ChemComm

FEATURE ARTICLE

View Article Online
View Journal | View Issue



Cite this: *Chem. Commun.*, 2023, **59**, 8032

# α-Diazo-λ$^3$-iodanes and α-diazo sulfonium salts: the umpolung of diazo compounds

Sven Timmann and Manuel Alcarazo *

Received 2nd April 2023,
Accepted 30th May 2023

DOI: 10.1039/d3cc01620j

rsc.li/chemcomm

This minireview aims to cover the developments of the last few years in the design of reagents able to accomplish the umpolung of the azomethine carbon in diazo compounds namely, α-diazo-λ$^3$-iodanes and α-diazo sulfonium salts. Specifically, the routes available for their preparation and a classification of their unique reactivity patterns (either acting as equivalents of carbene-radical or carbene-carbocation synthons) are discussed. We also present a detailed overview of the synthetic utility of such species and, when possible, a critical comparation their reactivity and properties.



## 1. Introduction

Due to the broad variety of chemical transformations that they are able to promote, diazo compounds have well deserved their position as indispensable reagents in the toolbox of the synthetic practitioner. By irreversible elimination of $N_2$, a process that can be induced thermally, photochemically or by treatment with transition metals, diazo compounds generate short lived carbenes or carbene–metal complexes,[1] which further react either *via* addition to unsaturated substrates (*e.g.* cyclopropanation reactions)[2] or *via* insertion into σ-bonds (*e.g.* C–H or X–H functionalizations).[3,4] Diazo compounds also react with electrophiles at their carbon atom delivering aliphatic diazonium ions that subsequently lose $N_2$ to form carbocations;[5] and not less important, diazo compound additionally participate in a number of 1,3-dipolar cycloadditions in which the $N_2$-fragment stays as a constitutional fragment of the newly-constructed heterocycle.[6]

Interestingly, these three modes of reaction have a common origin, a nucleophilic character at the carbon atom of the $CN_2$ moiety, which can be understood by observation of the frontier orbitals and charge distribution already in the parent diazomethane **3**. Natural population analysis at the B3LYP[7]/def2SVP[8,9] level indicates that in **3** the C-atom bears a substantial negative charge (−0.483 e), while both N-atoms remain nearly neutral (+0.020 e (N1); −0.033 e (N2)). Moreover, inspection of the HOMO orbital in **3** reveals that the electron pair is mainly localized in a p-orbital at C1 (Fig. 1a and b). This situation also explains why the stability of diazo compounds increases when electron withdrawing groups (EWG) are attached to the carbon bearing the diazo functionality. The decomposition enthalpies for model compounds **1–3** are also shown in Fig. 1c.[10]

To better harvest the synthetic potential of diazo compounds, chemist have unsurprisingly tried to reverse their inherent polarity from nucleophilicity to electrophilicity by introducing a good leaving group at the C-atom of the diazo unit. That was probably what led Weiss to directly attach a positively charged and extremely nucleofuge phenyl iodonium moiety to the diazo unit in **4a**.[11] However, comparison of the NBO charge distribution in **2** and **4a** counterintuitively reveals that the partial negative charge at the azomethine carbons remains basically unchanged in both compounds. The umpolung of C1 does not seem to be achieved by introduction of the phenyl iodonium group (Fig. 1 and 2). On the other hand, in **4a** the iodine atom bears a complete positive charge (+1.020 e$^-$), and the low lying LUMO, which is characterized by its considerable coefficient at the I-atom, corresponds to the σ*(I–C1) orbital. These two properties make possible the direct attack of nucleophiles ($Nu^-$) to the iodine centre, a process that is often followed by reductive elimination of the Nu–R moiety from the iodine centre. It is actually that reaction pathway the one that explains the apparent umpolung of the azomethine carbon in **4a** and structurally related compounds.

The parallelism in terms of reactivity often observed between the reactivity of hypervalent I(III) reagents and sulfonium salts is also illuminated when the same analysis is carried out for compound **5a** (Fig. 2b). The sulfur atom is highly electron deficient and also bears an almost full positive charge (+0.882 e$^-$). In addition, the LUMO corresponds to the σ*(S–C1) orbital, which is again significantly localized at the S-atom. A similar electronic structure generates analogue reactivity, and hence, sulfonium salts are often employed in synthesis when the necessary iodine-based reagent is thermally too unstable to

*Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen Tammannstr. 2, 37077 Göttingen, Germany.*
*E-mail: manuel.alcarazo@chemie.uni-goettingen.de*

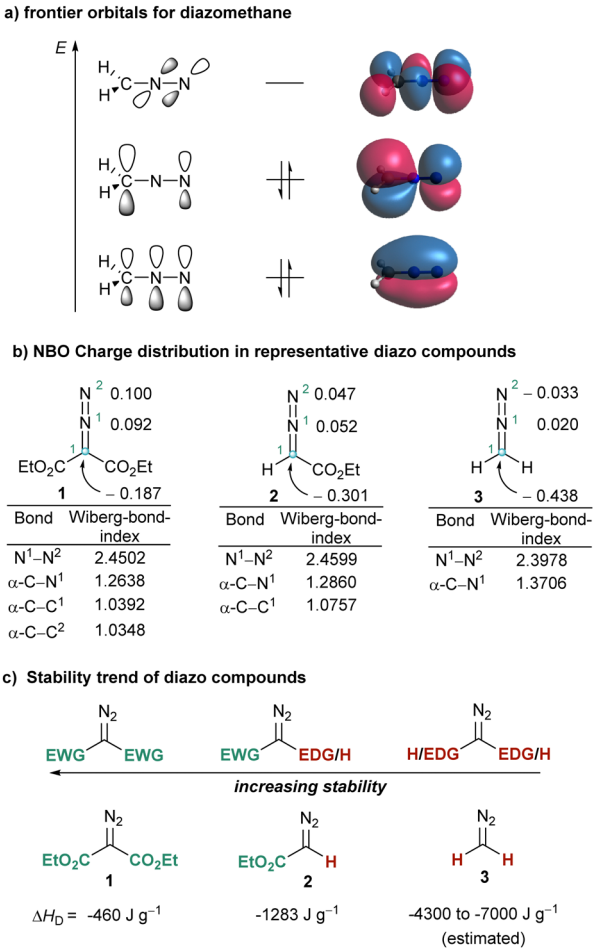



Fig. 1 Structural features of diazo compounds. (A) Representation of the frontier orbitals of diazomethane calculated at B3LYP/def2SVP level; (b) partial NBO charges and Wiberg bond orders at the same level; (c) reactivity trend. EWG = electron-withdrawing group, EDG = electron-donating group. $\Delta H_D$ = average enthalpy of decomposition.

