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Temperature induced rotation in a [4.4]cyclophane

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ABSTRACT

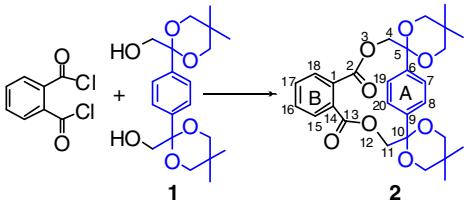
The synthesis, the X-ray, NMR and molecular modeling structure determination of a new ortho-para[4.4]cyclophane are reported. The similarity of the π(CO)–π(Ar) driven conformational equilibrium of this compound to the work of an amusement ride machinery is also revealed.

Although their importance beyond chemical curiosities is yet to be demonstrated, the design (at molecular or supramolecular level) of architectures and machineries that can reproduce the work of motors,[1,2] muscles,[3–6] or (home) devices[7,8] is a well-represented field of chemical research.[9–16] Recent papers reveal the building of molecular shuttles,[17–20] giant gyroscope,[21–25] hinges,[26] tweezers,[27] and scissors.[28,29] In a previous work,[30,31] we obtained [7.7]cyclophane-based molecular rudders, wringer and rocking chair. Herein, we describe and investigate the unusual conformational behavior of more hindered [4.4]cyclophanes that could be used for building new molecular devices.

Orthopara[4.4]cyclophane **2** was obtained in fair yields starting from 1,3-dioxane diol **1** and phthaloyldichloride (Scheme 1).

The solid state molecular structure of **2** (Fig. 1) reveals as its most salient feature the proximity of the 1,4-phenylene ring to one of the CO groups (C^2O^4 in Fig. 1) and indicates π–π interactions between these units.

According to the literature data,[32] the short distance from O^4 to the center of ring A (3.12 Å) and the slightly tilted orientation of the planes of the ester group ($O^3C^2O^4$) and the opposite aromatic ring A (the dihedral angle between the two planes is $\omega = 28.53°$) suggest the important overall stabilization of the structure by the



Scheme 1. Synthesis of cyclophane **2**.

CO-aromatic interactions. These π–π interactions are brought about by the *anti–anti* conformation of one of the chains $–C^{14}–C^{13}(O)–O^{12}–C^{11}H_2–C^{10}–$ [torsion angles for the bonds $–C^{13}(O)–O^{12}–$ and $–O^{12}–C^{11}H_2–$ are −176.63 and 167.46], the twisting of the other bridge to the *anti–anticlinal* conformation [the torsion angles for the bonds $–C^2(O)–O^3–$ and $–O^3–C^4H_2–$ of the similar $–C^1–C^2(O)–O^3–C^4H_2–C^5–$ moiety are −173.82 and −101.17], the deformation of the *para*-phenylene ring (the angle between the bonds $C^5–C^6$ and $C^9–C^{10}$ is 31.86°) and the *face-tilted-to-face* arrangement of rings A and B ($\alpha_{A/B} = 36.35°$). Additionally, C–H–π and π–π interactions of rings A and B are found in the lattice (shown in SI).

To investigate the molecular motions characteristic to this cyclophane, we took into account several conformational equilibria (Scheme 2). The dioxacyclohexane parts of the cyclophane are anancomeric (rigid) with axial disposition of the *para*-phenylene

