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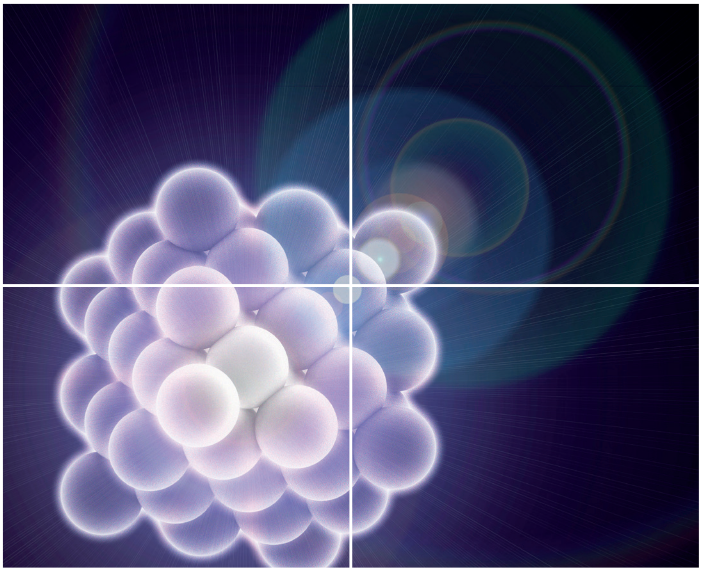

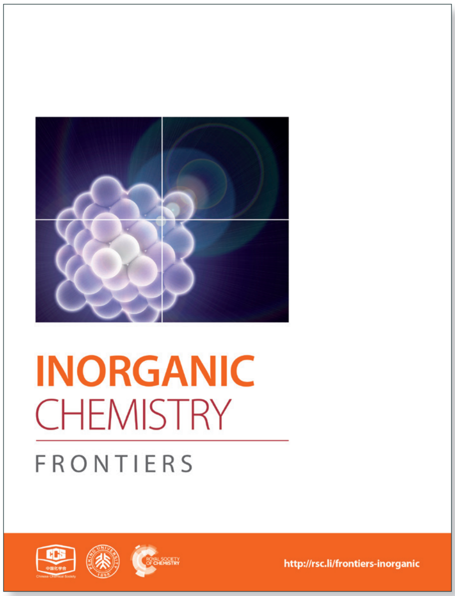

On the Flexibility of Carboranylalkylthio Substituents in Porphyrazines and Its Relevance to the Photophysical Properties[†]

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ABSTRACT: Ultrafast transient absorption spectrometry and DFT/TDDFT calculations reveal that following photoexcitation carboranyl- and carboranyl-free alkylthioporphyrazines deactivate by the pathway $S_1(\pi,\pi^*) \rightarrow S_n(C_\beta\text{-}2p_z/S_{l.p.},\pi^*) \rightarrow$ ground state. The presence of quenching singlet excited states with predominant $C_\beta\text{-}2p_z/S_{l.p.},\pi^*$ character immediately below the primarily photogenerated $S_1(\pi,\pi^*)$ state is a consequence of the electronic structure changes induced by the inherent flexibility of the alkylthio chains.

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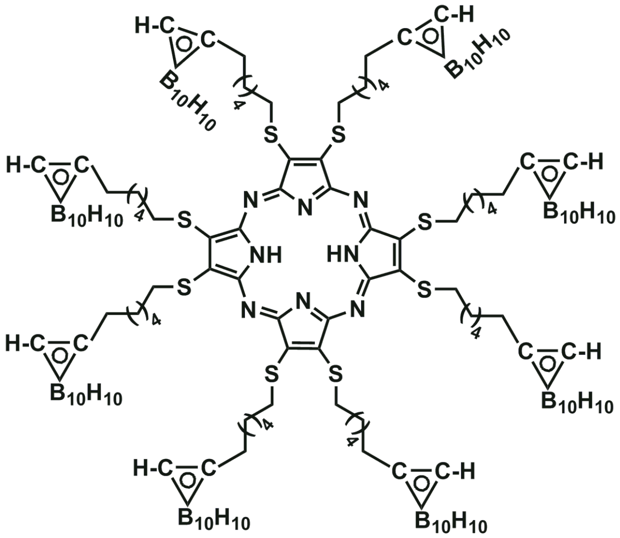
Alkylthioporphyrazines (ATPzs) are a widely investigated class of tetrapyrroles because of their potential applications in high-tech fields and biomedicine.[1-5] Dissimilar from alkylthioporphyrins[6] and arylsubstituted porphyrazines,[7] which show luminescence and $^1O_2$ photosensitizing properties, ATPzs are only weakly fluorescent, if any. According to preliminary photophysical studies, ATPzs undergo fast radiationless decay upon photoexcitation into the intense near-IR Q-band, that makes them promising candidates as sensitizers in photothermal therapy (PTT) of cancer.[8]

