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Silylation of cellobiose as a model reaction for the synthesis of silylated cellulose. A DFT and PM3 approach.

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Abstract

The object of the present study is the isodesmic reaction of cellobiose (the repeating unit in cellulose) with different kinds of silanes, R-SiH_3, to form silylated cellobiose (Cello-SiH_3) and the corresponding alcohols (R-OH). The size and the chemical reactivity of the substituent R is varied as well as the position where O-silylation at the cellobiose takes place. In contrast to experimental observations where the O6 position is favored for silylation, for the computed reactions, energy differences are smaller than 3 kcal/mol for the different positions at the B3LYP/6-311G* as well as at the B3LYP/6-311+G* level of theory. Depending on the silane, reaction energies in a range from -17 kcal/mol (R=$NHSiH_3$) and +18 kcal/mol (R=F) have been calculated. In addition, semi-empirical calculations on the PM3 level of theory have been performed. These results are set into contrast with the results derived from DFT calculations to assess whether semi-empirical methods may be useful for the description of larger systems containing silylated cellobiose units.

Keywords: *Cellobiose, DFT, PM3, Silanes, magnetically induced ring currents*

Computational Methods

All calculations have been performed using the *Gaussian03*[1] program suite (DFT) and the program *HYPERCHEM 8.0* (PM3). For DFT calculations, different Pople type basis sets (6-31G*, 6-311G* and 6-311+G*) in combination with the Barr-Lee-Young functional B3LYP were applied. For all calculations, vibrational analysis was performed after geometry optimization showing only positive elements in the Hessian matrix. For the calculation of the Free Enthalpy ΔG^{298}, zero point correction to T=298 K was applied. Magnetically induced ring currents have been calculated by the method of *Sundholm and coworkers*.[2] The PM3 calculations have been performed using *HYPERCHEM 8* from Hypercube Inc. PM3 is an optimized parameter set for semi-empirical molecular modeling calculations and bases on a modified neglect of diatomic overlap (MNDO) method. This method uses two Gaussian functions for the core repulsion function. The geometric optimization was done via Polak-Ribiere algorithm, which is a conjugated gradient method. The termination conditions were set to a RMS gradient of 0.1 kcal/(Åmol) or 60 maximum cycles. All computations have been performed in vacuo.

Introduction and Background

One of our research interests involves the preparation of polysaccharide model films, in particular cellulose model films.[3-6] Model films offer many advantages compared to ‘real’ cellulose samples because of their homogeneity in terms of composition, surface morphology and thickness. However, the obvious way to prepare cellulose model films from cellulose solutions is somewhat limited due to the few commercially available cellulose solvents. A more convenient strategy for the preparation of cellulose model films is the use of soluble cellulose derivatives which are converted back to cellulose after the film has been deposited by e.g. spin-coating on a substrate. Several derivatives (xanthogenates, cellulose acetates) have been considered for this purpose, however, from our point of view, the most straightforward approach to prepare cellulose model surfaces is the use of trimethylsilylated cellulose (TMSC).[7] After coating on a flat substrate such as silicon wafers or glass substrates, the silyl groups can be removed very easily by simple exposure to an acidic atmosphere yielding cellulose model films, whose thickness can be tuned up to a certain degree.

The synthesis of TMSC is usually performed by reaction of cellulose with hexamethyldisilazane (HMDS) using ionic liquids as reaction media. [8, 9] The driving force of the reaction seems to be the cleavage of the weak silicon-nitrogen bond in HMDS and subsequent formation of a strong silicon-oxygen bond in the resulting cellulose ether. In the course of our research dealing with sol gel chemistry and polysaccharides, we became interested whether reactions and formation of covalent bonds between polysaccharides and silicon compounds may also occur with other precursors, for instance with alkoxysilanes.

Results and Discussion

The object in this study is the investigation of silylation reactions on cellobiose which should serve as model reaction for the silylation of cellulose. Although the molecular structure of cellobiose seems to be a simple task on first glance, recent theoretical publications proved the existence of more than 30 conformers which are all minima on the potential energy surface.[10-12] The energy difference between the conformer with lowest and with the highest energy was calculated to be ca. 7 kcal/mol. However, a principal problem in quantum chemistry is the evaluation of intramolecular hydrogen bond strengths which is of course influencing total energies of different conformers. While intermolecular hydrogen bonds can be easily calculated by several methods, intramolecular hydrogen bonds are often underestimated by quantum chemical calculations. In this context, a recent publication can be considered as breakthrough which uses magnetically induced ring currents for the determination of intramolecular hydrogen bonds in DNA.[2] It is obvious that such calculations are not limited to DNA and detailed investigations on cellobiose and other oligosaccharides are already in progress and will be the topic of a later full paper.

