

Fig. 2 | Schematic representation of the extracted time-resolved circular dichroism spectra of the high-spin state. The blue line shows the symmetric band shapes at early time delays. At longer delays, an asymmetric band shape (orange) develops because of the sensitivity of TRCD to symmetry-breaking torsional twisting modes. The asymmetry in the figure has been exaggerated compared to the spectra presented by Oppermann and colleagues for display purposes.

spatial distribution and alignment of dipoles in the ensemble of photoexcited molecules because the pump will preferentially excite molecules aligned along the laser polarization direction and the probe will monitor the decay of this alignment. The rich, spectrally resolved data were fitted to a global model, enabling Oppermann and colleagues to conclude that there was a narrower distribution of the ligand angles for the enantiopure sample than for the racemic mixture. This meant that the diastereomeric interactions were limiting the lability of the metal–ligand bonds and hindering the decay back to the low-spin ground state.

To better understand the structural dynamics during relaxation Oppermann and colleagues turned to their improved circular dichroism set up. Due to the excellent signal-to-noise ratio in their TRCD measurements, they could carefully separate the CD spectrum of the high-spin state from that of the ground state. The CD spectrum for excitonically coupled ligand-centred transitions in a rigid octahedral environment, which are dominant for $[\text{Fe}^{\text{II}}(\text{dm-bpy})_3]^{2+}$, should yield a symmetric shape (a positive and negative feature at higher and lower energies, respectively, compared to the associated peak in the absorption spectrum), and this is indeed what was observed at early time delays for the enantiopure sample (Fig. 2). However, the symmetric ratio of the intensities of the peaks decayed over tens of picoseconds, which indicates a structural change that breaks the octahedral symmetry. Based on previous theoretical work, Oppermann and colleagues could conclude that a separate reaction coordinate besides the commonly assumed (symmetrical) radial breathing mode is involved in the conversion of the high to the low-spin state.

The distortion of the octahedral symmetry is important because it mixes the singlet and quintet states with intermediate triplet states, which couple the low and high-spin states. The nuclear motion that is involved in the torsional motion is identified by Oppermann and colleagues as the Ray–Dutt twist (Fig. 1) because of the asymmetric decay of the band shape in the TRCD spectrum. The importance of twisting motion in the relaxation from high to low spin has previously been emphasized^{7–9}, and now the TRCD spectra demonstrate the specific role of the Ray–Dutt twist. The TA, TAA, and TRCD measurements show that the diastereomeric interaction limits

the Ray–Dutt twist and therefore prolongs the lifetime of the high-spin state. These findings open up new synthetic design challenges to stabilize the high-spin state by supramolecular chemistry and solid-state approaches.

The successful use of time-resolved circular dichroism to reveal structural changes in the excited state is significant because it had previously not been possible to assign the specific nature of the symmetry-breaking mode. There is a rapidly growing interest in the photophysics of earth-abundant metal complexes with the prospect of replacing ruthenium-based complexes for more sustainable materials in applications in lighting, solar capture, and photocatalysis. Now, Oppermann and colleagues provide a textbook example of how technical methodological advances coupled with well-chosen systems for study can further advance insights into inorganic photophysics and photochemistry. □

J. Olof Johansson

EaStCHEM School of Chemistry, University of Edinburgh, David Brewster Road, Edinburgh, UK.

✉e-mail: olof.johansson@ed.ac.uk

Published online: 1 July 2022
<https://doi.org/10.1038/s41557-022-00986-1>

References

- McCusker, J. K. *Acc. Chem. Res.* **36**, 876–887 (2003).
- Auböck, G. & Chergui, M. *Nat. Chem.* **7**, 629–633 (2015).
- Chergui, M. & Collet, E. *Chem. Rev.* **117**, 11025–11065 (2017).
- Gaffney, K. J. *Chem. Sci.* **12**, 8010–8025 (2021).
- Oppermann, M., Zinna, F., Lacour, J. & Chergui, M. *Nat. Chem.* <https://doi.org/10.1038/s41557-022-00933-0> (2022).
- Oppermann, M. et al. *Optica* **6**, 56–60 (2019).
- Purcell, K. F. *J. Am. Chem. Soc.* **101**, 5147–5152 (1979).
- Vanquickenborne, L. G. & Pierloot, K. *Inorg. Chem.* **20**, 3673–3677 (1981).
- McCusker, J. K., Rheingold, A. L. & Hendrickson, D. N. *Inorg. Chem.* **35**, 2100–2112 (1996).

Competing interests

The author declares no competing interests.

AROMATICITY

Baird's rules at the tipping point

This year marks the 50th anniversary of Baird's rules of aromaticity — a set of perturbational molecular orbital theory analyses that has garnered considerable attention in the past ten years in light of its many real-world applications in photochemistry.

