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Graphical Abstract

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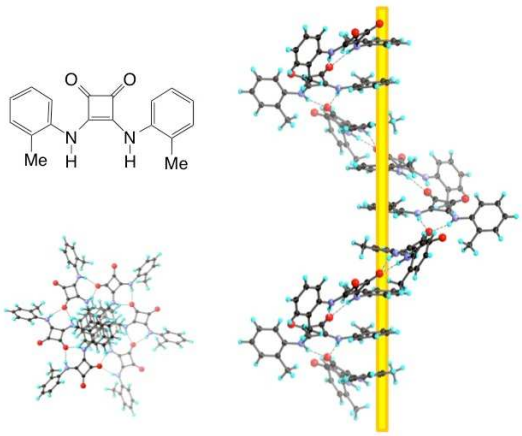

Spontaneous Chiral Resolution of *N,N'*-Diarylsquaramides : Formation of Various Types of One-handed Helical Networks During Crystallization

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Abstract

N,N'-Bis(*ortho*-substituted phenyl)squaramides afforded chiral crystals, in which squaramide molecules are arranged in one-handed helical networks, upon simple recrystallization. Three types of crystals with different helices were obtained, depending on the substituents or recrystallization solvent. Folded-type intermolecular hydrogen-bonding interactions of squaramides play a key role in forming the helical networks.

Keywords: Squaramide, Helical structure; Chiral resolution; Hydrogen bond network

1. Introduction

Tectons are defined as molecules whose positive interactions generate well-ordered three-dimensional assemblies of aggregates; they are important in the field of crystal engineering because of their interesting crystal packing structures, and have also been utilized in the development of functional solid materials [1]. Among various noncovalent interactions, hydrogen bond networks play a major role in tectons, due to their precise spatial orientations and restricted lengths [2]. For example, simple *N*,*N'*-disubstituted ureas such as *N*,*N'*-diphenylurea, which favor (trans, trans) conformation, can form head-to-tail type hydrogen bonds between the carbonyl oxygen atom of one molecule as the acceptor and two hydrogen atoms on nitrogen atoms of the adjacent molecule as the donor, resulting in linear chain structures in the crystal (Figure 1a) [3]. These properties of *N*,*N'*-disubstituted ureas, as well as their ability to interact with various guest molecules (hydrogen bond acceptors and donors), make such compounds suitable for construction of nano-scale materials [4].

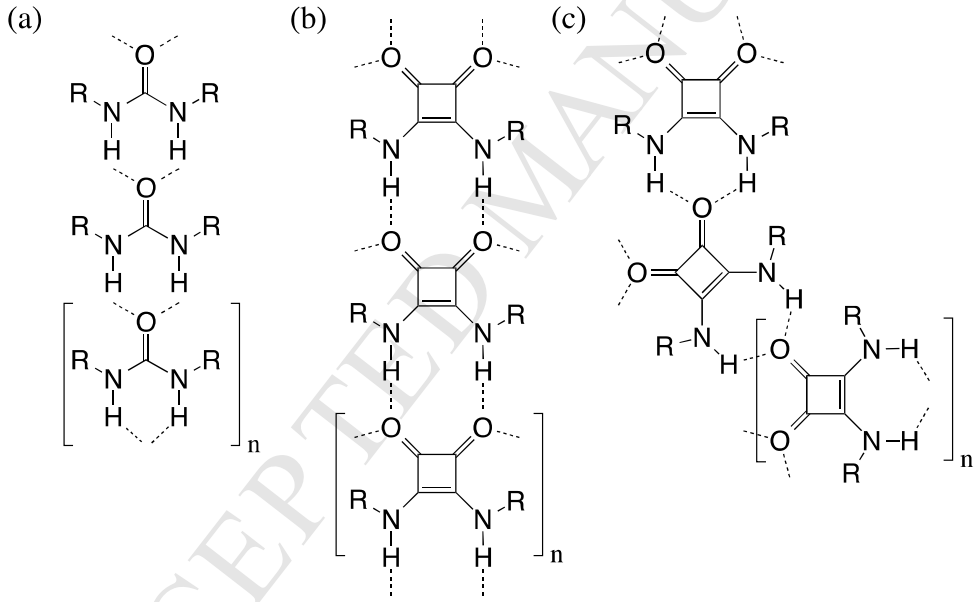


Figure 1. Possible hydrogen-bonding chain structures of (a) *N*,*N'*-disubstituted urea in (trans, trans) form, and (b) linear and (c) bent types of *N*,*N'*-disubstituted squaramide in (trans, trans) form.

