Inter- and intramolecular aryl-aryl-interactions in partially fluorinated ethylenedioxy-bridged bisarenes

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Abstract: Several ethylenedioxy-bridged bisarenes with a variety of type and number of aryl groups were synthesized to study non-covalent dispersion-driven inter- and intramolecular aryl-aryl-interactions in the solid state and gas phase. Intramolecular interactions are preferably found in the gas phase. DFT calculations of dispersion-corrected energy scans for rotations around the ethylenedioxy-bridge and optimized structures show larger interacting aromatic groups to increase the dispersion energy. Single molecule structures generally adopt folded conformations with short intramolecular aryl-aryl-contacts. Gas electron diffraction experiments were performed exemplarily for 1-(pentafluorophenoxy)-2-(phenoxy)ethane. A new procedure for structure refinement was developed to deal with the conformational complexity of such molecules. The results are an experimental confirmation of the existence of folded conformations of this molecule with short -intramolecular aryl-aryl distances in the gas phase. Solid-state structures are dominated by stretched structures without intramolecular aryl-aryl-interactions but interactions with neighboring molecules.

Introduction

Intra- or intermolecular interactions between aromatic systems are of importance for different categories in molecular science. Supramolecular recognition processes,[1] interplay of DNA side-chains[2] or host-guest complexation[3] as well as crystal engineering[4] are some prominent examples. Many experimental and theoretical studies dealt with such interactions, however, they are still far from being completely understood. The simplest model for aryl-aryl-interactions is the benzene dimer.[5] In the solid-state the benzene rings arrange in T-shaped or herringbone structures, described as o-π-interaction;[6] a parallel arrangement of the rings is not favored. In contrast to the arrangement in the solid-state, the results of gas phase and theoretical studies show the parallel displaced or offset as well as the rare sandwich structures to be more important under these conditions.[7] Easier to predict are the interactions between benzene (C₆H₆) and its perfluorinated analogue hexafluoro-benzene (HFB, C₆F₆). Both pure substances arrange in herringbone-like structures in the solid-state,[8] but the equimolar mixture of benzene and HFB crystallizes in a parallel displaced structure of alternating HFB and benzene units. Strong intermolecular C₆H₆:−C₆F₆ π-stacking interactions increase the melting point by about 18 °C relative to the individual solid substances.[9,10] This phenomenon was discovered by Patrick and Prosser[10] and was first interpreted by an interaction of opposing quadrupole moments of both substances (C₆H₆: −6.69, C₆F₆: 7.89 a.u.).[9] Later studies pointed out that London dispersion (LD) forces, the attractive part of van-der-Waals interactions,[11] have a significant impact on the total interaction energy.[12] To analyze this phenomenon, different aromatic groups were linked with rigid or flexible backbones and investigated in different phases and by different methods.[13]

Recently, our group studied π-stacking interactions between different types of halogenated and non-halogenated phenyl groups linked by different backbones in various phases. Compounds with phenyl and perfluorophenyl rings bridged by (sila)-propyl chains receive stabilization by intermolecular aryl-aryl stacking interactions in the solid-state,[14] whereas free molecules, studied by gas electron diffraction (GED), find their energetic minima as conformers bearing intramolecular aryl-aryl interactions. 1,1,2,2-Tetramethyl-disilanes, substituted with symmetric or asymmetric pairs of phenyl and/or perhalogenated (F, Cl) phenyl groups also show strong π-interactions.[15,16] The aggregation in solid-state was found significantly stabilized by intramolecular aryl-aryl interactions. Gas electron diffraction and SAPT (symmetry-adapted perturbation theory) calculations demonstrate the untypical syn-conformers to be stabilized by large dispersion contributions.

From our experience with bridged bisarenes we learned, that the type of interaction partners and the linking-backbone is important for the stabilization of gas-phase and solid-state structures. We were interested if more flexibility and modified electronic surrounding, by heteroatoms in the bridge, would influence such interactions. Therefore, we report here investigations employing a new four-atomic ethylenedioxy linker unit (-OCH₂CH₂O-) between a variety of interacting aromatic systems.

