Watching bonds move in a large antiaromatic ring

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Summary

In antiaromatic molecules, single and double bonds interconvert via a process called bond-shift valence tautomerization, which is often so fast that its rate is difficult to measure experimentally. In this issue of *Chem*, Wu and coworkers use dynamic NMR spectroscopy to study valence tautomerization in a giant antiaromatic macrocycle.

Body

“How rapidly do the resonance forms of benzene interconvert?” It is depressing when students ask this question because it normally means they have not understood the difference between resonance and equilibrium. One must gently explain that the true structure of benzene is D_{6h} symmetric with all C–C bond lengths equal. But it is not such a stupid question. Benzene’s smaller antiaromatic cousin, cyclobutadiene, exhibits pronounced bond-length alternation (BLA) and bond-shift valence tautomerization. The structural dichotomy between benzene and cyclobutadiene is shown by the potential energy surfaces for bond-length reorganization (Figure 1A).[1]

Kekulé thought that benzene could be described as two rapidly interconverting cyclohexatriene tautomers. We now call this oscillation the Kekulé vibration; it effects an increase in BLA (b_{2u} vibrational mode; frequency ~1310 cm^{-1}, time period ~25 fs). Importantly, the equilibrium geometry has no bond length alternation (BLA = 0).

In contrast, cyclobutadiene's valence tautomerization is represented by a double well potential. There are two equilibrium geometries (D_{2h} rectangles) separated by a low activation barrier: the transition state at the top of this barrier is the D_{4h} square cyclobutadiene. It has been difficult to evaluate the height of the bond-shift barrier in cyclobutadiene. High-level calculations suggest 27–32 kJ/mol, but low temperature solidstate ^{13}C NMR spectroscopy experiments set an upper-bound of ~4 kJ/mol (at 25 K, interconversion time < 1 ms), and it appears that heavy-atom tunneling substantially accelerates the tautomerization.[2]

Another well-known difference between benzene and cyclobutadiene is that benzene is aromatic, satisfying the famous $4n+2$ rule for aromaticity, whereas cyclobutadiene is antiaromatic, with $4n$ π-electrons (with $n = 1$). Frost-Musulin diagrams explain how the difference in electron count causes structural distortions in antiaromatic molecules (*i.e.* high BLA), while small aromatic molecules tend to be symmetrical with low BLA. An annulene $(CH)_n$ is represented by drawing an n-sided polygon inside a circle, with one corner of the polygon at the bottom (Figure 1B). The relative resonance energies of the π-orbitals are given by the points at the corners of the polygon, on a vertical energy scale. The diagram for benzene confirms its exceptional resonance stabilization — all the occupied π-orbitals are strongly bonding. In contrast, square (D_{4h}) cyclobutadiene has a diradical configuration, with two degenerate non-bonding HOMOs. A pseudo-Jahn-Teller distortion introduces significant BLA and reduces the symmetry to D_{2h}, while stabilizing the HOMO (Figure 1B right) and lowering the energy of the system.

There are many other examples of valence tautomers, broadly defined as pairs of molecules, in equilibrium with each other, which differ only in the nature of bonding, without a substantial change in the spatial arrangement of atoms (Figure 1C and 1D). The valence tautomerization in cyclobutadiene is called “bond-shift tautomerization” because it only involves a change in π-bonding. This tautomerization is much too fast to be observed by solution-phase NMR spectroscopy. In contrast, the bond-shift barriers for cyclooctatetraene and some higher annulenes with [$4n$] π-electrons have been determined experimentally using variable temperature (VT) NMR. For cyclooctatetraene, the barrier for the bond-shift process is about 55 kJ/mol, with an interconversion time of 8.3 ms at 273 K (from analysis of ^{13}C satellites in the ^{1}H NMR spectra).[3] Other examples, including 1,7-methano[12]annulene and [24]annulene, have barriers of 21–45 kJ/mol (Figure 1D).[3–5]

The main limitation of VT-NMR studies is that the rate of reaction must be close to the chemical shift timescale at some accessible temperature; as a rule of thumb, the activation barrier for the dynamic process should be in the range 20–60 kJ/mol. There are many ways of changing this activation energy. One approach is to change the molecular structure, as illustrated by studies of the interconversion of cycloheptatriene (CHT) and norcaradiene (NCD) (Figure 1C). This tautomerization was too quick to observe by NMR until Vogel *et al.* studied the benzene-fused derivatives (Figure 1D).[6] In these systems the interconversion is retarded to such an extent that the two benzo-NCD conformers, which exchange via the benzo-CHT, are in slow exchange by NMR at temperatures of up to 180 °C. In this example the tautomerization barrier is increased by the loss of benzene aromaticity in the benzo-CHT intermediate. In general, benzene's aromatic stability persists in local form in extended π-systems, as described by Clar's rule[7] and beautifully demonstrated by some of Jishan Wu's other work on graphene nanoflakes.[8]