For our computed isodesmic reaction, a *syn*-conformer of cellobiose (Fig.1) is used. In the *syn*-form of cellobiose, the protons attached to C1 and C1’ are directing in the same direction leading to dihedral angles ϕ and ψ which are in the range between -30 – 41° and -62 - -8°. The cellobiose conformer which is used for the isodesmic reactions reported here has ϕ and ψ values of +24 and -25°, respectively. This conformer was chosen by removing a piece from a modeled cellulose crystal structure with two present intramolecular hydrogen bridges (O2-H2···O6’; O5···H3’-O3’).

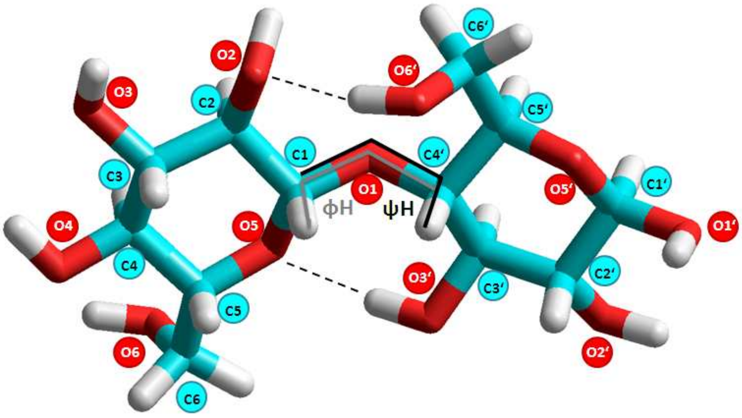

Fig. 1. The *syn*-conformer of the used cellobiose.

The silanes $RSiH_3$ which are employed for the isodesmic reactions with the *syn*-conformer of cellobiose differ in size, chemical reactivity and polarity (R=H, NH_2, $NHSiH_3$, OH, OMe, F, Cl). These silanes are models for ‘real’ reagents in the silylation of cellulose such as HMDS, tetramethoxysilane and trimethylsilylchloride. It turned out that the B3LYP/6-311+G* basis set yields the best results therefore in the following only values referred to this basis set are discussed in the text.

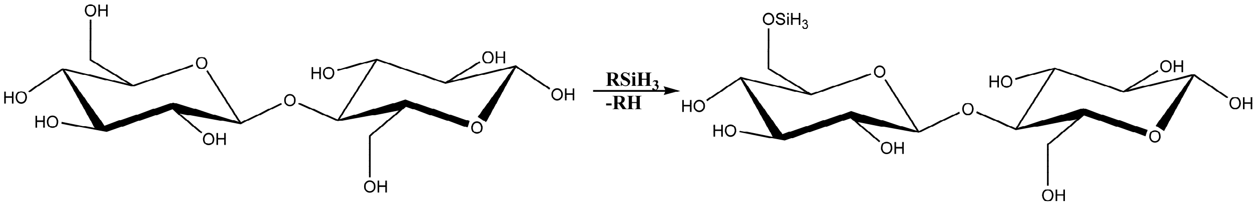

Fig. 2. Computed isodesmic reaction of cellobiose with silanes. For reasons of clarity only silylation at O6 is shown.