Results and Discussion

Before we started synthesizing such model systems we performed preliminary calculations, in order to evaluate intramolecular aryl–aryl-interactions to be also possible with the ethylenedioxy linker unit. Basic computational methods at low levels of theory were used to calculate structures of single molecules in the free state. We used these predictions as a simple model for possible gas-phase structures. The experimental gas-phase structures should be determined experimentally by means of gas electron diffraction. With such fast calculations we could decide if the examined compound was worthy to be synthesized and analyzed.
The refinement of structures using experimental gas electron diffraction data was supported by different computational methods. This will be described later on and is outlined in detail in the Supporting Information.

![Scheme 1](image)

Scheme 1. Model compounds 2–10.

We explored the conformational landscapes of molecules of 2–10 (Scheme 1) using dispersion-corrected (D3BJ) [17,18] energy scans (B3LYP-D3BJ/6-31G) [19] along the torsion angles $\theta_1$ (CAr–O–C–C) and $\theta_2$ (CAr’–O’–C–C) (Scheme 2). The resulting potential energy surfaces for 2–10 have different forms and number of minima (Figure 1). Minimum structures deduced from potential energy surfaces were manually inspected and subsequently optimized at different DFT levels (B3LYP, TPSS, B97D3) [17,18,20] using different basis sets (6-31G; 6-311G) [21]. All stationary points were proven to be minima by frequency analyses.

All structure-optimized minima from the potential energy surface of compounds 2–10 are listed in the Supplementary Information. For all compounds the TPSS-D3BJ/6-311G level of theory was applied and the results of the calculations are listed in Table 1 and shown in Figures 2–5. To analyze intramolecular aryl–aryl interactions, minima with folded and stretched structures and their structural parameters are listed in Table 1. Minima for molecules with at least one pentafluorophenyl group are exclusively found for folded structures with intramolecular π–π interactions.

![Scheme 2](image)

Scheme 2. Torsion angles for ethylenedioxy-bridged bisarenes ArAr'.

![Figure 1](image)

Figure 1. Potential energy surface grid of 2 at B3LYP-D3BJ/6-31G level of theory.

### Table 1. Selected structural parameters of compounds 2–10 with stretched and folded structures. The relative energies of the minima $\Delta E$ are given in kJ mol$^{-1}$ and structural parameters in Å.

| Structure$^{[a]}$ | f | f | s | f | s | f | s | f | s | f | s | f | s | f | s |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\Delta E$       | 0 | 0 | 37.2 | 0 | 33.6 | 0 | 22.3 | 0 | 8.0 | 0 | 47.9 | 4.1 | 0 | 0 | 14.7 | 0 | 28.4 |
| $d_{c_{\text{center}}}$ | 3.438 | 3.242 | 9.122 | 3.251 | 9.076 | 3.412 | 5.435 | 3.410 | 6.012 | 3.383 | 10.971 | 6.416 | 8.803 | 3.584 | 8.784 | 4.159 | 7.939 |
| Plane shift      | 1.360 | 0.654 | - | 0.403 | - | 1.220 | - | 1.028 | - | 1.091 | - | 6.124 | - | 1.335 | - | 2.824 | - | 7.392 |

[a] f: folded; s: stretched [b] only minimum with folded structure for 2 was found [c] centroids distances to both Phf groups are identically in the range of rounding; both –CH2CH2OPhf groups were scanned independently [d] minimum for stretched structure.
The stretched structures are unfavorable with relative energy differences to the folded forms of $\Delta E = 22-49$ kJ mol$^{-1}$ (Table 1). All centroid-centroid distances are shorter than in those bisarene compounds our group investigated earlier in the solid state (XRD) and by gas electron diffraction (e.g. shortest centroid distances: PhCH$_2$CH$_2$CH$_2$Ph: 3.50(2) Å; PhSiMe$_2$SiMe$_2$Ph: 3.76(3) Å). Surprisingly, the shortest aryl–aryl contact was found for bisarene 4 with 3.251 Å. The question, if the enlargement of the non-fluorinated (2 to 3 to 5) or fluorinated (4 to 10) ring system influences the strength of the interactions could not be answered by simply comparing the centroid distances (Figure 2). The ethylenedioxy-bridge generally allows closer intramolecular aryl-aryl-contacts than the earlier tested linker units do, but there is no clear relationship between the size of the aromatic systems and the centroid-centroid distances. Furthermore, the introduction of a second CH$_2$CH$_2$OPh$_2$ unit (6) does not lead to significantly shorter aryl-aryl contacts. Optimized minima for symmetric bisarenes 8 and 9 also reveal folded structures (Figure 3).

