

Suero Research Group



Group Leader: Marcos Garcia Suero

Postdoctoral researchers: Zhaofeng Wang / Liyin Jiang / Ana Maria del Hoyo (until March)

PhD students: Ana Garcia Herraiz / Pau Sarro Grane

Visiting students: Yuan Yuchao (Sep.-Nov.)

Abstract

Dr Suero's group major goal is to develop the catalytic generation of unexplored carbon-based reactive species, and to study their behaviour towards chemical feedstocks. Their strategy is revealing new reactivity rules at carbon that chemists have been missing, not only in the design and discovery of new chemical reactions, but also in their use to build molecular

complexity. They have pioneered the catalytic generation of diazomethyl radicals as direct equivalents of monovalent carbyne species. The latter process, published in *Nature*, clearly revealed the distinct dual radical–carbene behaviour of carbynes, and its application in discovering elusive disconnection approaches for chiral centre construction.

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Carbon has the unique ability to bind four atoms and form stable tetravalent structures prevalent in nature. The lack of one or two valences leads to a set of species – carbocations, carbanions, radicals, carbenes – that are fundamental to understand chemical reactivity (Fig. 1A). In contrast, carbynes – the monovalent carbon with three non-bonded electrons – are one of the least explored reactive intermediates in chemical science (Fig. 1B). Despite that the simplest methylidyne ($:\dot{\text{C}}\text{-H}$) was one of the first molecules detected in interstellar space, and currently considered one of the very basic ingredients of life; it is surprising that this reactive carbon class has not previously been exploited for reaction invention. Pioneering efforts by Strausz and Patrick in the 1960s and 1970s for the generation of a doublet ground-state carbyne ($:\dot{\text{C}}\text{-CO}_2\text{Et}$) – with $\text{Hg}(\text{C}(=\text{N}_2)\text{CO}_2\text{Et})_2$ and UV light – established that these species had a dual radical and carbene behavior. Alongside this, the expansion of this field and its application in synthesis have not blossomed yet due to challenges associated with controlling its extreme reactivity and lack of efficient sources. In this context, the development of a catalytic method to generate carbyne species or stabilized forms under mild conditions would open a new frontier in chemical reactivity, and reveal previously elusive disconnection approaches scoring into the logic of chemical synthesis.

We became attracted by three important fundamental features of carbyne intermediates: (i) the highly electrophilic nature, (ii) the distinct radical/carbyne reactivity on the same carbon atom and, (iii) the natural ability to form three sigma bonds to complete the valence shell. Considering this, we wondered whether a new strategy for the construction of chiral centers using simple aryl C–H bonds would be possible by using the assembly-point functionalization of carbynes (Fig. 1B). However, to secure control of the sequence around the monovalent carbon, a blueprint for the design of the carbyne source might be conceived. Drawing inspiration from Strausz reports, we speculated that the monovalent carbon could be decorated with two orthogonal leaving groups that, upon subsequent catalytic activations, would reveal the dual radical/carbene reactivity and underpin a sequencing control for a desired chiral center (Fig. 1C). In this sense, we hypothesized that a diazo compound bearing an appropriate redox-active leaving group (LG) could generate – through catalytic single-electron reduction – a diazomethyl radical, which could induce aryl C–H bond

cleavage. After this, the prochirality of the diazo-functionalized intermediate would be exploited using the broad range of known metal-catalyzed processes.

Our group has recently demonstrated an unprecedented strategy for the catalytic generation of diazomethyl radicals as monovalent carbon equivalents. Essential for this achievement was the combination of photoredox catalysis and a new class of hypervalent iodine reagents that enabled a useful aryl C–H bond diazomethylation reaction and underpinned a late-stage assembly-point functionalization of therapeutic agents (Fig. 1D). Considering the prevalence of chiral centers in natural products and their interlocked relationship with drug bioactivity, we believe that this novel strategy will create a high interest in the broad synthetic community.

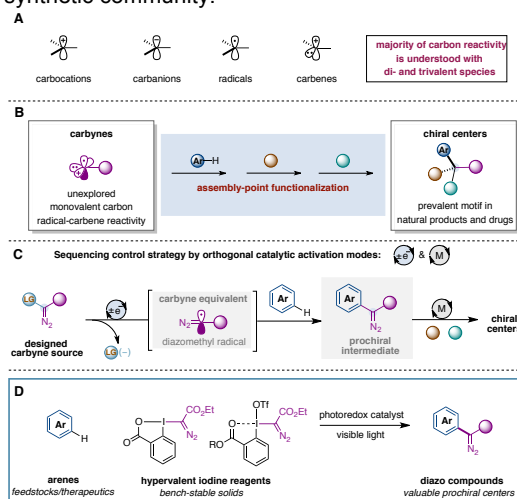


Fig. 1 – (A) Fundamental carbon-based reactive species. (B) Monovalent carbyne species for chiral center synthesis. (C) Designed carbyne source for sequencing control. (D) Arene C–H diazomethylation with hypervalent iodine reagents via photoredox catalysis.