In the present work it is shown that the unusual photophysical behavior of ATPzs is related to the inherent flexibility of the alkylthio groups. The photophysical properties of ATPzs are investigated using 2,3,7,8,12,13,17,18-octakis-(1,2-dicarba *closo*-dodeca-boran-2-*yl*)hexylthio-5,10,15,20-(21*H*, 23*H*) porphyrazine, H_2HEHCSPz, as a case study.



H_2HEHCSPz

This molecule, which has been synthesized by innovative, "soft" methods,[1] † has the advantage to conjugate the biologically relevant characteristic of being free from transition metals with potential in PTT and, because of the high boron content, also in neutron capture therapy (BNCT) of cancer.[1] To ascertain whether the encumbering carboranyl cages can influence the flexibility of the alkylthio groups, the carboranyl-free ethylthioporphyrazine, H_2OESPz, is also studied. The photophysical behavior of H_2HEHCSPz and H_2OESPz is investigated by ultrafast transient absorption spectroscopy in solution and interpreted with the help of dynamic ^{1}H NMR experiments and density functional theory (DFT) and time-dependent DFT (TDDFT) calculations on the methylthioporphyrazine model system, H_2OMSPz.

The emission spectrum of $H_2HEHCSPz$ in CH_2Cl_2, normalized to the $Q_x(0,0)$ band maximum, is characterized by a structureless band centered at 738 nm with a Stokes shift of ~ 530 cm^{-1},† as previously observed in other ATPzs.[9] A very low value (0.0017) was obtained for the absolute emission quantum efficiency (q_M) from the Strickler-Berg equation. A comparably small q_M value was obtained for H_2OESPz. Aggregation-induced fluorescence quenching was ruled out on the basis of Lambert-Beer experiments.†

Time-resolved transient absorption changes and kinetic data were acquired in CH_2Cl_2 at room temperature using 640 nm (Q band envelope) and 340 nm (B band maximum) excitation wavelengths. No dependence on the excitation wavelength was observed. The spectrum formed within the instrument response time (ca. 200 fs) displayed negative signals due to the bleaching of the ground-state absorption bands at 725 nm, 650 nm, and 500 nm, and positive absorption signals between 760-810 nm and 540-600 nm (Fig. 1).