On first sight, this parallel displaced arrangement of the aromatic groups seems to be disfavored because of the steric hindrance of the halogen substituents and the electrostatic repulsion through the quadrupoles of the aromatic rings —although the centroid-centroid distances are quite short. Such eclipsed conformations were also found for the perhalogenated disilanes Ph$_x$SiMe$_2$SiMe$_2$Ph$_x$ and are stabilized by London dispersion interactions.$^{[19]}$ Symmetric bisarenes without halogen substitution do not preferably arrange in folded sandwich structures. This is also the case for compound 7.

The minimum for 7 was found for a planar structure (Figure 4) with coplanar phenyl groups and linker unit. None of the minima on the potential energy surface shows significant intramolecular aryl-aryl interactions. The electrostatic repulsion and steric hindrance is not compensated for by dispersion energy. A similar free-molecule structure for the same compound was already found by calculations and fluorescence dip infrared spectroscopy (FDIR) by E. G. Buchanan et al.$^{[23]}$ Relative energy differences between stretched and folded minima are up to 47 kJ mol$^{-1}$ (Table 1). Intramolecular aryl-aryl interactions stabilize free molecules. These interactions are mainly driven by dispersion and electrostatic effects. The magnitude of dispersion energy of minima structures is shown in Figure 5.
The magnitude of dispersion energy increases within the size of the non-fluorinated aromatic part of the molecules (2–5). Among the compounds with one pentafluorophenyl group, compound 5 receives the strongest stabilization by dispersion interactions \((E_{\text{disp}}=237 \text{ kJ mol}^{-1})\). The energy for compound 6 \((E_{\text{disp}}=255 \text{ kJ mol}^{-1})\) is somewhat larger, also that for compound 10 \((E_{\text{disp}}=244 \text{ kJ mol}^{-1})\). Therefore, we can assume, that the size of the interacting aromatic systems plays a relevant role for the amount of dispersion energy. Expectedly, more interaction partners lead to higher stabilization energies.

**Synthesis**

For a preparative access to the model compounds, we used a modified protocol of Guo et al.\[24\] Scheme 3 displays an exemplary way to the asymmetric compound 1-(pentafluorophenoxy)-2-(phenoxy)ethane (2).

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\begin{align*}
\text{Ph-OH} & \quad \text{CH}_3\text{CN}, \text{K}_2\text{CO}_3, \text{reflux}, 4\text{h} \quad \text{Ph-O} \quad \text{Br} \\
\text{Ph-O} & \quad \text{O} \quad \text{Ph} \\
\text{Ph-OH} & \quad \text{CH}_3\text{CN}, \text{K}_2\text{CO}_3, \text{reflux}, 4\text{h}
\end{align*}
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Scheme 3. Synthesis of 2 starting from pentafluorophenol.\[24\]

Starting from pentafluorophenol, dibromoethane and potassium carbonate we generated 2-(pentafluorophenoxy)ethyl bromide (1). Based on this building block we could introduce a second aryloxy group under the same conditions. This procedure allowed generating various asymmetric bisarenes (2–4, 6). The syntheses of symmetric bisarenes (7–9) required extended reaction times for the first etherification step. In order to obtain compound 5 we generated 2-(9-anthroxy)ethyl bromide (5a) from anthrone and 2-bromoethanole. 5a and pentafluorophenole were then converted into 5. Detailed information is provided in the Supporting Information. Purification by column chromatography, sublimation and crystallization afforded the bisarenes in moderate to good yields. Compound 10 could not be synthesized yet. The compounds were characterized by NMR-spectroscopy, high resolution mass spectrometry, CHN analysis and single crystal X-ray diffraction.

