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Chemistry A European Journal



Accepted Article

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This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Chem. Eur. J. 10.1002/chem.202003259

Link to VoR: https://doi.org/10.1002/chem.202003259

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

Jan-Henrik Weddeling, Yury V. Vishnevskiy,* Beate Neumann, Hans-Georg Stammler and Norbert W. Mitzel*

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 with and without dispersion-correction show larger interacting aromatic groups to increase the stabilization energy of folded conformers and decrease the intermolecular centroid-centroid-distance. Single molecule structures generally adopt folded conformations with short intramolecular arylaryl-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 sidechains^[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 $\sigma-\pi$ -interaction;^[6] a parallel arrangement of the rings is not favored. In contrast to the arrangement in the solidstate, 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.

[a] J.-H. Weddeling, Dr. Yu. V. Vishnevskiy, B. Neumann, Dr. H.-G. Stammler, Prof. Dr. N. W. Mitzel Lehrstuhl für Anorganische Chemie und Strukturchemie Fakultät für Chemie, Universität Bielefeld Universitätsstraße 25, 33615 Bielefeld (Germany) E-mail: mitzel@uni-bielefeld.de Supporting information for this article is given via a link at the end of the document. Strong intermolecular C_6H_6 ··· C_6F_6 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 (C_6H_6 : -6.69, C_6F_6 : 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 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-Tetramethyldisilanes, 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. At first we investigated the electronic and mesomeric effect of the new linker and whether the oxygen atoms have an influence on conformations or electron-density of the interacting aromatic systems. As the simplest model system for our linkerunit we performed a potential energy scan (PBE0-D3/def2-TZVP) around the C–C-bond of H₃C-OCH₂CH₂O-CH₃ (Figure S38). We found two minima, *gauche* and *anti*, of nearly the same energy. Therefore, we can assume that the relative positions of the

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oxygen atoms to each another in the $-OCH_2CH_2O$ - unit, do not significantly influence the conformational energies.

The electronic effects of the oxygen substituents on the aryl groups were analyzed by inspection of the electrostatic potential (ESP) surface of compound **2** in its stretched form. As shown in Figure 1, the effect of the oxygen atoms on the electron density of both aromatic rings is not very pronounced, in terms of a distortion of the ESP. As earlier mentioned for aromatic systems investigated before^[17] the electrostatic potential values on the surface of the phenyl group are negative (blue) while the surface of the perfluorophenyl group has a positive ESP (yellow/red). The complementary polarization of the aryl groups should lead to attractive interactions between these functions. These interactions would necessarily be intramolecular for isolated molecules in the gas phase, but difficult to predict for the solid state, where alternative intermolecular interactions are possible.



Figure 1. Stretched conformation of 2 (a) and its total electrostatic potential (ESP, b) mapped onto isosurface (0.0005 a.u.) of the electron density using AIMAII^[18] at PBE0-D3/def2-TZVP level of theory. Blue and red areas correspond to the negative and positive ESP values with maximal magnitudes, respectively.

In order to see whether folded conformers with intramolecular stacking interactions represent the favored conformation in the gas phase, we used the CREST procedure^[19] for a global search of stable conformers at the GFN2-xTB^{[20)} level of theory for compounds **2–10**. We additionally inspected compound **1**, the analogue of **2**, C_6H_5 -(CH_2)₄- C_6F_5 , with an oxygen-free four-atomic bridge, to prove that the predicted conformers are largely independent of the preferred stereochemical effects of the ethylene-dioxy-linker.

With a series of calculations on compounds **1–10** (Scheme 1) we decided if the examined compound was worthy of being synthesized and analyzed experimentally. For one example, compound **2**, we determined the structure of a free molecule in the gas phase by means of gas electron diffraction (GED). This investigation was supported by a more detailed description with computational methods. This will be described below and is outlined in detail in the Supporting Information.