In a first step, the influence of the silanes on ΔG^{298} has been evaluated. For R=H, NH_2 and $NHSiH_3$ strongly negative ΔG^{298} values have been computed at all levels of theory (Fig. 3, Fig. 4). This can be explained by the substitution of the weak hydrogen-silicon (average bond dissociation energy (BDE): 323 kJ/mol[13]) and nitrogen-silicon (BDE: 335 kJ/mol[13]) bonds by rather strong silicon-oxygen bonds (BDE: 440 kJ/mol[13]). For R= H, ΔG^{298} was calculated between -14 and -17 kcal/mol depending on basis set and the position of substitution. For R=NH_2, slightly different values have been calculated (-9 – -11 kcal/mol). A special case is the silylation involving $H_3SiNHSiH_3$. This compound reacts in a first step with cellobiose resulting in silylated cellobiose and NH_2SiH_3 which in turn can react with another molecule of cellobiose to give silylated cellobiose. The ΔG^{298} values given in Figs. 3 and 4 are the sum of both reactions. In contrast, for R=F strongly endothermic enthalpies (+10 – +17) have been computed. This can be attributed to the strong silicon-fluorine bond (BDE: 565 kJ/mol[13]) which must be cleaved for silylation. Reactions involving the oxygen containing silanes (R=OMe, R=OH) yielded ΔG^{298} close to 0 kcal/mol. Independently of the basis set, R=OH is energetically favored by ca. 1 kcal/mol over R=OMe which can be explained by the stronger Si-O bond in alkoxysilanes compared to silanols. This behavior can be understood by negative hyperconjugation[14] where electron density is transferred from the π into the σ^* molecular orbitals. This negative hyperconjugation is more pronounced in case of silanols (which is the reason for their oligomerization tendency) compared to alkoxysilanes.[15]

In real cellulose, substitution reactions usually take place at the oxygen bound to C6 which is caused by the best accessibility of this functional group in the bulk. However, in the work presented here, only changes in conformation and hydrogen bond capability may play a role. Indeed, reaction enthalpies for silylations at O3 and O4 are in a similar range, as well as those at O2 and O6. Silylation at O3 and O4 do not induce significant conformational modifications upon silylation; therefore the dihedral angles ϕ and ψ remain nearly unchanged compared to cellobiose. In contrast, after silylation at O2 the conformation is altered. Both, ϕ and ψ, exhibit values of -1.4 and +48.7° due to the steric demand of the silyl moiety. As a consequence also τ, the dihedral angle C4-C5-C6-O6, is changed from 44° to -73°. Surprisingly, the silylation at O2 is energetically favored compared to the ones at O3 and O4 by ca. 2-3 kcal/mol although the loss of the hydrogen bond O2-H2···O6’.

For an estimation of the energy contribution from the change in conformation, it seems reasonable to estimate the strength of hydrogen bonds first. According to *Steiner*[16], the hydrogen bonds in cellobiose can be classified as middle strong. Important geometric parameters for the estimation of hydrogen bond strength include the donor-acceptor distance (D···A), the angle between the donor-hydrogen···acceptor (DHA) as well as the distance between the hydrogen atom and the acceptor atom (H···A). However, following this concept the hydrogen bond O5···H3’-O3’ can be classified as weaker than the O6···O2’-H2’ one. This can be seen in the DHA angles which range from 147 to 150° (O5···H3’-O3’) and 166-168° (O6···O2’-H2’). However, there are arguments which indicate that O6···O2’-H2’ is weaker than O5···H3’-O3’ (D···A: 3.001 vs. 2.881 Å; H···A: 2.087 vs 2.012 Å, B3LYP/6-311+g*). In order to estimate the absolute strength of these particular intramolecular hydrogen-bonds, we employed a scheme which was proposed very recently by *Sundholm and coworkers*.[2] Using this method, magnetically induced ring current strengths flowing around the H-bond moiety are calculated.