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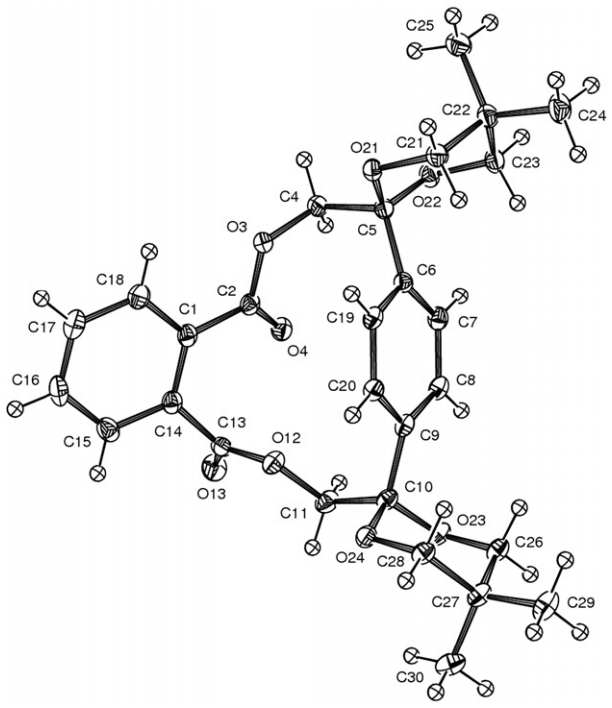
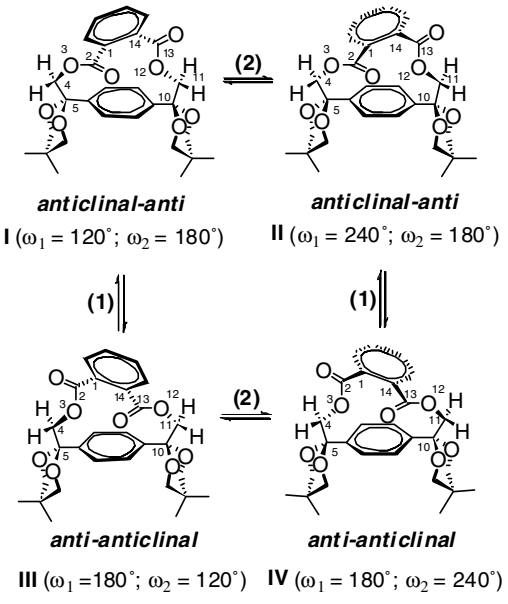


Figure 1. ORTEP diagram of compound **2**.



Scheme 2. Flipping of the bridges and *outside–inside* movement of the CO groups in [4.4]cyclophane **2**.

ring for both dioxacyclohexane units. The ester parts of the cyclophane (the bridges) are flexible and, therefore, allow the molecular motions of interest to take place. The conformational behavior of the bridges is complex and involves both the common (for [4.4]cyclophanes)[33] flipping of the *ortho*-phenylene ring (Scheme 2; equilibrium 2) and the *outside–inside* movement of the CO groups (Scheme 2, equilibrium 1, I⇆III; II⇆IV). This last conformational process requests the interchange of the *anti–anti* and *anti–anticlinal* conformations of the C(ar)–CO–O–CH_2–C(–O–CH_2–)$_2$– parts of the bridges. This conformational change amounts to +60° torsion around the O^3–C^4H_2 (ω_1) bond and −60° torsion around the O^{12}–$C^{11}H_2$ (ω_2) bond. The flipping of the bridges requests the modification of the *anticlinal* conformer (I) to its enantiomeric structure (II) [rotation of +120° or −120° around O^3–C^4H_2 (ω_1) for I⇆II and around O^{12}–$C^{11}H_2$ (ω_2) for III⇆IV]. We calculated the energies associated to these conformational changes (SI). The *inside–outside* movement of the CO groups (equilibrium denoted with 1 in Scheme 2) was found to have a small barrier (the value found by molecular modeling is $\Delta G^{\circ\#}$ = 6.6 kcal/mol), while for the flipping of the bridges (denoted with 2) the calculated barrier is considerably higher ($\Delta G^{\circ\#}$ = 23.4 kcal/mol).

These movements that push and pull at the same time in front and behind and shake the *ortho*-substituted phenylene ring can be compared with the work of a 'molecular amusement ride' (the support of the machine is represented by the *para*-phenylene moiety, the chair is the *ortho*-phenylene ring and the mechanism is formed by the –CO–O–CH_2– parts of the bridges, Fig. 2).

