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Computer Modeling and Simulations on Flexible Bifunctional Systems: Intramolecular Energy Transfer Implications[†]

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A conformational search of the potential energy surface using the single coordinate driving method CICADA, molecular dynamics calculations, and quantum mechanical studies using the 6-31G* basis set were used for a detailed analysis of the conformational behavior of various flexible bichromophoric compounds Ph−CO−(CH$_2$)$_x$−O−Ar ($x = 3-14$; Ar = 2-naphthyl, 2-biphenylyl, 3-biphenylyl, 4-biphenylyl). The results were used for the estimation of end-to-end intramolecular (exchange) energy transfer efficiency and for comparison to the data recently obtained from steady-state quenching and quantum yield measurements (Wagner, P. J.; Klán, P. *J. Am. Chem. Soc.* **1999**, *121*, 9626−9635). The conformational search clearly supported the dominance of a through-space interaction in longer molecules ($x = 5-14$), which was still remarkably high even for $x = 14$. Comparison of both computational and experimental results suggests that through-bond coupling is responsible for ~90% of the energy transfer in the shortest ($x = 3$) bichromophores. The molecular dynamics calculations seemed to validate the conclusion that only a small fraction of the energy transfer involved ground-state control (static quenching) by ground-state conformations with interchromophore distances within 4 Å. Rate-determining bond rotations to such geometries should be then responsible for the energy transfer within the lifetime of the excited donor. The influence of chromophore orientation was found insignificant for long-tether molecules, but important in short-tether ones due to different “reactive volumes” of different acceptors, such as naphthalene or biphenyl. In addition, a correlation of the calculated average distances between the γ-hydrogen and the carbonyl oxygen with the experimental hydrogen abstraction rate constants in the Norrish type II process strongly supported the right choice of the computational method.

1. Introduction

Intramolecular reactions and interactions in flexible bifunctional molecules is a field of continuing interest,[1] in which the studies of intramolecular electron and energy transfer in chain-linked donor−acceptor (bichromophoric) systems have provided most valuable insight. It is now well-established that rates of intramolecular triplet energy transfer (ITET) reactions are affected by structural and geometrical factors, and by medium effects.[2−4] An exchange mechanism for the triplet transfer implies an exponential decrease of the rate constants with increasing distance between the donor and acceptor chromophores.[5,6] Rigid spacers such as cyclohexane or decalin rings provided well-defined geometries, facilitating studies of the *through-bond* interaction of the ITET process, rate constants of which dropped ~1 order of magnitude for each additional bond between chromophores.[7−11] Flexible bichromophoric systems, on the other hand, afforded only a gradual drop in ITET rate constants as the connecting chain became longer indicating a presence of *through-space* transfer.[12−15] The time required for bimolecular exothermic energy transfer between an excited triplet donor and a ground-state acceptor is usually less than 100 ps.[16] Thus the corresponding intramolecular reaction is fast enough to compete with conformational motion of a flexible system when donor and acceptor are within van der Waals contact distance of each other. Such a competition requires a complex kinetic analysis that differs from what is normally employed in ground-state chemistry.[17]

Kinetic studies of intramolecular energy transfer reactions in flexible bichromophores usually interpret the experimental results in terms of chain conformation or chain dynamics. A detailed examination is undoubtedly required because energies of the conformations are separated only by subtle barriers, especially when the chain is very flexible. The rate of interconversion between conformational states then reflects the chain properties and the distribution of D−A distances results in a range of transfer rate constants. The transfer of triplet energy requires a close proximity of chromophores. Chromophores separated by 3−4 Å (within van der Waals parameters) undergo instantaneous energy transfer in <100 ps but most conformations with an interchromophore distance under ~6 Å should contribute to the total transfer.[13] Wagner[17] depicted the kinetics of intramolecular photochemical reactions with a zoomorphic model of a bug swallowing its own tail, showing that photochemistry involves one necessary presumption not present in a standard ground-state model: the actual reaction constants are

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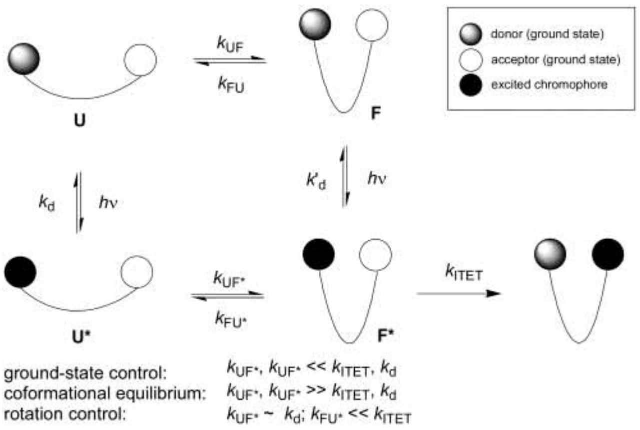
SCHEME 1: Competition between Energy Transfer and the Norrish Type II Reaction

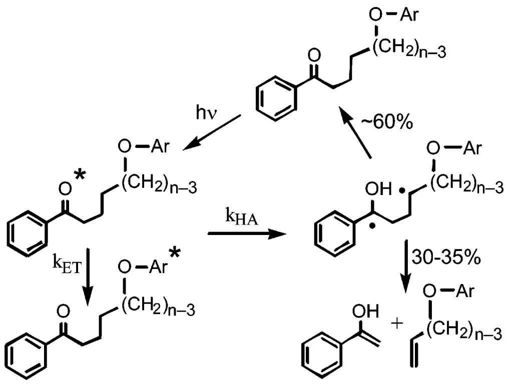


restricted to the excited-state molecules. Scheme 1 shows a general kinetic scheme of ITET in flexible molecules, where **F** and **U** represent favorable and unfavorable conformations, and k_{UF}, k_{FU}, and k_d coiling, uncoiling, and decay rate constants, respectively. Three distinct kinetic categories describe intramolecular energy transfer reactions whose observed rate constants are (1) much faster than the rate constants of conformational interconversions (*ground-state control*; intramolecular equivalent of "static" quenching[18]), (2) slower than rates of conformational change and thus dependent on the equilibrium population of different conformers (*conformational equilibrium*; intramolecular equivalent of the Winstein-Holness principle), or (3) determined by comparable rate constants for both decay and irreversible conformational motion to a rapidly reacting conformer (*rotation-controlled photochemical reaction*; intramolecular equivalent of "diffusion-controlled" quenching).[13,17] According to the last model, unfavorable conformers **U** with a longer excited-state lifetime may contribute to the total transfer if the excited system coils to the conformation **F**. In general, the excited-state conformational population may differ from the ground-state one because electronic excitation may change bond angles and lengths. However, this difference is considered insignificant for the purposes of this work, because excitation barely affects ketone conformations.

