π Interactions | Hot Paper

DOI: 10.1002/anie.201407161

Anion–π and Cation–π Interactions on the Same Surface**

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Abstract: *Herein, we address the question whether anion–π and cation–π interactions can take place simultaneously on the same aromatic surface. Covalently positioned carboxylate–guanidinium pairs on the surface of 4-amino-1,8-naphthalimides are used as an example to explore push–pull chromophores as privileged platforms for such "ion pair–π" interactions. In antiparallel orientation with respect to the push–pull dipole, a bathochromic effect is observed. A red shift of 41 nm found in the least polar solvent is in good agreement with the 70 nm expected from theoretical calculations of ground and excited states. Decreasing shifts with solvent polarity, protonation, aggregation, and parallel carboxylate–guanidinium pairs imply that the intramolecular Stark effect from antiparallel ion pair–π interactions exceeds solvatochromic effects by far. Theoretical studies indicate that carboxylate–guanidinium pairs can also interact with the surfaces of π-acidic naphthalenediimides and π-basic pyrenes.*

Cation–π interactions[1] take place on electron-rich aromatic surfaces, whereas the much more recent and still somewhat controversial anion–π interactions occur on the surface of electron-deficient aromatic systems.[2] With these interactions, counterions are usually ignored. However, the combination of anions and cations near aromatic rings has been reported in the context of molecular recognition,[3,4] the spectral tuning of green-, red-, and cyan-fluorescent protein probes,[5] and the understanding of firefly luciferase[6] as well as the chemistry of vision.[7] The molecular Stark effect that proximal ion pairs could impose on push–pull chromophores is broadly related to phenomena such as solvatochromism, electrochromism, and nonlinear optical processes.[8,9] However, in existing cation–anion–arene triads, interactions with the aromatic surface are either excluded or ignored for one or both ions. The question whether anion–π and cation–π interactions can take place on the same aromatic surface has never been answered (Figure 1 a). The only explicit considerations of such "ion pair–π" or "salt bridge–π" interactions either focus on theory with surfaces that are too small to accommodate both ions,[10] or remain purely speculative in context of cell-penetrating peptides.[11] Here, using oriented carboxylate–guanidinium pairs on the surface of 4-amino-1,8-naphthalimides as a specific example, we report experimental and theoretical support that ion pair–π interactions can occur, and that they can be relevant for function.