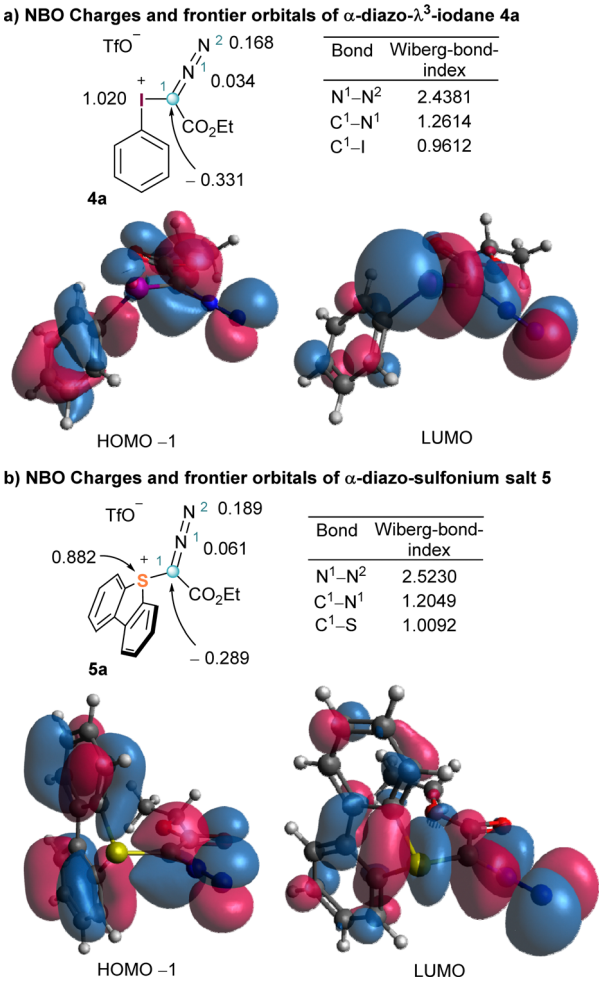
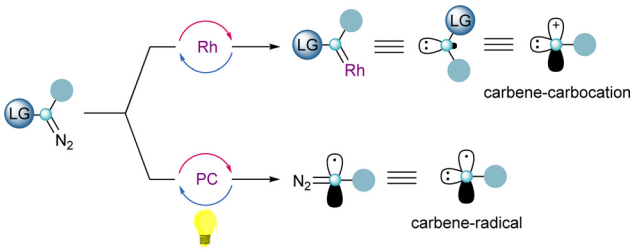



Fig. 2 Representation of the HOMO–1 (left) and LUMO (right) of iodonium salt **4** (a) and sulfonium salt **5** (b). Partial NBO charges and Wiberg bond orders are calculated at B3LYP/def2SVP level.




Scheme 1 Dual reactivity character of α-diazo-λ3-iodanes and α-diazo-sulfonium salts.

be used in multigram scale, or simply when there is no protocol available for its preparation.[10,12]

One of the key features of reagents **4** and **5** is the presence of two orthogonal leaving groups attached to the same carbon-atom. Careful control of the reaction conditions allows each of the groups to be selectively addressed, and by this, different reaction pathways arise. The reactivity of a formal carbene–carbocation can be achieved when **4** or **5** react with a transition-metal catalyst delivering a metal–carbene species and subsequently the iodoarene or sulfide moieties are released. Alternatively, utilizing photoredox-catalytic conditions, the homolytic cleavage of the sulfur– or iodine–carbon bond takes place first, resulting in the formation a carbon-centered diazo radical. Once the radical has been trapped, the carbene reactivity can be accessed by release of dinitrogen, either thermally or through metal catalysis (Scheme 1).

With this minireview we intend to provide the reader with an overview on the preparation and synthetic potential of these two families of compounds (α-diazo-λ3-iodanes and α-diazo sulfonium salts), together with a critical comparison between their reactivity and scope. Unsolved problems derived from the use of these reagents will be indicated, and possible developments in the area will also be anticipated.

## 2. Synthesis of α-diazo-λ3-iodanes and their sulfonium salts analogue

The prototype α-diazo-λ3-iodane **4a** can be accessed in one-pot by initial activation of commercially available λ3-iodane

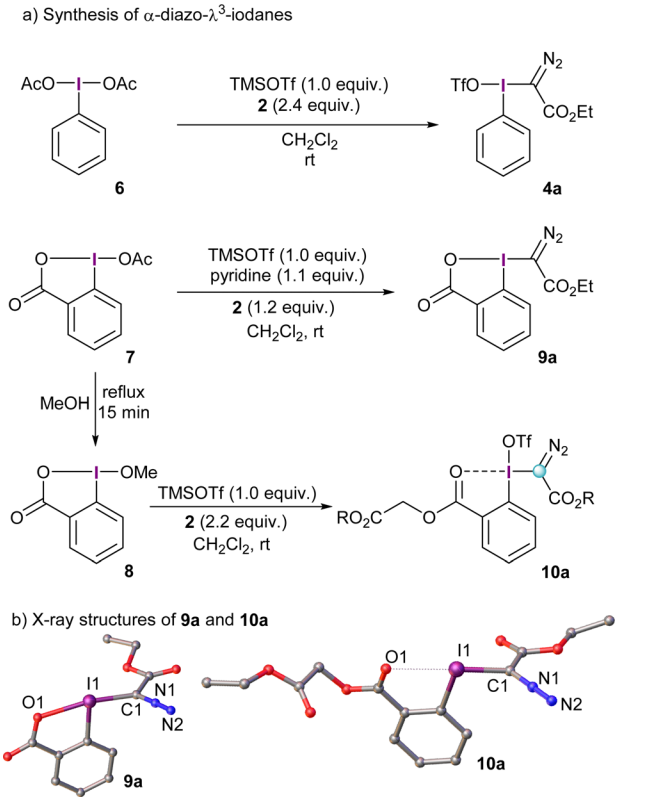
precursors, such as the diacetoxy iodobenzene **6** (PIDA), with trimethylsilyl triflate and subsequent reaction with excess of the desired diazo compound.[11] This route seems to be quite general and works equally well for several stabilized diazocompounds; substituents of different nature on the arene ring are tolerated as well. The use of reagent **4a** presents, however, a practical limitation. It is not thermally stable and needs to be stored under refrigeration.[13] Besides that, **4a** is characterized by a highly exothermic decomposition upon moderate heating to 80 °C (472.4 J $g^{-1}$),[13] which limits its utility to small scale reactions. To mitigate, at least partially, this inconvenience and improve the safety profile of these structures, cyclic derivatives have been prepared using, for example, the benziodoxolone platform. This strategy has proven to be satisfactory for many other I(III)-based reagents.[14]

α-Diazo-benziodoxolone reagent **9a** is prepared in a similar fashion as its non-cyclic analogues; namely, initial activation of the acetoxy precursor **7** with TMS triflate followed by addition of the diazo compound under basic conditions. Pyridine seems to be the ideal base to trap the triflic acid generated and avoid decomposition of **9a**. Alternatively, treatment of **8** with TMS triflate and excess of the desired diazo compound in the absence of base delivers the benzoate derivative **10a**. The formation of this species can be explained by protonation of **2** followed by loss of molecular nitrogen and trapping of the corresponding carbocation by the carbonyl moiety of *in situ* generated **9a**.[15]