Most studies of ITET were done on systems with relatively short chains.[19,20] Flexible molecules with 2−4 connecting atoms provide as efficient energy transfer as the Closs's rigid systems thanks to predominant through-bond mechanism.[10,11] Wagner and El-Taliawi extended the lengths of tether up to 7 atoms in the cinnamyl esters of ω-benzoylcarboxylic acids,[14] in which through-space transfer slowed the exponential drop in the ITET rate constants. Some of us reported the studies of ITET in flexible ω-naphthyl and ω-biphenylylalkanophenones having 4−15-atom interchromophore distance.[12,13] The rate constants decreased only 1 order of magnitude as the number of atoms increased from 5 to 15. Yamamoto et al. studied bichromophores connecting carbazole and naphthalene groups to a flexible chain.[21−24] Their experimental results supported by computational determination of the end-to-end distances indicated that through-space transfer dominates. Important insight was also gained from intramolecular electron transfer,[25−29] the formation of intramolecular exciplexes[26,30,31] studies, or spin−orbit exchange interaction in biradicals.[32−37]

There have been many attempts to model and simulate dynamic behavior of flexible bifunctional molecules.[3] An essential parameter that helps with determining the course of the reaction is the mutual distance of the end groups in the lowest energy conformer of the reactant. However, that information is not sufficient for explaining the experimental details in most cases.[38] The relative probability distribution over all possible conformations, obtained, for example, from Monte Carlo calculations,[25,38−42] seems to be the better approach. Several papers have reported attempts to reproduce experimental results using an equilibrium Monte Carlo method.[25,38−42] We have used an alternative approach based on complete description of conformational space, calculating Boltzmann probabilities of all important states, and relating the data to experimental observations. Moreover, we have combined this approach with molecular dynamics simulations.

SCHEME 2: Kinetics of ITET in a Flexible Bichromophore (Adapted from Reference 17)

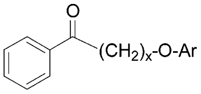


In our earlier works, the Norrish type II reaction[43] was utilized for the energy transfer studies; the kinetics of γ-hydrogen abstraction was adopted as the "system clock" to calculate the ITET rate constants.[12,13] Scheme 2 demonstrates the competition between the energy transfer (k_{ET}) and the Norrish type II reaction, with the benzoyl group and Ar being donor and acceptor chromophore, respectively. Those two independent processes are taken as model processes for the computational studies in this work.

Here we report the results from our computational studies of flexible bifunctional (bichromophoric) compounds and compare them to those obtained from the experimental studies reported recently.[12,13] The data will be discussed in terms of end-to-end energy transfer, the efficiency of which is strongly dependent on the distance between the chromophores, on the system dynamics and on the chromophore orientation as well.

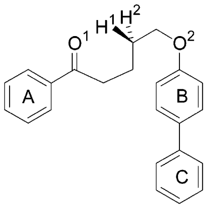
2. Methods

A general formula of the systems studied, practically identical to that used in the previous triplet energy studies,[12,13] is depicted in Figure 1. The functional groups (chromophores), the aromatic moiety Ar (2-naphthyl; 2-biphenylyl; 3-biphenylyl; 4-biphenylyl; phenyl), bonded through the oxygen atom, and the benzoyl group PhCO− (Bz), are connected by polymethylene chains. Structures of the bichromophores are abbreviated according to the following example: Bz7ONp corresponds to Ph−CO−$(CH_2)_7$−O−Np. Figure 2 shows a labeling used to describe interatomic distances; the benzene ring connected to the polymethylene chain through the oxygen atom is denoted as Ph1 whereas the terminal phenyl ring is denoted as Ph2 (benzene rings in the naphthyl group are denoted correspondingly). The d_{H1} and d_{H2} values relate to the distances between the γ-hydrogens and the carbonyl oxygen atom. The distances between the benzene rings, A−B (d_{PhPh1}) and A−C (d_{PhPh2}), are the distances between the geometrical centers of the rings, whereas the distances between the carbonyl oxygen and acceptor benzene



x = 3-7, 9-11, 14
Ar = 2-naphthyl (Np)
2-biphenylyl (oBP)
3-biphenylyl (mBP)
4-biphenylyl (pBP)
phenyl (Ph)

Figure 1. General formula of the systems studied.



abbreviation	connected atoms / sites
d_{H1}	O^1 - H^1
d_{H2}	O^1 - H^2
d_{OPh1}	O^1 - B
d_{OPh2}	O^1 - C
d_{PhPh1}	A - B
d_{PhPh2}	A - C

Figure 2. Description of interatomic distances.

ring, O^1−B (d_{OPh1}) and O^1−C (d_{OPh2}), are the distances between the O^1 atom and the geometrical center of the corresponding benzene ring.

Conformational Search. The conformational search of the potential energy surface (PES) was performed using the single coordinate driving (SCD) method CICADA.[44,45] The SCD can be described as an excursion through low-energy areas of the conformational space. The MM3[46] molecular mechanics (MM) force field was used. Geometries and energies of the conformers were extracted from the PES by program PANIC.[47] The Boltzmann probability was calculated for each conformer. Important distances from Figure 2 were measured for all conformers. The population P_H of the conformers that have $d_H \leq 3.1$ Å and, at the same time, the populations P_{ET} of the conformers with the distances between the chromophores of <4.5 Å were determined. These values were chosen as an example of the distances for very efficient hydrogen abstraction[43] and triplet energy transfer processes,[2] respectively.

The Boltzmann-weighted average values for the distances d_{PhPh1}, d_{PhPh2}, d_{OPh1}, and d_{OPh2} were evaluated from

$$d = \sum_{i}^{N} p_i d_i \tag{1}$$

where N is the total number of conformers and p_i and d_i are the Boltzmann probability and the distance calculated for the conformer i, respectively. The Boltzmann-weighted average values for the distance d_H (average of d_{H1} and d_{H2}) were calculated using a similar approach.

$$\log k_{ET} = 13 - \frac{2R_{DA}}{2.3} \tag{2}$$

Ermolaev's experimental equation[48] (eq 2) of the exchange (Dexter) triplet energy transfer was used for the estimation of the corresponding rate constants k_{ET}. R_{DA} is the distance between the donor and acceptor chromophores.