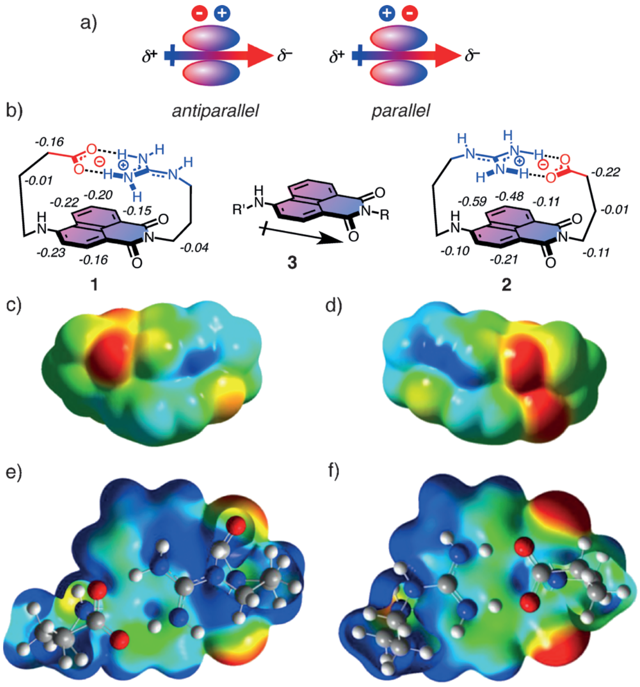

Figure 1. Ion pair–π interactions on push–pull chromophores. a) Definition of antiparallel or parallel ion pair–π interactions in comparison to the push–pull component of the ground-state dipole moment (arrows). b) Covalent positioning of antiparallel or parallel ion pair–π interactions in **1** and **2**, with indication of changes in chemical shifts ($\Delta\delta$, in ppm) in the ^{1}H NMR spectra in response to deprotonation of the conjugate carboxylic acids ([D$_6$]DMSO, 25 °C). Reference compounds **3 a** (hypothetical): R = R′ = CH$_3$, **3 b**: R = (CH$_2$)$_3$NHC(NHBoc)$_2$, R′ = (CH$_2$)$_3$COO-*t*Bu, **3 c**: R = (CH$_2$)$_3$COO-*t*Bu, R′ = (CH$_2$)$_3$NHC-(NHBoc)$_2$. c–f) Electrostatic potential surfaces of complete ground-state structures (c, d) and π-surfaces only (e, f) for antiparallel ion pair–π interactions in **1** (c, e) and parallel ion pair–π interactions in **2** (d, f). Red = negative, blue = positive, isovalue 0.0004 au/ ± 30 kcal mol^{-1}.

The 4-amino-1,8-naphthalimides (NMIs)[8] **1**–**3** were selected to explore the possible existence and functional relevance of ion pair–π interactions (Figure 1 b). With an electron-donating amine on one side and a π-accepting imide

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[**] We thank R. Letrun, S. Mosquera-Vázquez, and E. Vauthey for assistance and advise, the NMR and the Sciences Mass Spectrometry (SMS) platforms for services, and the University of Geneva, the European Research Council (ERC Advanced Investigator), the National Centre of Competence in Research (NCCR) Chemical Biology, the NCCR Molecular Systems Engineering, and the Swiss NSF for financial support.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201407161.

on the other, the compact polarized π-surface of these push–pull chromophores appeared ideal to possibly accommodate an anion and a cation next to each other. The covalent attachment of an anion and a cation was absolutely essential to control their position on the polarized aromatic surface, i.e., explore the existence of anion–π and cation–π interactions on the same surface with maximal precision and minimal ambiguities. Ion pairs[12] formed by carboxylate anions and guanidinium cations[3,11] were selected to support anion–π and cation–π interactions as much as possible with hydrogen bonding and π–π interactions. The carefully optimized[2i] linkers between ions and push–pull chromophores were adjusted for perfect positioning of anion and cation on the aromatic surface. Ion pairs could be placed parallel and antiparallel to the push–pull component of the ground-state dipole moment of the push–pull chromophore (Figure 1a). Antiparallel and parallel ion pair–π interactions are realized in the constitutional isomers **1** and **2**, respectively (Figure 1b).

Theoretical simulations revealed that the formation of both parallel and antiparallel ion pair–π interactions in the ground state is energetically favorable (Gaussian09;[13] B97D, 6-311G**;[14] Figure 1c–f, Table S1). The distances between anion or cation and the aromatic plane in the ground state were shorter in parallel **2** than in antiparallel **1** (Table 1). This difference could suggest that favorable ion pair–π interactions in isomer **2** could overcompensate for the repulsion between the ion pair and the push–pull dipole (Figure 1a). The electrostatic potential surfaces confirmed that the presence of ion pairs significantly affects the polarization of push–pull systems (MP2/6-311G**//B97D/6-311G**, GaussView 5.0,[15] VMD,[16] Figures 1c–f and S1). Parallel ion pair–π interactions in **2** increased the push–pull component of the intrinsic ground-state dipole moment $\mu_{\mathrm{DA}}{}^{\mathrm{GS}} = +7.1$ D of the unperturbed chromophore **3a** to $\mu_{\mathrm{DA}}{}^{\mathrm{GS}} = +12.1$ D (Table 1, Figure 1d), whereas antiparallel ion pair–π interactions in **1** reversed the same push–pull dipole to a very weak $\mu_{\mathrm{DA}}{}^{\mathrm{GS}} = -0.9$ D (M06-2X/def2-TZVP//B97D/6-311G**,[17–19] Figure 1c).