**Structures in the solid state**

Single crystals, suitable for X-ray diffraction, were obtained by slow evaporation of n-hexane solutions. Some selected structural parameters characterizing the \(\pi\)-stacking interactions are listed in Table 2. For ring systems bigger than phenyl, the centroid was defined as the centroid of all condensed six-membered rings. A \(\pi\)--\(\pi\)-interaction was defined by centroid–centroid distances smaller than 4 Å.

![Structure of 2 in the crystalline state](image)

**Table 2:** Selected structural parameters from solid state structures of 2–9.

|   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   |
|---|-----|-----|-----|-----|-----|-----|-----|-----|
| Space group | \(P2_1/c\) | \(P2_1/c\) | \(P2_1/n\) | \(P1\) | \(P2_1/c\) | \(P1\) | \(P2_1/c\) | \(P1\) |
| \(R[\%]\) | 3.18 | 4.85 | 4.03 | 3.69 | 4.47 | 5.55 | 2.00 | 2.74 |
| \(d_{C-C}[\AA]\) | \(3.348(2)\) (C1–C14) | \(3.338(3)\) (C2–C11) | \(3.403(2)\) (C3–C18) | \(3.288(2)\) (C1–C19) | \(3.278(3)\) (C3–C6) | \(3.580(3)\) (C5–C9) | \(3.585(3)\) | \(3.327(2)\) (C13–C9) |
| \(d_{\text{same-core}} [\AA]\) | \(3.688(1)\) | \(3.462(1)\) | \(5.026(1)\) | \(3.690(1)\); \(3.721(1)\) | \(4.431(1)\) | \(4.431(1)\) | \(5.423(1)\) | \(3.971(1)\) | \(3.553(1)\) | \(3.729(1)\) |
| \(d_{\text{same-inner}} [\AA]\) | \(1.554(2)\) | \(0.430(3)\); \(0.418(3)\) | \(-\) | \(1.544(2)\); \(1.371(2)\) | \(3.004(3)\); \(2.439(4)\) | \(-\) | \(1.739(3)\) | \(1.376(2)\) |

| Intermolecular \(\pi\)--\(\pi\) interaction | Ph/Ph | Naph/Ph | Anthr/Ph | Ph/Ph | Ph/Ph | Ph/Ph | Ph/Ph | Ph/Ph |
|---|---|---|---|---|---|---|---|---|
| Aggregation motif | polymeric | columnar | columnar | - | - | columnar | chainlike |
Within one column the centroid–centroid distances alternate with 3.462(1) Å and 3.550(1) Å (Figure 7). A is the shortest intermolecular aryl–aryl-distance for partially fluorinated flexibly bridged bisarenes found so far for sandwich structures in solid state (e.g. shortest centroid-centroid distances: F₂C₆(CH₂)₂Si-Me₂C₆H₅: 3.535(1) Å; F₂C₆(SiMe₂)₂C₆H₅: 4.425(1) Å) and is even shorter than in the C₆F₆/C₆H₆-cocrystal (3.77 Å). The variation from phenyl- to naphthyl-group enables each group to form two aryl contacts in solid state. A change in substitution position – 1-naphthyl (3) to 2-naphthyl(4) – to the constitution isomer 4 leads to an unexpected packing behavior. Compound 4 shows no preference for an arrangement in alternating columnar structures. Instead we found multiple intermolecular aryl-contacts (Phf/Phf, Naph/Naph, Naph/Phf) with long ranges (>5 Å) (see Supporting Information). There is no recognizable impact of π–π-interactions for the arrangement in the crystal lattice.

Compound 5 crystallizes in an alternating columnar structure with slightly longer intermolecular centroid distances 3.660(1) Å and 3.721(1) Å than for 3. This offset or parallel displaced orientation is commonly observed for π–π-interactions. The angle between the plane normal and the vector between the ring centroids is about 20°.

