

International Carbene and Nitrene Consortium (ICNC)
The ICNC Bulletin
Recent Publications of Members (June-December 2023)

Thermal/Blue light Induced Crosslinking of Acrylic Coatings with Diazo Compounds

de Zwart, F.J. Wolzak, L.A.; Laan, P.C.M.; Mathew, S.; Flapper, J.; van den Berg, K.J.; Reek, J.N.H.; de Bruin, B.*
University of Amsterdam, Van 't Hoff Institute for Molecular Chemistry, Science Park 904, Amsterdam, The Netherlands

Macromolecular Rapid Communications, **2023**, 2300380

<https://doi.org/10.1002/marc.202300380>



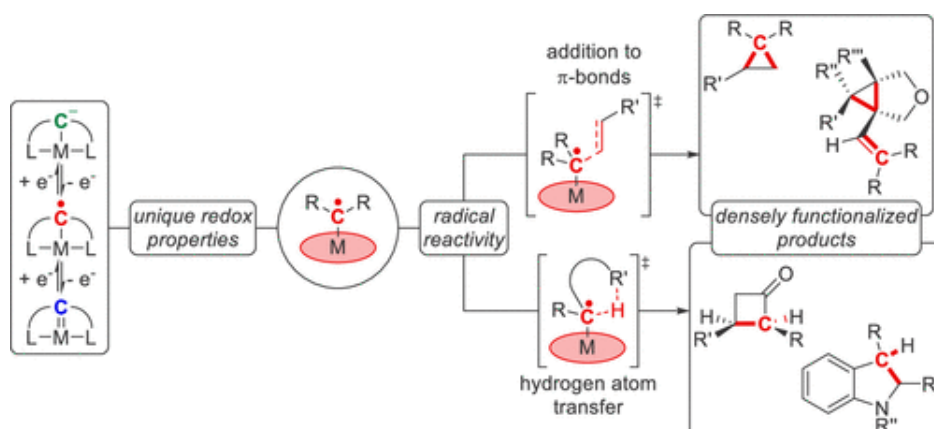
Abstract: This work presents the usage of diazo cross-linkers for the curing of acrylate-based coatings. Activation of these cross-linkers create free carbenes which are used to insert into O–H bonds, creating strong covalent linkages in the films. The composite films can be cured with blue light and provide excellent material properties, comparable to other acryl coatings. The thermal curing of industrial coatings (e.g., car painting and metal coil coatings) is accompanied by a substantial energy consumption due to the intrinsically high temperatures required during the curing process. Therefore, the development of new photochemical curing processes—preferably using visible light—is in high demand. This work describes new diazo-based cross-linkers that can be used to photocure acrylic coatings using blue light. This work demonstrates that the structure of the tethered diazo compounds influences the cross-linking efficiency, finding that side reactions are suppressed upon engineering greater molecular flexibility. Importantly, this work shows that these diazo compounds can be employed as either thermal or photochemical cross-linkers, exhibiting identical crosslinking performances. The performance of diazo-cross-linked coatings is evaluated to reveal excellent water resistance and demonstrably similar material properties to UV-cured acrylates. These studies pave the way for further usage of diazo-functionalized cross-linkers in the curing of paints and coatings.

Carbene Radicals in Transition-Metal-Catalyzed Reactions

Epping, R.F.J.; Vesseur, D.; Zhou, M.; de Bruin, B.*
University of Amsterdam, Van 't Hoff Institute for Molecular Chemistry, Science Park 904, Amsterdam, The Netherlands

ACS Catalysis **2023**, 13, 5428–5448.

<https://doi.org/10.1021/acscatal.3c00591>



Abstract: Discovered as organometallic curiosities in the 1970s, carbene radicals have become a staple in modern-day homogeneous catalysis. Carbene radicals exhibit nucleophilic radical-type reactivity orthogonal to classical electrophilic diamagnetic Fischer carbenes. Their successful catalytic application has led to the synthesis of a myriad of carbo- and heterocycles, ranging from simple cyclopropanes to more challenging eight-membered rings. The field has matured to employ densely functionalized chiral porphyrin-based platforms that exhibit high enantio-, regio-, and stereoselectivity. Thus far the focus has largely been on cobalt-based systems, but interest has been growing for the past few years to expand the application of carbene radicals to other transition metals. This Perspective covers the advances made since 2011 and gives an overview on the coordination chemistry, reactivity, and catalytic application of carbene radical species using transition metal complexes and catalysts.