The excitation of push–pull chromophores is accompanied by an intramolecular charge transfer (ICT) from the donor toward the acceptor.[8,9] This increase of the push–pull component of the excited-state dipole moments $\mu_{\mathrm{DA}}{}^{\mathrm{ES}}$ was confirmed in theoretical simulations of the first excited states (TURBOMOLE v.6.1,[20] ADC(2),[21] cc-pVTZ basis set,[22] Table 1). The change of the dipole moment was larger with antiparallel isomer **1** ($\mu_{\mathrm{DA}}{}^{\mathrm{T}} = +4.4$ D) than with parallel isomer **2** ($\mu_{\mathrm{DA}}{}^{\mathrm{T}} = +2.5$ D, Table 1). The antiparallel positioning of carboxylate–guanidinium pairs in isomer **1** was ideal for stabilizing the ICT excited state. In theoretical predictions, this intramolecular Stark effect caused a red shift of the absorption maximum by $\Delta\lambda_{\max} = +70$ nm (Table 1). Inversion of the orientation of carboxylate–guanidinium pairs in isomer **2** annihilated this bathochromic effect ($\Delta\lambda_{\max} = +2$ nm, Table 1). Comparisons with models without anion or cation showed that the contributions from anion–π and cation–π interactions to spectral tuning were additive (Tables S8 and S9, Figures S6 and S7).[19,23,24]

To verify the validity of our theoretical predictions experimentally, the constitutional isomers **1** and **2** were synthesized in a few steps from commercially available starting materials (Scheme S1). The formation of ion pair–π interactions could be followed in the ^{1}H NMR spectra of **1** and **2** in [D$_6$]DMSO. Deprotonation of their conjugate acids caused position-dependent upfield shifts of the NMI resonances, whereas the signals for the linker did not change significantly (Figure 1b). Particularly significant upfield shifts observed at positions 5 and 6 of **2** were consistent with the presence of a guanidinium group near these protons, and thus supported the occurrence of intramolecular ion pairing as depicted in Figure 1f.

The absorption spectra of **1** and **2** were recorded in comparison with their protected, uncharged precursors **3b** and **3c**. The largest red shifts in response to the formation of ion pair–π interactions were, not surprisingly, observed in the least polar solvent, i.e., CCl$_4$ (Figure 2c, Table 1). At high dilution, the antiparallel configuration in isomer **1** caused a red shift of $\Delta\lambda_{\max} = +41$ nm. Decreasing red shifts with increasing concentration were presumably due to aggregation, although the absorbance showed a perfectly linear concentration dependence (Figure 2e). Decreasing red shifts upon aggregation were consistent with ion pair–π interactions because any additional intermolecular contacts necessarily weaken the strong local dipoles in monomeric **1** and thus reduce the stabilization of the ICT-polarized excited state by intramolecular antiparallel ion pair–π interactions. Saturation behavior at high dilution suggested that the maximal $\Delta\lambda_{\max} = +41$ nm indeed originates from monomeric **1** (Figure 2e, solid). The red shift and even the position of the absorption

Table 1: Characteristics of guanidinium–carboxylate pairs on aromatic surfaces.[a]

Cpd.	Type[b]	Anion–π [Å][c]	Cation–π [Å][c]	$\mu_{\mathrm{DA}}{}^{\mathrm{GS}}$ [D][d]	$\mu_{\mathrm{DA}}{}^{\mathrm{ES}}$ [D][e]	$\lambda_{\max}$ calc[f]	$\lambda_{\max}$ CCl$_4$[g]	$\lambda_{\max}$ DMSO[h]	$\Delta\lambda_{\max}$ calc[i]	$\Delta\lambda_{\max}$ CCl$_4$[j]	$\Delta\lambda_{\max}$ DMSO[k]
1	antiparallel	3.33	3.31	−0.9	+3.5	450	462	453	+70	+41	+13
2	parallel	3.21	3.27	+12.1	+14.6	382	449	435	+2	+23	−4
3[l]	none	–	–	+7.1	+10.1	380	421	440	–	–	–
4	induced	3.13	3.24	–	–	–	380	380	–	0	0