In this issue of *Chem*, Wu and coworkers describe a series of π-conjugated [*n*]cyclo-*para*-biphenylmethine (**[*n*]CPBM-An**, *n* = 3–8) molecules.[9] The **[*n*]CPBM-An** series is similar to the well-studied [*n*]cyclo-*para*-phenylenes ([*n*]CPP),[10] but with an additional methine inserted between every biphenyl unit. These methine positions bear substantial radical character, and require protection with bulky anthracenyl groups. The spectacular synthesis relies on a late-stage remote reductive aromatization of the anthracene, avoiding steric challenges in the construction of the macrocycle. Remarkably, the entire series of molecules is stable under ambient conditions for several days.

The **[*n*]CPBM-An** macrocycles have interesting magnetic properties. Each **CPBM-An** repeating unit provides 9 π-electrons to the macrocycle. Thus *n* = 3,5,7 are paramagnetic molecules with a doublet ground state, whereas *n* = 4,6,8 are diamagnetic singlet ground states (albeit with appreciable radical character, according to both DFT and EPR/SQUID). In all cases the singlet-triplet gap is small (<16 kJ/mol), decreasing in the larger macrocycles.

The macrocycle **[4]CPBM-An** can be thought of as a "super-sized" analogue of cyclobutadiene. X-ray crystallography reveals a distinct structural distortion, from the idealized square to a more rectangular shape. This elongated structure results from quinoidal character in the biphenyls along two opposing sides of the molecule, with aromatic character for those on the other two sides (Figure 1E). Calculations of the nucleus-independent chemical shift (NICS), which is often diagnostic for (anti)aromaticity, reveal that although the high-symmetry "square" geometry would be antiaromatic (NICS = +10 ppm), the elongated rectangular ground state structure is non-aromatic (NICS ≈ 0 ppm).

In the room-temperature NMR spectrum of **[4]CPBM-An**, the ^{1}H resonances of the quinoidal and aromatic benzene rings are in fast exchange and thus indistinguishable. Only two pairs of **CPBM** proton resonances are apparent until the sample is cooled to about 223 K. Below this temperature, distinct resonances for the quinoidal and aromatic benzene protons are observed. The VT-NMR spectroscopic data were evaluated by lineshape analysis giving a barrier to bond-shift valence tautomerization of ~47 kJ/mol (coalescence temperature 263 K; interconversion time ~1 ms).

Why should this barrier be so much higher than that between other pairs of bond-shift tautomers? We return to the idea of inserting energetically robust benzene units to increase the barrier for valence tautomerization. The transition state for the bond-shift in **[4]CPBM-An** is, by calculation, the antiaromatic “square” geometry. It can be seen from Figure 1E that the establishment of a 36 π-electron antiaromatic circuit results in the loss of aromaticity in each benzene subunit: four π-electrons, which were formerly part of each privileged sextet, are now given up to this circuit. The loss of benzene aromaticity is accompanied by a dramatic increase in energy. This simple picture is supported by calculated ring currents and NICS values (Figure 6 in Wu’s paper[9]). The bigger macrocycles, **[6]-** and **[8]CPBM-An**, do not have measurable bond-shift interconversion barriers, probably due to their greater conformational flexibility. Both molecules remain in the fast-exchange regime relative to the NMR chemical shift timescale, down to the lowest accessible temperature (213 K).

This paper by Wu and coworkers presents spectacular insights into a fascinating series of molecules. It provides a clear illustration of how bond-shift tautomerization can be reconciled with resonance. **[4]CPBM** is a rare example in which bond-shift valence tautomerization can be observed directly by NMR spectroscopy, without contributions from other conformational or configurational exchange processes. Antiaromaticity probably contributes towards the large barrier to tautomerization in **[4]CPBM**. Antiaromatic systems inevitably have small HOMO–LUMO gaps, leading to potential applications as organic semiconductors and near-IR dyes. The family of **[*n*]CPBMs** is a remarkable set of materials with small HOMO–LUMO gaps and significant open-shell character across the entire series.

Figure caption:

Figure 1. Valence tautomerisms and **[4]CPBM-An**.
A: Sketch of the potential energy surfaces for resonance (as in benzene) and bond-shift valence tautomerization (as in cyclobutadiene).
B: Frost-Musulin diagrams explain benzene’s aromatic stabilization and rationalize the pseudo-Jahn-Teller distortion in cyclobutadiene.
C: Examples of fast valence tautomerization processes (see references 2 and 4).
D. Examples of slow valence tautomerization processes, which have previously been characterized by solution-phase NMR (see references 3–5).