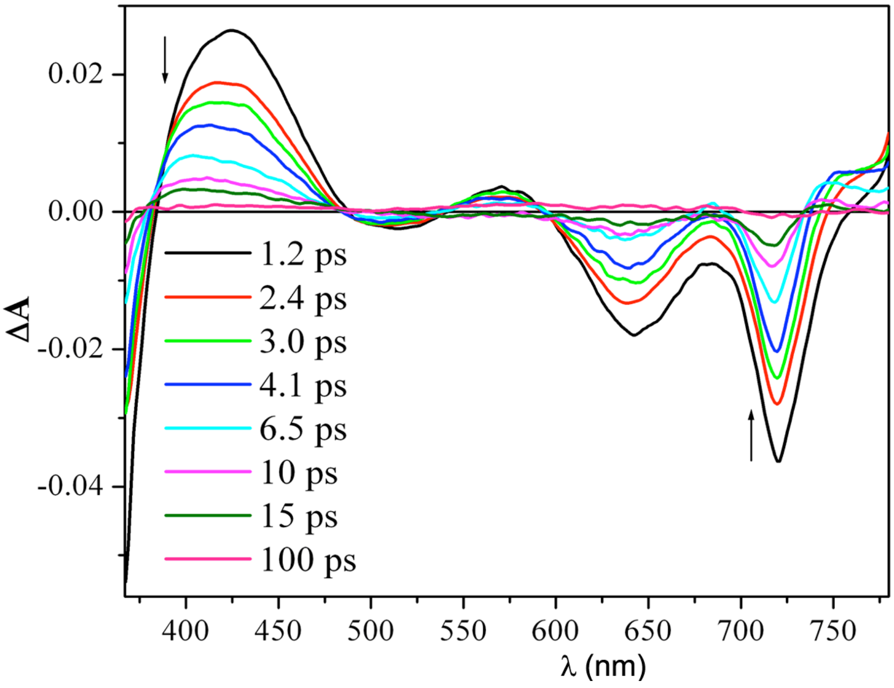


Fig. 1 Femtosecond transient absorption difference spectra of a 40 μM solution of $H_2HEHCSPz$ in CH_2Cl_2 at different delay times after 340 nm excitation.

A pronounced photoinduced absorption band at around 420 nm could also be detected superimposed on the strong bleaching signal due to the B band removal (1.2 ps spectrum in Fig. 1). This initially formed transient spectrum could be assigned to the $S_1(\pi,\pi^*)$ state responsible for the $Q_x(0,0)$ band. As the time delay between pump and probe increased, the intensity of the transient absorption signal decreased; however, no changes in spectral shape could be detected during decay of the transient, except for the blue shift of the positive signals in the red and blue region of the probe spectral window. After the blue shift was complete (ca. 8 ps), the transient absorption signal decayed to a small offset with isosbestic behavior. The blue shift of the transient absorption bands is generally associated with vibrational relaxation (cooling) of a vibrationally hot excited state.[10] Interestingly, the observed vibrational relaxation process had a similar lifetime, independent of the excitation wavelength. As the $S_1(\pi,\pi^*)$ state formed within the instrument response time is already in its relaxed energy minimum, there must be other states that lie closely below the $S_1(\pi,\pi^*)$ that might be populated in their high vibrational levels, also within the instrument response time. It is likely that these excited states, which absorb in the same spectral region as the $S_1(\pi,\pi^*)$, decay uniformly to the ground state, resulting in the observed isosbestic behavior of the transient absorption signal.

The decay of the positive absorption as well as the ground-state recovery was best fit by a double exponential function (lifetimes of ca. 3.2 ps and 24 ps) plus a small constant term.† This term can be attributed to the $S_1(\pi,\pi^*)$ state returning to ground state by a radiative process (fluorescence), although a small contribution to the residual absorption at longer time from the $T_1(\pi,\pi^*)$ state formed in very low-yield cannot be ruled out. H_2OESPz showed similar spectral and kinetic behavior.†

Variable temperature (VT) ^{1}H NMR experiments provided information on the flexibility of the alkylthio groups. The changes in the H_2HEHCSPz ^{1}H NMR spectrum down to –95°C are shown in Fig. 2. One sharp triplet was detected, at room temperature, at 4.10 ppm for the SCH_2 groups, implying the equivalence of the hexyl chains and division of the whole molecule in eight equivalent parts by symmetry. Lowering the temperature down to –65°C resulted in a broadening of the SCH_2 triplet that eventually split into two broad signals separated by 168 Hz at –95°C. Line-shape simulation of the experimental traces at various temperatures allowed to determine an activation free energy, $\Delta G^{\#}$, of 9.90 ± 0.15 kcal/mol for the twisting of the peripheral chains around the C_β–S bond.

