

## Harnessing Applied Potential: Selective $\beta$ -Hydrocarboxylation of Substituted Olefins

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The carboxylate moiety is prevalent in nature, and a wide range of biologically active drugs and bioactive compounds are carboxylic acids or derivatives. However, the incorporation of a carboxylic function in a selective manner, from low-value materials such as alkenes, remains a significant challenge for organic chemists. In particular, sustainable and straightforward methods for selective carboxylation are underdeveloped. Dr. Benjamin Buckley, Professor Andrei Malkov and team from Loughborough University (UK) have recently reported a new electrochemical approach to the selective  $\beta$ -hydrocarboxylation of alkenes with inexpensive and abundant carbon dioxide, thus avoiding the use of toxic, flammable carbon monoxide that is the current reagent of choice for this purpose. The reported method allows direct access to carboxylic acids derived from terminal, di-, tri-, and tetra-substituted alkenes, in a highly regioselective manner. Interestingly, the authors observed a selectivity which is opposite to that reported utilizing transition-metal complexes<sup>1</sup> and complementary to the photochemical approaches reported to date.<sup>2</sup>

Dr. Buckley noted: “There are a number of electrochemical processes reported that allow for CO<sub>2</sub> incorporation into organic molecules. In the majority of cases, these rely on a sacrificial electrode – such as magnesium – and this presents several difficulties, including the limited sustainability of the approach, the challenges in translation to industrial applications and implementation of continuous processes.”

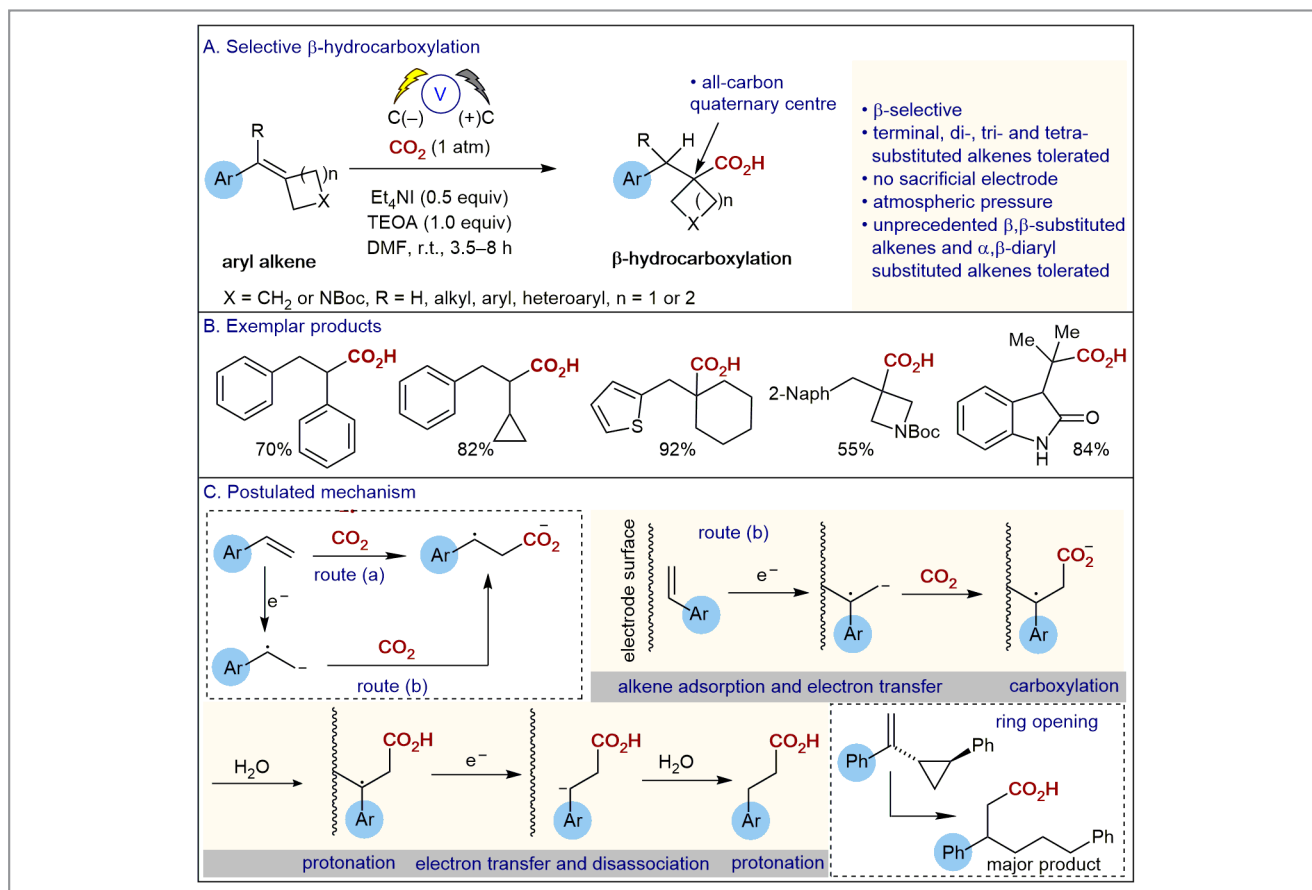
After reporting the use of a sacrificial electrode system for the formation of cyclic carbonates from epoxides and oxetanes, the team set themselves the target of developing a non-sacrificial electrochemical system in which they could utilize CO<sub>2</sub>.<sup>3</sup> “This was inspired by our unpublished findings on the nature of a precipitate that we observed during the original cyclic carbonate reaction,” explained Dr. Buckley. He continued: “Depending on the sacrificial electrode employed, we could isolate oxalic acid (after acidic work-up) and this now became really interesting from a C–C bond-forming point of view. Our interest increased even further following the publication of a paper by Bouwman and co-workers highlighting the importance of catalysts for oxalate synthesis.<sup>4</sup>” Prof. Malkov, Dr. Buckley and co-workers eventually found that this was not a unique process, as there was a precedent reported more than two decades before by Vasil’ev, although at much higher tem-