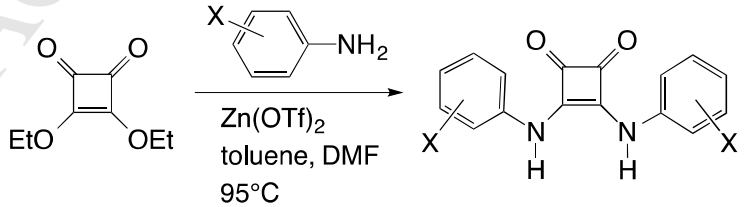
Squaramide (Figure 1b) is an amino derivative of squaric acid, a four-membered cyclic dibasic acid. The C–N bonds of squaramide have partial double bond character, like amide and urea bonds [5]. The squaramide skeleton has been used as a key structural motif for molecular recognition or in bifunctional organocatalysts for asymmetric synthesis [6]. Squaramide is also regarded as a bioisostere of urea or cyanoguanidine in the field of medicinal chemistry, an active derivatives of various bioactive molecules have been obtained

by replacement of a urea moiety with a squaramide moiety [7]. However, there are several differences in chemical properties between squaramide and urea [8]. For example, Costa et al. showed that squaramide is superior to urea as a hydrogen bond acceptor (cation receptor), and can also act as an anion receptor, due to the increased aromaticity of the squaramide upon complex formation with a hydrogen-bond donor or acceptor, or even both [9]. The structures of various squaramides and their complexes with guest molecules have been elucidated [10].

Several *N,N'*-disubstituted squaramides can form network structures with linear head-to-tail type hydrogen bonds (Figure 1b) [11], like *N,N'*-disubstituted urea derivatives. *N,N'*-Disubstituted squaramide itself also favors (trans, trans) conformation, in which both phenyl groups are located near the carbonyl oxygen atoms. In such linear networks, the aromatic character of the 4-membered ring of squaramide would contribute to sheet formation through π-π interactions between squaramides or between squaramide and other aromatic rings [12]. On the other hand, squaramides, unlike ureas, have other possible hydrogen-bonding interactions, due to the presence of two carbonyl and two amino groups on the 4-membered ring. For example, hydrogen-bonding interactions of one carbonyl group of one molecule with two amino groups of the adjacent molecule induce a bent arrangement of squaramide (Figure 1c). Thus, we hypothesized that bent-type networks of squaramides might be utilized to construct unique helical structures, different from linear hydrogen-bonding networks. Here, we report the spontaneous chiral resolution of simple *N,N'*-bis(*ortho*-substituted phenyl)squaramides with various types of one-handed helical structures generated by folded-type hydrogen-bonding networks, and we determined the absolute structure of one compound by means of X-ray crystallography.

2. Results and discussion

In this study, we focused on *N,N'*-diarylsquaramides, anticipating that aryl-aryl or aryl-squaramide interactions, as well as hydrogen-bonding interactions, would contribute to the packing structure. We synthesized compounds **1** – **7** from diethyl squarate and the corresponding anilines using literature methods (Shceme 1) [12].



1 X = H
2 X = *m*-CH_3
3 X = *o*-CH_3
4 X = *o*-Cl
5 X = *o*-Br
6 X = *o*-OMe
7 X = *o*-F

Scheme 1.

The crystal structures of several *N*,*N*'-diarylsquaramides and their complexes with guest molecules have been elucidated. The reported crystal structure (space group: *P*bcn) of simple *N*,*N*'-diphenylsquaramide **1** shows (trans, trans) conformation [13], and the crystal contains sheet structures due to the linear hydrogen-bonding network (Figure 1b) and intermolecular π-π interactions of the squaramide moiety. We also examined the crystal structure of **1**, and obtained a crystal pseudopolymorph (space group: $P2_1/c$, Table S1) including solvent of recrystallization (DMSO), in which the hydrogen-bonding network of **1** is not formed, due to the interaction of the oxygen atom of DMSO with the two amino groups of **1** (Figure S1). Sandwich-type interaction of the 4-membered ring with two phenyl groups of adjacent molecules results in the formation of a well-ordered sheet-type packing structure.

Compound **2** bearing *m*-toluyl groups shows a linear hydrogen-bonding network structure (Figure S2) similar to that in the reported crystal structure of **1**, while compound **3** bearing *o*-toluyl groups affords two types of crystals (crystal No. **3a** and **3b** in Table S1) upon recrystallization from methanol, depending on the conditions. These crystals showed distinct crystal shapes, and can be ditinguished each other by solid-state UV-vis spectra, although the reason of the difference in the spectra is unclear (Figure 2).

