.

The following combined AM1/MM calculations are performed with MAXIMOBY 3.3[20] running on an IBM-RS6000-32H workstation. Scheme 1 shows the procedure. Prior to the simulation, a "conjugate gradient" optimization (5000 steps) of a calixarene was performed while the fullerene was kept fixed in space. During the heating period, the temperature is raised by 10K per interval until 300K are attained. Now all atoms are allowed to move according to the forces exerted by all atoms. Each time step takes 1fs. Cut-offs of 10Å apply for the nonbonding interactions with a switching function starting at 9Å and a distance dependent dielectric constant is chosen. After an equilibration period of 300 time steps, the simulation itself is started. It runs for 32000 time steps at 300K; the temperature is adjusted every 100th cycle. During the time of the simulation, every 320th geometry is written to disk for later analysis (yields 100 geometries).

RESULTS AND DISCUSSION

The equilibrium constants of complex formation were determined by means of UV/Vis absorption techniques using the *Benesi-Hildebrand* evaluation method.[21] In Fig. 1 a typical example of the changes in the absorption spectrum of C_{60} by addition of p-^{t}butyl-calix[6]arene is shown. Following eq. 1 the complex constants were determined from the changes of the absorption in dependence on the concentration of added calix[n]arene (Fig. 2).

$$C_{C60} \cdot b/(A_0 - A) = 1/(K_{\text{Complex}} \cdot \Delta\varepsilon) \cdot 1/C\ \text{p-}^{t}\text{butylcalix[6]arene}) + 1/\Delta\varepsilon \qquad (1)$$

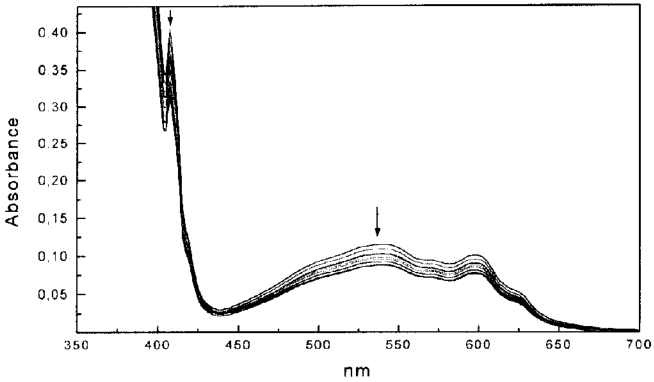


Fig. 1: Changes in the UV/Vis absorption spectrum of C_{60} in toluene solution resulting from addition of the p-^{t}butylcalix[6]arene. Concentration of C_{60} is $2.9{\cdot}10^{-5}$ M, concentration of p-^{t}butylcalix[6]arene varies from $2.8{\cdot}10^{-4}$ to $1.2{\cdot}10^{-3}$ M.

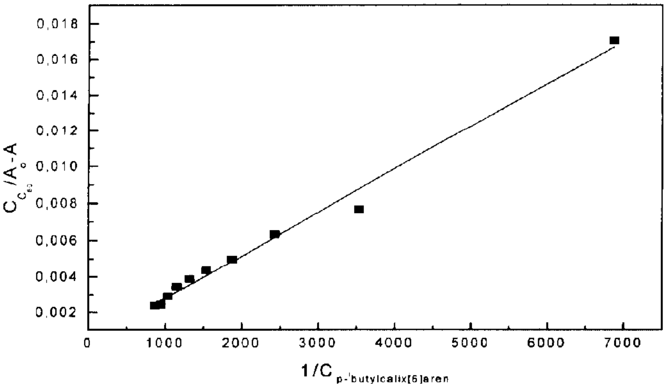


Fig. 2: Changes of UV/Vis absorbance of C_{60} versus concentration of p-^{t}butylcalix[6]arene according to the modified Benesi-Hildebrand equation 1.

Table 1 summarizes the results of both the experiments and the calculations. The experimentally determined complex constants are compared to the interaction energies [ΔE(interaction) = E(calix/fullerene) - E(calix)]. For a comparison of the results for C_{60} and C_{70}, the average interaction energy per carbon atom is given. The last column shows a detailed description of the interaction energy. "Arene" indicates the central phenyl unit inclusive hydrogen atoms whereas "rest" corresponds to the ^{t}butyl, the OH group, and methylene bridges.