The minima found for compounds **1–10** at the global search were structure-optimized at the PBE0/def2-TZVP level of theory using Gaussian 16^[22] and are listed in the Supplementary Information. The calculations were performed with and without D3 correction for dispersion interactions,^[21] in order to analyze if the intramole-cular aryl-aryl-interactions for folded conformers are caused solely by electrostatic effects. Along with the expected folded and stretched structures, we also found minima with half-folded structures (e.g. compound **2**; see Figure 2).



Figure 2. Calculated folded and half-folded structures of 2.

For these conformers the aromatic ring systems are not in a parallel offset orientation relative to one another; instead they are twisted or adopt T-shaped arrangements of their aryl rings (similar to the arrangements in the crystal structures of pure benzene or hexafluorobenzene). They also have generally longer centroidcentroid distances (see Supporting Information). These halffolded structures represent in many cases the global minima if no D3 dispersion correction was applied. For calculations with D3 dispersion correction, folded and half-folded conformers have similar energies. The stretched conformers were modelled by optimizing the structures found in the solid state (see below). In general, the application of D3 corrections for dispersion leads to significantly lower energies of (half)folded conformers, with small centroid-centroid distances. For all compounds with at least one pentafluorophenyl group the folded structures a more favorable than the stretched ones by $\Delta E = 2-24$ kJ mol⁻¹ (Table 1).



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Figure 3. Minima for folded conformers of 1-6 and of 10 calculated at the PBE0-D3/def2-TZVP level.

The centroid-centroid distances are comparable to those in bisarene compounds, which our group investigated earlier in the solid state (XRD) and by gas electron diffraction (e.g. shortest centroid distances: PhCH2CH2CH2Phf: 3.50(2) Å; PhSiMe2-SiMe₂Ph_f: 3.76(3) Å).^[14,22] The enlargement of the non-fluorinated (2, 3, 5) or fluorinated (4, 10) ring system influences the strength of the interactions and can be seen by comparing the decreasing centroid-centroid distances (Figure 3). Due to the greatest interacting surfaces, we found the largest stabilization energies for compound 10. The ethylenedioxy-bridge generally allows close intramolecular aryl-aryl-contacts and there is a clear relationship between the size of the aromatic systems and the centroid-centroid distances. Furthermore, the introduction of a second CH₂CH₂-OPh_f unit (2, 6) does lead to the significantly shorter aryl-aryl contacts.

Comparison of compound 2 to its oxygen-free analogue 1 again shows, that the oxygen atoms in the linker-unit do not influence the conformational preference significantly (Table 1). The relative energy differences of the calculations for 1 and 2 - with and without D3 correction - have the same tendency and range.

Table 1. Relative energy differences between stretched and folded conformers of compounds 1-10. The relative energies of the minima E are given in kJ mol⁻⁷ ΔE >0, folded conformer is more stable; ΔE < 0, stretched conformer is more stable

	$\Delta E = E_{\rm s} - E_{\rm f}^{\rm [a]}$									
method	1	2	3	4	5	6	7	8	9	10
[PBE0]	-0.3	1.1	-4.9	0.8	-16.5	3.2	-14.7	-13.2	-6.5	87.5
[PBE0-D3]	9.5	8.8	16.0	8.8	9.3	18.0	-5.6	3.1	2.1	24.0

[a] f: folded; s: stretched.

Considering the relative energy differences with and without D3 dispersion correction for each compound, 1-10 (Table 1), electrostatic interactions alone cannot explain the effect of stabilization of the folded conformers. If that were the case, folded conformers of compounds 3 and 5, calculated without D3 correction, would be more stable than the stretched ones. Only by taking into account electrostatic and dispersion forces, the stabilization of the folded conformers of partially fluorinated bisarenes can be explained properly.

In order to explore cases without important stabilizing electrostatic components, which are dominated by dispersion effects, we investigated bisarenes with two identical aromatic substituents. Due to the same electrostatic potential, both aryl groups should repel each other, however surprisingly, the optimized minima for the symmetric bisarenes 8 and 9 also reveal folded structures (Figure 4).



Figure 4. Folded minima of 8 (left) and 9 (right).