Molecular Dynamics. Molecular dynamics (MD) trajectories were obtained using the program DYNAMICS, which is a part of the software package TINKER.[49] The simulations were run in a vacuum with the dielectric constant set to 1.5 and temperature 300 K. The same force field as for the conformational search (MM3[46]) was used. The total length of each trajectory was 100 ns with the integration step of 1 fs. The important distances (except those of d_H) were monitored using the program gOpenMol.[50,51]

The frequencies ν_C of molecular coiling to a geometry favorable for the ITET were estimated from the MD trajectories using

$$\nu_C = \frac{1}{\tau} \tag{3}$$

where τ is defined as an average time needed for a conformational change between the structures with a geometry favorable for the triplet energy transfer process, *i.e.*, with the distances d_{OPh} and d_{PhPh} smaller than the defined limits (4.0 and 4.5 Å). In other words, τ is an average lifetime of geometry that is unfavorable for triplet energy transfer process.

Quantum Mechanical Studies. Low-energy conformers (coiled or uncoiled) of the system Bz4OPh, extracted from PES, were chosen for the geometry optimization. Their geometries were optimized using different quantum mechanical methods to validate the MM results: (a) restricted Hartree−Fock (HF); (b) DFT with B3-LYP functional; (c) MP2.

Each minimization was carried out using the 6-31G* basis set. The program Gaussian 98[52] was used for the computations. The resulting geometries were compared with those obtained by CICADA. The geometrical differences between the starting and optimized structures were quantified using the root-mean-square deviation (RMSD). The energetic preference of the coiled structure was calculated using

$$\Delta E = E_U - E_F \tag{4}$$

where E_U and E_F are enthalpies of the uncoiled and coiled structures, respectively. For the positive values of ΔE, the coiled structure is energetically preferred and hence more populated than the uncoiled one. However, the complexity of PES increases markedly with the size of the system. Consequently, the ability of CICADA to explore the whole conformational space decreases with the increasing size of the system studied, causing the overestimation of the low-energy conformers that prefer the coiled conformation with smaller distance values, eventually leading to less exact results for structures with larger x values ($x > 10$).

3. Results

Conformational Search. The rate constants calculated from the average distances using eq 2 are shown in Figure 3a−d. According to this calculation, average distances of 4, 5, or 6 Å correspond, for example, approximately to the ITET rate constants of 3.3×10^9, 4.5×10^8, or 6.1×10^7 s^{-1}, respectively. The conformational population of the molecules with Np, mBP, and pBP chromophores apparently differ from those of the oBP derivatives. Whereas the Ph1 is closer to the donor moiety than Ph2 in short (3−6-atom tether) Np, mBP, and pBP systems, the situation is reversed for longer systems. Subsequently, the distances between both phenyl rings and the donor chromophore become comparable for the longest molecules. The oBP systems display unique behavior. The average distances between the Ph2 ring and the donor moiety are shorter than those of Ph1 in the short-tether bichromophores but longer in the long-tether ones, which is an opposite trend from that observed for the remaining derivatives.

The calculated populations of the conformers, having *intentionally* either the Ph1 or Ph2 rings in the average distance to the donor aromatic ring (d_{PhPh1} or d_{PhPh2}) equal to or less than 4.5 Å (Figure 4a−d), provide also very interesting information about the systems. For short molecules ($x = 3, 4$), the structures with the Ph1 ring close to the donor benzene ring predominate

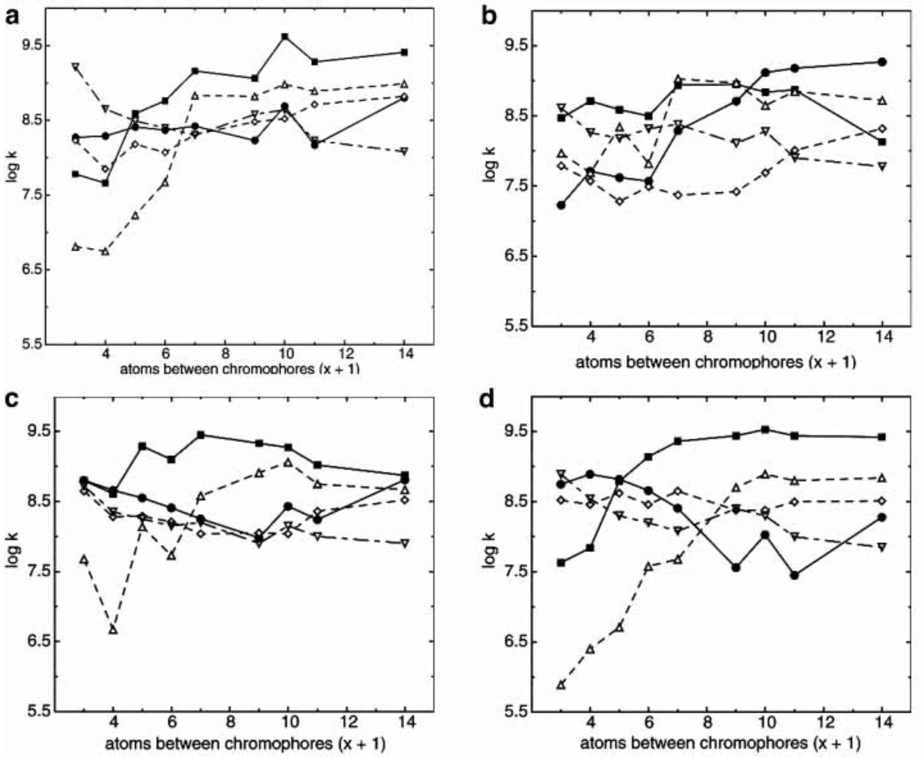


Figure 3. (a−d) Calculated ITET rate constants from the average distances for Bz-*x*-ONp (a), Bz-*x*-OoBP (b), Bz-*x*-OmBP (c), and Bz-*x*-OpBP (d) (●, d_{PhPh1}; ■, d_{PhPh2}; ◇, d_{OPh1}; △, d_{OPh2}; ▽, experimental values from literature[12,13]).

but, with increasing number of atoms between the chromophores, the population is favorable for the molecules having the Ph2 ring close to the donor group. The oBP system behavior is again unique. The conformers with the Ph2 ring close to the donor benzene ring are more populated in molecules having 9 or less methylene tether groups. Different results were obtained from the calculations of the molecular populations having either the Ph1 or Ph2 rings in the average distance to the carbonyl oxygen equal to or less than 4.5 Å (Figure 4e−h). The differences in the population distributions calculated for d_{OPh1} or d_{OPh2} distances are not too significant. Only Bz-*x*-OoBP systems show specific variations again.