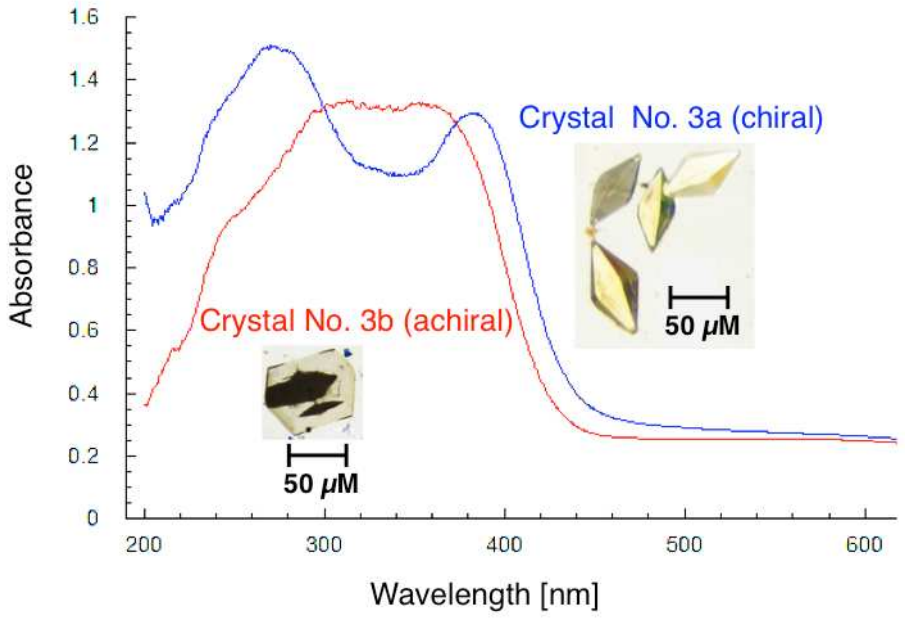


Figure 2. Crystal shapes and solid-state UV-vis spectra of the two types of crystals of **3**.

Crystal No. **3a** is a chiral crystal with space group $P2_12_12_1$. In both crystals, compound **3** exists in (trans, trans) form, like **1** and **2**. In the chiral crystal of **3**, continuous hydrogen bonding between two amino groups of one molecule and one of the two carbonyl groups of

the adjacent molecule (Figure 1c) forms a pseudo 6_1 helical structure (helical pitch: 20.6 Å), affording a one-handed helix containing only one enantiomeric conformer of **3** (Figures 3a and S3). The helical axis is located near the centers of the phenyl rings in the multi-layered structure, in which the inter-ring distances are 3.54, 3.57 and 3.58 Å, with a near-parallel arrangement (dihedral angles between adjacent phenyl rings: 11, 8, and 8°), and hydrogen-bonded squaramides surround the multi-layered phenyl groups. On the other hand, a racemic crystal (space group: $P2_1/c$) of **3** (Crystal No. **3b**) obtained from wet methanol contains both methanol and water molecules that interact with amino groups and carbonyl groups of the squaramide moiety, and no extensive hydrogen-bonding network is observed (Figure S4).

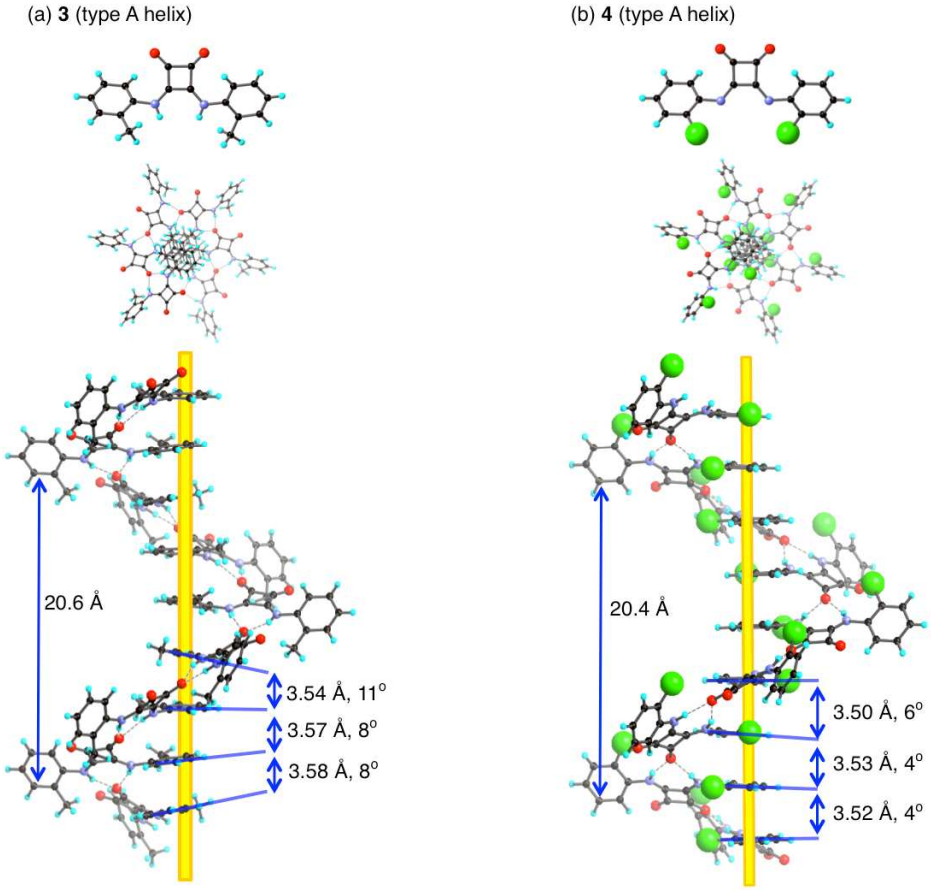


Figure 3. Helical structures of compounds (a) **3** (Crystal No. **3a**) and (b) **4** in the crystals.