[a] Wavelength $\lambda_{\max}$ of absorption maxima are given in nm (nanometers). [b] Compare text and Figure 1 and Figure 3. [c] Cation–π and anion–π distances were measured from the central carbon atom of guanidinium cation and from the centroid of carboxylate anion, respectively, towards the plane fitted through the naphthyl core of NMI. [d] Donor–acceptor (DA) component of the ground-state (GS) dipole moment, in Debye (Figure 1). [e] Same for the first excited state (ES). [f] Calculated $\lambda_{\max}$ in vacuum. [g] Measured $\lambda_{\max}$ in CCl$_4$. [h] Measured $\lambda_{\max}$ in DMSO. [i] Calculated red shift $\lambda_{\max}$(**1**, **2**)−$\lambda_{\max}$(**3a**) in vacuum. [j] Measured $\lambda_{\max}$(**1**, **2**)−$\lambda_{\max}$(**3b**, **3c**) in CCl$_4$. [k] Measured $\lambda_{\max}$(**1**, **2**)−$\lambda_{\max}$(**3b**, **3c**) in DMSO. [l] Measured with **3b**, **3c**, calculated with **3a**.

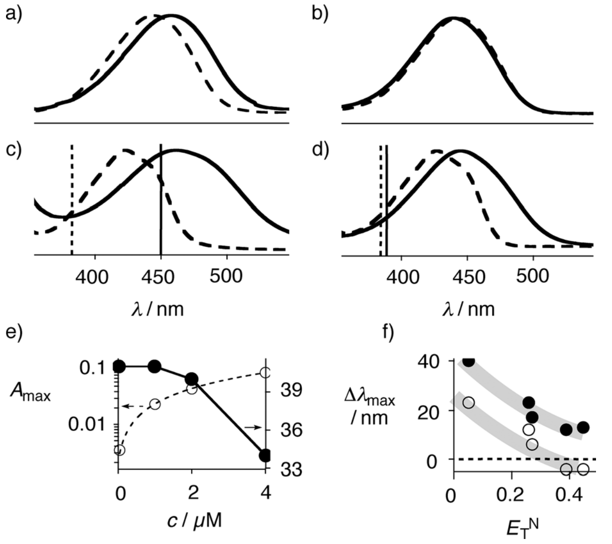

Figure 2. Spectroscopic relevance of ion pair–π interactions on push–pull systems. Absorption spectra of **1** (a, c, solid) and **2** (b, d, solid) in DMSO (a, b) and CCl_4 (c, d) compared to **3b** and **3c** (a–d, dashed). Theoretical predictions in vacuum are indicated as solid and dashed lines (c, d). e) Dependence of the absorbance A_{max} with linear curve fit (○, $R = 0.99992$) and $\Delta\lambda_{max}$ (●) on the concentration c of **1** in CCl_4. f) Dependence of the red shifts $\Delta\lambda_{max}$ of **1** (●) and **2** (○) in the polarity E_T^N of the solvent (CCl_4, $CHCl_3$, $Cl_2C_2H_4Cl_2$, DMF, DMSO).

maxima were in quite remarkable agreement with theoretical predictions and thus demonstrated the power of computational chemistry to predict relevant spectroscopic characteristics of fairly challenging systems (Figure 2c, Table 1).

Solvatochromism,[9] that is excited-state stabilization by polar solvents, could be observed as a red shift of $\Delta\lambda_{max} = +19$ nm from $\lambda_{max} = 421$ nm to $\lambda_{max} = 440$ nm for control **3b** in CCl_4 and DMSO (Figure 2a and c, dashed lines, Table 1). For the same change in solvent polarity, the antiparallel carboxylate–guanidinium pairs in **1** produced a small blue shift of $\Delta\lambda_{max} = -9$ nm from $\lambda_{max} = 462$ nm to $\lambda_{max} = 453$ nm, possibly due to weakened ion pair–π interactions in these more competitive solvents (Figure 2a and c, solid lines, Table 1). The opposite response to increasing solvent polarity with and without carboxylate–guanidinium pairs resulted in an overall decreasing red shift from $\Delta\lambda_{max} = +41$ nm in CCl_4 to $\Delta\lambda_{max} = +13$ nm in DMSO (Table 1). However, the separate opposing trends to solvent polarity contained additional important information: Antiparallel ion pair–π interactions 1) also exist in polar solvents, at least partially, 2) shield the chromophore from solvatochromism, and 3) generate an intramolecular Stark effect that exceeds solvatochromism by far.