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 of the aromatic rings -although the centroid-centroid distances are quite short. Such eclipsed conformations were also found for the perhalogenated disilanes $Ph_XSiMe_2SiMe_2Ph_X$ and are stabilized by London dispersion interactions.^[15] Symmetric bisarenes without halogen substitution do not preferably arrange in folded sandwich structures. This is also the case for compound 7.



Figure 5. Calculated minimum structure for 7.

The minimum for 7 was found for a stretched structure (Figure 5). In the latter the inclusion of dispersion correction lowers the relative energy of the folded conformation but the repulsion

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between the phenyl groups still plays the dominant role. A similar free-molecule structure for the same compound was already found by calculations and fluorescence dip infrared spectroscopy (FDIR) by Buchanan *et al.*^[24]

Synthesis

For a preparative access to the model compounds, we used a modified protocol of Guo *et al.*^[25] Scheme 2 displays an exemplary way to the asymmetric compound 1-(pentafluorophenoxy)-2-(phenoxy)ethane (2).



Scheme 2. Synthesis of 2 starting from pentafluorophenol.[25]

Starting from pentafluorophenol, dibromoethane and potassium carbonate we generated 2-(pentafluorophenoxy)ethyl bromide (2a). 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 etherfication 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 chromategraphy, 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.

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

	2	3	4	5	6	7	8	9
Space group	P21/c	P21/c	P21/n	ΡĪ	P21/c	PĪ	P21/c	ΡĪ
R[%]	3.18	4.85	4.03	3.69	4.47	5.55	2.00	2.74
dc₋c [Å]	3.348(2) (C1…C14)	3.338(3) (C2-C11) (C6-C9)	3.403(2) (C3- C18)	3.288(2) (C1C19)	3.278(3) (C3 C6)	3.580(3) (C5 C9)	3.585(3) C5 C4	3.327(2) (C13 […] C9)
d _{centr-centr} [Å]	3.688(1) 3.944(1) Å	3.462(1); 3.550(1)	5.026(1) 5.247(1))	3.660(1); 3.721(1)	4.431(1) 4.431(1)	5.423(1)	3.971(1)	3.553(1) 3.729(1)
d∕ _{plane-shift} [Å]	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 _f	Naph/Ph _f	-	Anthr/Ph _f	Ph/Ph; Ph _f /Ph _f	Ph/Ph	Ph _{o-Br} /Ph _{o-Br}	Ph _f /Ph _f
Aggregation motif	polymeric	columnar	-	columnar	-	- -	columnar	chainlike

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 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 aryl-aryl-interaction was defined by centroid–centroid distances smaller than 4 Å.



Figure 6. Molecular structure and primary aggregation of **2** in the crystalline state. a) Side view of aggregation in the crystal lattice. b) Interaction to neighboring molecules with an intermolecular centroid–centroid distance of 3.668(1) Å. Displacement ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity. Symmetry operations for generating equivalent positions: 1-x, 1-y, 1-z.

Compounds **2–9** show no intramolecular aryl-aryl-interactions in their solid-state structures. All molecules crystallize in stretched conformations. The arrangement of molecules in the crystal lattice follow different motifs. Compound **2** forms dimeric structures whereas the phenyl and perfluorophenyl arrange in a head-tail orientation to their neighboring counterpart and undergo aryl–aryl-interactions with short centroid distances [3.688(1) Å]. A second aryl–aryl-interaction was found between two perfluorophenyl groups of neighboring dimers, with a distance of 3.944(1) Å, leading to an 1D-polymer along the *a*-axis.