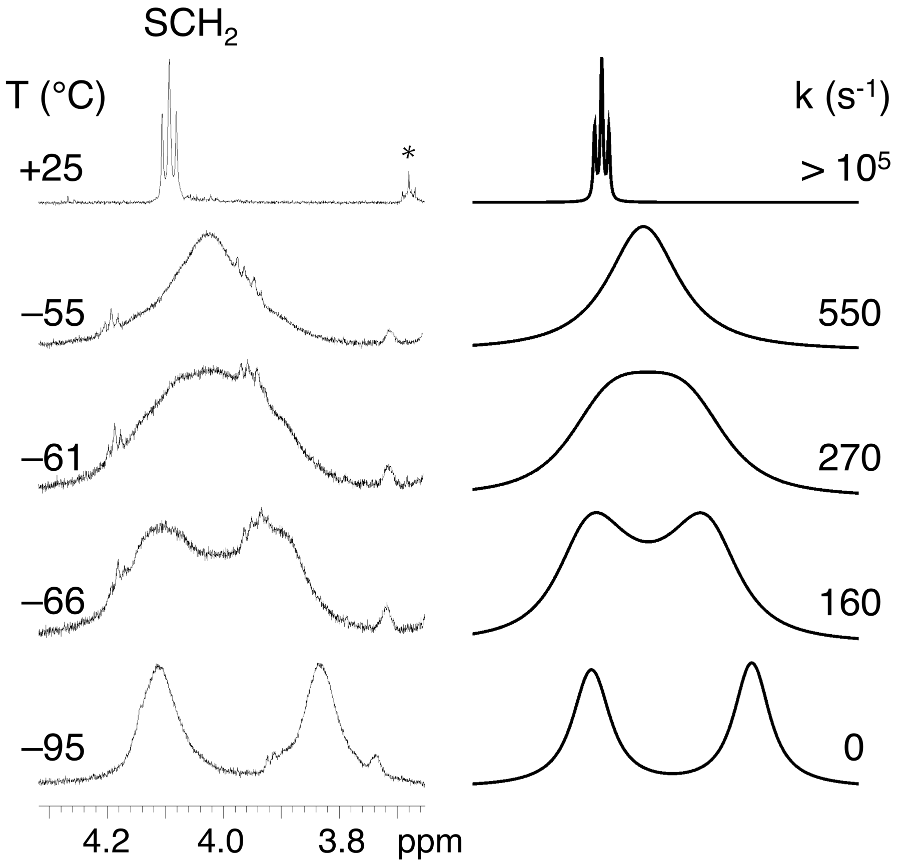


Fig. 2 ^{1}H NMR experimental traces for H_2HEHCSPz in CD_2Cl_2 showing the temperature dependence of the SCH_2 signal at 4.10 ppm (left); the starred signal at 3.7 ppm in the 25 °C trace refers to residual THF in the sample. Simulated traces and computed rate constants (right).

The observed diastereotopic behavior of the SCH_2 groups suggests that at low temperatures the elements of symmetry are reduced from eight to four, implying that vicinal SCH_2 groups have been locked in an *anti* arrangement. A comparable free-energy barrier (9.85 ± 0.15 kcal/mol) was found for H_2OESPz, suggesting that in the investigated ATPzs the flexibility of the peripheral chains is influenced neither by their size nor by the presence of terminal carboranyl groups.

To understand whether the observed flexibility of the alkylthio groups play a role in determining the unusual photophysical behavior of the investigated ATPzs, DFT/TDDFT calculations of the ground and lowest excited states of the H_2OMSPz model system were performed.[11]

A previous DFT analysis of the conformational behavior of this molecule by some of us revealed that the nearly degenerate C_{2h} and C_{2v} symmetry conformations, characterized by an *uu-ud-dd-du* (*u* = up; *d* = down) and *uu-dd-uu-dd* orientation of the methyl groups, respectively, are the preferred ones among several choices.[12] Therefore, only these two conformers were examined in this study.

To model the electronic effects of the twisting of the methyl groups around the C_{β}–S bond, for each conformer two structures were considered, the equilibrium structure, **a**, and a structure where the methyl groups were constrained to be nearly coplanar with the Pz ring, **b**.[13] The C_{2h} and C_{2v} **b** structures resulted, in CH_2Cl_2 solution, only 11.5 and 13.7 kcal/mol less stable than the corresponding equilibrium structures, so they are, in principle, thermally accessible. This fits in with VT ^{1}H NMR data pointing to a facile twisting of the alkyl groups around the C_{β}–S bond.