The protonation of the carboxylate anion with trifluoroacetic acid reproducibly and reversibly weakened or cancelled all red shifts in all solvents. This finding suggested that the exchange of the intramolecular by an intermolecular anion weakens or fully destroys ion pair–π interactions in this system under these conditions. Taken together, the overall impressive red shifts ($\Delta\lambda_{max} = +70$ nm expected in vacuum, $\Delta\lambda_{max} = +41$ nm found in the least polar CCl_4) and their decrease with solvent polarity, aggregation, and protonation afforded meaningful experimental support for the existence and spectroscopic relevance of antiparallel ion pair–π interactions.

Compared to these powerful antiparallel ion pair–π interactions, the spectroscopic impact of parallel carboxylate–guanidinium pairs was almost as modest as predicted theoretically. In CCl_4, the parallel carboxylate–guanidinium pair in **2** caused a still appreciable red shift of $\Delta\lambda_{max} = +23$ nm (Figure 2d). However, like with antiparallel **1**, the parallel **2** showed an even more pronounced blue shift of $\Delta\lambda_{max} = -14$ nm in response to increasing solvent polarity, from $\lambda_{max} = 449$ nm in CCl_4 to $\lambda_{max} = 435$ nm in DMSO (Figure 2b and d, solid spectra, Table 1). Because of the complementary red-shifting solvatochromism of the uncharged control **3c** (Figure 2b and d, dashed lines, Table 1), the presence of parallel carboxylate–guanidinium pairs in DMF and DMSO resulted in a small overall blue shift of $\Delta\lambda_{max} = -4$ nm (Figure 2b and f, empty circles, Table 1). This result was consistent with the predicted inability of parallel ion pair–π interactions to significantly stabilize the ICT excited state of push–pull chromophores.

The formation of ion pair-π interactions on the unpolarized π-acidic surfaces was considered as well (Figure 3a). Computational models of naphthalenediimide (NDI) **4** revealed the presence of the cation and particularly the anion in close proximity to the aromatic surface (Table 1). Electrostatic potential surfaces confirmed the transfer of electron density between anion and cation on the one side and the aromatic system, including the imide oxygen atoms, on the other side (Figure 3a). However, significant shifts were not observed in the absorption spectra of **4** (Table 1). Systems that are more environmentally responsive than the notoriously insensitive NDIs will be needed to eventually create induced push–pull chromophores with ion pair–π interactions.

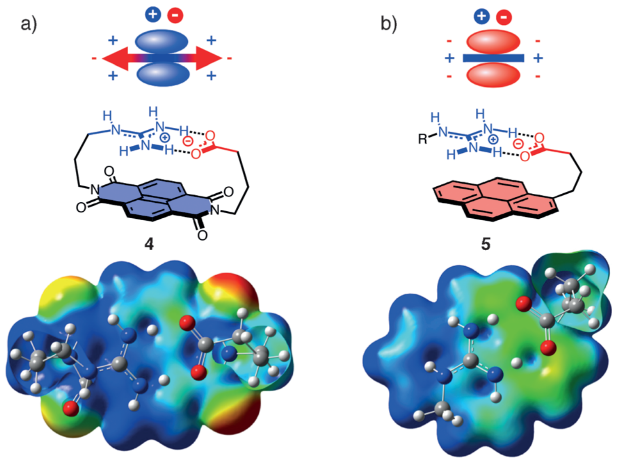

Figure 3. Ion pair–π interactions on π-acidic and π-basic surfaces. Definition, molecular structures, and ground-state electrostatic potential surfaces for anion–π and cation–π interactions on π-acidic (a) and π-basic aromatic surfaces (b) (isovalue 0.01 au/±38 kcal mol^{-1}).

A unique example for explicit anion–π and cation–π interactions on the same surface with biological relevance concerns cell-penetrating peptides.[11] The question how these guanidinium-rich peptides can cross the membrane barrier has been a subject of intense debate since their discovery in the late 1980s. The finding that pyrenebutyrate can accelerate their direct delivery into the cytosol has been rationalized by ion pairing on the π-basic pyrene surface.[11] To evaluate the validity of this purely speculative interpretation in the light of the present study, the ion pair–π complex was investigated theoretically. The energy minimum found for complex **5** revealed operational anion–π and cation–π interactions, with both anion (3.20 Å) and cation (3.34 Å) residing comfortably on the aromatic plane (Figure 3 b). Moreover, a lateral polarization of the aromatic system induced by the ion pair–π interaction was clearly visible in the electrostatic potential surface (Figure 3 b).