The X-ray structures of **9a** and **10a** are depicted in Scheme 2; interestingly, the benzoyl oxygen atom in **10a** also interacts with the neighboring iodine delivering an iodaxolane-type architecture, although not as tight as the one in **9a**. Actually, the reactivity of **10a** and analogue reagents can be tuned by addition of Lewis acids such as $Zn(NTf)_2$; they coordinate the benzoyl moiety and, consequently, reduce the donation of this group towards the $\lambda^3$-iodane unit.[15]

The first synthesis of α-diazo substituted sulfonium salts, compounds **11** and **12**, was also reported by Weiss.[11,16] These species were obtained with excellent yields by direct reaction of **4b** with dimethyl sulphide or tetrahydrothiophene, respectively (Scheme 3a); however, this route has two drawbacks that severely limit its practical use: (i) it requires the previous preparation of the corresponding $\lambda^3$-iodane precursors **4**, and (ii) the diazo transfer process is not general. Typically, only electron rich dialkyl sulphides are nucleophilic enough for the reaction to proceed.

To circumvent these shortcomings, we recently developed a general synthetic protocol towards α-diazo sulfonium salts starting from easily available sulfoxides. Activation of these starting materials with triflic or trifluoroacetic acid anhydride at low temperatures generates a highly electrophilic sulfurane intermediate, which is able to react with α-diazo compounds to afford the expected α-diazo-sulfonium salts.[17] Following that route, salts derived from dibenzothiophene (**13**), phenoxatiine (**14**) and thianthrene (**15**) were prepared in a one-pot procedure (Scheme 3b). The X-ray structures of **13** and **15** are shown in Scheme 3c. Interestingly, differential scanning calorimetry of a




Scheme 2 Synthetic pathways towards α-diazo reagents **4a**, **9a** and **10a** and X-ray structures of **9a** and **10a**. Hydrogen atoms and triflate-anion (**10a**) omitted for clarity; ellipsoids shown at 50% probability level.

sample of **13** shows decomposition above 130 °C leading to a significative energy release of 400 J $g^{-1}$;[17] for comparison, compound **9a** starts decomposing at 120 °C with a larger release of energy >600 J $g^{-1}$.[15] On the basis of these results, it can be concluded that the use of **13** is relatively safer; in particular for large scale laboratory syntheses.

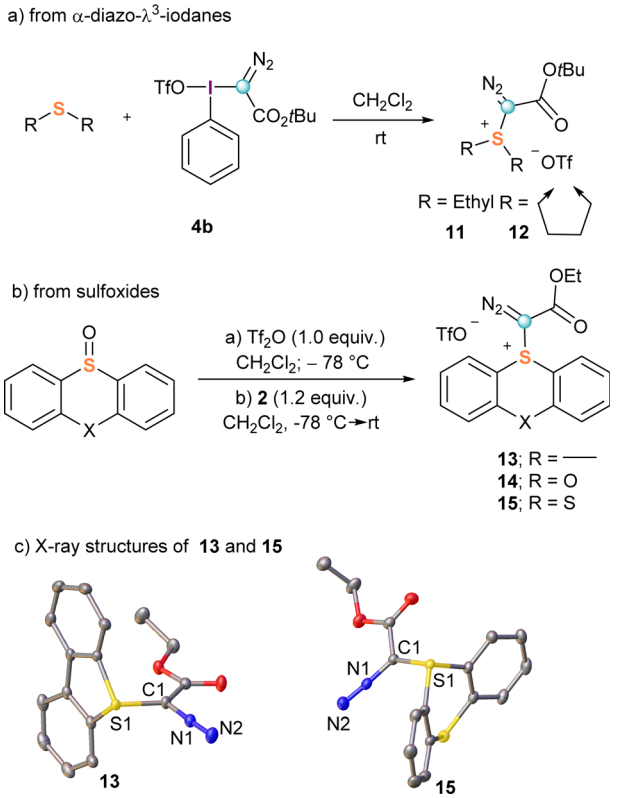
## 3. Reactivity of α-diazo-λ³-iodanes

The transformations in which α-diazo-$\lambda^3$-iodanes are involved have been grouped in three different sections according to the operating mechanism proposed by the authors. Section 3.1 describes reactions in which the diazo group transfer occurs *via* typical nucleophilic attack at its carbon atom. Section 3.2 lumps together those processes in which the diazo transfer reaction takes place *via* formation of a diazoalkyl radical, and finally, Section 3.3 compiles the family of reactions that initially exploit the carbene reactivity of the diazo group in **4**, **5**, **9** or **10**.

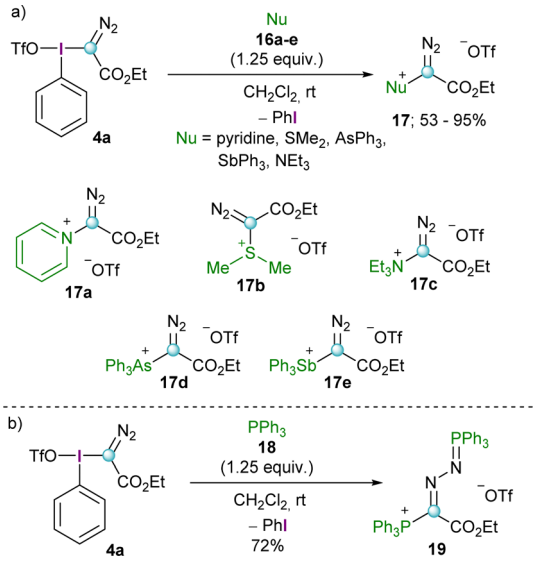
### 3.1 Transfer of the diazoalkyl group by reaction with nucleophiles

Initial studies by Weiss and co-workers showed that reagent **4a** is able to transfer the diazoalkyl moiety to a series of neutral nucleophiles such as tertiary amines, pyridines, arsines, stilbines and dialkyl sulfides furnishing the corresponding -onio products **17a–e** (Scheme 4a). Interestingly, the reaction with

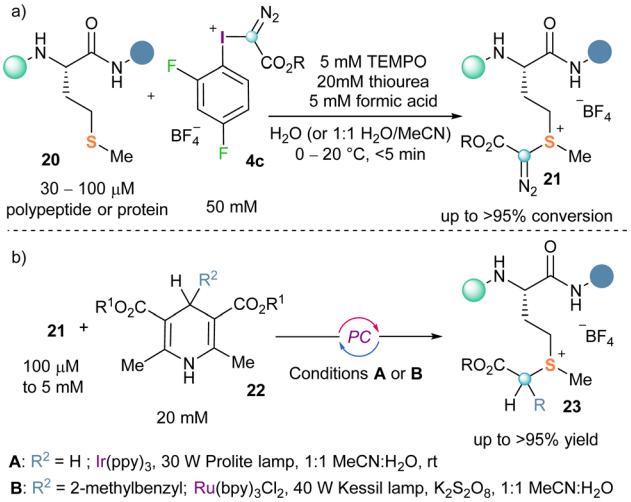



Scheme 3 Synthetic pathways towards α-diazo reagents **11–15** and X-ray structures of **13** and **15**. Hydrogen atoms and triflate-anions omitted for clarity; ellipsoids shown at 50% probability level.