The lowest singlet and triplet excited states of the **a** and **b** structures of each conformer were examined in CH_2Cl_2 solution, at TDDFT/B3LYP/TZ2P level of theory. The vertical absorption energies, composition, and oscillator strength computed for the whole set of singlet and triplet excited states up to ~0.2 eV above the $S_1(Q_x)$ state are gathered in Tables S1-S4.† The $S_1(Q_x)$ and the lower lying excited states computed for the **a** and **b** structures of the C_{2h} conformer, taken as representative, are plotted in Fig. 3.

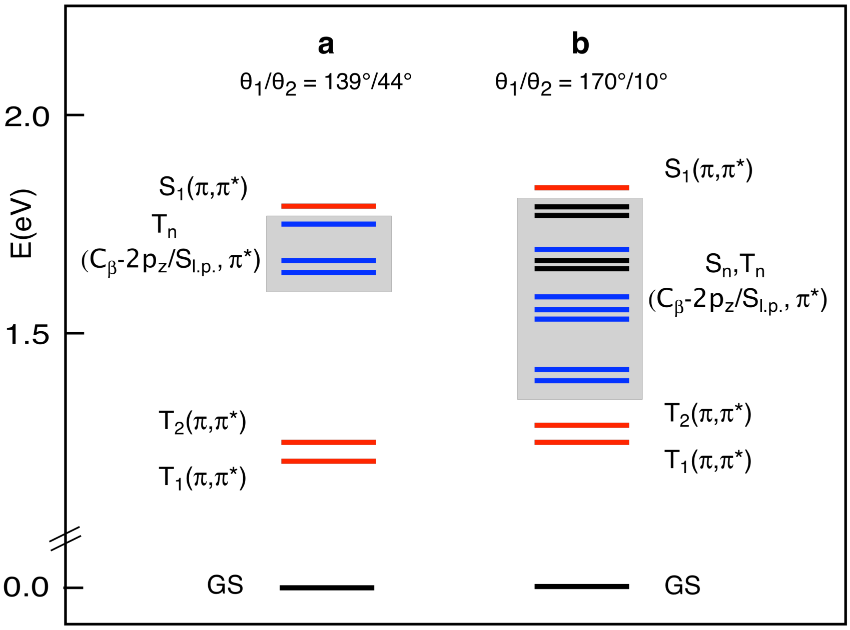


Fig. 3 Lowest excited states of the H_2OMSPz C_{2h} conformer in the **a** and **b** structures obtained at DFT/B3LYP/TZ2P level in CH_2Cl_2 solution. The singlet and triplet states with C_{β}-2p_z/$S_{l.p.}$,π* character are printed in black and blue, respectively.

At the equilibrium geometry (Table S1† and Fig. 3), four triplet excited states are found to lie vertically between the S_1(π,π*) state, which is located at 676 nm in nice agreement with the experiment, and the normally emissive T_1(π,π*) state. Save for the T_2(π,π*), which is the triplet corresponding to the $S_2(Q_y)$ state, these excited states involve transitions out of C_β-$2p_z$/sulfur lone pair ($S_{l.p.}$) π-antibonding MOs into the Gouterman π* MOs.

This scenario changes significantly when the methyl groups are nearly coplanar with the Pz ring, as in the **b** structure. Now, a manifold of excited states (singlets and triplets) is located between the $S_1(\pi,\pi^*)$ and the $T_1(\pi,\pi^*)$ states (Fig. 3). Except for the $T_2(\pi,\pi^*)$, these excited states are dominated by C_β-$2p_z/S_{l.p.}\rightarrow\pi^*$ transitions. In the **b** structure they end up in this spectral region essentially because of the upshift, visible in the energy level diagram of Fig. 4, of the involved C_β-$2p_z/S_{l.p}$ MOs, i.e., the $46b_u$, $41b_g$, $45b_u$, and $47a_g$.