Taken together, the results provide theoretical and experimental evidence that anion–π and cation–π interactions can occur on the same surface, and that they are relevant for function, here in particular for spectral tuning. Studies on scope, limitations, and applications of these "ion pair–π" interactions are ongoing and will be reported in due course.

Received: July 13, 2014
Revised: July 30, 2014
Published online: August 28, 2014

Keywords: computational chemistry · peptides · π interactions · push–pull chromophores · spectral tuning

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[1] D. A. Dougherty, *Acc. Chem. Res.* **2013**, *46*, 885 – 893.

[2] a) A. Frontera, P. Gamez, M. Mascal, T. J. Mooibroek, J. Reedijk, *Angew. Chem. Int. Ed.* **2011**, *50*, 9564 – 9583; *Angew. Chem.* **2011**, *123*, 9736 – 9756; b) D.-X. Wang, M.-X. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 892 – 897; c) P. Ballester, *Acc. Chem. Res.* **2013**, *46*, 874 – 884; d) H. T. Chifotides, K. R. Dunbar, *Acc. Chem. Res.* **2013**, *46*, 894 – 906; e) L. M. Salonen, M. Ellermann, F. Diederich, *Angew. Chem. Int. Ed.* **2011**, *50*, 4808 – 4842; *Angew. Chem.* **2011**, *123*, 4908 – 4944; f) M. Giese, M. Albrecht, C. Bohnen, T. Repenko, A. Valkonen, K. Rissanen, *Dalton Trans.* **2014**, *43*, 1873 – 1880; g) S. T. Schneebeli, M. Frasconi, Z. Liu, Y. Wu, D. M. Gardner, N. L. Strutt, C. Cheng, R. Carmieli, M. R. Wasielewski, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2013**, *52*, 13100 – 13104; *Angew. Chem.* **2013**, *125*, 13338 – 13342; h) Y. Zhao, Y. Domoto, E. Orentas, C. Beuchat, D. Emery, J. Mareda, N. Sakai, S. Matile, *Angew. Chem. Int. Ed.* **2013**, *52*, 9940 – 9943; *Angew. Chem.* **2013**, *125*, 10124 – 10127; i) Y. Zhao, C. Beuchat, Y. Domoto, J. Gajewy, A. Wilson, J. Mareda, N. Sakai, S. Matile, *J. Am. Chem. Soc.* **2014**, *136*, 2101 – 2111; j) Y. Zhao, N. Sakai, S. Matile, *Nat. Commun.* **2014**, *5*, 3911.

[3] a) S. E. Thompson, D. B. Smithrud, *J. Am. Chem. Soc.* **2002**, *124*, 442 – 449; b) X. Wang, J. Post, D. K. Hore, F. Hof, *J. Org. Chem.* **2014**, *79*, 34 – 40; c) P. Blondeau, M. Segura, R. Perez-Fernandez, J. de Mendoza, *Chem. Soc. Rev.* **2007**, *36*, 198 – 210; d) M. Haj-Zaroubi, F. P. Schmidtchen, *ChemPhysChem* **2005**, *6*, 1181 – 1186; e) S. Rensing, M. Arendt, A. Springer, T. Grawe, T. Schrader, *J. Org. Chem.* **2001**, *66*, 5814 – 5821.

[4] a) Y.-J. Huang, W.-J. Ouyang, X. Wu, Z. Li, J. S. Fossey, T. D. James, Y.-B. Jiang, *J. Am. Chem. Soc.* **2013**, *135*, 1700 – 1703; b) V. Sgobba, A. Troeger, R. Cagnoli, A. Mateo-Alonso, M. Prato, F. Parenti, A. Mucci, L. Schenetti, D. M. Guldi, *J. Mater. Chem.* **2009**, *19*, 4319 – 4324.