Unlike 2, the crystal structure of 3 contains columnar alternating stacks of perfluorophenyl and naphthyl groups from reversely oriented alternating molecules. The ring systems arrange almost perfectly above the centroid of the ring system of the neighboring

counterpart. Such sandwich orientation is rarely observed.[26] Within one column the centroidcentroid distances alternate with 3.462(1) (A) and 3.550(1) Å (B) (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 F₅C₆(CH₂)₂SiMe₂distances: C₆H₅: 3.535(1) Å; F₅C₆(SiMe₂)₂-C₆H₅: 4.425(1) Å]^[14-15] and is even shorter than in the C₆F₆/C₆H₆ cocrystal (3.77 Å).^[16]

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Figure 7. Molecular structure and aggregation of **3** in the crystalline state. a) Side view of aggregation in the crystal lattice. b) Interaction to neighboring molecules with intermolecular centroid-centroid distance of **A** 3.462(1) / **B** 3.550(1) Å. Displacement of ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity. Symmetry operation for generating equivalent positions: 1-x, $\frac{1}{2}+y$, $\frac{1}{2}-z$.

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 (Ph_f/Ph_f, Naph/Naph, Naph/Ph_f) 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 aryl-aryl interactions. The angle between the plane normal and the vector between the ring centroids is about 20°.



Figure 8. Molecular structure and aggregation of **5** in the crystalline state with intermolecular centroid-centroid distances of 3.660(1) and 3.721(1) Å. Displacement ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity. Symmetry operation for generating equivalent positions: 1-x, 1-y, 1-z.

In order to study the influence of a second $-OCH_2CH_2Ph_f$ 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.



Figure 9. Molecular structure and aggregation of **6** in the crystalline state with an intermolecular centroid-centroid distance of 4.311(1) Å. Displacement ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity. Symmetry operation for generating the second part of molecule (1-x, 2-y, 2-z) and equivalent positions: +x, -1+y, +z.

The offset structure of **6** (Figure 9) seems to be disfavored because the repelling surfaces of the aromatic systems and the aryl-aryl-distance of 4.311(1) Å being too long for an aryl-aryl 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 Ph_f 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 aryl-aryl 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 stacking interactions 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].



Figure 10. Molecular structures and aggregations of **7** (a) and **8** (b) in the crystalline state. Displacement ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity. a) Intermolecular centroid-centroid distance: 5.423(1) Å; symmetry operation for generating equivalent positions: -1+x, +y, +z. b) Intermolecular centroid-centroid distance: 3.971(1) Å; symmetry operation for generating second part of the molecule (1-x, -y, -z) and equivalent positions (1+x, +y, +z).

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 co-

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lumn 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 (Ph_xSiMe₂SiMe₂Ph_x; X = H, CI, F); we recognized that π -stacking was limited to halogenated aryl groups and was not observed for hydrocarbons.^[23] 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" centroid-centroid distance of 3.553(1) Å. The "outer" Ph_f 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 intercolumnar 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.

In contrast to the calculated gas-phase structures, most of the molecular structures of compounds are found to adopt stretched conformations in the solid state. Obviously, in this phase the number of stabilizing inter- and intramolecular interactions is larger for the stretched than for the folded conformer. As a simplest approximation of intermolecular interactions, for compound **2** we have optimized a system of two stacked molecules in stretched conformations (Figure 13).



Figure 13. Comparison of inter- and intramolecular stabilization of gas-phase (B) and solid state structures (A) of 2 at PBE0-D3/def2-TZVP level of theory.

For this we used the Cartesian coordinates of the dimer (A) in the crystal structure of **2**, optimized its structure and calculated its minimum energy at PBE0-D3/def2-TZVP level of theory. The energy of this dimeric system (A) was 54 kJ mol⁻¹ (BSSE corrected) lower than the twice the energy of the best folded conformation in the gas phase (B). Thus, the energetic stabilization due to intermolecular interactions between stretched conformers is more preferable than intramolecular stabilization in the folded conformation.



Figure 12. a) Molecular structure and aggregation of a 1:2 co-crystal of **7** and octafluoronaphthalene in the crystalline state. Displacement ellipsoids are drawn at 50% probability level. a) Top view with intercolumnar H $^{-}$ F-contacts. b) Hydrogen atoms are omitted for clarity. Interaction in the unit cell with intermolecular centroid-centroid distances of 3.548(1) and 3.807(1) Å. The neighboring unit cells are drawn at 50% transparency level. Symmetry operation for generating second half of the co-crystal (-x, 2-y, -z) and equivalent positions: +x, -1+y, +z.