To correlate our calculations with the experimental data,[12,13] the probabilities that the γ-hydrogen in the Norrish type II process (Scheme 2) will be abstracted by the carbonyl oxygen atom were calculated (Figure 5a−d). The calculated distances d_H are compared to the experimental hydrogen abstraction rate constants.[13] The distance d_H remains almost constant in the systems with $x \geq 5$. Only the systems with $x = 3$ exhibit a rather poor correlation with the experimental values.

The population distribution of the molecules having the geometry favorable ($d_H \leq 3.1$ Å and d_{PhPh} or $d_{OPh} < 4.5$ Å) for one of the processes (hydrogen abstraction only (HA); energy transfer only (ET); both HA and ET possible (ET & HA); none of the processes probable (N/A)) was also calculated. The distances d_{PhPh} and d_{OPh} were treated separately. For d_{PhPh} distances (Figure 6a−d), the HA probabilities are generally low; however, the probabilities for the energy transfer (ET) increase with the increasing number of tether atoms whereas the probabilities for both the hydrogen abstraction and energy transfer (ET & HA) decrease. In contrast, the calculations using d_{OPh} distances (Figure 6e−h) showed the probabilities (ET & HA) and (HA) to be high in short systems ($x = 3$, 4). As the tether becomes longer, the probabilities of all processes involved decrease, and when $x = 7$, the populations allowing the energy transfer dominate. The results with d_{OPh} distances should be very important, because the acceptor must donate a π electron to the *n* orbital of the n,π^* state whereas its π^* electron, in an orbital spread over the whole benzoyl group, is returned to an acceptor π^* orbital.

Molecular Dynamics. The molecular dynamics (MD) calculations were performed to obtain the frequencies of the coiling processes using eq 3. The calculated frequencies are compared with the corresponding (experimental) rate constants (Figure 7a−d). The interchromophore distance limits of 4.0 or 4.5 Å, respectively, were chosen to evaluate the conformational behavior of the compounds with chromophores in close proximity.

Quantum Mechanical Studies. Three quantum mechanical methods were used and compared in order to validate the results from the molecular mechanics. The results obtained for the uncoiled geometry of the Bz4OPh system by all three methods are almost identical. However, the results from HF and DFT methods differ from that of MP2 in coiled structures: whereas HF and DFT prefer the uncoiled geometry, MP2 favors the coiled one. This preference was found to be ∼3.2 and ∼2.2 kcal mol^{-1} for HF and DFT computations (Figure 8), respectively. The molecule uncoils during the optimization to achieve the geometry with a lower energy (RMSD ∼0.7 for both HF and DFT). On the other hand, MP2 prefers the coiled geometry by ∼3.6 kcal mol^{-1}, and the molecule tends to be coiled even more during the optimization to get the benzene rings closer to each other. The molecular mechanics results correspond well with the MP2 and experimental data; thus we consider the CICADA methodology and MM3 force field to be precise enough to describe our studied systems well.

4. Discussion

Inspired by the experimental data obtained from our study of ITET rate constants in various flexible bichromophoric systems D−(CH$_2$)$_x$−O−A, where D is benzoyl and A is

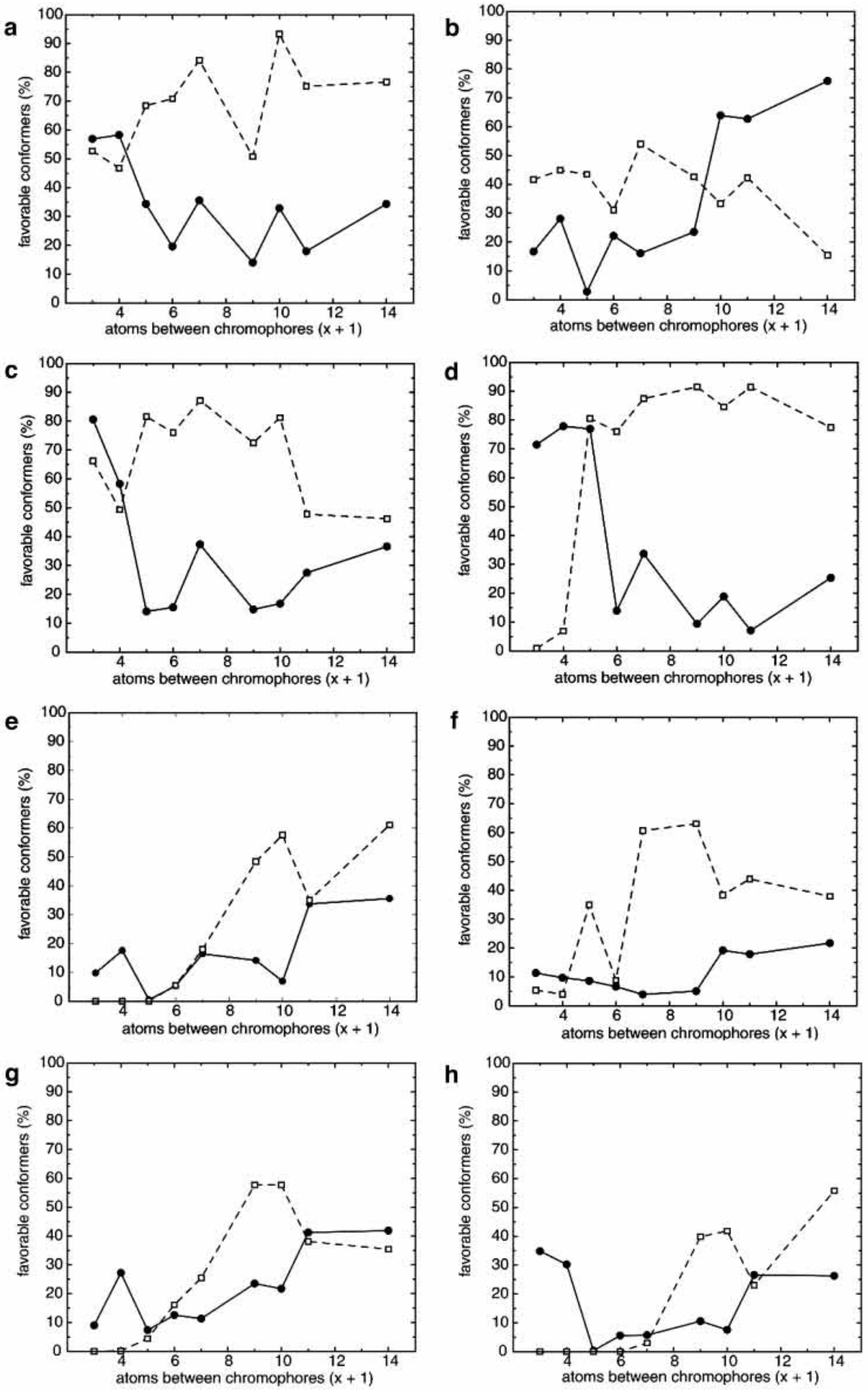


Figure 4. (a−d) Calculated populations of the conformers having d_{PhPh1} or $d_{\mathrm{PhPh2}} \leq 4.5$ Å for Bz-*x*-ONp (a), Bz-*x*-OoBP (b), Bz-*x*-OmBP (c), and Bz-*x*-OpBP (d) (●, Ph1; □, Ph2). (e−h) Calculated populations of the conformers having d_{OPh1} or $d_{\mathrm{OPh2}} \leq 4.5$ Å for Bz-*x*-ONp (e), Bz-*x*-OoBP (f), Bz-*x*-OmBP (g), and Bz-*x*-OpBP (h) (●, Ph1; □, Ph2).