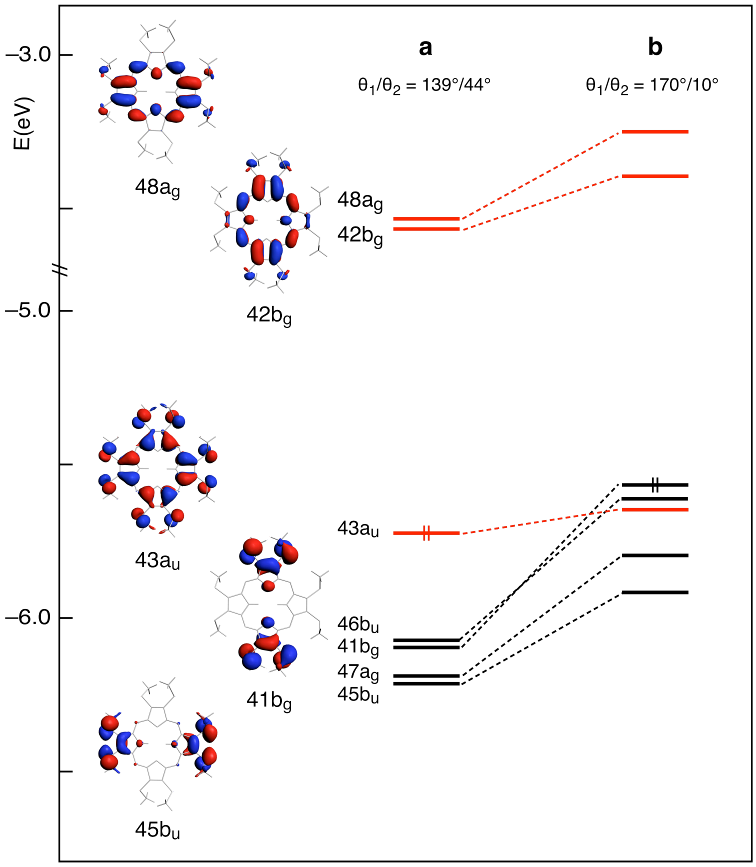


Fig. 4 Energy level diagram and molecular orbitals of the H_2OMSPz C_{2h} conformer in the **a** and **b** structures obtained at DFT/B3LYP/TZ2P level in CH_2Cl_2 solution. Double occupancy is indicated for the HOMO only. All lower lying levels are also doubly occupied. The $43a_u$, $42b_g$, and $48a_g$ Gouterman levels are printed in red.

The destabilization of these MOs can be explained in terms of enhancement of their π-antibonding character (see the plots of the $41b_g$ and $45b_u$ MOs in Fig. 4) in response to the improved overlap between C_β-$2p_z$ and sulfur lone pair orbitals upon twisting of the methyl groups.

The numerous singlets lying below the $S_1(\pi,\pi^*)$ are likely to highly favor the radiationless decay of this state, as suggested by ultrafast experiments showing that a very small fraction of the photogenerated $S_1(\pi,\pi^*)$ state of the investigated molecules returns directly to the ground state by radiative processes.

Thus, ultrafast experiments and TDDFT calculations clearly indicate that the twisting-induced π-conjugation between the sulfur lone pairs and the Pz π-system is detrimental to luminescence. That ATPzs appreciably fluoresce from both the Soret and Q bands when the vicinal alkylthio chains are locked in the most stable *anti* conformation as it happens in thin "solid" films[5] further supports this conclusion. As final remark, we note that H_2HEHCSPz and analogous ATPzs represent relevant examples of tetrapyrrolic compounds where fast radiationless decay of the photogenerated $S_1(\pi,\pi^*)$ state is related to the presence of low-lying ligand-centered excited states, rather than to the presence of low-lying metal-centered excited states, as it was shown to occur in several first-row transition-metal tetrapyrroles.[10]

The results described in this work present necessary background and basic knowledge in support of the prospective evaluation of the photothermal conversion performance[14] of H_2HEHCSPz and related molecules.

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Table of Content

Ultrafast transient absorption spectrometry reveals that following photoexcitation carboranyl-alkylthioporphyrazines undergo fast radiationless decay, with a very small fraction of the photo-generated $S_1(\pi,\pi^*)$ state returning directly to the ground state by fluorescence. DFT/TDDFT calculations and VT ^1H NMR spectroscopy indicate that this photophysical behavior is related to the inherent flexibility of the alkylthio chains.

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