In order to experimentally observe the conformational changes in cyclophane **2**, variable temperature ^{1}H and ^{1}C NMR experiments were carried out (Figs. 3 and 4 and SI). The temperatures were increased or decreased and ^{1}H NMR spectra were recorded after each 10 °C temperature modification. We also compared the conformational behavior of molecule **2** in $CDCl_3$ (non competing

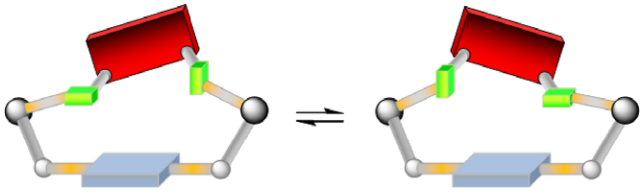


Figure 2. Macroscopic representation of the amusement ride machine.

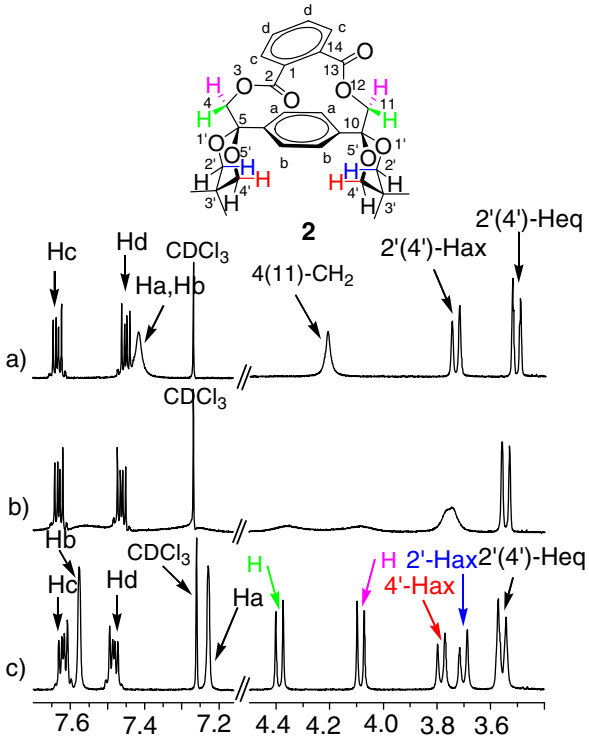


Figure 3. Variable temperature NMR experiments ($CDCl_3$) run with compound **2** (a: 330 K; b: 290 K; c: 220 K).

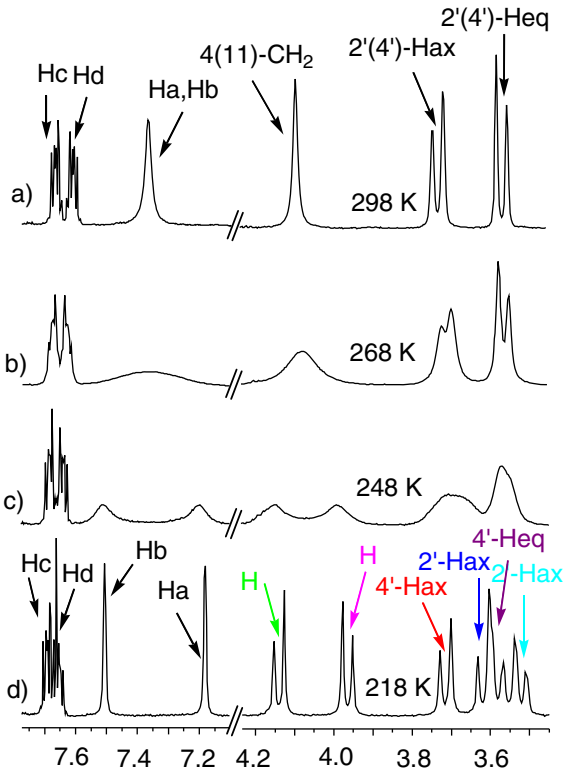


Figure 4. Variable temperature NMR experiments (acetone-d_6) run with compound **2** (a: 298 K; b: 268 K; c: 248 K, d: 218).