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Structure of 2 Determined by Gas Electron Diffraction

Gas-phase structures, i.e. the structures of free molecules undistorted by intermolecular interactions, ca 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.^[14,15,23]

First, a search for possible stable conformations of **2** was done theoretically using the Crest program^[19] utilizing the GFN2-xTB method^[20] 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 14).

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^[27] and the implemented method GFN1-xTB within.^[28] The relative energies and the most important torsion angles of the optimized structures are provided in Table S31. 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 (φ_1 , θ_1 , τ , θ_2 , φ_2 ; see Scheme 3) were obtained from these trajectories and analyzed (see Figures S69–S73).



Scheme 3. Torsion angles for ethylenedioxy-bridged bisarenes 2.

Guided by the distributions the individual trajectories were used for calculations of interatomic vibrational amplitudes and

corrections to equilibrium structure implying the Qassandra program.^[29]

For the refinement of molecular structures a new method has been implemented into the UNEX program.^[30] This method is based on the well-known regularization technique^[31] 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 methods^[32–35] apply flexible restraints only to the refined parameters. In some cases, e.g. for carbaboranes,^[36] it is convenient to refine and regularize Cartesian coordinates simultaneously. However, for flexible and large molecules this can either hinder the fitting of the model or can lead to highly unstable solutions. Thus, in this work the following least squares functional was minimized:

 $Q = \sum_{i} w_i \left(sM_{(i), exp} - sM_{(i), model} \right)^2 + \alpha \sum_{j} w_j \left(p_{(j), reg} - p_{(j), model} \right)^2$

where $sM_{(i),exp}$ and $sM_{(i),model}$ are experimental and model molecular intensity functions, $p_{(j),reg}$ and $p_{(j),model}$ are regularization and model internal geometrical parameters, wi and wi are respective weighting factors, α is the global regularization factor. Weighting factors for the experimental data were calculated from corresponding individual standard deviations σ_i as $w_i = \sigma_i^{-2}$. In the regularization part of the functional weighting factors w_i had different values depending on the location of parameters. Relative values of wi for valence angles in the -O-CH2-CH2-O- chain were by factor 10² smaller than for all other valence angles. Analogously, for the torsion angles in this fragment (φ_1 , θ_1 , τ , θ_2 , φ_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^[37] as implemented in the Turbomole 7.4 program package.^[38] The obtained torsion angles and relative energies are collected in Table S32. Note, that functional (1) consists of two parts, (a) the first part built



Figure 14. Selected conformers 2a-h obtained using GFN1-xTB method.

(1)

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on experimental sM(s) 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 α 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.^[39] 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 3. Note, the stated uncertainties are purely experimental errors, which were calculated using a method removing the influence of regularization.^[40] In comparison to these values, the least squares standard deviations were unrealistically small in many cases (see Table S33).



Figure 15. Experimental (dots) and best model (line) radial distribution functions of 2. Below are ordered difference curves for all tested models, highest for the first conformation 2a, lowest for 2h. Vertical bars indicate positions of interatomic distances in 2a.

Table 3: Refined torsion angles (in degrees), weighted R-factors (in %) and relative energies ΔE (in kJ mol⁻¹) for all tested conformers of **2**.^a

	$arphi_1$	θ_1	T	θ_2	\$\$	w₽⁵	Δ <i>Ε</i> (GFN1- xTB)	Δ <i>Ε</i> (PBEh- 3c)	
2a	-17.8(32)	-65.9(34)	-59.8(21)	75.9(14)	72.8(22)	3.62	0.00	0.00	
2b	-8.1(71)	-120.7(31)	82.1(25)	-54.3(47)	-76.4(16)	4.78	3.89	0.46	
2c	14.6(59)	166.7(51)	-71.0(36)	71.6(36)	-105.0(18)	3.59	3.10	0.21	
2d	-47.1(45)	-104.8(28)	58.9(19)	36.7(24)	-129.6(14)	3.60	6.44	6.02	
2e	23.3(150)	70.9(43)	50.2(10)	43.0(18)	71.4(17)	5.15	7.78	9.92	
2f	-20.0(300)	-80.5(130)	-179.7(25)	-78.5(88)	-57.2(20)	5.24	6.23	12.38	
2g	157.3(74)	109.7(21)	-70.9(33)	145.3(25)	63.4(20)	4.14	5.69	13.05	
2h	0.0	180.0	180.0	180.0	180.0	11.10	8.83	18.66	
^a In parentheses are 1g pure experimental errors, see text for details									