A comparison of the crystal structures of **1** – **3** suggested that the *ortho*-substituents on the phenyl rings play key roles in the helix formation. Next, the crystal structures of several *N*,*N*'-diphenylsquaramides **4** – **7** with *o*-substituents were examined. Some of them afforded crystal polymorphs (Table S1), while all of them afforded chiral crystals upon simple recrystallization [14]. Interestingly, the types of helical structures varied depending on the substituent. Compound **4** with *o*-chlorophenyl groups shows a pseudo 6_1 helix similar to that

of **3** (Figures 3b and S5), in which a folded-type hydrogen-bonding network of squaramides surrounds the multi-layered phenyl groups on the helical axis (helical pitch: 20.4 Å).

On the other hand, compounds **5** and **6** bearing *o*-bromophenyl or *o*-methoxyphenyl groups, respectively, form a one-handed 2_1 helix, in which the planar arylaminocyclobutene moieties are arranged alternatively around the helical axis to form multi-layered structures (Figures 4, S6, and S9). The helical pitch was 7.4 and 7.0 Å for compounds **5** (Crystal No. **5a**) and **6** (Crystal No. **6a**), respectively. In these crystal structures, squaramides form hydrogen bonds with solvent molecules (water and methanol for compounds **5** and **6**, respectively). Thus, both amino groups of squaramindes act as hydrogen-bond donors toward oxygen of solvent molecules that form hydrogen bonds with a carbonyl group of the adjacent squaramide, and consequently folded-type hydrogen-bonding chain structures of squaramide (Figure 1c) are generated via the solvent molecules.

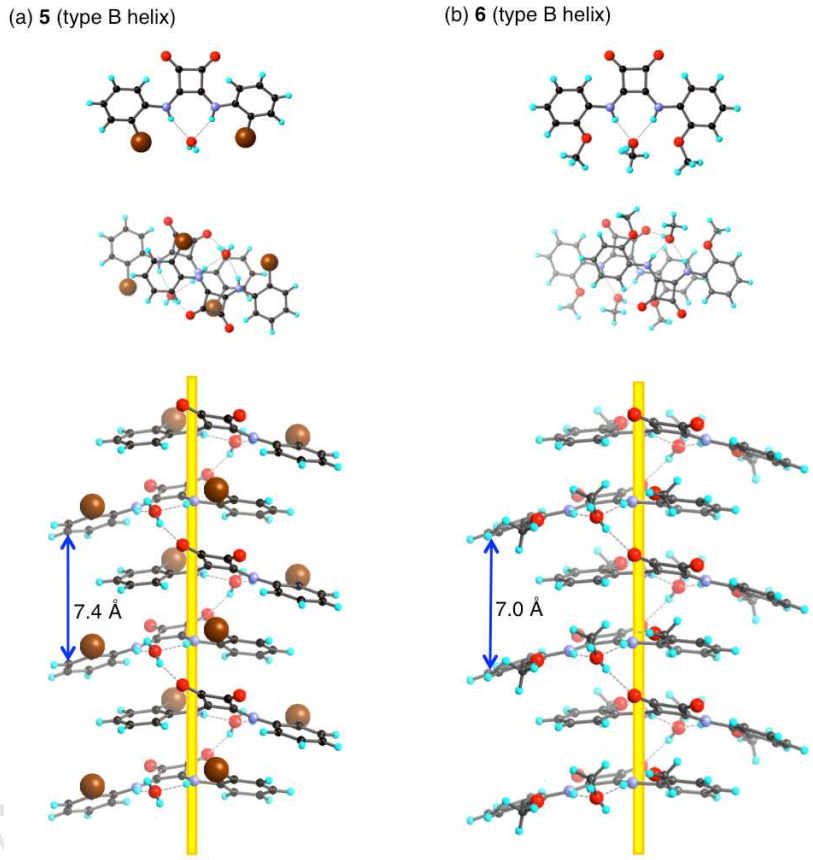


Figure 4. Helical structures of compounds (a) **5** (Crystal No. **5a**) and (b) **6** (Crystal No. **6a**) in the crystals.