E: Sketched potential energy surface for interconversion of bond-shift tautomers of **[4]CPBM-An**.

Acknowledgements

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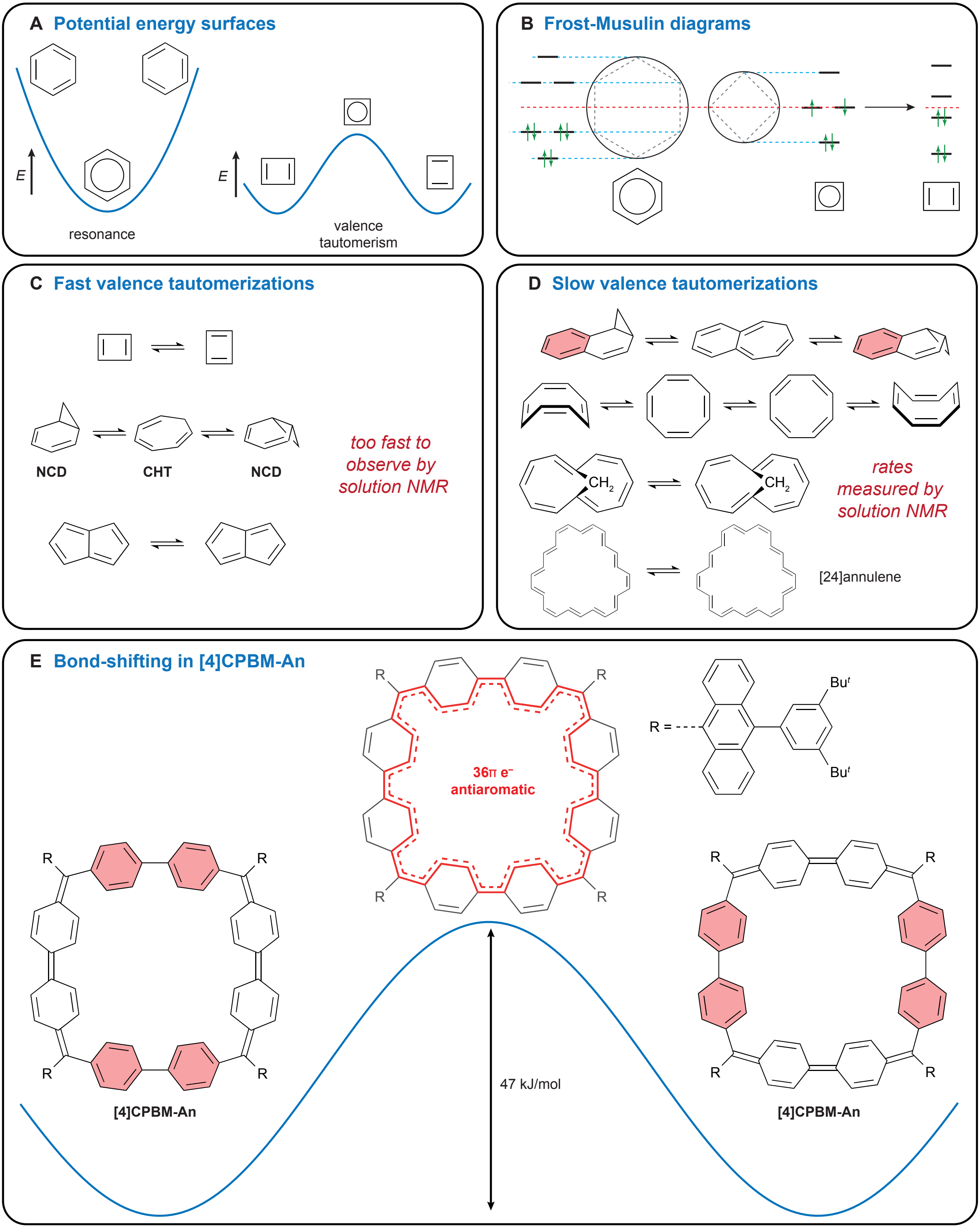
A Potential energy surfaces
E
resonance
E
valence tautomerism
B Frost-Musulin diagrams
C Fast valence tautomerizations
NCD
CHT
NCD
too fast to observe by solution NMR
D Slow valence tautomerizations
CH₂
CH₂
rates measured by solution NMR
[24]annulene
E Bond-shifting in [4]CPBM-An
R
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36π e⁻ antiaromatic
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47 kJ/mol
[4]CPBM-An
[4]CPBM-An