^b Calculated as $wR = [\sum w \{ sM_{(i),exp} - sM_{(i),model} \}^2 / \sum w \{ sM_{(i),exp} \}^2]^{1/2} \times 100 \%$

Other detailed information on refinements, including complete structures, is provided in the Supporting Information. The radial distribution functions are shown in Figure 15. 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 16). 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 still small systematic differences between experimental and model radial distribution functions (Figure 15) and molecular intensity functions (Figure S68). This was also seen by comparing the very low experimental wR-factors of 1.6 %, demonstrating the excellent reproducibility of the experimental sM(s) 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.



Figure 16. Conformers 2a, 2d, 2c with best description of GED.

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 S69–S73). 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 15. The model of **2g** showed an

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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 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.

The best GED models have folded structures with short intramolecular aryl-aryl interactions. The respective centroid-centroid distances (see Figure 16) are slightly longer than for our preliminary calculations for the gas phase (Figure 3) and comparable to GED data for bisarenes our group investigated recently (PhCH₂CH₂CH₂Ph_f: 3.50(2) Å; PhSiMe₂SiMe₂Ph_f: 3.76(3) Å).^[14,23] 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 aryl-aryl-interactions, the size of the aromatic group is important. Multiple ring systems (>Ph), support aryl contacts to more than one neighboring molecule in the crystal lattice and lead to highly ordered columnar structures. Solid state structures of symmetric bisarenes show that the intermolecular aryl contacts are disfavored for non-halogenated aromatic systems.

The investigation of molecules by computational methods predicts the preferred formation of folded structures with intramolecular interactions for halogenated bisarenes. The oxygen atoms in the flexible ethylenedioxy-backbone, do neither influence the polarization of the aromatic ring systems nor the conformational preference of the bisarenes significantly. Increasing the size and number of aryl interaction partners results in decreasing centroidcentroid distances and higher stabilization energies. Due to different methods we could proof, that the stabilization of folded conformers is caused by both, electrostatic attraction and dispersion interactions in the cases where two electronically different aryl groups interact with one another. For two identical groups, the electrostatic terms vanish, but a substantial stabilization by dispersion forces remains. Only in the case of the non-halogenated bisarene 7, neither electrostatic nor dispersion is strong enough to stabilize a folded conformer.

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.

Acknowledgements

We thank Klaus-Peter Mester and Marco Wißbrock for recording NMR spectra and Barbara Teichner for elemental analyses. We also thank Timo Glodde and Dr. Jan Schwabedissen for the gas electron diffraction experiments. This work was funded by DFG (German Research Foundation) in the Priority Program SPP 1807 "Control of LD in molecular chemistry" (grant MI477/28-2, project no. 271386299) and the core facility GED@BI (grant MI477/35-1, project no. 324757882). Yury Vishnevskiy is grateful for financial support by Deutsche Forschungsgemeinschaft (DFG, Grant VI 713/1-2, project no. 243500032) and to HPC facilities at the Universität zu Köln for providing computational time and programs.

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

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

J.-H. Weddeling, Yu. V. Vishnevskiy, B. Neumann, H.-G. Stammler and N. W. Mitzel

London dispersion driven interactions between two aryl groups, separated by ethylenedioxy-bridged linkers, lead to different conformations, dependent on the size and nature of the aryl groups and the phase, studied by X-ray (solid) and electron diffraction (gas).