Lucas J. Karas and Judy I. Wu

Aromaticity, an ever-evolving concept first developed to explain the properties of 'benzene-like' compounds, has since expanded to describe

a myriad of organic and inorganic species, in two and three dimensions, and in the ground and excited states. Hückel's early investigations into the stability of planar

conjugated annulenes led to the now widely known $[4n+2]$ π -electron rule of aromaticity. A couple of decades later, Baird reported his theoretical analysis for cyclic



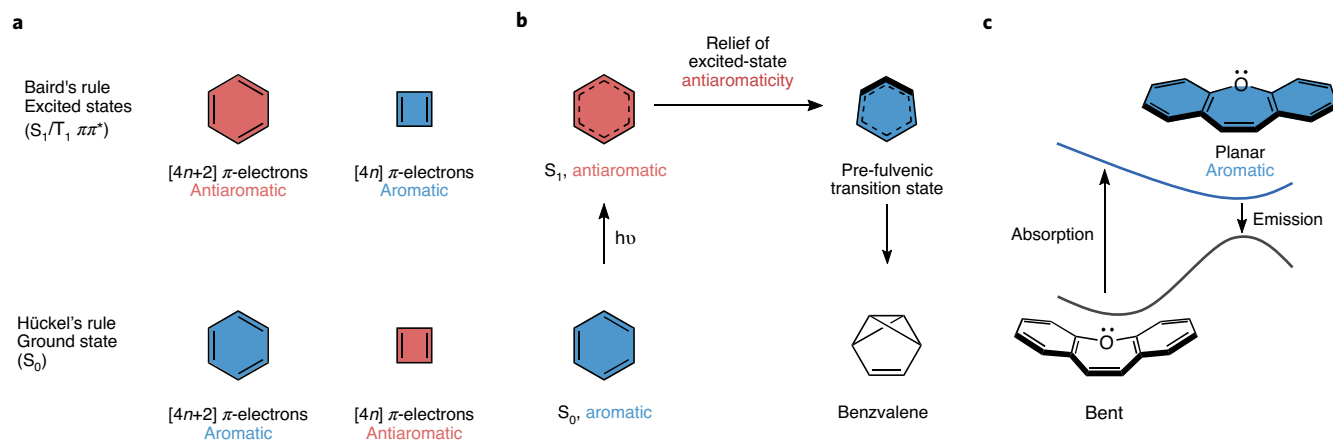


Fig. 1 | Baird's rule is a reversal of the Hückel electron-counting rule for aromaticity and antiaromaticity in the S_1 and T_1 $\pi\pi^*$ states. **a**, Ground- and excited-state aromaticity and antiaromaticity for benzene and cyclobutadiene. **b**, Photorearrangement of benzene to fulvene and benzvalene. **c**, Dibenz[*b,f*]oxepin displays a large Stokes shift due to excited-state aromaticity.

polyenes showing that, in their lowest triplet state, [$4n$] rings were instead aromatic and [$4n+2$] rings antiaromatic (Fig. 1a).

This reversal of electron-counting rules for aromaticity and antiaromaticity in the lowest $\pi\pi^*$ excited states — which arose from a set of perturbational molecular orbital theory analyses¹ — didn't immediately attract all that much excitement in the community. In the first four decades after its publication, Baird's 1972 paper¹ had garnered just shy of 150 citations. Yet, references to this theory have more than tripled in the ten years since. What sparked this increased interest?

It wasn't that manifestations of Baird's rules were lacking during those four first decades — it was relating observation to theory that was often missed. Photorearrangement of benzene to fulvene and benzvalene (Fig. 1b)², for example, has been known since the mid-1960s; Baird¹, and later Aihara³, had even linked the photoreactivity of benzene to its excited-state antiaromatic character at the time. These conclusions were overlooked for many years, however.

The first direct spectroscopic evidence for the reversal of excited-state aromaticity and antiaromaticity in the lowest excited state compared to the ground state had come in 1993⁴. Wan and Krogh⁵ showed that dibenz[*b,f*]oxepin (Fig. 1c) displayed large Stokes shifts resulting from planarization of the 8π -electron core in the S_1 state. They commented that: "The driving force for this geometry change is the attainment of a cyclically conjugated system of 8 electrons in the central ring, which is believed to have inherent stability on the excited-state surface." This experiment formed the basis for many recent designs of fluorophores by use of Baird's rules. Reversal of excited-state

aromaticity and antiaromaticity was also evident in many of the experiments performed by Wan and co-workers during the 1980s and 1990s, including a pioneering 1985 paper that showed that photolysis of fluorene-9-ol generated exceptionally stable 4π cationic systems, which was insightfully interpreted as a consequence of excited-state aromaticity⁵.