[5] a) N. H. List, J. M. H. Olsen, H. J. A. Jensen, A. H. Steindal, J. Kongsted, *J. Phys. Chem. Lett.* **2012**, *3*, 3513 – 3521; b) H. W. Ai, S. G. Olenych, P. Wong, M. W. Davidson, R. E. Campbell, *BMC Biol.* **2008**, *6*, 13.

[6] D. Cai, M. A. L. Marques, F. Nogueira, *J. Phys. Chem. B* **2013**, *117*, 13725 – 13730.

[7] a) M. Sheves, K. Nakanishi, B. Honig, *J. Am. Chem. Soc.* **1979**, *101*, 7086 – 7088; b) P. D. Kiser, M. Golczak, K. Palczewski, *Chem. Rev.* **2014**, *114*, 194 – 232.

[8] R. M. Duke, E. B. Veale, F. M. Pfeffer, P. E. Kruger, T. Gunnlaugsson, *Chem. Soc. Rev.* **2010**, *39*, 3936 – 3953.

[9] a) C. Reichardt, *Chem. Rev.* **1994**, *94*, 2319 – 2358; b) E. W. Miller, J. Y. Lin, E. P. Frady, P. A. Steinbach, W. B. Kristan, R. Y. Tsien, *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 2114 – 2119.

[10] M. Mitra, P. Manna, S. K. Seth, A. Das, J. Meredith, M. Helliwell, A. Bauzá, S. R. Choudhury, A. Frontera, S. Mukhopadhyay, *CrystEngComm* **2013**, *15*, 686 – 696.

[11] a) N. Sakai, S. Matile, *J. Am. Chem. Soc.* **2003**, *125*, 14348 – 14356; b) K. Inomata, A. Ohno, H. Tochio, S. Isogai, T. Tenno, I. Nakase, T. Takeuchi, S. Futaki, Y. Ito, H. Hiroaki, M. Shirakawa, *Nature* **2009**, *458*, 106 – 109.

[12] a) D. J. Barlow, J. M. Thornton, *J. Mol. Biol.* **1983**, *168*, 867 – 885; b) K. Brak, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2013**, *52*, 534 – 561; *Angew. Chem.* **2013**, *125*, 558 – 588.

[13] Gaussian 09 *revision B.01*, M. J. Frisch, et al., Gaussian, Inc., Wallingford CT, **2009**.

[14] a) S. Grimme, *J. Comput. Chem.* **2006**, *27*, 1787 – 1799; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648 – 5652.

[15] GaussView *5* R. Dennington, T. Keith, J. Millam, Semichem Inc., Shawnee Mission KS, **2009**.

[16] W. Humphrey, A. Dalke, K. Schulten, *J. Mol. Graphics* **1996**, *14*, 33 – 38.

[17] a) Y. Zhao, D. G. Truhlar, *J. Chem. Phys.* **2006**, *125*, 194101 – 194118; b) Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215 – 241.

[18] A. Bauza, D. Quiñonero, P. M. Deya, A. Frontera, *J. Phys. Chem. A* **2013**, *117*, 2651 – 2655.

[19] In compliance with Ref. [18], diffuse functions were not included in ground-state calculations. Diffuse functions were used in TDDFT excited-state calculations (Tables S8 and S9) and shown to have negligible effect.

[20] TURBOMOLE V6.1 2009, a development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989 – 2007, TURBOMOLE GmbH, available from http://www.turbomole.com.

[21] J. Schirmer, A. B. Trofimov, *J. Chem. Phys.* **2004**, *120*, 1449 – 11464.

[22] a) C. Hättig, F. Weigend, *J. Chem. Phys.* **2000**, *113*, 5154 – 5161; b) C. Hättig, *Adv. Quantum Chem.* **2005**, *50*, 37 – 60.

[23] ADF, scm, theoretical chemistry, Vrije Universiteit, Amsterdam, the Netherlands, http://www.scm.com.

[24] a) A. D. Becke, *J. Chem. Phys.* **1997**, *107*, 8554 – 8560; b) C. T. Lee, W. T. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785 – 789; c) B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* **1989**, *157*, 200 – 206.