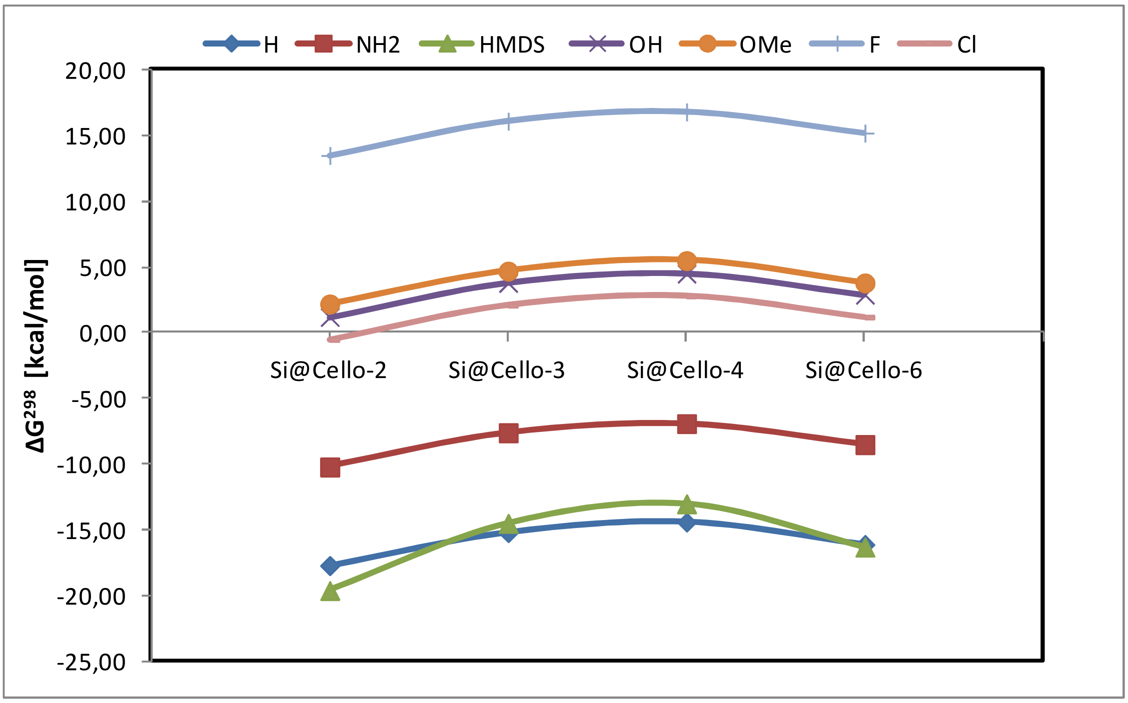

Fig. 3. Calculated reaction enthalpies of the reaction of cellobiose with various silanes, $RSiH_3$, at the B3LYP/6-311+G* level of theory. The lines between the different positions where silylation takes place are connected due to clarity reasons and have no physical meaning.

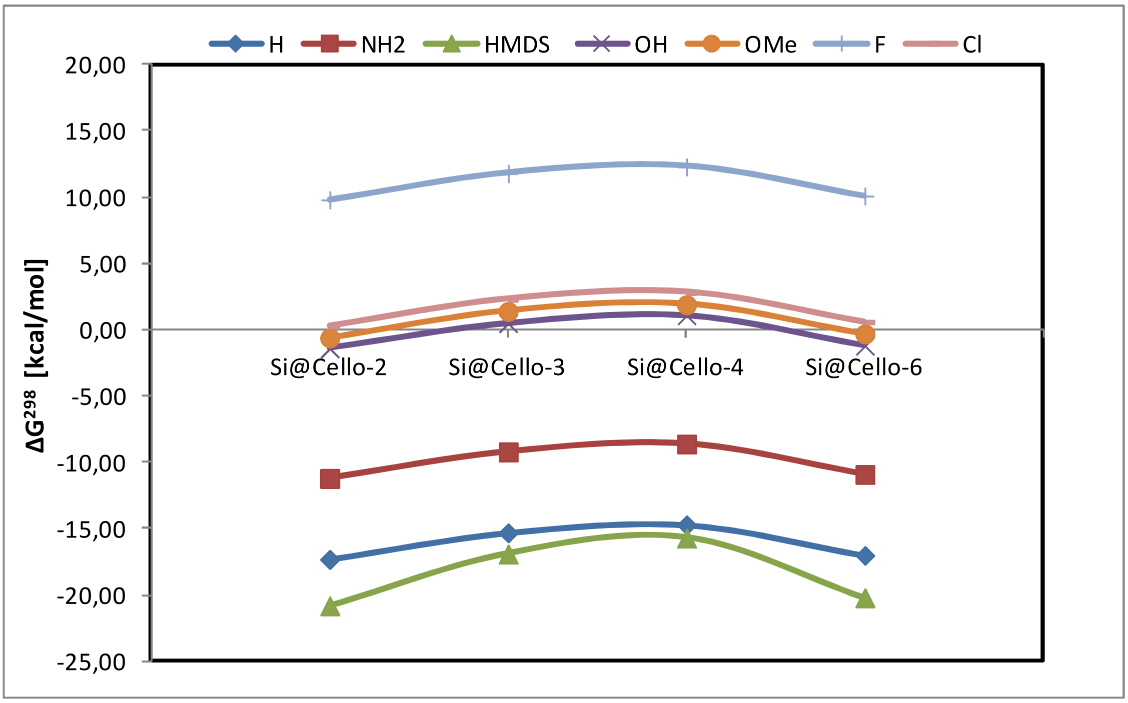

Fig. 4. Calculated reaction enthalpies of the reaction of cellobiose with various silanes, $RSiH_3$, at the B3LYP/6-311G* level of theory. The lines between the different positions where silylation takes place are connected due to clarity reasons and have no physical meaning.