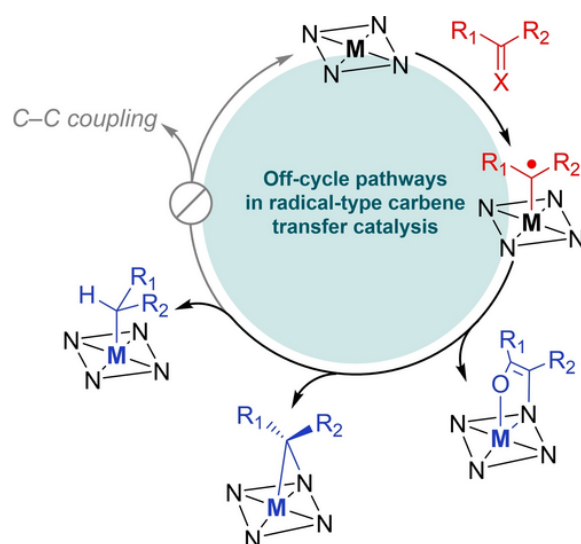
Understanding Off-Cycle and Deactivation Pathways in Radical-Type Carbene Transfer Catalysis

Snablić, D.D.; Meeus, E.J.; Epping, R.F.J.; He, Z.; Zhou, M.; de Bruin, B.*

University of Amsterdam, Van 't Hoff Institute for Molecular Chemistry, Science Park 904, Amsterdam, The Netherlands

Chem. Eur. J. **2023**, 29, 30, e202300336

<https://doi.org/10.1002/chem.202300336>



Abstract: Radical-type carbene transfer catalysis is an efficient method for C–C coupling reactions, but also suffers from off-cycle and deactivation pathways, such as hydrogen atom transfer and the formation of N-enolate and bridging carbenes. In this concept article, we demonstrate that off-cycle species not always lead to a dead-end and can even unlock new reactivity. Transition metal radical-type carbene transfer catalysis is a sustainable and atom-efficient method to generate C–C bonds, especially to produce fine chemicals and pharmaceuticals. A significant amount of research has therefore been devoted to applying this methodology, which resulted in innovative routes toward otherwise synthetically challenging products and a detailed mechanistic understanding of the catalytic systems. Furthermore, combined experimental and theoretical efforts

elucidated the reactivity of carbene radical complexes and their off-cycle pathways. The latter can imply the formation of N-enolate and bridging carbenes, and undesired hydrogen atom transfer by the carbene radical species from the reaction medium which can lead to catalyst deactivation. In this concept paper, we demonstrate that understanding off-cycle and deactivation pathways not only affords solutions to circumvent them, but can also uncover novel reactivity for new applications. In particular, considering off-cycle species involved in metalloradical catalysis can stimulate further development of radical-type carbene transfer reactions.

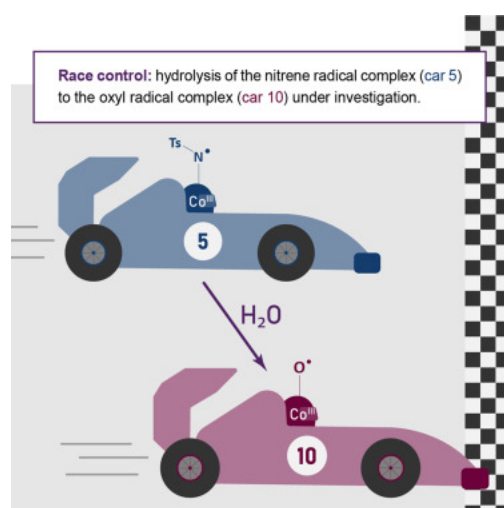
Styrene aziridination with $[\text{Co}^{\text{III}}(\text{TAML}^{\text{red}})]^-$ in water: Understanding and preventing epoxidation via nitrene hydrolysis

Meeus, E.J.; Derks, M.T.G.M; van Leest, N.P.; Verhoef, C.J.; Roithova, J.; Reek, J.N.H.; de Bruin, B.*

University of Amsterdam, Van 't Hoff Institute for Molecular Chemistry, Science Park 904, Amsterdam, The Netherlands

Chem Catalysis, **2023**, 3, 100700.