Scheme 4 Nucleophilic substitution reaction of the α-diazo aryliodonio compounds with neutral nucleophiles by Weiss and co-workers.

triphenylphosphine (**18**) resulted in the formation of a phosphino phosphazine **19**, regardless of the reaction conditions applied and the stoichiometry used (Scheme 4b).[11] This particular reactivity has been further investigated by Podrugina *et al.* using phosphines with different substitution pattern.[16]



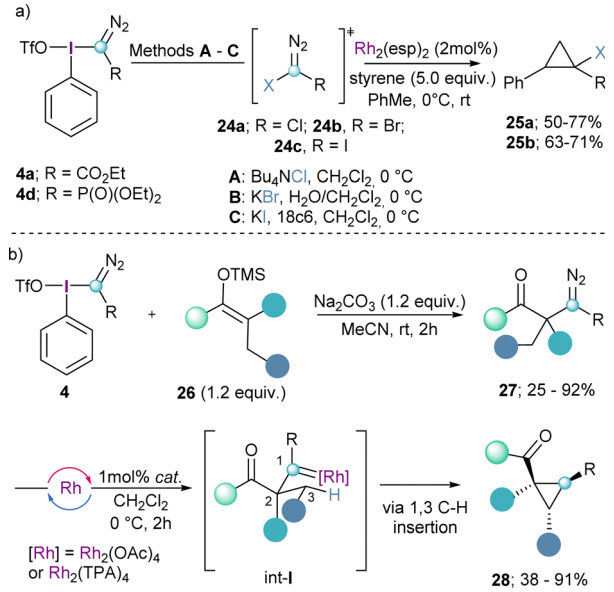

Scheme 5 (a) Methionine-selective bioconjugation strategy; (b) protein diversification *via* photo-redox catalysis.

Making use of this reactivity mode Gaunt and co-workers recently conceived that α-diazo-λ3-iodanes could be applied to the selective functionalization of polypeptides and proteins at methionine residues. For this purpose, they designed an electron poorer derivative than the original Weiss reagent by introducing two fluorine atoms in the arene moiety (**4c**). The desired bioconjugation reaction using **4c**, proceeds selectively delivering the expected sulfonium salt **21** (Scheme 5a).

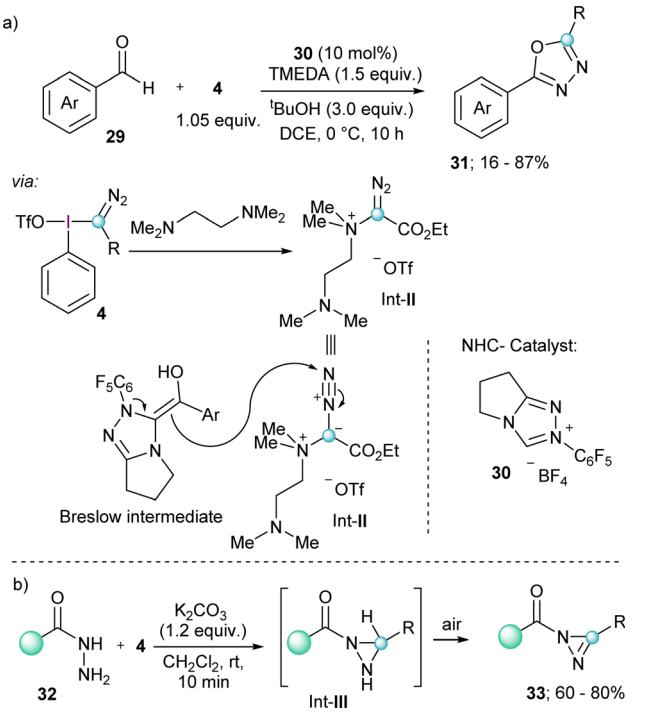
The advantages associated with the targeting of the methionine residue are two-folded; its low abundance in proteins (around 2%) makes the reaction extremely site-selective and, additionally, the functionalization of methionine residues is not likely to interfere with the protein function.[18,19] Also remarkable is the fact that the diazo unit once attached to the methionine residue could be used for further derivatization of the protein *via* photocatalytic approaches (Scheme 5b).[20]

The same reaction mode has been employed by the group of Bonge-Hansen on the synthesized α-halo diazocompounds **24a–c** by reaction of **4a** and **4d** with halide anions. These compounds were subsequently converted into the corresponding halo-substituted cyclopropane derivates **25a** and **25b** *via* catalytic carbene addition to the double bond of styrenes employing $Rh_2(esp)_2$ as catalyst (Scheme 6a).[21]

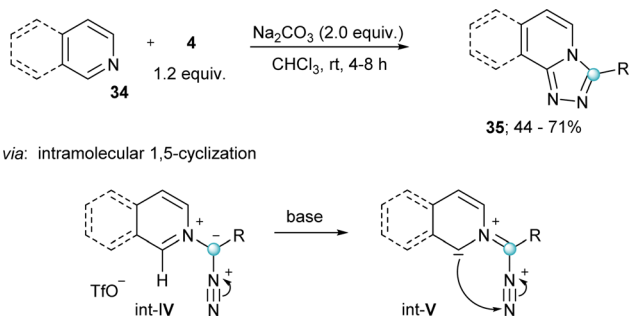
The synthesis of α-diazocarbonyl compounds is straightforward and can be achieved through diazo-transfer reactions such as the Regitz diazo-transfer, which makes react sulfonylazides with enolates.[22] However, the synthesis of the β-homologes **27** is much more challenging and the diazo products lack the stabilization of an electron withdrawing group. Suero and co-workers realized that by reaction of the Weiss-reagent **4** with silylenol ethers (**26**), the desired β-diazocarbonyl compounds **27** could be obtained (Scheme 6b). Subsequently, compounds of general formula **27** were transformed into the corresponding cyclopropanes **28** *via* initial Rh-promoted carbene formation (int-**I**) followed by the highly diastereoselective insertion of the carbene into the C($sp^3$)–H bond in position 3 of that species (Scheme 6b).[13]




Scheme 6 (a) Nucleophilic halogenation of α-aryliodonio diazo reagents with following catalytic cyclopropanation; (b) electrophilic diazomethylation of ketone silyl ethers.




Scheme 7 (a) NHC-catalyzed formation of 2,5-disubstituted 1,3,4-oxadiazoles; (b) formation of substituted diazirines.




