

Borsley, S.; Kreidt, E.; Leigh, D. A.; Roberts, B. M. W. Autonomous Fuelled Directional Rotation about a Covalent Single Bond. *Nature* **2022**, 604 (7904),80–85. <https://doi.org/10.1038/s41586-022-04450-5>.

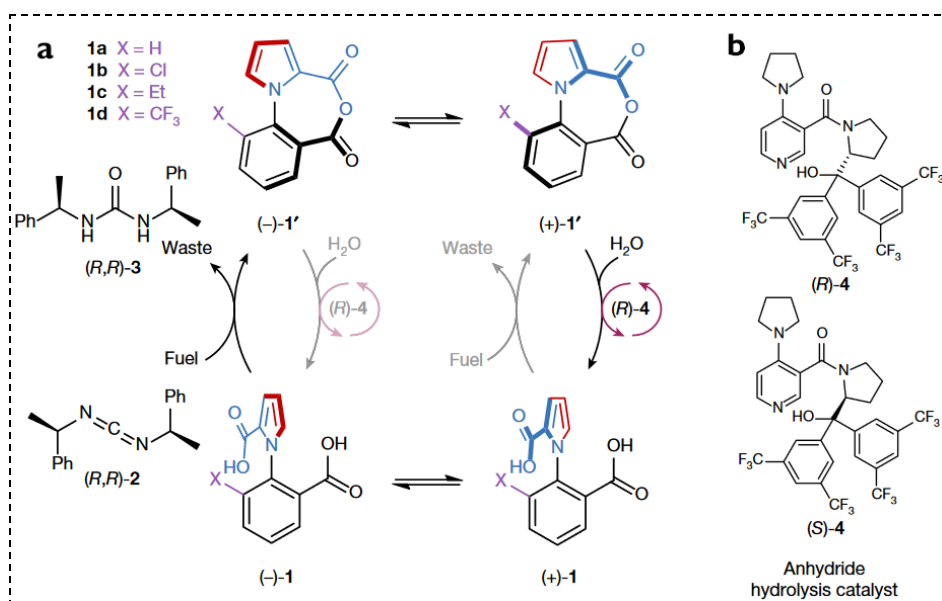


Figure 1 | (a) Chemomechanical cycle for autonomous chemically fuelled rotation of **1a–d**. In practice, only **1a** undergoes full 360° rotation on the timescale of the fuelling reactions. The grey arrows indicate slower transformations than the corresponding transformations indicated by black arrows (that is, (–)-1→(–)-1' faster than (+)-1→(+)-1'; (+)-1'→(+)-1 faster than (–)-1'→(–)-1). To be consistent with microscopic reversibility, all transitions should be considered reversible, although under the experimental conditions the position of equilibrium of the fuel-to-waste reaction heavily favours carbodiimide hydration. **(b)**, Chemical structures of anhydride hydrolysis catalysts (S)-4 and (R)-4.

Who are the corresponding authors and what are their research areas?

David A. Leigh - professor of chemistry at the University of Manchester, UK.

His research area is related to exploring, inventing and discovering ways to control non-covalent interactions and molecular topology - *mostly in the context of molecular-level dynamics* - to produce nanomotors and molecular machines.

What is the main claim of the article?

Synthesis of a molecular motor capable of autonomous 360° directional rotation about a single bond. Previous design attempts of this type of molecular engine proved to be quite challenging and have lacked either autonomous fuel or rotational directionality.

How is it demonstrated?

By attesting to the three essential requirements of the proposed chemical engine cycle:

1) The two sets of conformational changes ($(-)-1' \rightleftharpoons (+)-1'$ and $(-)-1 \rightleftharpoons (+)-1$) occur in different chemical states (diacid or anhydride) of the motor - Preparative HPLC separation of atropisomers (to **1b-d**, the stability of the enantiomers allows to obtain an enantiopure compound in rt) followed by reaction with a carbodiimide and then hydrolysis give raise to a racemic mixture. X-ray structure analysis was also employed.

2) The chemical transformations (diacid-to-anhydride and anhydride-to-diacid) occur predominantly in the chemical engine cycle through different mechanisms under the same set of reaction conditions - ^1H NMR spectra studies shown the presence of two mechanisms (**Figure | 2 a**) and confirmed that both chemical transformations occurs at the same time under the same experimental conditions (**Figure 2 | b**).