<https://doi.org/10.1016/j.checat.2023.100700>



Abstract: (Radical-type) nitrene transfer catalysis is an elegant strategy allowing fast and direct functionalization of C–H and C=C double bonds under mild conditions. The respective reaction products, aziridines for instance, are generally highly valued because they are frequently encountered motifs in pharmaceuticals. However, the synthesis of such motifs typically requires harsh conditions and multiple steps, highlighting the importance of nitrene transfer reactions. Despite considerable efforts to develop base-metal complexes that facilitate (radical-type) nitrene transfer in organic media, their application in water remains a long-standing challenge. Enabling such transformations in water has the potential to open up a wider range of applications, such as the *in vivo* synthesis of medicines and other bioactive compounds. Therefore, understanding and controlling the reactivity of nitrene radical complexes in water is of substantial interest. Enabling (radical-type) nitrene transfer reactions in water can open up a wide range of (novel) applications, such as the *in vivo* synthesis of medicines. However, these reactions typically suffer from oxygen-containing side-product formation, the origin of which is not fully understood. Therefore, we investigated aqueous styrene aziridination by using a water-soluble $[\text{Co}^{\text{III}}(\text{TAML}^{\text{red}})]^-$ catalyst known to be active in radical-type nitrene transfer in organic solvents. The cobalt-catalyzed aziridination of styrene in water (pH = 7) yielded styrene oxide as the major product, next to minor amounts of aziridine product. On the basis of ^{18}O -labeling studies, catalysis, and mass spectrometry experiments, we demonstrated that styrene oxide formation proceeds via hydrolysis of the formed nitrene radical complexes. Computational studies support that this process is facile and yields oxyl radical complexes active in oxygen-atom transfer to styrene. On the basis of these mechanistic insights, we adjusted the pH to afford selective aziridination in water.

A Crystalline Doubly Oxidized Carbene

Ying Kai Loh,^{*a} Mohand Melaimi,^a Milan Gembicky,^a Dominik Munz,^b Guy Bertrand^{*a}

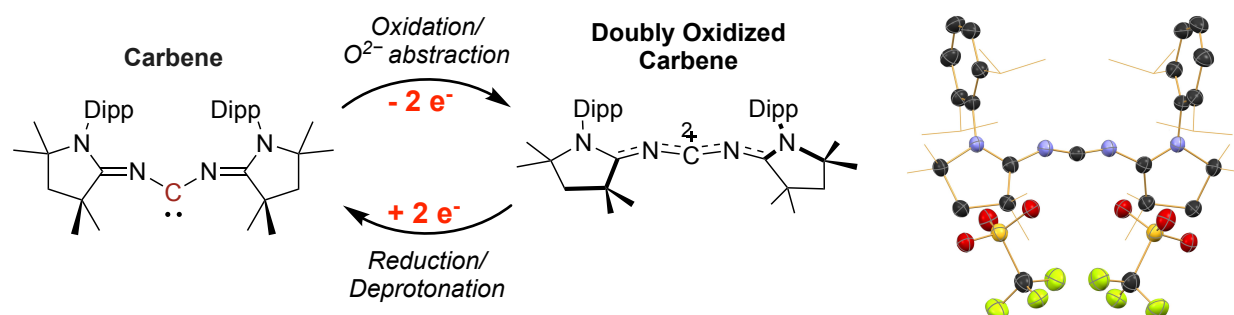
^a UCSD–CNRS Joint Research Laboratory (IRL 3555), Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, California, USA.

^b Coordination Chemistry, Saarland University, Campus C4.1, 66123 Saarbrücken, Germany.