Scheme 8 Synthesis of [1,2,4]triazolo[4,3-*a*]pyridines starting from pyridines.

A related transformation that also exploits the reactivity of electron rich olefins with **4** has been reported by the group of Wang; however, in this case the nucleophile was a Breslow intermediate catalytically generated by the umpolung of aldehydes with a bicyclic N-heterocyclic carbene **30**. The products obtained from this transformation are 2,5-disubstituted-1,3,4-oxadiazoles **31**, which originate from the attack of the electron rich olefin to the electrophilic terminal nitrogen of the diazo group, and not to the azomethine carbon.

Fundamental for the understanding of this unique mechanism and reaction outcome was the isolation of Int-**II**, which is formed by the initial reaction of TMEDA with **4** under the conditions applied (Scheme 7a).[23]

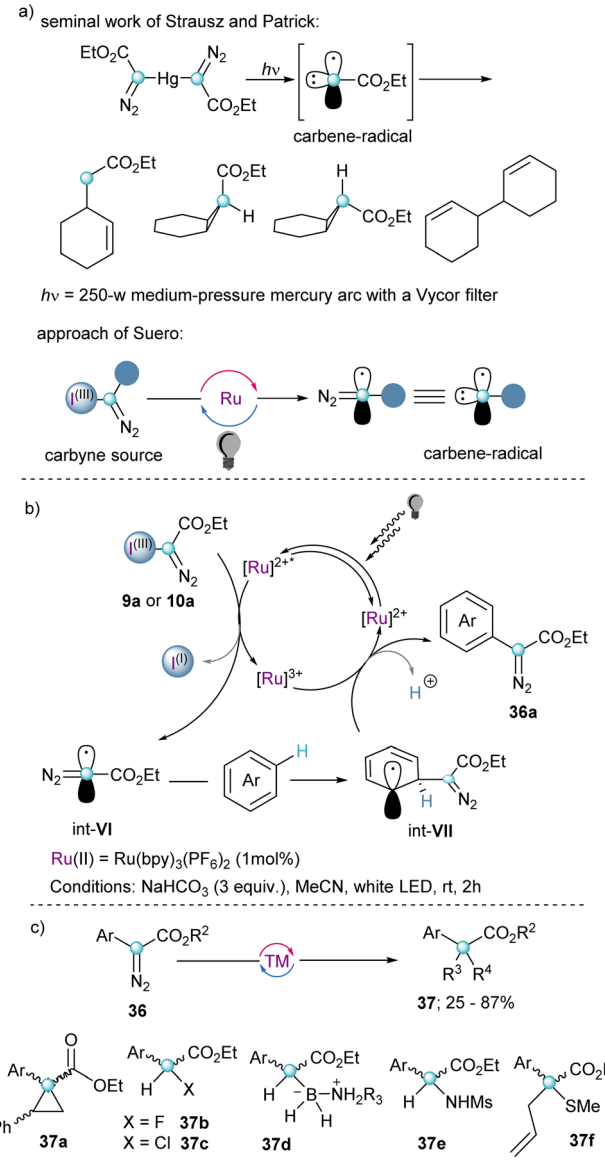
Finally, two additional transformations were reported in 2022 exploiting the electrophilicity of **4** and the excellent properties of iodobenzenes as leaving groups. The group of Singh described a novel route towards the synthesis of substituted diazirines **33** by reaction of semicarbazides **32** with **4**, followed by oxidation of the diaziridine intermediate (Int-**III**) by air (Scheme 7b).[24] Also in the same year Rastogi and coworkers published a base assisted synthesis of [1,2,4]triazolo[4,3-*a*]pyridines **35**, by reaction of **4** with pyridines and isoquinolines (Scheme 8).[25] Intermediates in this reaction are α-diazoalkyl pyridinium salts (Int-**IV**); compounds already described by Weiß in his seminal work.[11] Treatment of these species with base result in the deprotonation of the iminium moiety and subsequent cyclization towards the desired heterocycles.[25] A variant of this reaction, but using piperidines and tetrahydroisoquinolines as the nucleophilic reaction partner has been very recently reported by Singh and coworkers.[26]

### 3.2 Transfer of the diazo group *via* radical processes

As previously indicated, α-diazo-λ$^3$-iodanes of general formula **4** have been known for three decades; however, they were sporadically used as transfer reagents. It was only after the work of Suero in 2018 that their broad synthetic potential was first recognized, and their reactivity intensively explored.

Probably inspired by the pioneering work of Strausz and Patrick towards the generation of carbynes by treatment of Hg{C(=N$_2$)CO$_2$Et}$_2$ with ultraviolet light,[27] Suero and coworkers hypothesized that the generation of diazomethyl radicals (Int-**VI**) could be achieved more efficiently under the mild conditions offered by photocatalysis; specifically, by single electron transfer to **9** and **10** with concomitant elimination of the iodoarene moiety (Scheme 9b). After optimizing the experimental conditions, these authors succeeded in bringing to practise their hypothesis using white light as radiation source and [Ru(bpy)$_3$](PF$_6$)$_2$ as the most adequate photocatalyst. Furthermore, they developed a C–H arene diazomethylation reaction by trapping the thus generated diazomethyl radicals

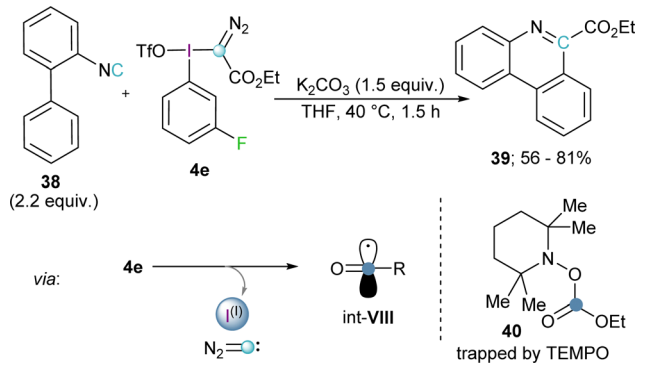
 




Scheme 9 (a) Seminal work of Strausz and Patrick. (b) Photoredox catalysed C–H arene diazomethylation; proposed mechanism. (c) Diazo diversification.

with an array of (hetero)arenes. The transformation showed impressively broad functional group tolerance, and even a series of different pharmaceutically relevant molecules could be functionalized in acceptable yields. Subsequently, the initially obtained diazo-compounds were further elaborated into α-amino, α-thio, α-bora, α-haloesters and cyclopropanes **37** using the native carbene-type reactivity of the diazo moiety (Scheme 9c).[15]

