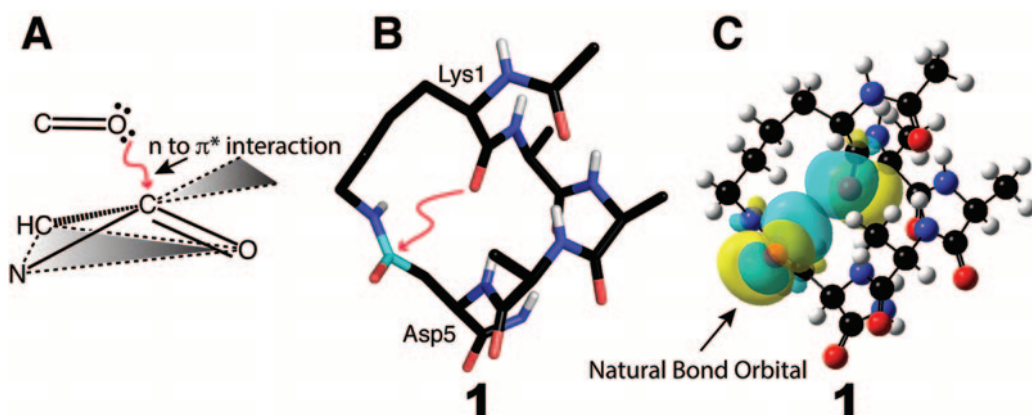


## Novel long-range interaction for alpha helix stabilisation in peptides

Researchers from the University of Queensland have shown that a novel long-range  $n$  to  $\pi^*$  interaction between a main-chain amide oxygen and a uniquely positioned carbonyl group in the linker of a cyclic pentapeptide (**1**) is able to help optimally stabilise the smallest known alpha helix in water (Hoang H.N., Wu C., Hill T.A., Dantas de Araujo A., Berhardt P.V., Fairlie D.P. *Angew. Chem. Int. Ed.* 2019, **58**, 18 873–7). An  $n$  to  $\pi^*$  interaction is the sharing of lone-pair electron density from a carbonyl oxygen into the empty  $\pi^*$  orbital of a nearby carbonyl group (**A**) and in protein backbone amide units has been demonstrated to help stabilise  $\alpha$ -helices. This research highlights a novel interaction, with a

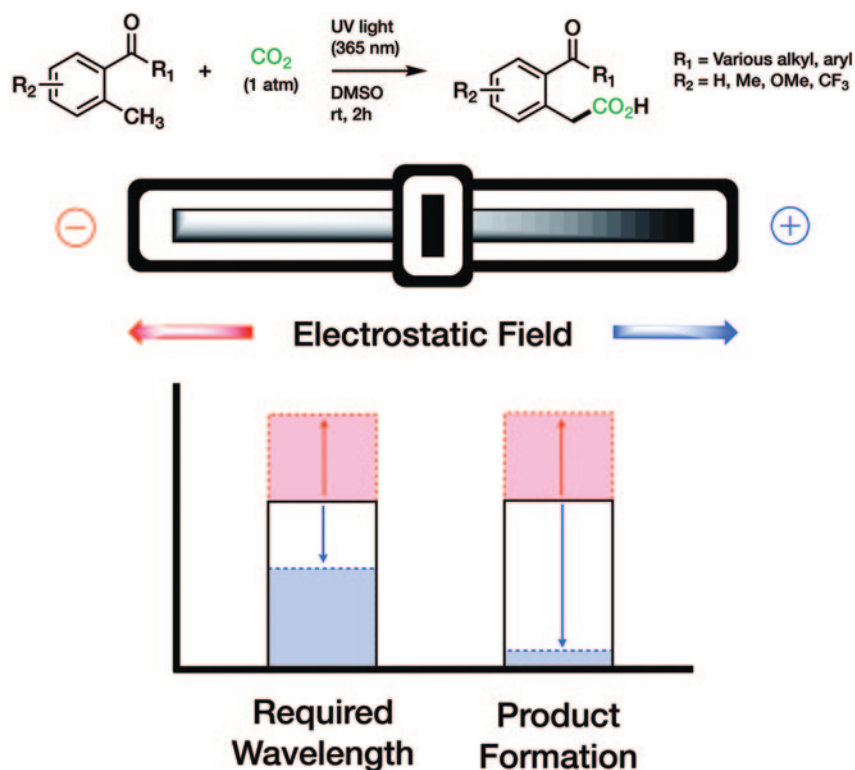


covalent amide bond outside of the helical backbone (**B**, **C**), and could lead to new approaches to synthetically stabilise peptide structures in water. The discovery of this novel  $n$  to  $\pi^*$

interaction and its structure-inducing properties highlights that greater recognition of  $n$  to  $\pi^*$  interactions should be given in medicinal, computational and structural chemistry.

## Electric fields cooperatively promote ground and excited state reactivity

The demonstration that electric fields can be used to catalyse and control the reactivity or selectivity of chemical reactions has recently sparked immense interest, with both theoreticians and experimentalists exploring a range of avenues for harnessing these effects. Now researchers from the Australian National University have shown that the electric fields from remote charged functional groups can selectively and cooperatively promote both ground- and excited-state chemical reactivity in the same system (Blyth M.T., Noble B.B., Russell I.C., Coote M.L. *J. Am. Chem. Soc.* 2020, **142**, 606–13). As a demonstration of this principle, the team used electrostatics to both red shift and improve the efficiency of Murakami's photochemical  $\text{CO}_2$  storage reaction (*J. Am. Chem. Soc.* 2015, **137**, 14 063–6). Strikingly, they showed that, contrary to the conventional understanding of electrostatic effects, catalysis can actually *increase* with solvent polarity. This counterintuitive result occurs when polarisation is significant, and provides a way forward for addressing the solvent



polarity versus solubility trade-off normally associated with using charged functional groups for electrostatic catalysis.