*e-mail: yloh@ucsd.edu; gbertrand@ucsd.edu

Nature **2023**, 623, 66–70

<https://doi.org/10.1038/s41586-023-06539-x>



Abstract: The chemistry of carbon is governed by the octet rule, which refers to its tendency to have eight electrons in its valence shell. However, a few exceptions do exist, for example the trityl radical ($\text{Ph}_3\text{C}\cdot$)¹ and carbocation (Ph_3C^+)² with seven and six valence electrons respectively, and carbenes ($\text{R}_2\text{C:}$) – two-coordinate octet-defying species with formally six valence electrons³. Carbenes are now powerful tools in chemistry, and have even found applications in material and medicinal sciences⁴. Can we undress the carbene further by removing its non-bonding electrons? Herein, we describe the synthesis of a crystalline doubly oxidized carbene (R_2C^{2+}), through a two-electron oxidation/oxide-ion abstraction sequence from an electron-rich carbene⁵. Despite a cumulenec structure and strong delocalization of the positive charges, the dicoordinate carbon center maintains significant electrophilicity, and possesses two accessible vacant orbitals. A two-electron reduction/deprotonation sequence regenerates the parent carbene, fully consistent with its description as a doubly oxidized carbene. This work demonstrates that the use of bulky strong electron-donor substituents can simultaneously impart electronic stabilization and steric protection to both vacant orbitals on the central carbon atom, paving the way for the isolation of a variety of doubly oxidized carbenes.

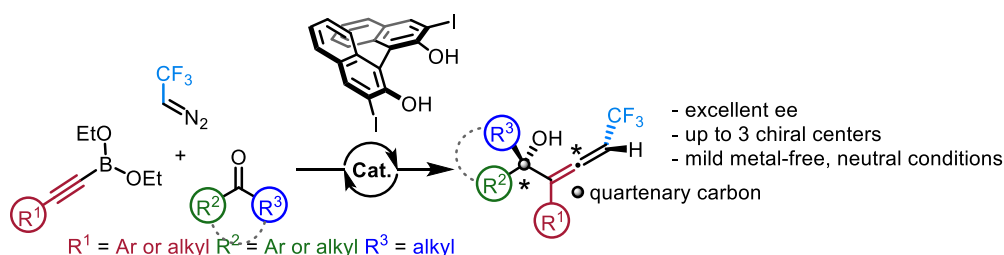
Three-Component Approach to Densely Functionalized Trifluoromethyl Allenols by Asymmetric Organocatalysis

Marie Deliaval, Ramasamy Jayarajan, Lars Eriksson, and Kálmán J. Szabó*

Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-10691 Stockholm, Sweden

J. Am. Chem. Soc. **2023**, 145, 10001–10006

doi.org/10.1021/jacs.3c02852

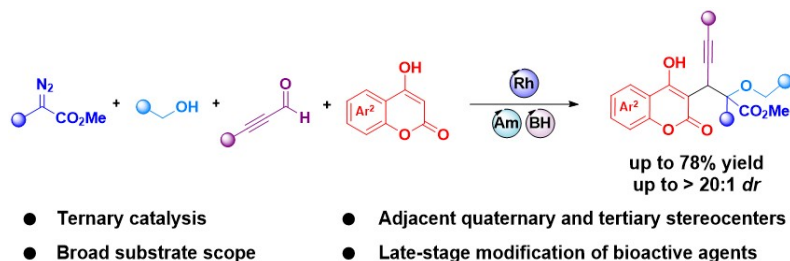


Abstract: We have developed a new three-component catalytic coupling reaction of alkynyl boronates, diazomethanes and aliphatic/aromatic ketones in the presence of BINOL derivatives. The reaction proceeds with a remarkably high enantio- and diastereoselectivity (up to three contiguous stereocenters) affording tertiary CF_3 -allenols in a single operational step. The reaction proceeds under mild, neutral, metal-free conditions, which leads to a high level of functional group tolerance.