Compound **7** with *o*-fluorophenyl groups afforded chiral crystals with pseudo 4_1 helical structure (Figures 5 and S11). In this case, the crystal contained two remarkably different conformers, that is, both planar and twisted structures exist, and the alternate arrangement of

these two conformers constructs the helical chain with a folded-type hydrogen-bonding structure (Figure 1c). Interestingly, the cyclobutene rings in the 4_1 helical structure of **7** are nearly parallel to the helical axis, different from the case in the pseudo 6_1 and 2_1 helical structures, in which the 4-membered rings and phenyl groups are nearly perpendicular to the helical axis.

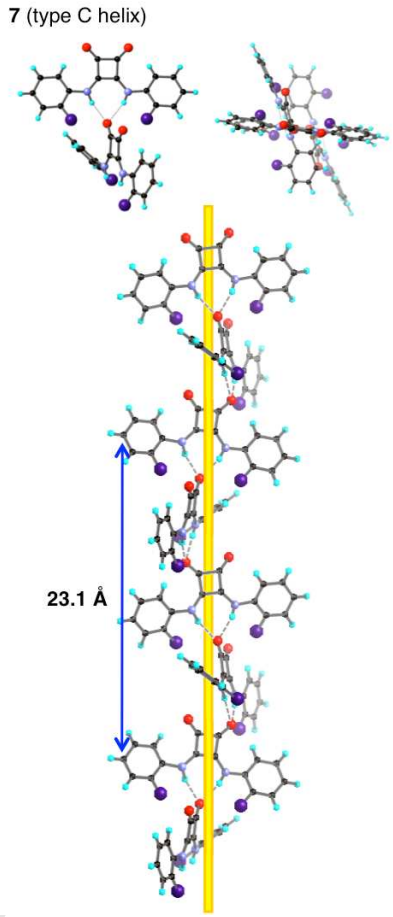


Figure 5. Helical structures of compound **7** in the crystals.

All *N,N'*-diarylsquaramides **1** – **7** exist in (trans, trans) conformations in the crystals. The conformations can be classified into two types, depending on the dihedral angles between aryl and aryl/squaramide (Table 1). In the chiral crystals of type A (compounds **3** and **4**), two *N*-aryl groups are twisted with respect to the plane of cyclobutene rings, with large dihedral angles (32 – 39°), and as the directions of twist are opposite to each other, the dihedral angles between two aryl rings are large (67 – 74°). Compound **2** has a similar twisted conformation (dihedral angle: 109.8°), but forms chain structure in the achiral crystal, in which each chain structure consists of one enantiomer. In the crystals of compounds **5** and **6** (type B helices), two aryl groups are twisted in the same direction with respect to the cyclobutene rings, and the dihedral angles between two aryl groups are small (**5**: 20.1° and **6**: 29.9°). Compound **7**

(type C helix) has both twisted and planar conformations. The three-dimensional structures, that is, twisted or planar conformations, did not correspond to the chirality or helix formation in the crystals. The hydrogen-bonding interactions between squaramide moieties or between squaramide and solvent (guest) molecules, as well as aromatic-aromatic/squaramide interactions, apparently determine the packing structures and chirality of the crystals.

Table 1. Dihedral angles of squaramides **1** – **7**.

Compound	Crystal No.	Space group	Dihedral angles (deg)	
			Aryl–Aryl	Aryl–Cyclobutene
1	**1**	$P2_1/c$	10.7	4.8, 8.2
2	**2**	$C2/c$	109.8	35.7, 38.1
3	**3a**[a]	$P2_12_12_1$	71.8	35.9, 37.4
			72.6	34.0, 38.6
			73.4	35.0, 38.8
	3b	$P2_1/c$	15.6	35.6, 48.1
4	**4**[a]	$P2_12_12_1$	67.4	32.4, 35.5
			68.9	32.9, 36.0
			68.9	33.8, 36.3
5	**5a**	$P2_1$	20.1	34.4, 40.8
	5c	$Pna2_1$	6.3	39.9, 44.5
	5d	$P2_1/n$	26.0	39.6, 49.6
6	**6a**	$P2_1$	29.9	12.3, 30.2
	6b[a]	$P2_1/c$	7.2	22.9, 29.7
			18.2	27.2, 29.6
			39.2	9.5, 33.0
7	**7**	$P2_12_12_1$	3.0	19.5, 21.9
			62.8	17.6, 46.5

[a]Three independent molecules exist in the asymmetric unit.

[b]Two independent molecules exist in the asymmetric unit.

In order to identify the absolute structures of helical squaramides, we carried out X-ray crystallographic analysis of compound **5** bearing heavy atom (bromine) substituents, and measured the CD spectra. Each crystal was cut into two parts; one was used to measure the solid-state CD spectrum [15] and the other for X-ray crystallography. We obtained both enantiomeric crystals (crystal No. **5a** and **5b** in Table S1) with mirror-image CD spectra in KBr (Figure 6). Analysis of *R* factor and Flack parameter (Table S4) indicated that the absolute structures in the crystals of **5a** (red line in Figure 6) and **5b** (blue line in Figure 6) could be assigned as left-handed and right-handed helices, respectively.