In order to study the influence of a second –OCH₂CH₂Phf group, trisarene 6 was synthesized. Because the molecule has twice as many fluorinated than non-fluorinated aryl rings, it is not possible to arrange in 1:1 alternating structure as was observed for 3 or 5, and consequently we expected a mixture of inter- and intramolecular aryl-interactions.

The offset structure of 6 (Figure 9) seems to be disfavored because the repelling quadrupoles of the aromatic systems and the aryl-aryl-distance of 4.311(1) Å being too long for a π–π interaction. The fact that benzene and HFB, as pure substances, both prefer T-shaped arrangements in their solid-state structures, makes this structure even more interesting. Due to the symmetry, the Phf groups are coplanar and the central phenyl unit is twisted by 64.1(1°) relative to them.

In order to analyze if the phenomenon of π–π-interactions is limited to partially fluorinated bisarenes, we also investigated symmetric bisarenes with phenyl, perfluorophenyl, and 1,2-dibromophenyl groups. The solid state structures of these compounds do not feature typical intramolecular interactions. Whereas compound 7 shows no π–π-stacking in the solid-state structures, compound 8 crystallizes in columnar structure with a centroid–centroid distance slightly below the 4 Å limit [3.971(1) Å].
Because of long centroid distances to neighboring molecules, the interaction between two phenyl groups seems to be disfavored. The phenyl groups within one molecule of 7 are twisted against each other by 63.1°. The substitution with bromine in ortho-position (8) leads to co-planarity of the aromatic rings within the column and short centroid-centroid distance to neighboring molecules. This phenomenon was recently discovered in our group by investigating inter- or intramolecular π-stacking for perhalogenated groups in symmetric disilanes (Ph₂SiMe₂X-SiMe₂Ph₂; X = H, Cl, F); we recognized that π-stacking was limited to halogenated aryl groups and was not observed for hydrocarbons. Such stacking interactions are stabilized primarily by London dispersion forces.

Figure 11. Molecular structure and aggregation of 9 in the crystalline state with intermolecular centroid-centroid distances of 3.553(1) Å and 3.729(1) Å. Displacement ellipsoids are drawn at 50% probability level. Symmetry operation for generating equivalent positions: 1−x, 1−y, 1−z.

The perfluorinated compound 9 aggregates differently. The primary aggregation motif is a dimeric structure, with a short "inner" Ph groups interact with the corresponding counterparts of neighboring dimers. This leads to endless chains running along 111 in the crystal lattice with alternating shorter and longer aryl-aryl interactions.

In order to find out if we can intentionally generate the different aggregation motifs, i.e. control the crystallization to some extent, we attempted to co-crystallize compounds 2–9 with different aromatic compounds (HFB, benzene, octafluoronaphthalene) from n-hexane solutions. We generated a 1:2 co-crystal of 7 and octafluoronaphthalene (OFN). It has a columnar structure of alternating entities, either one molecule of 7 or a pair of OFN molecules. Each phenyl group of 7 interacts with two neighboring OFN units (Figure 12, b). The shorter contact of 3.548(1) Å is to the OFN molecule within the same unit cell, the slightly longer [3.807(1) Å] contact to an OFN molecule of a neighboring unit cell. This packing leads to columnar structures, similar to the benzene/HFB co-crystal. The neighboring column, is displaced by a half of a repetitive unit, that the structure is additionally stabilized by inter-columnar H···F-contacts [e.g.: 2.48(2) Å H(6)···F(4)]. Within one sheet (along the c-axis) the aromatic groups are coplanar, between two sheets twisted by 6.2(1) and 3.6(1)°. Other attempts of co-crystallization could not be analyzed yet, because of the insufficient quality of the resulting crystals.