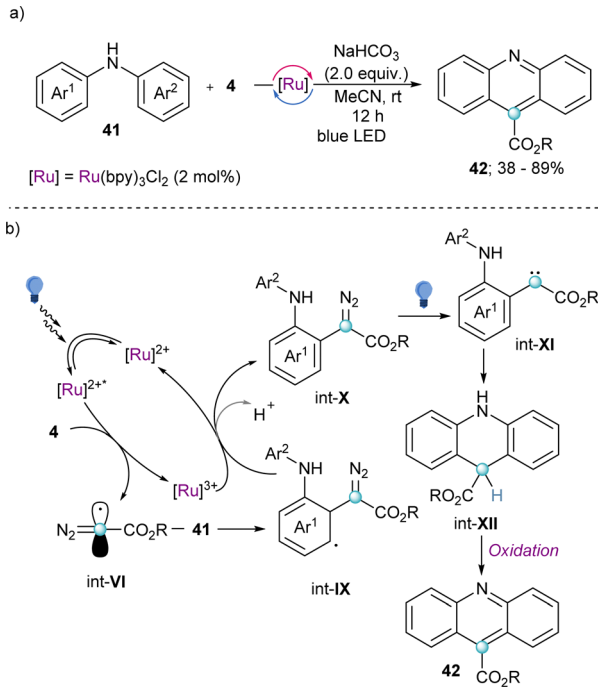
Inspired by this work, Wang and coworkers hypothesized that a good radical scavenger such as isonitrile **38** should also be able to react with electrophilic diazomethyl radicals (int-**VI**) to afford ethyl diazo-6-phenanthridinyl acetates. Interestingly, no trace of the expected product was formed; in fact, this reaction effectively delivers phenanthridine-6-carboxylates **39**. Radical trapping experiments using 2,2,6,6-tetramethylpyperidine



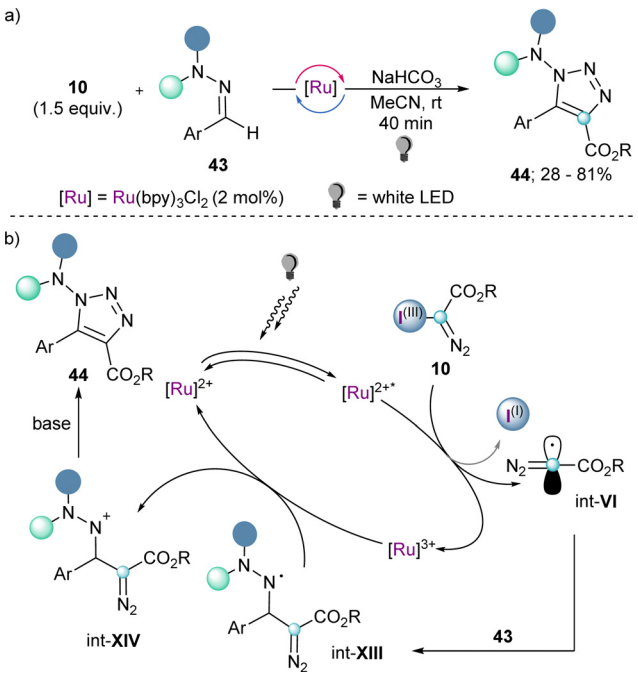

Scheme 10 Phenanthridine synthesis *via* radical, diazo-methane elimination pathway.

oxide (TEMPO) as scavenger allowed the isolation of the carboxylic ester adduct **40**, which is a clear proof of the formation of the carboxylic radical int-**VIII**. Hence, Wang and co-workers proposed that under the reaction conditions employed, the initially formed diazomethyl radical thermally decomposed *via* extrusion of diazocarbene to form the corresponding carboxylate radical.[28] Reaction of this open shell species with **38** followed by radical addition to the neighbouring phenyl ring, oxidation, and deprotonation, leads to the formation of **39** (Scheme 10).[29]

Also making use of the mesolitic C–I bond cleavage after one electron reduction, Li and co-workers recently reported a photoredox catalysed cascade transformation that delivers substituted acridines by reaction of **4** with diarylamine substrates **41**. The authors propose the initial generation of the diazomethyl radical intermediate (int-**VI**) from **4** and subsequent interception of this species by **41** to generate the radical adduct (int-**IX**). Subsequent single-electron oxidation delivers int-**X**. Finally, photochemical decomposition of the diazo compound by irradiation with blue light delivers a free carbene (int-**XI**), which is intramolecularly trapped by the second aromatic ring of the diarylamine-substrate (int-**XII**). Oxidation of this intermediate produces the observed acridines **42** (Scheme 11).[30] Other unsaturated organic nucleophiles can serve as diazomethyl radical acceptors as well. For example, a visible light-induced [3+2] cyclization reaction of hydrazones (**43**) with reagent **10**, to form 1-amino-1,2,3-triazoles (**44**) was reported by the group of Li in 2021 (Scheme 12a). The reaction is initiated by single-electron reduction of reagent **10** under photochemical conditions to generate the diazomethyl radical (int-**VI**). Subsequent addition to the aldehyde-derived hydrazone **43** forms a *N*-centred radical intermediate (int-**XIII**), which is oxidized to int-**XIV** by the photocatalyst. In the presence of a base, deprotonation of int-**XIV** delivers an α-diazoalkylhydrazone, which cyclizes to the desired 1-(dialkylamino)-1,2,3-triazole product **44** (Scheme 12b).[31] Interestingly, the same transformation was shortly earlier published by the Alcarazo group using α-diazo sulfonium triflates as the radical precursor;[17] this variant of the reaction will be discussed in the next section of this minireview. A structurally related photoredox catalyzed [3+2] cyclization able to deliver 1,2,3-triazole fused quinoxalinones *via* an analogue mechanism has also been reported.[32]

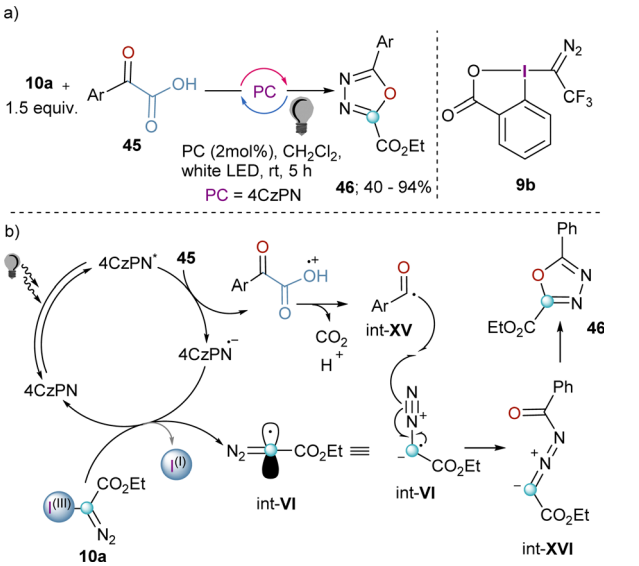



Scheme 11 (a) Photoredox catalysed cascade reaction towards substituted acridines. (b) Proposed mechanistic pathway for the formation of acridines.




Scheme 12 (a) Visible light-induced [3+2] cyclization of hydrazones to 1-amino-1,2,3-triazoles. (b) Proposed mechanism for the cyclization towards 1-amino-1,2,3-triazoles.