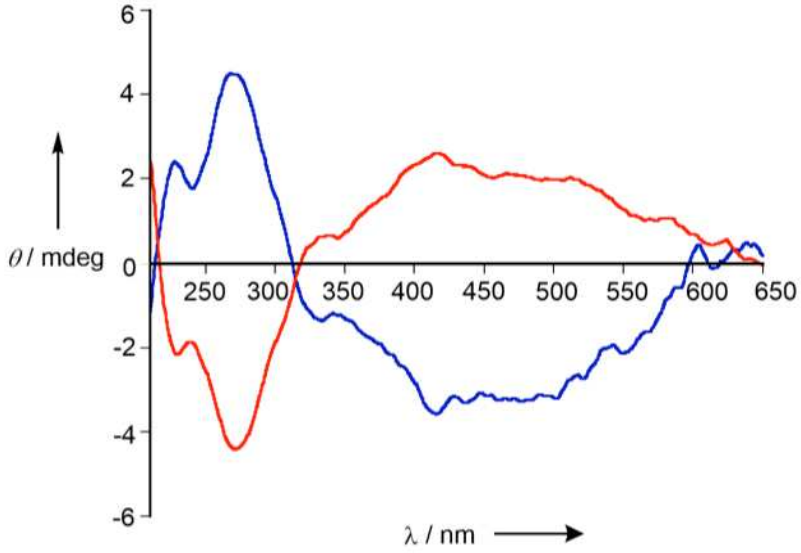


Figure 6. Solid-state CD spectra of enantiomeric crystals of compound **5** (150 mg in 100 mg of KBr). See Tables S1 and S2: **5a** (red line) and **5b** (blue line).

3. Conclusion

We found that *N*,*N*'-bis(*ortho*-substituted phenyl)squaramides **3** – **7** formed one-handed helical structures based on the folded-type hydrogen-bonding networks of the squaramide moiety. There reported various compounds taht afforded polymophic crystals including chiral crystals [14], while the *N*,*N*'-bis(*ortho*-substituted phenyl)squaramides are unique, because of high frequent chiral resolution and constractuon of various types of one-handed helical networks. Studies of several aromatic squaramides indicated that *ortho*-substituents play key roles in helix formation and spontaneous asymmetric induction in the crystals. Sterically bulky *ortho*-substituents hinder the formation of linear-type hydrogen bonds (Figure 1b), and instead, bent-type hydrogen-bonding networks (Figure 1c) are preferred. There are several types of one-handed helices depending on the substituents on the phenyl rings or on the

existence of solvent molecules in the crystals. The absolute one-handed helical structure of compound **5** was determined. Various unique artificial helical structures have been constructed based on the multi-hydrogen bond-forming properties [16] and conformational properties of amide and urea bonds [17]. Our results show that squaramide also has the ability to form unique helical structures, depending on the recrystallization conditions. Squaramide has distinct properties from amide and urea bonds as regards multi-hydrogen bond formation, and these features, together with the aromaticity of the 4-membered ring, suggest that it will be a useful building block for aromatic architectures with unique three-dimensional structures and chiral properties.

4. Experimental section

4.1. General

^{1}H spectra were recorded on Bruker Avance 400 spectrometer or Bruker Avance 600 spectrometer. ^{13}C NMR spectra were recorded on Bruker Avance 500 spectrometer. Mass spectra were collected on a Bruker Daltonics microTOF-2focus spectrometer in the positive ion modes. Elemental analysis was performed on MT-6 elemental analyzer (Yanagimoto). Melting points were determined on a RFS-30 melting point apparatus (Round Science). UV spectra were recorded with a JASCO V-650, and CD spectra were recorded with a JASCO J-820 spectropolarimeter.

4.2. Synthesis

*4.2.1. Synthesis of 3,4-Bis(phenylamino)cyclobut-3-ene-1,2-dione (**1**)*

Aniline (770 ml, 9.53 mmol) was added to a mixture of 3,4-diethoxy-3-cyclobutene-1,2-dione (681.5 mg, 4.01 mmol) and zinc trifluoromethanesulfonate (294.8 mg, 0.811 mmol) in toluene/DMF (19:1, 4 ml), and the mixture was heated at 95°C for 12 h. Cooling to room temperature afforded a pale yellow precipitate, which was collected and washed with methanol to give **1** (1.002 g, 3.79 mmol, 95%). Pale yellow plates (DMSO); mp > 300°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (2 H, br s), 7.49 (4 H, d, J = 7.6 Hz), 7.38 (4 H, t, J = 7.4 Hz), 7.08 (2 H, t, J = 7.4 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 181.66, 165.72, 138.67, 129.43, 123.29, 118.53; Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C 72.72, H 4.58, N 10.60, Found: C 72.77, H 4.73, N 10.60; HRMS (ESI+) Calcd. for $C_{16}H_{13}N_2O_2$ $[M + H]^+$: 265.0972. Found 265.0966.