Construction of 4-hydroxycoumarin derivatives with adjacent quaternary and tertiary stereocenters via ternary catalysis

Mengchu Zhang, Tianyuan Zhang, Sifan Yu, Huang Qiu, Abdulla Yusuf, Xinfang Xu, Yu Qian*, and Wenhao Hu*
School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, Guangdong 510006, China

Chem. Sci. **2023**, *14*, 11850-11857
doi.org/10.1039/D3SC03452F

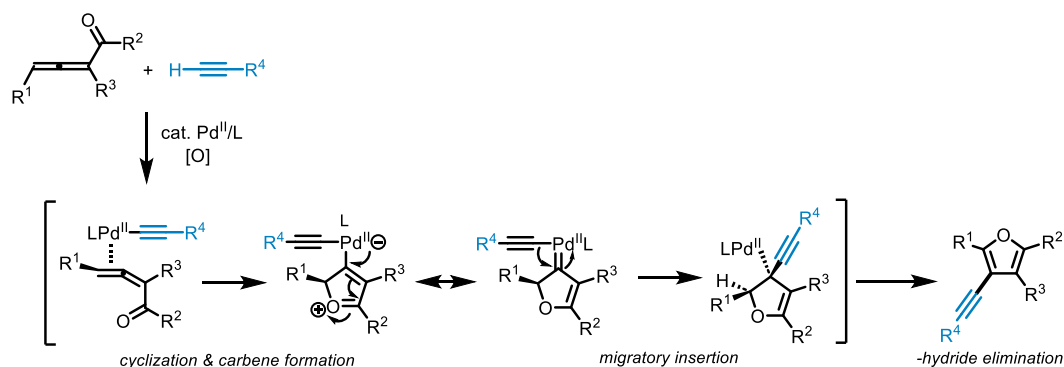


Abstract: A Rh/amine/Brønsted acid co-catalyzed four-component reaction of diazoacetates, alcohols, alkynaldehydes and 4-hydroxycoumarins is presented for the synthesis of substituted 4-hydroxycoumarin derivatives with adjacent quaternary and tertiary stereocenters *via* carbene *gem*-difunctionalization. This process provides an efficient strategy for convergent assembly of oxonium ylides derived from diazoacetates and alcohols with active electrophilic intermediates generated *in situ* from 4-hydroxycoumarins and alkynaldehydes. Furthermore, the late-stage transformations of coumarin derivatives and their *in vitro* trial of antitumor activity successfully demonstrated the potential utilities of the products as platform molecules.

Palladium-Catalyzed Oxidative Alkynylation of Allenyl Ketones: Access to 3-Alkynyl Poly-substituted Furans

Bowen Dou, Kang Wang, and Jianbo Wang*
College of Chemistry, Peking University, Beijing 100871, China

Chin. J. Chem. **2023**, *41*, 3598-3604.
<https://doi.org/10.1002/cjoc.202300465>



Abstract: Furans bearing alkynyl substituents are highly useful in organic synthesis. However, the methodologies to access these important furan derivatives are rather limited. We herein report an efficient synthesis of alkynylated furan derivatives based on Pd-catalyzed oxidative cross-coupling reaction between allenyl ketones and terminal alkynes. This novel synthesis of alkynylated furans with wide substrate scope is operationally simple and tolerates various functional groups. Mechanistically, the formation of the palladium carbene through cycloisomerization and the subsequent alkynyl migratory insertion are proposed as the key steps in the transformation. The reaction reported in this manuscript further demonstrates the generality of the carbene-based cross coupling.

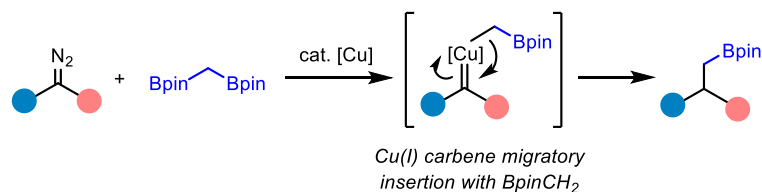
Copper-Catalyzed Cross-Coupling of Aryldiazoacetates with Bis[(pinacolato)boryl]methane

Zhicheng Bao, Muyao Li, Jianbo Wang*

College of Chemistry, Peking University, Beijing 100871, China

Chin. J. Org. Chem. **2023**, *43*, 1808-1814.

http://sioc-journal.cn/Jwk_yjhx/EN/10.6023/cjoc202301027



Abstract: We report herein the copper-catalyzed cross-coupling reaction between α -diazophenylacetate as carbene precursor with 1,1-bis[(pinacolato)boryl]methane, leading to the construction of C(sp³)-C(sp³) bonds. Reaction optimization experiments showed that Monophos ligand was critical for the success of this reaction. In situ oxidation afforded the corresponding primary alcohols instead of the relatively unstable boronates. The reaction has high efficiency and good functional group compatibility. The two-step transformation represents a formal hydroxymethylation of diazoacetates.