naphthyl or biphenyl,[12,13] we have examined the same molecules by means of several computational methods, conformational search, molecular dynamics simulations, and quantum mechanical calculations. Results obtained by current computational tools have become respected components of scientific papers that involve experimental studies. One of the reasons is that they allow for deep understanding of processes on molecular and atomic level. We have used the highly respected MP2 level of theory within ab initio quantum chemical methods to show the ability of MM3 force field to handle systems such as ours. Then we have performed very careful search of conformational space by the program CICADA, which has been shown to compete with total search techniques such as the grid search approach.[44] Finally, we have run several long time molecular dynamics trajectories. Although the conformational search provides a static picture of the conformational space and, thus, more or less thermodynamics related information, molecular dynamics shows the behavior of the system within a time scale. Even if the time

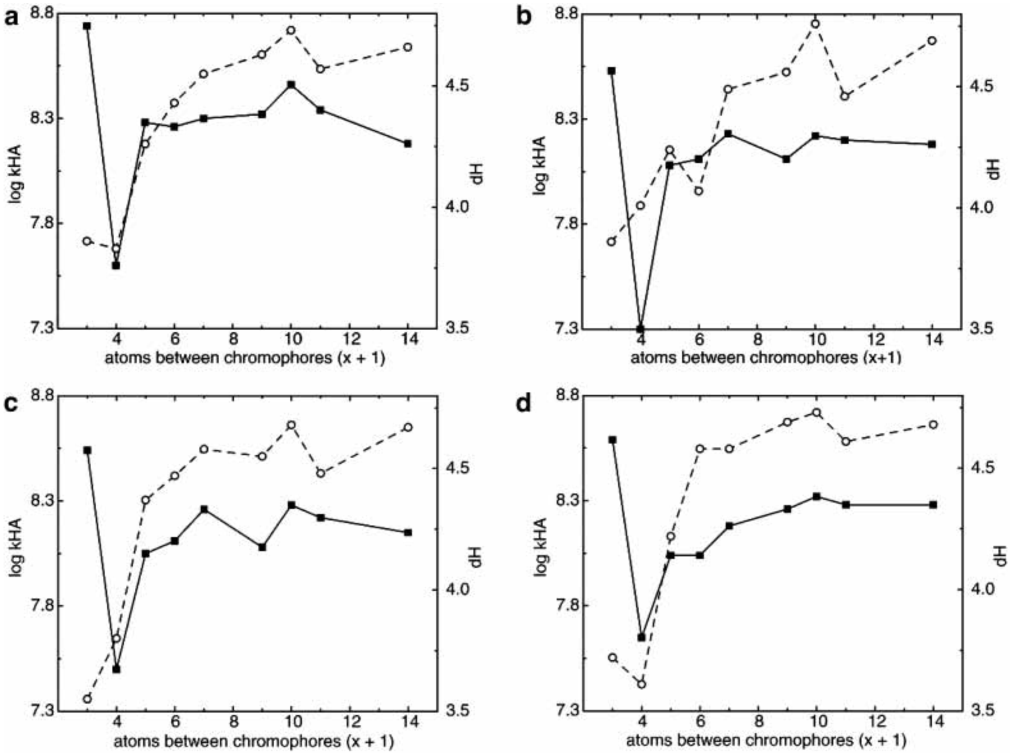


Figure 5. (a−d) Calculated probabilities of the γ-hydrogen abstraction in the Norrish type II process (dashed line) for Bz-*x*-ONp (a), Bz-*x*-OoBP (b), Bz-*x*-OmBP (c), and Bz-*x*-OpBP (d), in comparison with the experimental rate constants found for HA process (solid line; from refs 12 and 13).

interval covered is usually very short (100 ns in our case), the information obtained is very detailed, allowing us to trace processes on a femtosecond level. Altogether, it implies that molecular dynamics provides us with kinetic oriented information. In further text, we therefore discuss results obtained by both methods.

Length of the Tether and Isomeric Differences. The initial presumption that the exchange energy transfer occurs from one end of the system to the other is that end-to-end proximity is controlled by conformational motion. The magnitude of the interaction in real systems strongly depends on the character of the interaction, mutual group orientations, time of the contact, environment, and most importantly the distance. For ITET process, the proximity has the meaning of a distance over which molecular orbitals of the end groups can overlap.

Conformational search provided 4 different Boltzmann-weighted average distances (d_{PhPh1}, d_{PhPh2}, d_{OPh1}, d_{OPh2}) for all bifunctional molecules and each value is characteristic for a conformational family with specific end-group orientations. Parts a−d of Figure 3 show the dependence of the tether length on the rate constants of ITET calculated directly from the distance values according to Ermolayev's[48] eq 2. The equation serves only as a quantitative guide to the decrease in k_{ET} as a function of interchromophore distance, and it was derived from the experiments of bimolecular triplet energy transfer in a rigid matrix. Our calculation was based on the presumption that *any* close contact (within the defined limits) can provide the energy transfer. The shape of the plots suggests that the average distances between differently located geometrical points on two end groups vary significantly in the short-tether molecules ($x = 3-5$) whereas they level off for higher x values. For flexible bifunctional molecule with $x = 3$, the rate constants calculated from the distance d_{PhPh1} is higher than that calculated from d_{PhPh2} approximately by 1 order of magnitude in Bz3OpBP and to some extent also in Bz3ONp. In contrast, $d_{\mathrm{PhPh2}} \gg d_{PhPh1}$ in Bz3OoBP. Similar results were obtained for d_{OPh1} and d_{OPh2} distances, but the differences are not so dramatic. The carbonyl oxygen has a more favorable position in the molecule and it is "closer" to the acceptor moiety. The situation can be clearly illustrated by Figure 9 (the ground-state conformation of the biphenyl group is shown as twisted[53]). In low-energy conformations the ring C cannot move toward the benzoyl group in pBP derivatives, whereas in oBP molecules it can approach very closely. The question of the "reactive volume" in our calculations, *i.e.*, the space around the end group within which the interaction occurs, was raised when we defined the end-to-end distances in the systems. Geometrical points (centers) of the atom or a part of the molecule finally served as its good representation. Comparing the calculated data with those from the experimental ITET measurements is not fully adequate because we could not focus on the problem of an ideal orbital overlap and the electronic factors that accompany the energy transfer. It is clear that the phenyl ring is larger than the carbonyl oxygen and may provide more efficient overlap with the phenyl acceptor moiety. However, it is more sensitive to orientation factors, because an electron must be returned to the *n* orbital.[13] The conformational search also does not evaluate the through-bond interaction that will be discussed in the following paragraph.