*4.2.2. Synthesis of 3,4-Bis(3-methylphenylamino)cyclobut-3-ene-1,2-dione (**2**)*

m-Toluidine (705.8 mg, 6.59 mmol) was added to a mixture of

3,4-diethoxy-3-cyclobutene-1,2-dione (507.0 mg, 2.98 mmol) and zinc trifluoromethanesulfonate (249.7 mg, 0.687 mmol) in toluene/DMF (19:1, 4 ml), and the mixture was heated at 95°C for 2 h. Cooling to room temperature afforded a pale yellow precipitate, which was collected and washed with methanol to give **2** (758.8 mg, 2.60 mmol, 87%). Colorless plates ($CH_3OH/CHCl_3$); mp 211-215°C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.33 (2 H, br s), 7.29 (2 H, d, *J* = 7.6 Hz), 7.23 (2 H, t, *J* = 7.5 Hz), 6.93 (2 H, d, *J* = 7.5 Hz), 2.35 (6 H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ 181.65, 165.68, 138.77, 138.59, 129.26, 124.03, 119.05, 115.72, 21.21; Anal. Calcd. for $C_{18}H_{16}N_2O_2 \cdot 1/2H_2O$: C 71.74, H 5.69, N 9.30, Found: C 71.75, H 5.79, N 9.27; HRMS (ESI+) Calcd. for $C_{18}H_{17}N_2O_2$ $[M + H]^+$: 293.1285. Found 293.1279.

*4.2.3. Synthesis of 3,4-Bis(2-methylphenylamino)cyclobut-3-ene-1,2-dione (**3**)*

o-Toluidine (765.8 mg, 7.12 mmol) was added to a mixture of 3,4-diethoxy-3-cyclobutene-1,2-dione (515.0 mg, 3.03 mmol) and zinc trifluoromethanesulfonate (262.7 mg, 0.723 mmol) in toluene/DMF (19:1, 4 ml), and the mixture was heated at 95°C for 2 h, then evaporated to dryness. The residue was taken up in a mixture of AcOEt and water. The organic layer was dried over sodium sulfate, filtered and evaporated to give **3** (933.5 mg, quant). Yellow pyramids (CH_3OH); mp 212-216°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (2 H, br s), 7.31 (2 H, d, *J* = 7.5 Hz), 7.21 (2 H, d, *J* = 7.1 Hz), 7.18 (4 H, m), 7.04 (3 H, td, *J* = 7.4, 1.0 Hz), 2.33 (6 H, s) ; ^{13}C NMR (125 MHz, DMSO-d_6) δ 182.65, 166.53, 136.20, 130.49, 128.68, 126.44, 124.64, 122.41, 17.80; Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C 73.95, H 5.52, N 9.58, Found: C 73.66, H 5.52, N 9.36; HRMS (ESI+) Calcd. for $C_{18}H_{17}N_2O_2$ $[M + H]^+$: 293.1285. Found 293.1288.

*4.2.4. Synthesis of 3,4-Bis(2-chlorophenylamino)cyclobut-3-ene-1,2-dione (**4**)*

2-Chloroaniline (540.2 mg, 4.23 mmol) was added to a mixture of 3,4-diethoxy-3-cyclobutene-1,2-dione (339.3 mg, 1.99 mmol) and zinc trifluoromethanesulfonate (148.9 mg, 0.410 mmol) in toluene/DMF (19:1, 2 ml). The reaction mixture was heated at 95°C for 11.5 h. Cooling to room temperature afforded a pale yellow precipitate, which was collected and washed with methanol to give **4** (354.2 mg, 1.06 mmol, 53%). Yellow plates (CH_3OH); mp 228-230°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ□9.93 (2 H, s), 7.55 (2 H, dd, *J* = 8.0, 1.4 Hz), 7.52 (2 H, dd, *J* = 8.1, 1.4 Hz), 7.37 (2 H, ddd, *J* = 8.1, 8.1, 1.5 Hz), 7.18 (2 H, ddd, *J* = 8.0, 8.0, 1.5 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 182.72, 166.16, 134.53, 129.60, 127.78, 125.71, 123.94, 123.88; Anal. Calcd. for $C_{16}H_{10}Cl_2N_2O_2$: C 57.68, H 3.03, N 8.41, Found: C 57.41, H 3.27, N 8.40; HRMS (ESI+) Calcd. for

$C_{16}H_{11}Cl_2N_2O_2$ $[M + H]^+$: 333.0192. Found 333.0195.