Structure of 2 Determined by Gas Electron Diffraction

Gas-phase structures, i.e. the structures of free molecules undistorted by intermolecular interactions, can be determined by means of gas electron diffraction (GED). Due to the very high effort to be spent, we chose 2 as a model compound for the partially fluorinated ethylenedioxy-bridged bisarenes to be studied exemplarily in the context of this present study. The structure of 2 is suitable for comparison with those of other flexibly bridged bisarenes, we investigated earlier. First, a search for possible stable conformations of 2 was done theoretically using the Crest program utilizing the GFN2-xTB method for solving the electronic problem. Structures with relative energies below 3 kcal mol⁻¹ were manually inspected and (symmetry) duplicates were sorted out. This resulted in seven distinct conformations, denoted here as 2a–2g (see Figure 13). An additional stretched conformation 2h was also included into this set as a structure with the largest distance between the phenyl rings. The selected structures were optimized using the CP2K program and the implemented method GFN1-xTB within. The relative energies and the most important torsion angles of the optimized structures are provided in Table S37. Path integral molecular dynamics simulations were performed using the same program and method. Eight simulations with 16
beads were performed starting from structures of each conformation. Each trajectory was 100 ps long with a step size of 0.5 fs. Distributions of the most important torsion angles ($\phi_1$, $\theta_1$, $\tau_1$, $\phi_2$, see Scheme 2) were obtained from these trajectories and analyzed (see Figures S71–S75). Guided by the distributions the individual trajectories were used for calculations of interatomic vibrational amplitudes and corrections to equilibrium structure implying the Qassandra program.\textsuperscript{[31]} For the refinement of molecular structures a new method has been implemented into the UNEX program.\textsuperscript{[32]} This method is based on the well-known regularization technique\textsuperscript{[33]} and allows decoupled definition of refined structural parameters and regularization parameters of different types. For example, in this work we defined and refined molecular structures in terms of Cartesian coordinates but the regularization was applied in terms of internal parameters, that is bond lengths, valence, torsion and out of plane angles. In contrast, the already available mesoscopic coordinates but the regularization was applied in terms of model internal geometrical parameters,\textsuperscript{[34–37]} apply flexible restraints only to the refined parameters.

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Amplitudes of vibrations were refined in groups keeping the ratios within groups fixed at theoretical values. Models of all conformers were refined in exactly the same manner with the same extents of regularization. The resulted $wR$-factors of all models and corresponding torsion angles are collected in Table S38. Note, that functional (1) consists of two parts, (a) the first part built on experimental $sM_{ij}$ functions and (b) the second regularizing theoretical part. As the structures are determined by minimizing the complete functional $Q$, both parts of the functional can determine the refined parameters. However, the extent of influence of each part of $Q$ on different parameters can also be different. Accordingly, contributions can be defined (as a measure of influence) of the parts of $Q$ onto refined parameters.

The global regularization factor $\alpha$ was manually adjusted so that contributions of the experimental GED data onto the refined parameters were maximized while the solutions were still stable. The contributions of experimental data and regularization data, respectively, were calculated according to the W2 method.\textsuperscript{[41]} Amplitudes of vibrations were refined in groups keeping the ratios within groups fixed at theoretical values. Models of all conformers were refined in exactly the same manner with the same extents of regularization. The resulted $wR$-factors of all models and corresponding torsion angles are collected in Table S38. Note, that functional (1) consists of two parts, (a) the first part built on experimental $sM_{ij}$ functions and (b) the second regularizing theoretical part. As the structures are determined by minimizing the complete functional $Q$, both parts of the functional can determine the refined parameters. However, the extent of influence of each part of $Q$ on different parameters can also be different. Accordingly, contributions can be defined (as a measure of influence) of the parts of $Q$ onto refined parameters.

In order to refine the model or can lead to highly unstable solutions. Thus, in this work the following least squares functional was minimized:

\[
Q = \sum_i w_i (sM_{ij,\text{exp}} - sM_{ij,\text{model}})^2 + \alpha \sum_j w_j (p_{ij,\text{reg}} - p_{ij,\text{model}})^2
\]