The molecules with increasing number of tether atoms exhibit lower sensitivity to orientational factors, which means that the rate constants level off for all distances calculated and become nearly identical in long-tether molecules. The Boltzmann-weighted average distances give us information about the average distances in the steady-state conformational distribution, *i.e.*, distribution of all realistically populated states at a given temperature.

The *experimental* ITET rate constants measured in the same bichromophores[12,13] displayed abnormal behavior for the tether lengths $x = 7-11$, depending what acceptor moiety was present.

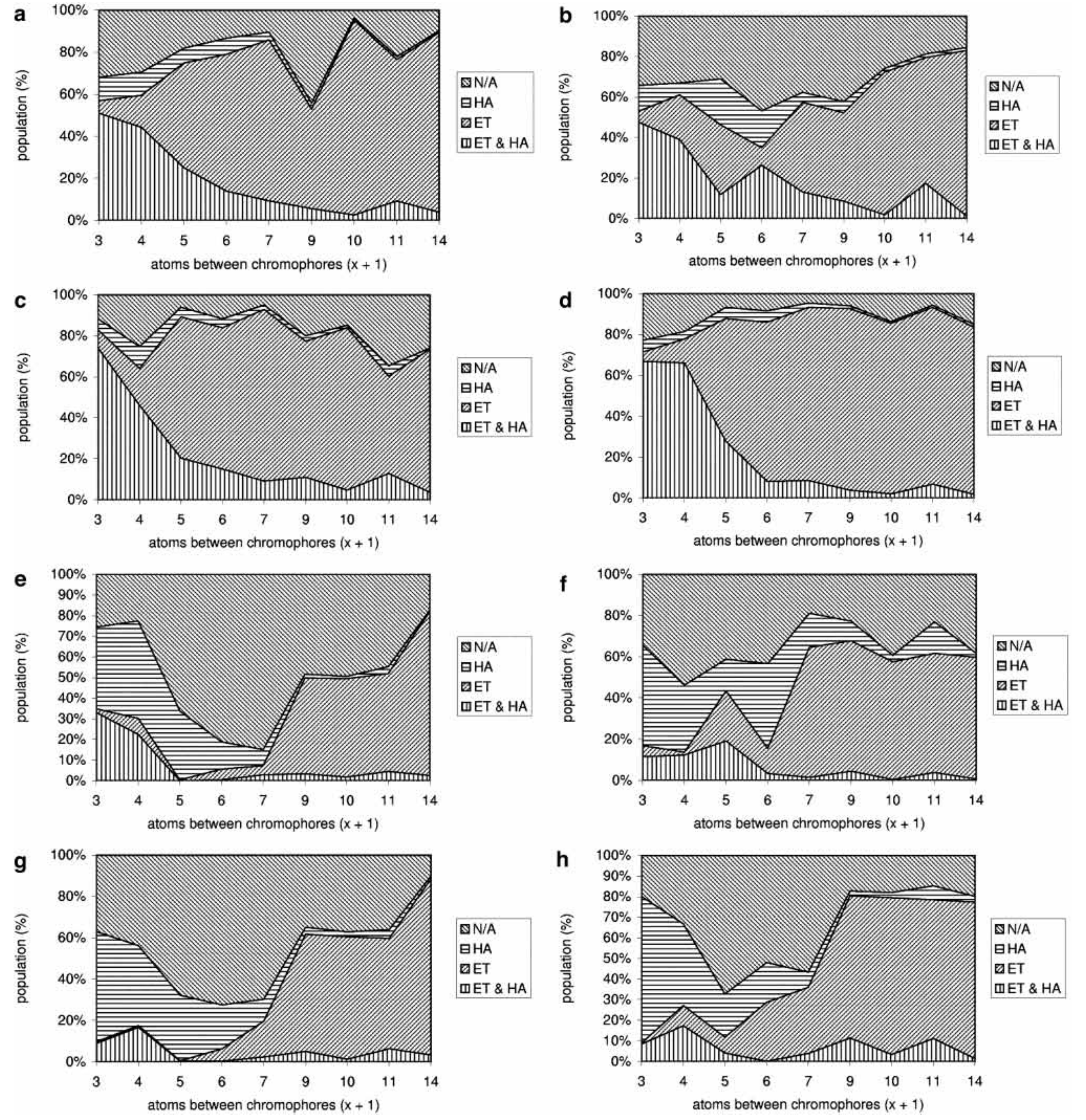


Figure 6. (a−d) Population distribution based on a fixed d_{PhPh} distance for Bz-*x*-ONp (a), Bz-*x*-OoBP (b), Bz-*x*-OmBP (c), and Bz-*x*-OpBP (d). (e−h) Population distribution based on a fixed d_{OPh} distance for Bz-*x*-ONp (a), Bz-*x*-OoBP (b), Bz-*x*-OmBP (c), and Bz-*x*-OpBP (d).

Sudden increases in the rate values were explained partially by a different "reactive volume" of the acceptor that is based on the outcome of a single bond (C−O) rotation in a given conformer (Figure 10). The more distant phenyl in pBP group cannot get close to the donor by simple C−O bond rotation, whereas in oBP and mBP groups it does. Such a behavior was expected and it is well represented by the population distribution of conformers having *intentionally* either the Ph1 or Ph2 rings in the average distance to the donor aromatic ring (d_{PhPh1} or d_{PhPh2}) equal to or less than 4.5 Å in Figure 4a−h. For d_{PhPh1} and d_{PhPh2}, the populations of the conformers significantly differ, especially in Bz-*x*-OpBP. Of course, energy in the real system can be transferred to both phenyl rings of the acceptor moiety; the observed rate constant is proportional to the sum over all the independent rate constants for reactive (favorable) conformers.[17] The rate constant k_{obs} depends on the independent kinetic pathways, with χ being the percent population with the two end chromophores in a discrete distance ($k_{obs} = \Sigma\chi_n k_n$). However, the availability of the whole biphenyl chromophore expands the "reactive volume" and so increases the probability of the transfer. Of course, the conformational search is not considering a specific rotation-controlled photochemical reaction (Scheme 1).