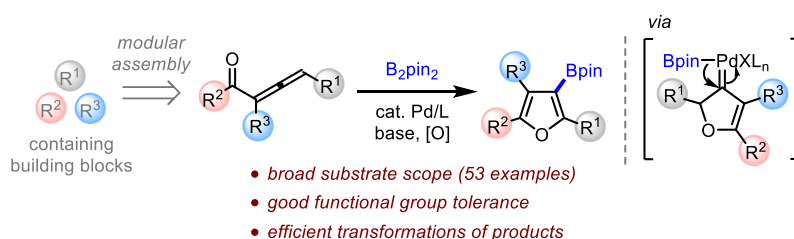
Palladium-Catalyzed Cyclizative Borylation of Allenyl Ketones through Carbene Boryl Migratory Insertion: Access to Densely Substituted Furyl Boronates

Kang Wang, Yan Xu, and Jianbo Wang*

College of Chemistry, Peking University, Beijing 100871, China

Chem. Eur. J. **2023**, *29*, e202203697.

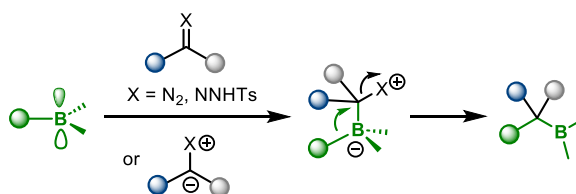
<https://doi.org/10.1002/chem.202203697>



Abstract: We report herein the palladium-catalyzed cyclizative borylation of allenyl ketones with diboron compounds which involves the carbene boryl migratory insertion as the key step. This reaction features mild conditions, good functional group tolerance and broad substrate scope. Thus, it represents an efficient methodology for the assembly of diverse tri-substituted furyl boronates. In addition, a series of transformations of the resultant multi-substituted furyl boronates were conducted to provide various densely substituted furan derivatives in good yields, further illustrating the potential synthetic utility of this methodology.

Transition-Metal-Free Insertion of Diazo Compounds, *N*-Arylsulfonylhydrazones or Ylides into Organoboronic Acids or Their Derivatives

Zhicheng Bao, and Jianbo Wang*

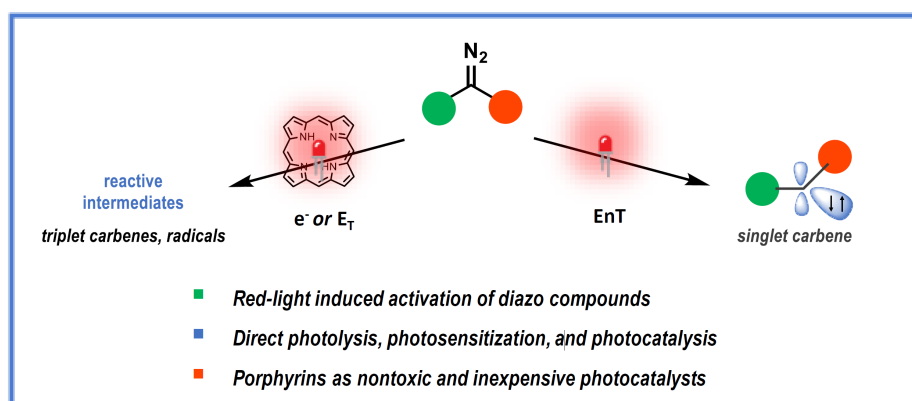


Abstract: The insertion reactions of carbenes or ylides with organoboronic acids or their derivatives have emerged as valuable methods for coupling or homologation of organoboron compounds under metal-free conditions. The crucial steps of these reactions are the coordination of electron-rich carbon centers of the carbene precursors or ylides to the electron-poor boron center, followed by 1,2-migration of the corresponding tetracoordinated boron intermediates. This type of unique transformations provides efficient methods for the construction of C–C bonds or C–X (X = H, B) bonds. Moreover, the C–B bonds generated by such transformations can be utilized as a handle for further derivatization or iterative homologations. In this review, we summarize the developments in this arena according to the reactive diazo compounds, *N*-arylsulfonylhydrazones or ylide species involved.