where $sM_{ij,\text{exp}}$ and $sM_{ij,\text{model}}$ are experimental and model molecular intensity functions, $p_{ij,\text{reg}}$ and $p_{ij,\text{model}}$ are regularization and model internal geometrical parameters, $w_i$ and $w_j$ are respective weighting factors, $\alpha$ is the global regularization factor. Weighting factors for the experimental data were calculated from corresponding individual standard deviations $\sigma_i$ as $w_i = \alpha_i^{-2}$. In the regularization part of the functional weighting factors $w_j$ had different values depending on the location of parameters. Relative values of $w_i$ for valence angles in the -O-CH$_2$-CH$_2$-O- chain were by factor 10$^3$ smaller than for all other valence angles. Analogously, for the torsion angles in this fragment ($\phi_1$, $\theta_1$, $\tau_1$, $\phi_2$, $\theta_2$) $w_j$ were 25 times smaller than for other torsion angles. Thus, in the refinements the inverse problem was more flexible for parameters determining conformations while for the benzene rings and atoms connected to them a stronger regularization was applied.

For obtaining regularization parameters of reasonable accuracy the structures were additionally optimized at the PBEh-3c level of theory\textsuperscript{[39]} as implemented in the Turbomole 7.4 program package.\textsuperscript{[40]} The obtained torsion angles and relative energies are collected in Table S38. Note, that functional (1) consists of two parts, (a) the first part built on experimental $sM_{ij}$ functions and (b) the second regularizing theoretical part. As the structures are determined by minimizing the complete functional $Q$, both parts of the functional can determine the refined parameters. However, the extent of influence of each part of $Q$ on different parameters can also be different. Accordingly, contributions can be defined (as a measure of influence) of the parts of $Q$ onto refined parameters.

The global regularization factor $\alpha$ was manually adjusted so that contributions of the experimental GED data onto the refined parameters were maximized while the solutions were still stable. The contributions of experimental data and regularization data, respectively, were calculated according to the W2 method.\textsuperscript{[41]} Amplitudes of vibrations were refined in groups keeping the ratios within groups fixed at theoretical values. Models of all conformers were refined in exactly the same manner with the same extents of regularization. The resulted $wR$-factors of all models and corresponding torsion angles are collected in Table S38. Note, the stated uncertainties are purely experimental errors, which were calculated using a method removing the influence of regularization.\textsuperscript{[42]} In comparison to these values, the least squares standard deviations were unrealistically small in many cases (see Table S39). Other detailed information on refinements, including complete structures, is provided in the Supporting Information. The radial distribution functions are shown in Figure 14.

Summarizing the results of the structural analysis of 2 by GED we conclude that the experimental gas electron diffraction intensities are best described by the models of conformers with folded structures 2a, 2c and 2d (see Figure 15). However, it was impossible to determine exactly which of these three conformations exist in the gas phase at the experimental conditions. Although the models described above fit the data well, there are

Figure 13. Selected conformers 2a–h obtained using GFN1-xTB method.
still small systematic differences between experimental and model molecular intensity functions (Figure S69). This was also seen by comparing the very low experimental wR-factors of 1.6%, demonstrating the excellent reproducibility of the experimental $sM(i)$ functions, with the best structural wR-factors of 3.6%. It is possible that all three conformers, 2a, 2c and 2d, exist in the gas phase simultaneously. However, a refinement of the conformational composition could not be done with sufficient accuracy using solely the GED data due to instability of the inverse problem.

Interestingly, model 2b had a somewhat larger wR-factor in spite of its folded structure and low relative energy at the PBEh3-c level. We do not exclude that this was due to imperfections in the description of molecular vibrations on the level of molecular dynamics used in this work. For 2 this problem is very complicated due the occurrence of large amplitude motions and its rich conformational landscape, which can be seen on distributions of torsion angles (Figures S70–S74). In general, the stretched structures showed a worse agreement with the experimental intensities. This is also clear by comparing the difference curves of the radial distribution functions in Figure 14. The model of 2g showed an interesting possible case of a σ-π interaction. The energy of this conformer was fairly high but the wR-factor was relatively low. We cannot exclude small fractions of this conformer in the gas phase. The worst agreement with experimental data had model 2h with the largest distance between phenyl rings. A special note should be made concerning the refined torsion angles in Table 3. Due to the aforementioned vibrational complexity and ambiguity in the conformational composition they can only be significantly biased away from true equilibrium values. Moreover, in the rejected models they do not indicate a correspondence to real structures, possibly existing in small fractions under experimental conditions.