Parts a−d of Figure 5 show a nice correlation of the calculated average distances d_H, *i.e.*, the distances between the γ-hydrogen and the carbonyl oxygen, that are compared to the experimental hydrogen abstraction rate constants in the Norrish type II process[13] (Scheme 2). The shape of the curve perfectly matches the experimental data except for $x = 3$ (the computations do not recognize the inductive and conjugative effects of the

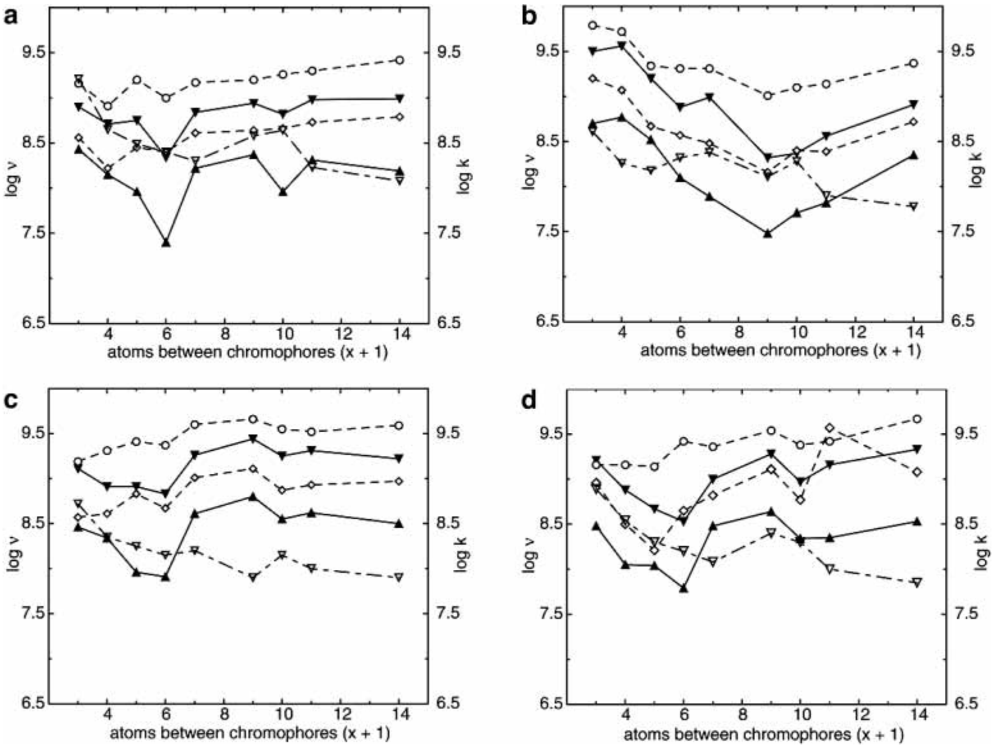


Figure 7. (a−d) MD calculation results: Bz-*x*-ONp (a), Bz-*x*-OoBP (b), Bz-*x*-OmBP (c), and Bz-*x*-OpBP (d). The interchromophore distances d_{OPh} or d_{PhPh} were set to 4.0 (▲ or ◇, respectively) or 4.5 Å (▼ or ○, respectively).

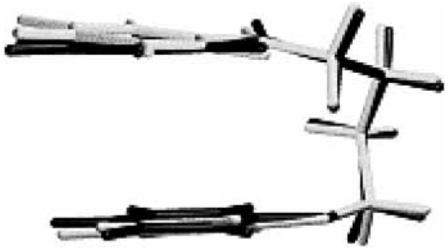


Figure 8. Example of the difference between molecular mechanics (white) and MP2 (black) minimized structures in a 5-atom-tether molecule.

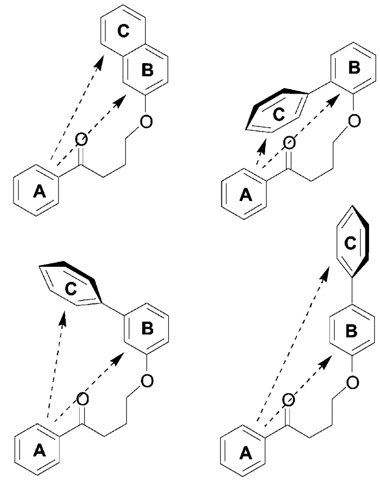


Figure 9. Illustration of the isomeric differences in short-tether molecules.

aryloxy oxygen on k_H, which explains this discrepancy). This strongly supports the application of the computational method we have chosen for our end-to-end interaction calculations.

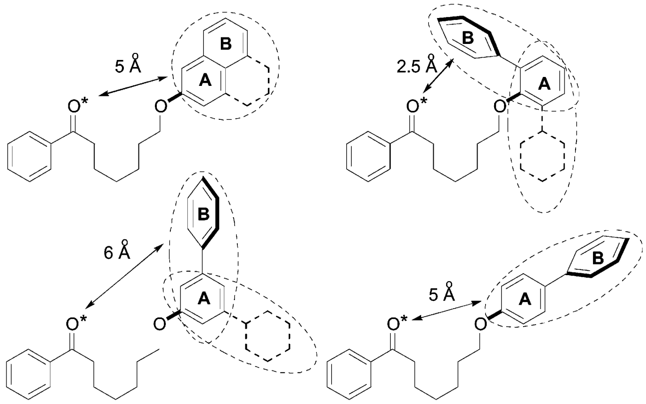


Figure 10. Illustration of the isomeric differences that influence the “reactive volume”. Adapted from ref 13.