The community's interest in Baird's rules first took a turn in 1998 when Schleyer and co-workers⁶ published an important paper demonstrating that magnetic shieldings for open-shell species — while not accessible by NMR experiments — could be readily computed, and that the results obtained for neutral and charged [$4n$] π -electron annulenes supported Baird's theory. Triplet state [$4n$] π -electron annulenes exhibited negative nucleus-independent chemical shifts values, downfield chemical shifts and prominent diamagnetic susceptibility exaltations in line with their expected aromatic character. Quoting the authors: "These open-shell calculations of magnetic properties may be 'unphysical' but they are instructive and useful for many purposes." And indeed, they were.

Although the conclusions of the 1998 paper were derived by calculation, the simplicity of the nucleus-independent chemical shifts method and its apparent connection to real NMR measurements made the findings valuable to a wide community of chemists. It spawned theoretical and experimental interest in Baird's rules. Between 1998 and 2008, Baird's rules were extended to the lowest singlet excited-state of annulenes and then expanded significantly to include many organic and inorganic species.

In 2014, an influential Review published by Ottosson, Kilså and co-workers⁷

proved to be a tipping point that propelled the field of excited-state aromaticity and antiaromaticity research towards real-world applications. The 64-page opus amassed an enormous collection of examples demonstrating the significance of Baird's rules for excited-state properties, synthesis and photoreactions. It provided important reinterpretations for hundreds of experiments and highlighted the tremendous potential of Baird's rules for photophysics and photochemistry.

Then in 2015, Ottosson and Papadakis⁸ described the reactivity of benzene with reference to the Scottish horror fiction: *Strange Case of Dr Jekyll and Mr Hyde*. They related the ground state to the mild-mannered Dr Jekyll and its excited state to the turbulent Mr Hyde⁸. This vivid picture influenced the work of many, including our own⁹. Benzene — perhaps the most well-known aromatic compound — was also the archetype of excited-state antiaromaticity!

Now Baird's theory is realizing many of its promised impacts, including for developments of synthetic methods¹⁰, light-active molecules and materials^{11,12}, and fluorophores¹³. Alabugin and Ottosson showed that synthetic routes to a stereoelectronically disfavoured cycloaromatization reaction could be achieved by twisting a benzannulated double bond via antiaromaticity relief of a triplet-state benzene ring¹⁰. The smallest red-light emitter resulting from excited-state antiaromaticity relief and ring bond length elongation of a benzene core was just reported¹¹. Using time-resolved electron diffraction, Hada and co-workers¹² captured dynamic structural changes induced by reversal of excited-state aromaticity for stacked columns of cyclooctatetraenes.

It was shown that aggregation-induced emission — a phenomenon with tremendously attractive biomedical engineering applications — can arise from large conformation changes resulting from reversal of excited-state aromaticity¹³.

Using time-resolved spectroscopy, Kim and Osuka¹⁴ reported the first direct experimental evidence for aromaticity and antiaromaticity reversal in the lowest triplet state. Reversed spectroscopic signatures were recorded for a pair of aromatic and antiaromatic bis-rhodium hexaphyrins, which interconverted to antiaromatic and aromatic, respectively, in their triplet states. Synergy between experiment and theory was critical to forming the conclusions of this landmark paper; experiments provided evidence, but theory endorsed the interpretation.

Yet, Baird's rules must be applied with care. Aromatic rings with S_1 and T_1 states of $n\pi^*$ character can preserve aromaticity

and are not subject to Baird's rules. Some Craig-type Möbius aromatic organometallic rings can be aromatic in both the S_0 and T_1 states due to metal-to-ring excitation¹⁵. The photophysics of annulenes are often assumed to occur from the lowest singlet or triplet states but can actually involve higher excited states. Polycyclic compounds can retain Hückel aromaticity by altering ring current pathways in the S_1 and T_1 states versus the S_0 state¹⁶.

Beyond their implications and limitations, the story of Baird's rules is an excellent example of experiments guided by theory.

Lucas J. Karas¹✉ and Judy I. Wu¹✉

¹Department of Chemistry, University of Houston, Houston, TX, USA.