The synthetic potential of int-**VI** might be even wider if this species could be trapped by another radical. Willing to explore this possibility and being aware of the fact that acyl radicals can



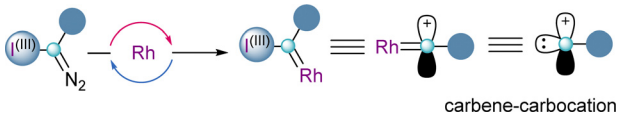

Scheme 13 (a) Photoredox catalytic decarboxylative cyclization of α-oxocarboxylic acid and hypervalent iodine(III) reagents. (b) Proposed mechanism.

be prepared from the decarboxylation of α-ketoacids by photoredox catalysis, Liu and co-workers developed a decarboxylative coupling towards 2,5-disubstituted 1,3,4-oxadiazoles from **10a** and α-oxocarboxylic acids that relays on the simultaneous generation of both radicals (Scheme 13a). After excitation of the organic photocatalyst, single-electron oxidation of the α-oxocarboxylic acid delivers the corresponding radical cation, which undergoes decarboxylation to generate radical intermediate int-**XV**. Subsequently, the reduced photocatalyst is able to reduce the $I^{(III)}$-reagent **10a** liberating the diazomethyl radical int-**VI**. Radical combination leads to the formation of int-**XVI**, which finally delivers the desired 2,5-disubstituted 1,3,4-oxadiazoles **46** after intramolecular ring-closure.[33] Unfortunately, the extension of this method to heterocyclic or aliphatic α-oxocarboxylic acids was unsuccessful; this remains as a clear synthetic limitation of this route.

In 2021 the group of Han also reported a variant of this reaction using the $CF_3$-substituted reagent **9b**. In this case no photocatalyst is needed and the diazotrifluoroethyl radical is directly generated from the hypervalent iodine reagent by visible-light irradiation. Moreover, the methodology developed allowed the introduction of trifluoromethyl-substituted 1,3,4-oxadiazole moieties in pharmaceuticals and other bioactive molecules.[34]

### 3.3 Initial reaction of the diazo group

In all the examples shown so far, from the two innate reactivities present in α-diazo-$\lambda^3$-iodanes, the nucleofuge character of the iodonium group has always been exploited in the first instance. However, there is no reason to believe that in the presence of the appropriate catalyst, the carbene-type reactivity might be used primarily, followed by elimination of the aryl iodide moiety. This succession of steps turns




Scheme 14 Dual reactivity character of hypervalent iodine(III) diazo reagents.

α-diazo-λ³-iodanes into synthetic equivalents of carbene carbocations (Scheme 14).

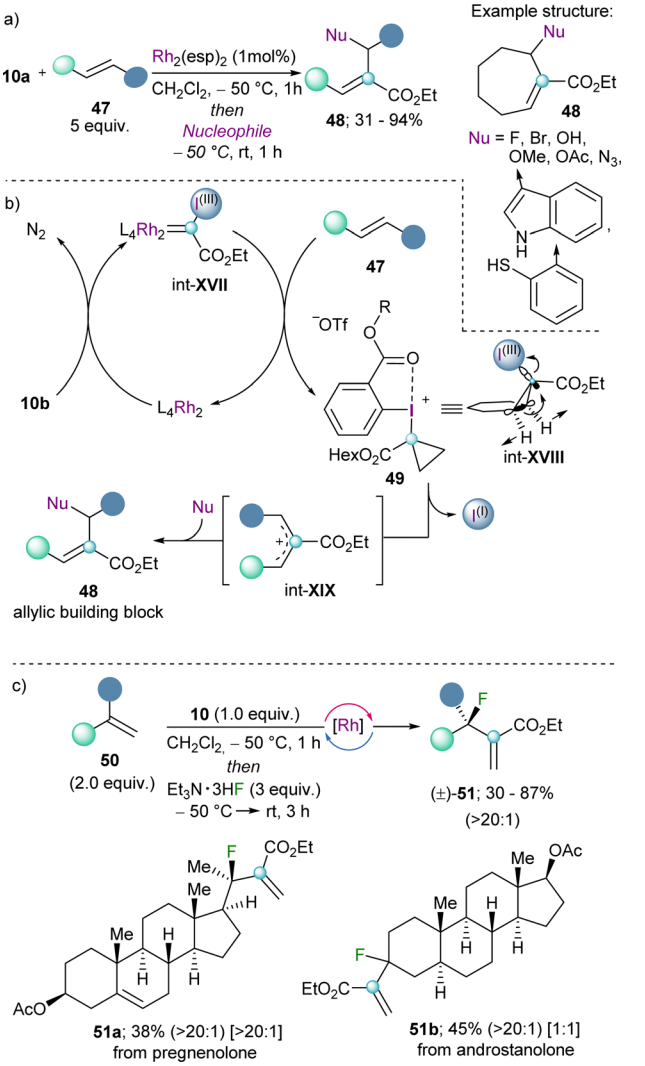
The group of Suero pioneered the work in this direction and published in 2019 a strategy to insert a carbon atom into the double bond of olefins by using the well-established dirhodium-catalyst $Rh_2(esp)_2$. Specifically, they discovered that after initial generation of a highly electrophilic Rh-carbynoid int-**XVII** by reaction of the Rh-catalyst with **10a**, insertion of the carbine into the C($sp^2$)–C($sp^2$) double bond generates the transient cyclopropyl-I$^{(III)}$ intermediate int-**XVIII**, which undergoes disrotatory electrocyclic ring-opening with concomitant elimination of the iodo arene fragment (Scheme 15a).[35] The mechanism of that step was studied in detail in the 60's of the twentieth century using cyclopropyl tosylates or bromides as model substrates.[36] Subsequent attack of nucleophiles to the allylic cation int-**XIX** delivers the corresponding building block **48.** The scope of the reaction is broad, and halides, alcohols, azide anions and electron rich arenes serve as productive nucleophiles.[35] By applying this methodology to terminal alkenes in combination with a fluoride source, the late-stage incorporation of fluorine-substituents to structurally complex olefins is also possible. Indeed, Suero has shown that this method provides access to the desired fluorinated targets with high selectivity towards the branched products (**51**) (Scheme 15c).[37]

Cyclopropenium cations **53** can also be synthesized using the same concept *via* the Rh-catalysed carbene addition to alkynes. The reaction seems to proceed by initial formation of cyclopropene intermediate int-**XX**, followed by elimination of the iodoarene moiety. This step is facilitated by the aromatization of the cyclopropenium cations, which were isolated with a variety of different substituents (**53**). Moreover, the addition of nucleophiles of different nature to **53** proceeds efficiently and is highly regioselective at the carbon atom that bears the ester functionality (Scheme 16).[38]