perature and pressure. In that interesting paper, the authors also added ethylene and observed C–C bond formation.<sup>5</sup> “We adapted our process and added styrene, which provided good yields of dicarboxylation across the double bond, similar to that reported by Duñach,<sup>6</sup>” said Dr. Buckley. From that point, the team implemented a regime to replace the sacrificial electrode, finally settling on a system that contained two carbon electrodes, tetraethylammonium iodide as electrolyte, and triethanolamine as a proton source with CO<sub>2</sub> at ambient pressure (Scheme 1A). Dr. Buckley remarked: “Surprisingly, under these conditions, we observed mono-carboxylation at the  $\beta$ -carbon of styrene, and not dicarboxylation. On further investigation we found that triethanolamine is essential for selectivity and a recent report has highlighted triethanolamine’s non-innocent role in activating CO<sub>2</sub>. Excitingly, further substrate screening revealed that our system works well for substrates that previously were challenging for metal-catalyzed and photochemical approaches. For example, we could successfully carboxylate stilbenes, tri- and tetra-substituted alkenes (Scheme 1B). This gives unprecedented access to all-carbon quaternary carboxylic acids, which are also challenging to prepare using the traditional metal-catalyzed carbonylation processes.”

Delineating the mechanism of these reactions is somewhat challenging given the similar reduction potentials of alkenes and CO<sub>2</sub> (Scheme 1C). Dr. Buckley said: “Collaboration with the Wright group enabled cyclic voltammetric analysis of the reaction process indicating formation of the radical anion of the alkene as a preferred approach, indeed we also observed the ring opening of a cyclopropane-derived alkene, suggesting the formation of a radical at the benzylic position. However, further studies in this area are required to fully understand the process.”