Twitter: @lucaskaras1; @JudyWuChem

✉e-mail: lucaskaras@gmail.com;

jwu@central.uh.edu

Published online: 1 July 2022

<https://doi.org/10.1038/s41557-022-00988-z>

References

1. Baird, N. C. *J. Am. Chem. Soc.* **94**, 4941–4948 (1972).
2. Slanina, T. et al. *J. Am. Chem. Soc.* **142**, 10942–10954 (2020).
3. Aihara, J.-I. *Bull. Chem. Soc. Jpn.* **51**, 1788–1792 (1978).
4. Shukla, D. & Wan, P. *J. Am. Chem. Soc.* **115**, 2990–2991 (1993).
5. Wan, P. & Krogh, E. *J. Chem. Soc. Chem. Commun.* 1207–1208 (1985).
6. Gogonea, V., Schleyer, P. v. R. & Schreiner, P. R. *Angew. Chem. Int. Ed.* **37**, 1945–1948 (1998).
7. Rosenberg, M. et al. *Chem. Rev.* **114**, 5379–5425 (2014).
8. Papadakis, R. & Ottosson, H. *Chem. Soc. Rev.* **44**, 6472–6493 (2015).
9. Karas, L. J., Wu, C.-H. & Wu, J. I. *J. Am. Chem. Soc.* **143**, 17970–17974 (2021).
10. Mohamed, R. K. et al. *J. Am. Chem. Soc.* **137**, 15441–15450 (2015).
11. Kim, H. et al. *Nat. Commun.* **12**, 5409 (2021).
12. Hada, M. et al. *J. Am. Chem. Soc.* **139**, 15792–15800 (2017).
13. Zhao, Z. et al. *Nat. Commun.* **10**, 2952 (2019).
14. Sung, Y. M. et al. *Nat. Chem.* **7**, 418–422 (2015).
15. Chen, D. et al. *Commun. Chem.* **1**, 18 (2018).
16. Zeng, W. et al. *Chem. Sci.* **12**, 6159–6171 (2021).

Competing interests

The authors declare no competing interests.

PREBIOTIC CHEMISTRY

Making nucleic acid monomers

Amino-containing four-carbon threose nucleic acids (TNAs) have long been considered to be prebiotically irrelevant due to their difficult formation. Now, a prebiotically plausible route to 3'-amino-TNA nucleoside triphosphate has been developed, raising the possibility of 3'-amino-TNA as a non-canonical nucleic acid during the origin of life.

Yingyu Liu and Yajun Wang

The ability of RNA to perform dual roles of encoding genetic information and catalysing essential reactions in extant life lays the foundation for the “RNA world” hypothesis, which suggests that RNA was the first nucleic acid for the origin of life¹. However, the prebiotic chemistry that gave rise to RNA might have produced nucleic acid molecules with alternative sugar backbones in the structural neighbourhood^{2,3}. Motivated by exploring alternative nucleoside structures that can be formed under prebiotically plausible conditions, and investigating the question of why nature chose RNA as the molecular basis of life's genetic material, researchers pioneered by Albert Eschenmoser and colleagues have discovered non-canonical nucleotides, which might be possible genetic polymers at the origin of life^{4,5}.

Among these nucleotides, the four-carbon threose nucleic acids (TNAs), 2'-amino-TNA, and 3'-amino-TNA,

are of particular interest due to their constitutionally simpler sugar structure, as well as their capability to self-hybridize and cross-talk with RNA (and DNA) through Watson–Crick base pairing^{6,7}. Completely oxygenous TNA has been considered as a candidate nucleic acid preceding RNA due to the simplicity both of its structure and of its formation⁸. By contrast, amino-TNA nucleoside monomers have been considered prebiotically irrelevant by Eschenmoser due to the complexity of their formation caused by “huge chemical complications” arising from nitrogenous compounds⁹. Such compounds are normally involved in Amadori and Mannich-type chemistry, alongside aldol reactions, which generate nucleoside monomers under prebiotic conditions^{6,7}. Now, writing in *Nature Chemistry*, Daniel Whitaker and Matthew Powner have re-examined the possibility and simplicity of amino-TNA formation by systematically demonstrating the facile

synthesis of 3'-amino-TNA nucleoside triphosphates starting from prebiotically plausible materials of two- and three-carbon units¹⁰.

The Powner laboratory has previously reported the diastereo- and regio- selective prebiotic synthesis of α -L-threocytidine — a component of TNA — starting from glycolaldehyde **1** and 2-aminooxazole **2** (itself produced from glycolaldehyde **1**, Fig. 1a)⁸. However, the synthesis of amino-TNA presents the additional difficulty of regioselective incorporation of an amino group into a tetrose sugar. Here, by means of three-component coupling of glycolaldehyde **1**, 2-aminooxazole **2** and a glycine nitrile **4** (or other aminonitriles) under slightly acidic conditions (pH 5), the formation of 3'-amino-aminooxazoline **5** was observed with both the 3'-amine and glycosidic bond regiospecifically positioned (Fig. 1b). Whitaker and Powner found that the aminonitrile species acted as the ideal