Table 3: Refined torsion angles (in degrees), weighted R-factors (in %) and relative energies $\Delta E$ (in kcal mol$^{-1}$) for all tested conformers of 2.

| $\phi_1$ | $\theta_1$ | $\gamma_1$ | $\phi_2$ | wR$^b$ | $\Delta E$ (GFN1-xTB) | $\Delta E$ (PBEh3-c) |
|---|---|---|---|---|---|---|
| 2a | −17.8(32) | −65.9(13) | −59.8(6) | 75.9(11) | 72.8(20) | 3.62 | 0.00 | 0.00 |
| 2b | −8.1(66) | −120.7(19) | 82.1(11) | −54.3(18) | −76.4(16) | 4.78 | 0.93 | 0.11 |
| 2c | 14.6(58) | 166.7(41) | −71.0(25) | 71.6(32) | −105.0(18) | 3.59 | 0.74 | 0.05 |
| 2d | −47.1(45) | −104.8(16) | 58.9(11) | 36.7(30) | −129.6(13) | 3.60 | 1.54 | 1.44 |
| 2e | 23.3(130) | 70.9(210) | 50.2(60) | 43.0(22) | 71.4(14) | 5.15 | 1.86 | 2.37 |
| 2f | −20.0(160) | −80.5(170) | −179.7(23) | −78.5(67) | −57.2(20) | 5.24 | 1.49 | 2.96 |
| 2g | 157.3(120) | 109.7(43) | −70.9(37) | 145.3(38) | 63.4(17) | 4.14 | 1.36 | 3.12 |
| 2h | 0.0 | 180.0 | 180.0 | 180.0 | 180.0 | 2.11 | 4.46 |

* In parentheses are 1σ pure experimental errors, see text for details.  
* Calculated as $wR = \{\sum wi[(sM_i^{(exp)} - sM_i^{(model)})^2/\sum wi(sM_i^{(exp)})^2]\}^{1/2} \times 100\%$

Figure 15. Conformers 2a, 2d, 2c with best description of GED data.

The best GED models have folded structures with short intramolecular aryl-aryl interactions. The respective centroid-centroid distances (see Figure 8) are slightly longer than for our preliminary calculations for the free state (Figure 2, 3.438 Å) and comparable to GED data for bisarenes our group investigated recently (PhCH$_2$CH$_2$CH$_2$Ph: 3.50(2) Å; PhSiMe$_2$SiMe$_2$Ph: 3.76(3) Å).$^{14,22}$ Note, the distances between centroids in 2 refined in this work were essentially experimental in spite of using quantum-chemically calculated restraints. W2-contributions of the GED data to these parameters as described above and which were 97, 57 and 82 % in 2a, 2c and 2d, respectively.

**Conclusion**

The aggregation motifs in the solid state structures of partially fluorinated ethylenedioxy-bridged bisarenes are stabilized by intermolecular interactions. Short centroid-centroid distances to neighboring molecules in the crystal lattice are found between aromatic ring systems and fluorinated aromatics. For stronger
π–π-interactions, the size of the aromatic group is important. Multiple ring systems (>Ph), support arec contacts to more than one neighboring molecule in the crystal lattice and lead to highly ordered crystal sturctures. Solid state sturctures of symmetric bisarenes show that the intramolecular π–π interactions a are disfavored for non-halogenated aromatic systems.

The investigation of free molecules by computational methods predicts the preferred formation of folded structures with intramolecular π–π interactions for halogenated bisarenes. The flexible ethylenedioxy-backbone leads to the shortest observed intramolecular centroid-centroid distances for these model compounds. Variation of the size and number of arec interaction partners results in stabilization by higher dispersion energies. A new method for structure refinement from the measured GED data allowed the detailed investigation of conformations for compound 2. The obtained results confirm the hypothesis that in the gas phase for this compound folded conformations are primarily populated.

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Keywords: bridged arenes • dispersion • halogenated arenes • inter/intramolecular π-stacking • solid-state structures • gas electron diffraction

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