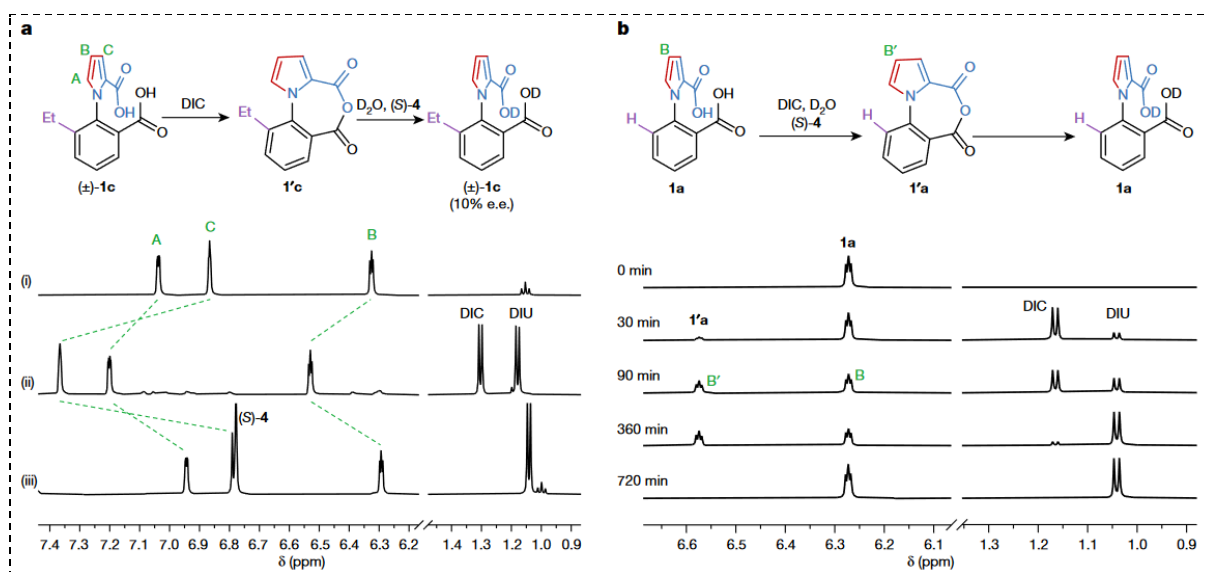


Figure 2 | Chemical transformations of 1-arylpyrrole 2,2'-dicarboxylic acids (**1**). **(a)** Stepwise anhydride formation and hydrolysis of **1c**, including partial ^1H NMR spectra (CD_3CN , 600 MHz, 298 K) of stepwise operation. **(b)** Autonomous operation of motor **1a**. Partial ^1H NMR spectra ($\text{CD}_3\text{CN}:\text{D}_2\text{O}$ 7:3 v/v, 600 MHz, 298 K) showing the transient formation of anhydride **1'a**.

3) Anhydride formation $(-)-1 \rightarrow (-)-1'$ proceeds at a different rate to $(+)-1 \rightarrow (+)-1'$, and anhydride hydrolysis $(+)-1' \rightarrow (+)-1$ at a different rate to $(-)-1' \rightarrow (-)-1$ - The use of a chiral fuel and chiral hydrolysis catalyst induces enantioselectivity in the process, resulting in a dynamic kinetic double resolution and enantio-enrichment of the final diacid. - Reaction with chiral/achiral fuel and hydrolysis catalyst followed by evaluation of the enantiomeric excess obtained by separation via HPLC were employed (**Figure | 3**).

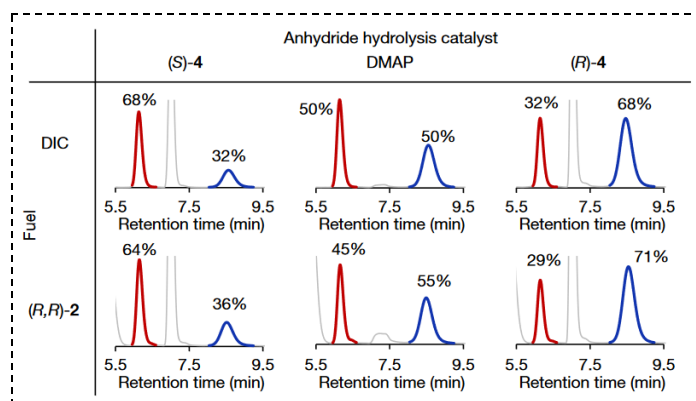


Figure 3 | The effect on chemical gating of fuels and anhydride hydrolysis catalysts of different handedness. The samples were analysed by chiral HPLC to determine enantio-enrichment.

What are the typical experimental conditions?

^1H NMR (CD_3CN or $\text{CD}_3\text{CN}:\text{D}_2\text{O}$ mixtures, 298 K), mM amounts.

Chiral HPLC, ChiralPak IF column, 25 °C, $\text{CH}_2\text{Cl}_2:\text{i-PrOH}:\text{CF}_3\text{CO}_2\text{H}$ (95:5:0.1, v/v/v) : n-hexane (7:3, v/v) 1 ml min $^{-1}$, mM amounts - For enantiomeric separations.

DFT functional/basis set = $\omega\text{B97X-D/6-31+G}^{**}$ - Gas phase minima and transition state energies.

Which are the key related papers?

Borsley, Stefan, David A. Leigh, and Benjamin MW Roberts. "A doubly kinetically-gated information ratchet autonomously driven by carbodiimide hydration." *Journal of the American Chemical Society* 143.11 (2021): 4414-4420.

Jayalath, Isuru M., et al. "Chemically fueled transient geometry changes in diphenic acids." *Organic Letters* 22.19 (2020): 7567-7571.

Koumura, Nagatoshi, et al. "Light-driven monodirectional molecular rotor." *Nature* 401.6749 (1999): 152-155.