Dr. Buckley concluded: “We are currently examining the potential of this approach to a wide variety of carboxylation chemistries and expect this to inspire many other electrochemical approaches that will no longer need to rely on a sacrificial electrode approach.”

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**Scheme 1** (A) General approach to the hydrocarboxylation process. (B) Example products from the process. (C) Postulated routes towards the mono-carboxylated products.

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## About the authors



Dr. B. Buckley

**Benjamin Buckley** is currently a Reader at Loughborough University (UK). In 2003 he received his PhD with Prof. Philip C. Bulman Page on organocatalytic asymmetric epoxidation. He then took up a post-doctoral position in the Page group for a further five years, working on a range of projects with industrial and academic partners. In late 2007 he was appointed to a Research Councils UK Fellowship at Loughborough and initiated independent research in the areas of catalysis, electro-synthesis and carbon dioxide utilisation. He was promoted to a Senior Lectureship in 2014 and also moved to the University of Utah, USA on sabbatical leave for a year with Professor Matthew S. Sigman's group. In February 2020 he was appointed to a Readership in Chemistry at Loughborough.



Prof. A. Malkov

**Andrei Malkov** started his career with the award of MSs (Hons) from the Moscow State University (Russia) in 1982, which was followed by PhD studies at the Institute of Organo-Element Compounds (Moscow, Russia), successfully completed in 1986. He continued his work in the area of organometallic synthesis and catalysis, which intensified with his move to the UK in 1992 where he had two postdoctoral spells at the UEA (1992–1995) and the University of Leicester (1995–1999). He started his independent career in the UK at the University of Glasgow (UK) in 1999 where he rose through the ranks to become Reader. In 2008 he was appointed as Professor of Organic Chemistry at Loughborough University (UK). He is currently active in the following research areas: Asymmetric organocatalysis: new catalysts, new methodology, synthetic applications; Catalytic functionalization of C–H bonds: method development, synthetic applications; Electrosynthetic methods for utilisation of carbon dioxide; Total synthesis of bioactive natural products, biological investigations.



Dr. A. Alkayal

**Anas Alkayal** obtained his B.Sc. in 2006, and his M.Sc. degree in chemistry in 2011 at Al-Baath University (P. R. of Syria). He then began his Ph.D. research under the supervision of Doctor Ayman Karam also at Al-Baath University focusing on drug discovery. He received his PhD in 2016, and in 2018, moved to Loughborough University (UK) to conduct postdoctoral research with Dr. Buckley which centres around reducing our reliance on fossil-fuel-based raw materials, utilising electro-synthesis and carbon dioxide.



Dr. V. Tabas

**Volodymyr Tabas** received his M.Chem in chemistry from Loughborough University (UK) in 2014. He then started his PhD in the group of Dr. Buckley and Prof. Malkov, focusing on electro-synthesis and CO<sub>2</sub> utilisation. In 2016 he won the RSC Catalysis Science and Technology Poster award at the 14<sup>th</sup> International Conference on Carbon Dioxide Utilization (ICCDU) and in 2017 the Outstanding Young Researcher Award at the 15<sup>th</sup> ICCDU in Shanghai, China. In 2019 he was awarded his PhD in chemistry.



Dr. I. Wright

**Iain Wright** pursued his undergraduate degree at the University of Strathclyde (UK) where he stayed to complete his PhD in 2011 advised by Professor Peter Skabara and focused on oligothiophene-based materials. This was followed by postdoctoral appointments at Universität Basel (Switzerland) with Professors Ed Constable and Catherine Housecroft and Durham University (UK) with Professor Martin Bryce. In November 2016 he was appointed as a Lecturer (Assistant Professor) in Chemistry at Loughborough University (UK). His research streams concern the synthesis, photophysics and electro-chemistry of new organic and organometallic materials for optoelectronic devices.

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**Stephanie Montanaro** received her M.Chem degree from Durham University (UK) in 2016. In 2017 she started her PhD at Loughborough University (UK) in the group of Dr. Wright, focused on the synthesis and study of organic electronic materials.

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