Unlocking the reactivity of diazo compounds in red light with the use of photochemical tools

Katarzyna Orłowska, Klaudia Łuczak, Piotr Krajewski, João V. Santiago, Katarzyna Rybicka-Jasińska and Dorota Gryko
 Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52 01-224, Warsaw, Poland.

Chem. Commun., **2023**, 59, 14649-14652
 DOI:10.1039/D3CC05174A

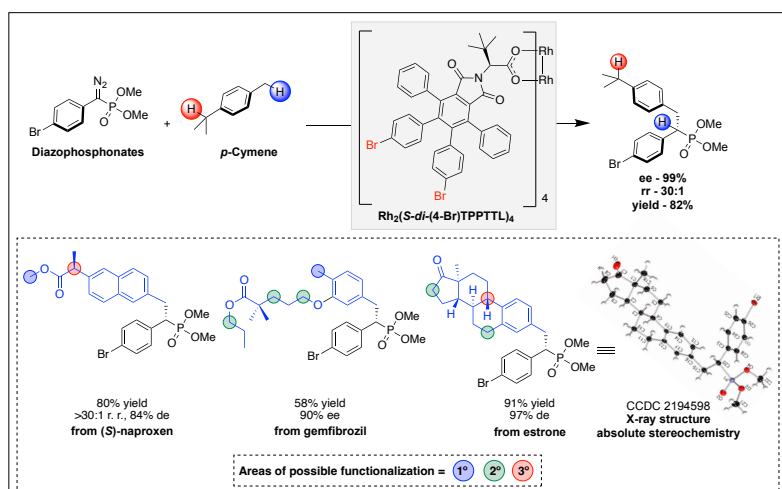


Abstract: The red light-irradiation of structurally diversified diazoalkanes gives access to reactive intermediates via direct photolysis and via photosensitization or photoredox approaches.

Enantioselective Intermolecular C–H Functionalization of Primary Benzylic C–H Bonds Using ((Aryl)(diazo)methyl)phosphonates

Yasir Naeem, Bianca T. Matsuo, and Huw M. L. Davies*
 Department of Chemistry, Emory University, 1515 Dickey Drive. Atlanta, GA 30322, USA.

ACS Catal. **2024**, 14, 124–130
 Publication Date: December 11, 2023
<https://doi.org/10.1021/acscatal.3c04661>



Abstract: Catalyst-controlled C–H functionalization using donor/acceptor carbenes has been shown to be an efficient process capable of high levels of site control and stereocontrol. This study demonstrated that the donor/acceptor carbene C–H functionalization scope can be extended to systems where the acceptor group is phosphonate. When using the optimized dirhodium catalyst, $\text{Rh}_2(\text{S-di-(4-Br)TPPTTL})_4$, ((aryl)(diazo)methyl)phosphonates undergo highly enantioselective (84–99% ee) and site-selective (>30:1 r.r.) benzylic C–H functionalization. The phosphonate group is much more sterically demanding than the previously studied carboxylate ester group, leading to higher selectivity for a primary site versus more sterically crowded positions. The effectiveness of this methodology has been demonstrated by the late-stage primary C–H functionalization of estrone, adapalene, (S)-naproxen, clofibrate, and gemfibrozil derivatives.

Diruthenium Tetracarboxylate-Catalyzed Enantioselective Cyclopropanation with Aryldiazoacetates

Joshua K. Sailer,¹ Jack C. Sharland,¹ John Bacsa,¹ Caleb F. Harris,² John F. Berry,² Djamaladdin G. Musaev*,^{1,3} and Huw M. L. Davies*,¹