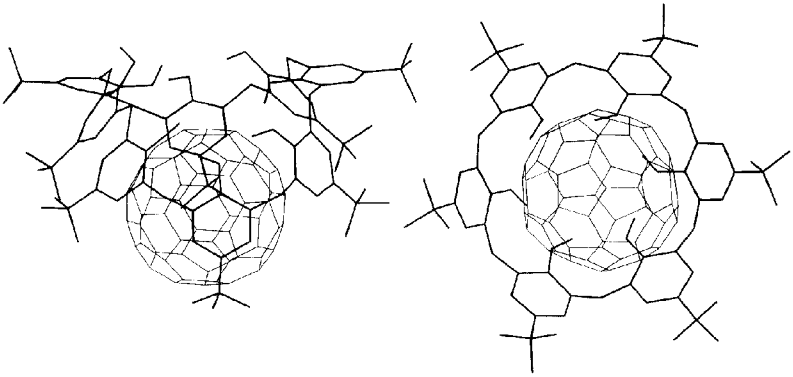
Table 1: Comparison of complex constants with calculated interaction energies

Complex of fullerene and p-^{t}butylcalix[n]arene	Complex constant $^{a)}$ [l/mol]	Interaction energy ΔE [kcal/mol]	Interaction energy per carbon atom [kcal/mol]	per cent distribution arene/rest $^{b)}$
C_{60}+[4]	-	-12.75	-0.21	
C_{60}+[6]	230	-62.61	-1.04	58 / 42
C_{60}+[8]	381	-67.26	-1.12	60 / 40
C_{70}+[6]	154	-64.82	-0.93	57 / 43
C_{70}+[8]	179	-69.08	-0.98	59 / 41

a) in solution at 25°C, b) rest corresponds to ^{t}butyl, OH, CH_2

The trend of the calculated interaction energies per atom are in accord with the experimentally observed complex constants, i.e. the values for the complexes of C_{60} are larger than for C_{70}. By considering the distribution of the interaction, all complexes show a uniform pattern. The arene's part equals barely 60% emphasizing the influence of the alkyl substituent to stabilize the complex as well.

Fig. 3 shows the geometries of the complexes between C_{60} and calix[n]arenes (n=6,8). Non-acidic hydrogen atoms are omitted for reasons of clarity. In the latter complex there are two arene units that stand out from the cone and thus do not participate in the complexation. This geometry proved to be characteristic for calix[8]arenes after the simulations. In accord with earlier findings,[18] there was no flip-flop mechanism detectable for intramolecular hydrogen bonds of complexes throughout the simulations. Although no complex was detectable between C_{60} and calix[4]arene experimentally, an interaction energy of -0.21 kcal/mol per carbon atom was calculated. An analysis of the molecular movement in the simulation revealed that an intact complex existed at the very beginning comparable to those in Fig. 3. However, C_{60} began to leave the calix[4]arene after 15ps and the entire process was completed after 23ps. Obviously the strain energy of the cone conformation was too large and was releaved by releasing the guest.



(a) C_{60} complexed by calix[8]arene (b) C_{60} complexed by calix[6]arene

Fig. 3: Geometries of complexes between C_{60} and calix[n]arenes

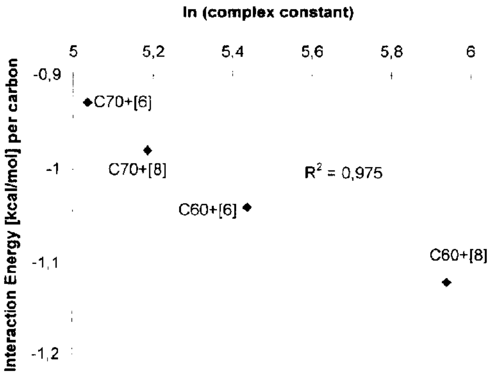
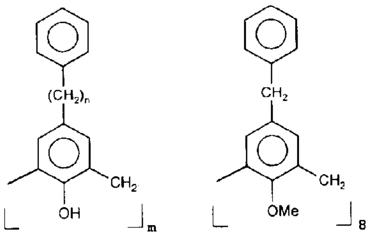


Fig. 4: Correlation between ln(complex constant) and interaction energy

Table 1 showed that the relative stability of the complexes was predicted correctly. By applying the thermodynamic relation $\Delta G = -RT\ln K$ for the interaction energies per carbon atom and the complex constants, a correlation coefficient of $R^2=0.975$ was determined (Fig. 4). Therefore, calculations based on our procedure should be able to predict the relative stability of new calix[n]arenes (Fig. 5).