It turned out that the size of these currents is strongly correlated with the calculated H-bond interaction energy at the same level of theory. We employed this scheme for a 'non-invasive' estimation of both intramolecular H-bonds in the cellobiose conformer under investigation (O2-H2···O6' and O3-H3···O5') and found interaction energies of about 2.5 and 5.0 kcal/mol, respectively. Therefore, we are able to distinguish between the contribution arising from conformational changes and hydrogen bonding in case of silylation at O2. The conformational change in energy accounts for ca. -4.5 and -5.5 kcal/mol compared to the silylated products at O3 and O4.

Surprisingly, silylation at O6 yields only slightly increased ΔG^{298} (~+0.3 kcal/mol) compared to silylation at O2. While the changes in ϕ and ψ are negligible in comparison to cellobiose, τ is changed significantly from 44.7 to 55.9 which origins also from the steric pressure of the silyl group. For comparison, τ’ (C4’-C5’-C6’-O6’) remains very close to the original value of cellobiose (35.2 vs 35.9° in cellobiose).

However, while the above computational methods can be applied on cellobiose, the computation of larger systems is associated with high computational costs. Therefore, we decided to screen the PM3 method on its applicability on these silylation reactions. As starting point, the optimized geometries obtained at the B3LYP/6-311+G* level of theory have been used. In the first step, the cellobiose conformer was investigated. The optimized geometry at the B3LYP/6-311+G* level of theory is not maintained at the PM3 method. Instead, the hydrogen bonding mode is changed according to Fig. 5, possibly due to an insufficient description of the hydrogen bonds in the PM3 parametrization. As a consequence, the dihedral angles ϕ and ψ are changed to values of 20.8 and -18.9°, respectively, as well as τ (57.4°) and τ’(61.8°).

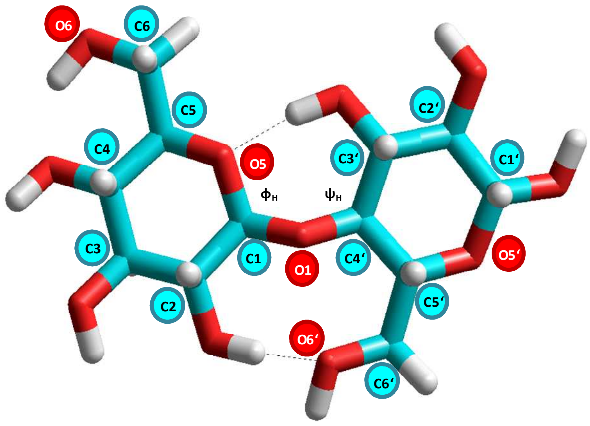

Fig. 5. Optimized geometry for cellobiose using the PM3 method. As starting geometry, the optimized structure calculated at the B3LYP/6-311+G* level of theory was used.

Although the results are not directly comparable with DFT due to the different conformations, a silylation was performed at each position using the same isodesmic reaction scheme as for DFT. The results are in clear contrast to the ones obtained with the DFT method. An optimistic point of view on the data may assume that the trends are at least similar (Fig. 6). However, a closer look reveals that the nitrogen containing silanes (R=NH_2, $NHSiH_3$) yield values which do not make sense and which are far away from the reasonable results obtained with B3LYP/6-311+G*.