Totally stretched molecules are sparsely populated, with an energy of >1.5 kcal mol^{-1} and a Boltzmann probability less than 5%. The populations of molecules having a geometry favorable ($d_H \leq 3.1$ Å and d_{PhPh} or $d_{\mathrm{OPh}} < 4.5$ Å) for HA (hydrogen abstraction), ET (*i.e.*, ITET), both ET and HA processes, or none of the processes (according to Scheme 2), are shown in Figure 6a−h. The *intentionally* chosen distances are the border limits for successful reactions. The distributions show similar trends for all bichromophoric systems. For d_{PhPh} distances, short molecules provide mostly both HA and ET, but for $x \geq 6$, conformers favorable only for ET dominate. It is very interesting that unfavorable conformations are not highly populated (<30%), which means that stretched molecules are not preferred. It may be π-stacking between terminal groups or simple hydrophobic van deer Waals interactions that induces coiled conformations of such molecules in solution. Hydrogen abstraction occurs only in a small portion of conformations, thus an interplay between HA and ET decides which way the system goes. Application of d_{OPh} distances enhanced conformations favorable only for HA at the expense of ET only conformations. The O1 atom is preferentially oriented on the side opposite the acceptor: the $\alpha-\beta$ C−C bond eclipses the carbonyl so that a γ C−H bond is always close to the oxygen but properly oriented only when the $\beta-\gamma$ C−C bond is gauche rather than anti. This is why k_H is known to be relatively constant for $x > 5$.

Molecular dynamics is considered to be the best simulation technique of today. It provides information about molecular and atomic movement in time. Because some processes are very fast (bond vibrations), the time step used must be very short (1 fs in our case). It means, on one hand, that the information about the dynamics of the system is very detailed. On the other hand, one needs many computational steps to cover time intervals close to abilities of experimental methods. In our study, we have simulated a period of 100 ns, which we consider to be long enough to collect statistics and to follow processes occurring on a nanosecond time scale where ITET belongs. The simulations were run in a vacuum where explicit molecules of solvent were not present. The reason is computational complexity of the problem, which would increase several times if solvent were present. The influence of solvent molecules on the computational results presented here should be large, especially in long molecules, causing a decrease in the frequency of molecular coiling. The frequencies ν_C of molecular coiling to a geometry favorable for ITET, with the distances d_{OPh} and d_{PhPh} smaller than the defined limits, are a direct measure of the dynamic properties of the system (Figure 7a−d). The frequency values for all compounds decrease with increasing x and then again raise approximately to the same order of magnitude. The magnitude of the distance generally influences the offset but not the shape of the curve. The decrease in ν_C for medium-length tethers is logical and would be even larger in the presence of a solvent.

Correlation with Experimental Data. Parts a−d of Figures 3 and 7 show comparison of our calculated data with those obtained from the experiments.[12,13] Although a conformational search (Figure 3a−d) would provide information useful for understanding the model of the conformational equilibrium,[17,18] molecular dynamics (Figure 7a−d) is focused on examining the molecule in motion, *i.e.*, the particular rate constants of chromophores approaching each other (k_{UF}, k_{FU} in Scheme 1), or even the time scales important for evaluating the applicability of the rotation controlled model.

The intramolecular interactions between two functional groups occur by a through-bond[26,54,55] or through-space[14,21,26,28] mechanism. Whereas the latter can be simulated by both conformation search and molecular dynamics, the former cannot. The through-bond interaction certainly predominates in all 4-atom tethered molecules, as is well-known from rigid systems studies,[8,10,11] for which there is not strong likelihood of significant population of conformers having an efficient orbital overlap (see a relatively smaller calculated k_{ET} for $x = 3$). We also recently assumed that through-bond interactions alone could not produce energy transfer rate constants much larger than those measured for the optimal rigid systems and that molecules having more than 6 tether atoms provide >99% of the total energy transfer by through-space mechanism.[13] The calculated k_{ET} values for $x = 3$ are lower than those in the experiments by 1−2 orders of magnitude, especially in Bz3ONp and Bz3OpBP systems. From this calculation, one can estimate that through-bond interaction dominates by ~90% in those systems. In the longer molecules, comparison of experimental values with those obtained from the conformational search provides a good parallel, showing that molecules with tethers as long as 15-atoms still afford very efficient ITET.

In contrast, molecular dynamics calculations provided the curves, the shapes of which match the experimental ones surprisingly well (Figure 7a−d). The initial conditions (*i.e.*, the end-to-end distances) had to be adjusted to obtain a good comparison with the experiment and we still have to keep in mind that the calculations were done without considering the ambient solvent molecules. The rate of coiling/uncoiling motion for all systems is of the same order of magnitude as the benzoyl chromophore lifetime. It clearly supports the idea that the system *must be rotationally controlled*, approaching the initial condition $k_{UF^*} \sim k_d$; $k_{FU^*} \ll k_{ITET}$ (Scheme 1). The shape of the curves resembles profiles of cyclization reactions operating rather under conformational equilibrium[3] and can be well compared to Monte Carlo calculations of Closs, Forbes, and co-workers,[25] or exact enumeration calculations of Shimada et al.[56,57] Similar humps in the rate constants for medium-size bichromophores were found in both theoretical and computational outcomes and may be caused by expanding the “reactive volume” of the acceptor, *i.e.*, enabling both benzene rings to be available for the transfer, as we suggested before.[12,13] The molecular mechanics calculations also proved that the fraction of coiled molecules is large even in the long-tethered systems.

5. Conclusions

This work presents a detailed analysis of the conformational behavior of various flexible bichromophoric compounds based on computational studies. The results are compared to those obtained from experiments on the same systems, in which the rate constants of intramolecular energy transfer provided a direct insight of how the connecting chain length affects end-to-end transfer.[12,13] For longer molecules in which through-space interaction dominates, conformational search provided an excellent match with experiment: the compounds with tethers as long as 5−15 atoms undergo relatively efficient transfer. Despite the fact that the computations did not evaluate through-bond interaction, they became an excellent tool for estimating its magnitude by comparing the calculated data with the experimental rate constants, especially in the $x = 3$ systems. The choice of molecular mechanics was supported well by the fact that it gave as good relative energies as high-level ab initio calculations.

The experimental paper[13] suggested that all three kinetics models for intramolecular interactions are involved, with ground-state control by a very small population of molelcules in highly coiled geometries with interchromophore distances of $d \leq 4$ Å accounting for only a few percent of the ITET. Our molecular dynamics calculations seem to confirm that rotational and equilibrium control prevail in conformations having the ends farther apart but still able to undergo energy transfer within the lifetime of the excited donor (~10 ns) by bond rotation to favorable geometries. Chromophore orientation was found to be important in short-tether molecules when parts of the chromophore moiety cannot fully reach the other chromophore due to steric problems.

It is not always clear whether comparison of computations with experiments is meant to validate one or the other, but when they agree, one can reasonably assume that both would not be wrong. For the reasons mentioned above, we are comfortable with the results of both approaches toward understanding ITET and believe that the computations do validate the conclusion presented in the experimental paper that through bond interactions dominate for the shortest tethers but rapidly are replaced by through space interactions as the tethers get longer.

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