for the CO–π interactions) and acetone, competing for the CO–π interactions. The room temperature (290 K) ^{1}H NMR spectrum in $CDCl_3$ (Fig. 3) shows the coalescence of three sets of signals. The spectrum run at high temperature (330 K) is very simple and suggests the flipping of the structure. It exhibits one singlet (δ = 4.21 ppm) for the protons of the CH_2 groups of the bridges, doublets for the axial (δ = 3.76 ppm) and equatorial protons (δ = 3.53 ppm) of the heterocycles, and a broad singlet for the aromatic protons of the 1,4-phenylene unit (δ = 7.41 ppm). The low temperature ^{1}H NMR spectrum (220 K) is more complex, yet well resolved, and suggests the hindrance of the flipping of the bridges. It shows the diastereotopicity (characteristic for the frozen structure) of positions 2′ and 4′ of the dioxacyclohexane units ($\delta_{2'ax}$ = 3.70 and $\delta_{4'ax}$ = 3.78 ppm), of the protons of the CH_2 groups belonging to the bridges (δ = 4.08 and δ' = 4.38 ppm), and of the protons denoted with a and b of the 1,4-phenylene ring (δ_a = 7.22 and δ_b = 7.57 ppm). During these experiments, several coalescences were observed (see SI). Using the temperatures of coalescence (SI), the δ values of the separated signals in the low temperature spectrum, and Eyring's equations,[34,35] the barrier for the flipping of the chains could be estimated at $\Delta G^{\circ\#}$ = 13.78 ± 0.41 kcal/mol (see SI).

If $CDCl_3$ is replaced with acetone-d_6, the rt spectrum already corresponds to the flexible structure (Fig. 4). The variable temperature NMR experiments (Fig. 4) showed the achievement of several coalescences. The spectrum of the frozen structure was recorded at 220 K. Using the NMR data the barrier for the flipping of the chains could be estimated at $\Delta G^{\circ\#}$ = 12.44 ± 0.46 kcal/mol (see SI).

The lower barrier measured in acetone ($\Delta\Delta G^{\circ\#}$ = 12.44 ± 0.46 kcal/mol) is due to the fact that the solvent (acetone) interacts with the aromatic units,[36,37] as well as the ester groups[38] of the cyclophane, both in the ground state and during the flipping of the bridges. These acetone-based interactions are competing-out the intramolecular C=O to 1,4-phenylene π–π interactions, therefore depriving the ground-state conformation of the corresponding stabilization energy. The direct consequence of this fact is a decrease in the barrier of the flipping of the bridges. This smaller barrier is presumably at a comparable value with that found in the similar ether orthopara[4.4]cyclophane in which the π–π interactions which stabilize the ground state are missing.[39]

The ^{13}C NMR spectrum at low temperature (250 K) in $CDCl_3$ is more complex than the spectrum obtained at rt (293 K) (for the dynamic ^{13}C NMR experiments in acetone-d_6 see SI). At rt the secondary carbon atoms of the dioxacyclohexane ring give only one signal. The a and b type carbon atoms of the 1,4-phenylene ring are rendered equivalent by the flipping of the bridges and also give only one signal. Due to the diastereotopicity of the carbon atoms at positions 2′ and 4′ of the dioxacyclohexane units and of the tertiary carbon atoms of the *para*-phenylene unit, the low temperature spectrum exhibits two signals for the similar positions of the carbon atoms (293 K: $\delta_{2',4'}$ = 71.6; $\delta_{a,b}$ = 129.1 ppm; 250 K: $\delta_{2'}$ = 71.7, $\delta_{4'}$ = 72.0, δ_a = 128.97, δ_b = 129.04 ppm). The CO groups exhibit only one signal (δ = 165.7 ppm) both at low and room temperature. This is in line with the fast *outside–inside* movement of the carbonyl groups (equilibrium 1), consistent with the low barrier conformation change calculated by molecular modeling (equilibrium 1, Scheme 2).

In conclusion, the dynamic NMR and molecular modeling investigations of compound **2** revealed the control of the conformational equilibria of the compound by the π(CO)–π interactions. Beyond the anecdotical similarity between the conformational modifications in **2** and the work of an amusement ride machinery, the π–π driven conformational changes described herein expand the repertoire of tools available for the finely tuned control of molecular movement. Their modulation by external factors, such as the nature of the solvent, adds further relevance to the described phenomena. In particular, one can envision the use of such dynamically modulable structures as basic units of small-molecule conformation-based catalysts.[40–43]

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.06.045.

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