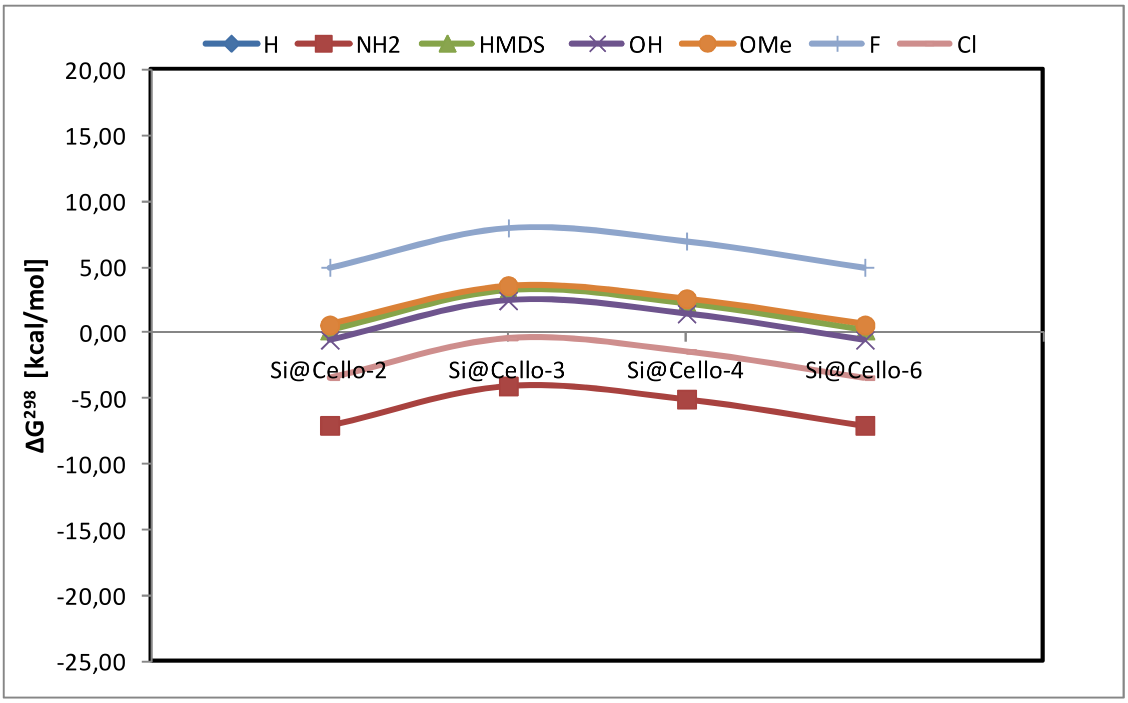

Fig. 6. Calculated reaction enthalpies of the reaction of cellobiose with various silanes, $RSiH_3$, obtained with the PM3 method. The lines between the different positions where silylation takes place are connected due to clarity reasons and have no physical meaning.

In addition, the geometries around the silicon centers are completely different in comparison to the results obtained in DFT. C-Si-O angles are in the range of 115-118° (PM3) while for DFT values between 125 and 129° are computed. The Si-O bond lengths have been calculated to range from 1.704 to 1.709 Å (PM3) while DFT leads to values of 1.666 to 1.677 Å. It is known that DFT underestimates the polarity of Si-O bonds and therefore these calculated bond lengths tend to be always larger than the ‘real’ values (av. Si-O: 1.64 Å) obtained from X-ray crystallography[17, 18] and gas electron diffraction[19, 20]. The poor description of the bonding situation around the silicon atom seems to be a major reason for the rather modest performance of PM3 in comparison to DFT methods.

Summary and Conclusion

The isodesmic reaction of a *syn*-conformer of cellobiose with different silanes is presented at different levels of theory using density functional theory. The choice of the silane determines whether the reaction is exo- or endothermic. In contrast to bulk cellulose where the O6 position is favored for silylation, in the calculations the position where silylation preferentially takes place is O2. This position is slightly favored over O6 by 0.3 kcal/mol followed by O3 and O4 (2-3 kcal/mol). In addition, preliminary results on the strength of the hydrogen bonds in this particular cellobiose conformer have been calculated using magnetically induced ring currents. This ‘non-invasive’ method yields hydrogen bond strengths of 2.5 (O2-H2···O6') and 5.0 (O3-H3···O5') kcal/mol (B3LYP/6-311+G*). However, in order to make more precise statements whether e.g. alkoxysilanes may be used for the experimental preparation of silylated cellulose, more detailed studies are necessary which will include the investigation of transition states and activation barriers. Finally, an attempt to use a semi-empirical approach (PM3) is described, however, the results obtained with this method cannot be considered as reliable as those obtained with DFT.

Acknowledgements

The research leading to these results has received funding from the European Community’s Seventh Framework Programme [FP7/2007–2013] under grant agreement no. 214015 (S.S. and H.M.A.E.). Dr. Raphael J.F. Berger (Paris-Lodron-University Salzburg) is gratefully acknowledged for providing data for the estimation of hydrogen bond strengths by magnetically induced ring currents.

MARIE CURIE ACTIONS

SEVENTH FRAMEWORK PROGRAMME

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