1:m = 8 , n = 1
2:m = 8 , n = 2
3:m = 6 , n = 1

4

Fig. 5: Modified calix[n]arenes for improved complex formation with fullerenes

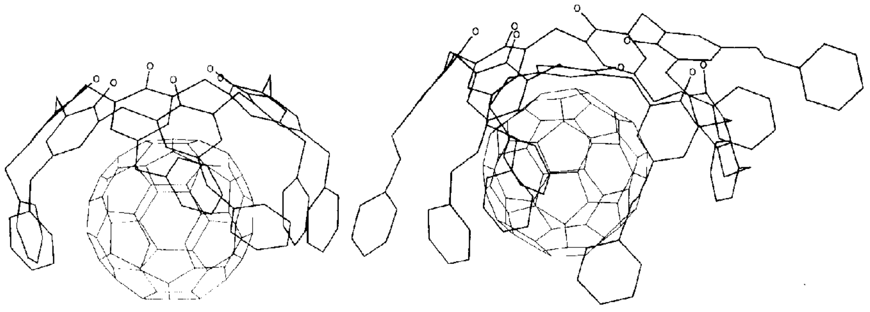
Surprisingly the largest interaction energy per carbon atom is calculated for the complex C_{60}+**3** (Table 2). By analyzing the geometry, it becomes obvious that the additional phenyl group is in closer contact with C_{60} (42% ≅ -35.6 kcal/mol) than in the complex of the calix[8]arene **1** and C_{60} (30% ≅ -23.9 kcal/mol). In agreement with the results in Table 1 the interaction of the arene unit is larger in **1** (50% ≅ -39 kcal/mol) than in **3** (42% ≅ -35.6 kcal/mol). The absolute values for the contributions of the "rest" are comparable.

Table 2: Calculated interaction energies of complexes with new calix[n]arenes

Complex of fullerene and calix[n]arene	Interaction energy ΔE [kcal/mol]	Interaction energy per carbon atom [kcal/mol]	per cent distribution arene/rest/p-phenyl [a]
C_{60}+**1**	-78,25	-1,30	50 / 20 / 30
C_{60}+**2**	-70,85	-1,18	46 / 23 / 23
C_{60}+**3**	-84,77	-1,41	42 / 16 / 42
C_{60}+**4**	-65,95	-1,01	46 / 19/ 35

a) rest corresponds to ^{t}butyl, OH, CH_2

Fig. 6 visualizes for the relatively small interaction of C_{60} with **2**. An alternative conformation becomes impossible with the introduction of a second methylene group because the tetrahedron at the sp^3-hybridized carbon atoms forces the phenyl group to point away from the fullerene.


a) Complexation of C_{60} by 3

b) Complexation of C_{60} by 2

Fig. 6: Geometries of complexes between C_{60} and calixarenes **2** and **3**

At the time when these calculations were performed[1] no experimental results were known so far. However, meanwhile the groups of Atwood and Shinkai found some indications for complexation of C_{60} with **1** and **3**.[22,23,24]

In summary, quantum chemical calculations are not only useful for elucidating the origin of the complexation between calix[n]arenes and fullerenes. They can also be used for designing modified macrocylces to improve selective complex formation.

EXPERIMENTAL

The p-^{t}butyl-calix[n]arenes (n=4,6,8) were synthesized following Gutsches' procedures.[25] C_{60} and C_{70} were supplied by *Hoechst AG* (Frankfurt) in *Gold grade* purity. The UV/Vis absorption spectra were measured using a *Shimadzu* spectrophotometer (Münster) and a *Specord 500* spectrophotometer (Kielce). Toluene was used as delivered by *Fluka* in *UV-spectroscopy* purity.

General procedure for UV/Vis spectroscopic measurements: A series of solutions containing C_{60} ($2.9 \cdot 10^{-5M}$) and varying concentrations of calix[n]arenes ($2.8 \cdot 10^{-4} - 1.2\,10^{-3M}$) were measured in a UV cell of 5.0 cm path length at 25°C. The equilibrium constants of complex formation for the 1:1 complexes were determined according to the *Benesi-Hildebrand* method taking into account the dilution effect (cf. eq. 1). In each case the *Benesi-Hildebrand* plots gave straight lines with correlation coefficients $r \geq 0.98$ (cf. fig. 2).

ACKNOWLEDGEMENTS

Support provided by the *Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie* (BMBF, Bonn), the *Fonds der Chemischen Industrie* (Frankfurt) and *Hoechst AG* (Frankfurt) is gratefully acknowledged.