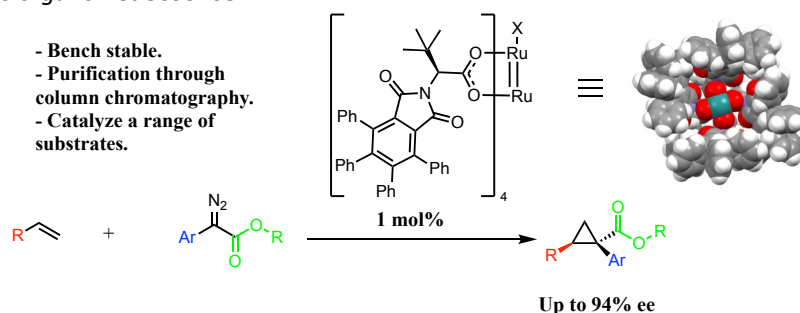
¹Department of Chemistry, Emory University, 1515 Dickey Drive. Atlanta, GA 30322, USA.

²Department of Chemistry, University of Wisconsin, 1101 University Avenue, Madison, Wisconsin 53706, United States

³Cherry L. Emerson Center for Scientific Computation, Emory University, 1521 Dickey Drive, Atlanta, Georgia 30322, United States

Organometallics **2023**, *42*, 2122–2133.

<https://doi.org/10.1021/acs.organomet.3c00268>.



Abstract: Five chiral bowl-shaped tetracarboxylate diruthenium paddlewheel complexes have been synthesized, characterized, and applied to the cyclopropanation of various olefins using aryl diazoacetate compounds as carbene precursors. These catalysts are shown to afford cyclopropane products in moderate to high yield with good to excellent enantioselectivity. React IR kinetics studies showed the diruthenium catalyst is capable of completing the reaction at loadings as low as 0.5 mol %. Additionally, we show that the dicopper and dicobalt tetracarboxylate analogues are not viable in affording the cyclopropanes in high enantioselectivity, suggesting the destruction of the high-symmetry catalyst during the reaction. These experimental results are corroborated via computational analysis, as well as highlighting the similarities and differences between the diruthenium and dirhodium congeners of the tetracarboxylate catalysts.

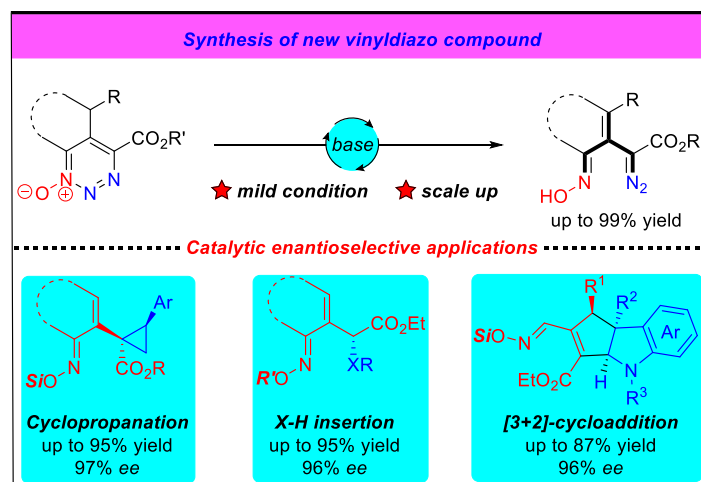
Expanded access to vinyl diazo compounds and their catalytic enantioselective applications

Ming Bao,¹ Luca De Angelis, Marlyn S. Rada, Marriah Baird, Hadi Arman, Daniel Wherritt, and Michael P. Doyle*

Department of Chemistry, The University of Texas at San Antonio, San Antonio, Texas 78249, United States

CHEM Catal. **2023**, 3, 100770

<http://doi.org/10.1016/j.checat.2023.100770>



Abstract: A variety of oximido vinyl diazoacetates with an oxime functional group at the β -position was synthesized via base catalyzed Dimroth-type rearrangement of multiply-substituted 1,2,3-triazine 1-oxides. Cyclopropanation, cycloaddition, N-H and O-H insertions processes were selected to exemplify the suitability of silylated oximido vinyl diazoacetates for catalytic metal carbene transformations, and high product yields with exceptional enantiocontrol were achieved under very mild conditions, suggesting that these new vinyl diazoacetates will be appropriate for use in a larger array of metal carbene transformations, as well as in the increasing number of non-metal transformations of vinyl diazoacetates.