*4.2.5. Synthesis of 3,4-Bis(2-bromophenylamino)cyclobut-3-ene-1,2-dione (**5**)*

2-Bromoaniline (1.5052 g, 8.85 mmol) was added to a mixture of 3,4-diethoxy-3-cyclobutene-1,2-dione (682.7 mg, 4.01 mmol) and zinc trifluoromethanesulfonate (302.2 mg, 0.831 mmol) in toluene/DMF (19:1, 4 ml). The reaction mixture was heated at 95°C for 1 d. Cooling to room temperature afforded a pale yellow precipitate, which was collected and washed with methanol. Combined filtrate was evaporated, and the residue was washed with ethanol to give **5** (1.1067 g, 2.62 mmol, 65%). Colorless prisms (CH_3OH); mp 210-218°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (2 H, s), 7.67 (2 H, dd, *J* = 8.0, 1.3 Hz), 7.45 (2 H, dd, *J* = 8.0, 1.4 Hz), 7.38 (2 H, ddd, *J* = 7.2, 7.2, 1.3 Hz), 7.11 (2 H, ddd, *J* = 7.3, 7.3, 1.5 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 182.81, 166.12, 135.72, 132.74, 128.29, 126.30, 124.52, 114.62; Anal. Calcd. for $C_{16}H_{10}Br_2N_2O_2$: C 45.55, H 2.39, N 6.69, Found: C 45.57, H 2.47, N 6.64; HRMS (ESI+) Calcd. for $C_{16}H_{11}Br_2N_2O_2$ $[M + H]^+$: 420.9182. Found 420.9173.

*4.2.6. Synthesis of 3,4-Bis(2-methoxyphenylamino)cyclobut-3-ene-1,2-dione (**6**)*

o-Anisidine (527.3 mg, 4.28 mmol) was added to a mixture of 3,4-diethoxy-3-cyclobutene-1,2-dione (343.2 mg, 2.02 mmol) and zinc trifluoromethanesulfonate (158.6 mg, 0.436 mmol) in toluene/DMF (19:1, 2 ml), and the mixture was heated at 95°C for 6.5 h. Cooling to room temperature afforded a pale yellow precipitate, which was collected and washed with methanol to give **6** (332.6 mg, 1.03 mmol, 51%). Yellow plates (CH_3OH); mp108-110°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (2 H, br s), 7.58 (2 H, d, *J* = 8.0 Hz), 7.10 (4 H, m), 6.95 (2 H, ddd, *J* =8.2, 6.0, 2.8 Hz), 3.90 (6 H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ 182.11, 165.87, 149.56, 126.97, 124.68, 121.48, 120.53, 111.40, 55.81; Anal. Calcd. for $C_{18}H_{16}N_2O_4$: C 66.66, H 4.97, N 8.64, Found: C 66.41, H 4.97, N 8.59; HRMS (ESI+) Calcd. for $C_{18}H_{17}N_2O_4$ $[M + H]^+$: 325.1183. Found 325.1183.

*4.2.7. Synthesis of 3,4-Bis(2-fluorophenylamino)cyclobut-3-ene-1,2-dione (**7**)*

A solution of 2-fluoroaniline (135.7 mg, 1.22 mmol) in toluene (0.5 ml) was added to a mixture of 3,4-diethoxy-3-cyclobutene-1,2-dione (95.5 mg, 0.56 mmol) and zinc trifluoromethanesulfonate (65.0 mg, 0.179 mmol) in toluene/DMF (19:1, 1 ml). The reaction mixture was heated at 95°C for 1 d. Cooling to room temperature afforded a pale yellow precipitate, which was collected and washed with methanol to give **7** (141.9 mg, 0.473 mmol, 84%). Colorless needles (CH_3OH); mp 244-246°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12

(2 H, s), 7.87(2 H, ddd, *J* = 8.0, 8.0, 1.6 Hz), 7.31(2 H, ddd, *J* = 11.6, 8.1, 1.4 Hz), 7.22(2 H, ddd, *J* = 7.9, 7.9, 1.4 Hz), 7.14(2 H, m); ^{13}C NMR (125 MHz, DMSO-d_6) δ 182.16, 165.99, 153.72, 151.78, 126.35, 124.88, 122.11, 115.72; Anal. Calcd. $C_{16}H_{10}F_2N_2O_2$for : C 64.00, H 3.36, N 9.33, Found: C 63.86, H 3.59, N 9.20; HRMS (ESI+) Calcd. for $C_{16}H_{11}F_2N_2O_2$ [M + H]$^+$: 301.0783. Found 301.0774.

4.3. X-ray crystallography

Crystallographic data were collected on a Bruker Apex II ultra CCD detector with graphite-monochromated Mo Kα radiation and a Bruker Apex II ultra CCD detector with graphite-monocromated Cu Kα radiation. The crystal structures were solved by direct methods using SHELXS-97 and refined by full-matrix least-squares SHELXL-97.[18] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included at their calculated positions.

Acknowledgements

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Graphical Abstract (Figure was modified)

Spontaneous Chiral Resolution of *N,N'*-Diarylsquaramides : Formation of Various Types of One-handed Helical Networks During Crystallization

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