REFERENCES AND NOTES

1. a) I. Schlachter, taken in part from the Ph.D. thesis, Universität Münster, **1995**.
   b) For a preliminary report see: J. Averdung, T. Budwach, W. Iwanek, I. Schlachter, G. Torres-Garcia, J. Mattay in *Progress in Fullerene Research*, H. Kuzmany et al. (Eds.), World Scientific Singapore, **1995**, p. 137-141.
2. a) H.W. Kroto, J.R. Heath, S.C. O'Brien, R.F. Curl, R.E. Smalley, *Nature* **1985**, *318*, 162-163.
   b) H.W. Kroto, *Angew. Chem.* **1992**, 104, 113-252; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 111.
3. W. Krätschmer, L.D. Lamb, K. Fostiropoulos, D.R. Huffman, *Nature* **1990**, *347*, 354-358.
4. a) A. Hirsch, *Chem. unserer Zeit* **1994**, *28*, 79-87.
   b) A. Hirsch, The Chemistry of Fullerenes, *Thieme Verlag, Stuttgart* **1994**.
5. a) J. Averdung, G. Torres-Garcia, H. Luftmann, I. Schlachter, J. Mattay, *Full.Sci.Techn.* **1996**, *4*, 633-654.
   b) J. Mattay, G. Torres-Garcia, J. Averdung, C. Wolff, I. Schlachter, H. Luftmann, C. Siedschlag, P. Luger, M. Ramm, *J. Phys.Chem. Solids*, **1997**, *58*, 1929-1937.
   c) J. Averdung, J. Mattay, *Praxis der Naturwissenschaften Chemie* **1997**, *46*, 28-34.
6. For a spectacular example of an endohedral fullerene compound containing atomic nitrogen see: H. Mauser, N.v.E. Hommes, T. Clark, A. Hirsch, B. Pietzak, A. Weidinger, L. Dunsch, *Angew. Chem.* **1997**, *109*, 2858-2861; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2835-2838.
7. J. Averdung, H. Luftmann, I. Schlachter, J. Mattay, *Tetrahedron* **1995**, *51*, 6977-6982
8. T. Grösser, M. Prato, V. Lucchini, A. Hirsch, F. Wudl, *Angew. Chemie* **1995**, *107*, 1462-1464; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1343-1345.
9. E.C. Constable, *Angew. Chemie* **1994**, *106*, 2359-2361; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2269-2271.
10. T. Andersson, G. Westman, O. Wennerström, M. Sundahl, *J. Chem. Soc., Perkin Trans. 2* **1994**, 1097-1101.
11. R.M. Williams, J.W. Verhoeven, *Recl. Trav. Chim. Pays-Bas* **1992**, *11*, 531-532.
12. J. Atwood, G.A. Koutsantonis, C.L. Raston, *Nature* **1994**, *368*, 229-231.
13. T. Suzuki, K. Nakashima, S. Shinkai, *Chem. Lett.* **1994**, 699-702.
14. J.L. Atwood, L.J. Barbour, P.J. Nichols, C.L. Raston, C.A. Sandoval, *Chem. Eur.J.* **1999**, *5*, 990-996 and refs. therein.
15. V. Böhmer, *Angew. Chem.* **1995**, 107, 785-818; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745 and literature cited therein.
16. P. Timmerman, W. Verboom, D.N. Reinhoudt, *Tetrahedron* **1996**, *52*, 2663-2704.
17. a) S.J. Weiner, P.A. Kollman, D.A. Case, U.C. Singh, C. Ghio, G. Alagona, S. Profeta Jr., P. Weiner, *J. Am. Chem. Soc.* **1984**, *106*, 765-784
    b) AMBER, 3.0: U.C. Singh, P.K. Weiner, J. Caldwell, P.A. Kollman, University of California, San Francisco, 1987.

18. P.D. Grootenhuis, P.A. Kollman, L.C. Groenen, D.N. Reinhoudt, G.J. van Hummel, F Ugozzoli, G. Andreetti, *J. Am. Chem. Soc.* **1990**, *112*, 4165-4176.
19. S. Fischer, P.D. Grootenhuis, L.C. Groenen, W.P. van Hoorn, F.C. van Veggel, D.N. Reinhoudt, M. Karplus, *J. Am. Chem. Soc.* **1995**, *117*, 1611-1620.
20. a) I. Schlachter, J. Mattay, J. Suer, U. Höweler, G. Würthwein, E.-U. Würthwein, *Tetrahedron*, **1997**, *53*, 119-132.

    b) U. Höweler, T. Bäcker, M. Klessinger, M. Eckert-Maksic, Z.B. Maksic, *Croat. Chem. Acta* **1990**, *64*, 539-549.

    c) Program MAXIMOBY 3.3: Implementation of force field and semiempirical methods for calculation of structures and properties of large chemical systems. Current Version 5.1, CHEOPS, U. Höweler, 48341 Altenberge, Germany (e-mail: hoeweler@muenster.de).
21. H. A. Benesi, J.H. Hildebrand, *J. Am Chem. Soc.* **1949**, *71*, 2703-2707.
22. a) J.W. Steed, P.C. Junk, J.L. Atwood, M.J. Barnes, C.L. Raston, R.S. Burkhalter, *J. Am. Chem.Soc.* **1994**, 10346-10347.

    b) J.L. Atwood, M.J. Barnes, M.G. Gardiner, C.L. Raston, *Chem. Commun.* **1996**, 1449-1450.
23. A. Ikeda, M. Yoshimura, S. Shinkai, *Tetrahedron Lett.* **1997**, *38*, 2107-2110.
24. See also ref. 14: p. 994-995.
25. C.D. Gutsche et al. in *Organic Synthesis, Coll. Vol. 8*, J.P. Freeman et al. (Eds.), **1993**, p. 75-77, p. 77-79, and p. 80-81.