Furthermore, we exploit the dual radical and carbene character of the generated carbyne equivalent $\text{N}_2=\text{C}(\bullet)\text{-CO}_2\text{Et}$ in the direct transformation of abundant chemical feedstocks into valuable chiral molecules. These results clearly show that we can efficiently exert sequencing control in an assembly-point functionalization process of carbyne equivalents by means of photoredox catalysis. Key to our success was the use of blue LEDs as a source of visible light, which decomposes the diazo group into a free carbene in the corresponding aryl diazo intermediate.

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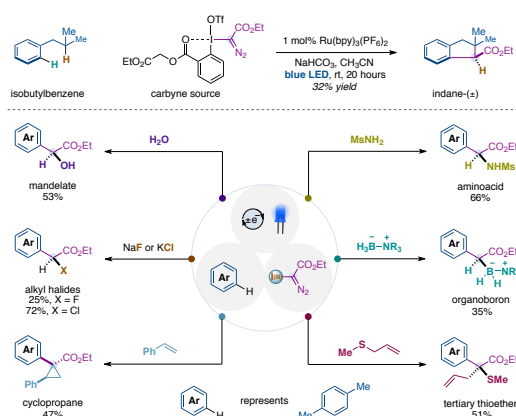


Fig. 2 – Catalytic assembly-point functionalization of carbyne equivalents with feedstock chemicals.

Our work in carbyne generation was accepted in late 2017 and published on 2018 in the journal *Nature* (1st of February). It was highlighted on a [Nature News & Views](#) article by Dr Rohan E. J. Beckwith (Novartis, Boston) and also on the cover of the same issue as “CARBYNE HARVESTING: Reactive carbon species made available for synthesis”.



Fig. 3 – *Nature* cover of issue No 7690, vol 554 2018 (1 February)

We wanted to show the link between our work in carbyne generation with the fact that carbynes, in particular methyldiyne, were the first molecules

detected in the interstellar space. In this sense, we designed with Ella Maru studies a beautiful cover for our article (Fig. 4).

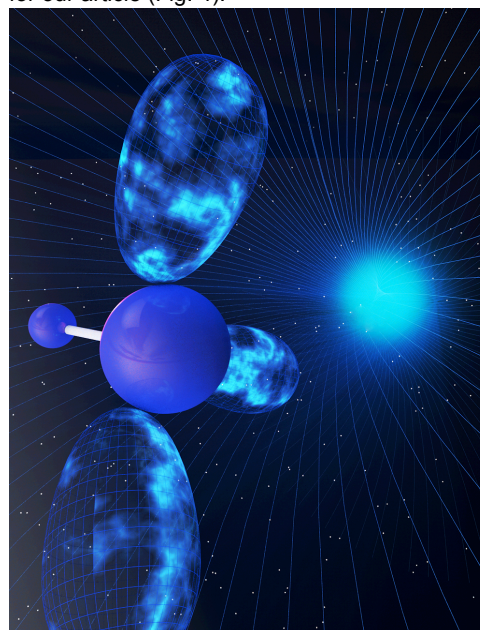


Fig. 4 – Artwork of a monovalent carbon by © Ella Maru Studio, Inc.

Our results were also highlighted on the prestigious [C&EN](#) (Tien Nguyen) by Prof Huw M. L. Davies (Emory University) and Tim Cernak (Merck, Boston), on [Chemistry World](#) (Andy Extance) by Prof Steven V. Ley (University of Cambridge), in [La Vanguardia](#), [El Periodico](#), [La Nueva España](#), and in many other Spanish newspapers. In addition, I was interviewed in the programme *La Buena Tarde de RPA* explaining our discoveries and my vision about science and in the [Agencia Cubana de Noticias](#).

Finally, we made a video to reach the general public with [Scienseed](#) and sponsored by Agilent technologies. It is currently one of the ICIQ videos with more views (>2400).

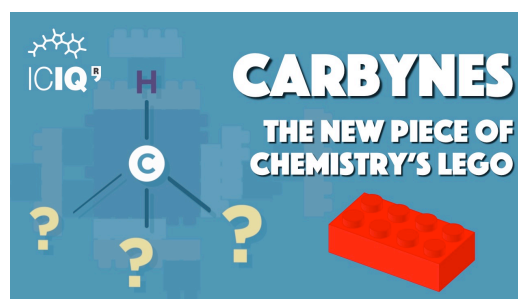


Fig. 5 – Video: <https://youtu.be/y7TIZ8GR6PA> © ICIQ / Scienseed. This video was sponsored by Agilent Technologies. Subtitles by Scienseed (English), ICIQ (Spanish, Catalan), Zhaofeng Wang (Chinese) and Pablo X. Suárez (Asturian).



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Articles

“Generating carbyne equivalents with photoredox catalysis”

Nature (2018) 554, 86-91.

Z. Wang, A.G. Herraiz, A.M. del Hoyo, M.G. Suero