Finally, early in 2023 the group of Suero reported the reaction of unsaturated carboxylic acids with *in situ* generated int-**XVII** to form transient Fisher-type acyloxy Rh(II)-carbenes (int-**XXI**) in a catalytic fashion (Scheme 17a). The subsequent intramolecular alkene cyclopropanation of such intermediate leads to the formation of cyclopropyl-fused δ-lactones **56** with high diastereoselectivity (Scheme 17b). Moreover, complex tricyclic lactones (**56b**) could be obtained by using already cyclic alkenyl carboxylic acids as starting materials (Scheme 17c).[39]

## 4. α-Diazo sulfonium salts

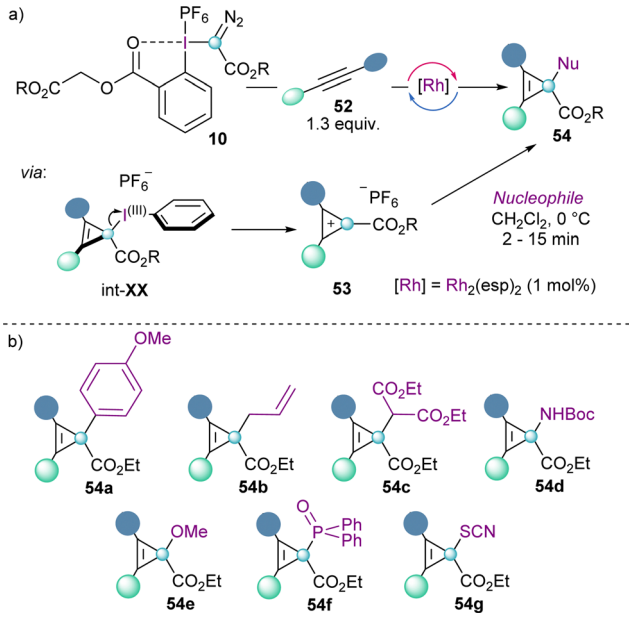
During the last years sulfonium salts have gained rising attention as versatile reagents in synthetic chemistry.[40] As mentioned in the



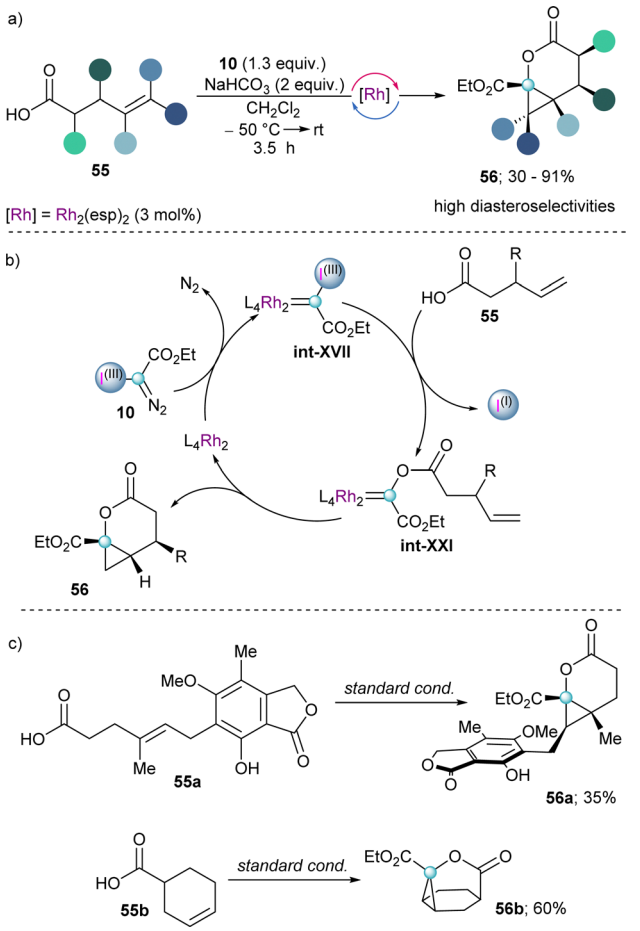

Scheme 15 (a) Catalytic scission of C(sp2)–C(sp2) by Rh-carbynoids. (b) Proposed mechanism for the construction of allylic building blocks. (c) Generation of fluorinated cuaternary stereocenters; branched/linear ratio, indicated in parentheses, diastereoselectivity ratio indicated in brackets.

introduction, they share many aspects of their reactivity with hypervalent I(III) reagents of analogue structure and, consequently, they are often employed as their surrogates.

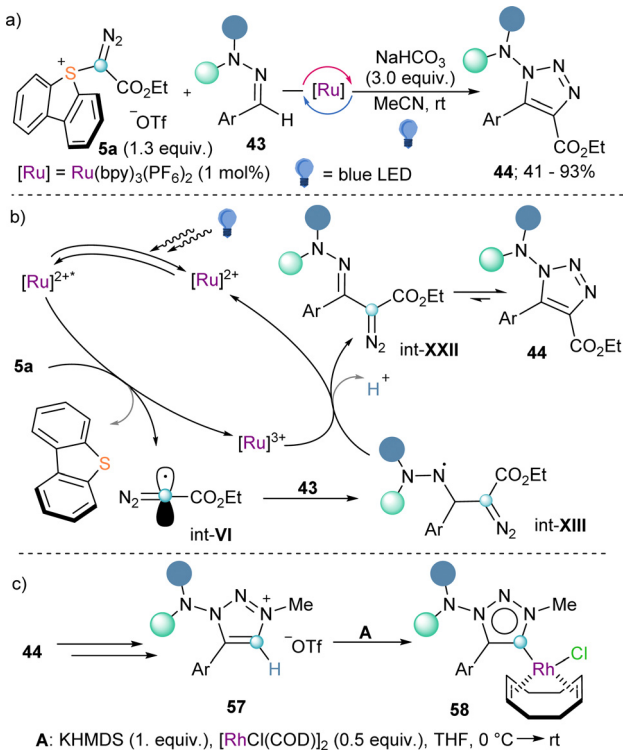
Awared of the synthetic versatility of reagents **9** and **10**, we asked ourselves about the possibility to prepare a sulfur(IV) based reagent bearing a diazoester substituent directly attached to the S-atom. Actually, the preparation of such structures was possible using the same synthetic strategy that we had previously developed for the synthesis of cyano-,[41] alkyne-,[42] and aryl-substituted[43] dibenzothiophenium salts. As originally hypothesized, α-diazo sulfonium triflate **5a** demonstrated to be a suitable precursor of diazomethyl radicals int-**VI** under photocatalytic conditions identical to those used for **9a** or **10a.** In addition, we were able to employ the electrophilic radical int-**VI** thus prepared on the synthesis of 1-amino-1,2,3-triazoles from hydrazones (Scheme 18a and b).[17] Interestingly, after *N*-alkylation, decarboxylation and deprotonation of **44**, we were




Scheme 16 Rh-catalysed synthesis of cyclopropenium cations *via* carbene insertion.



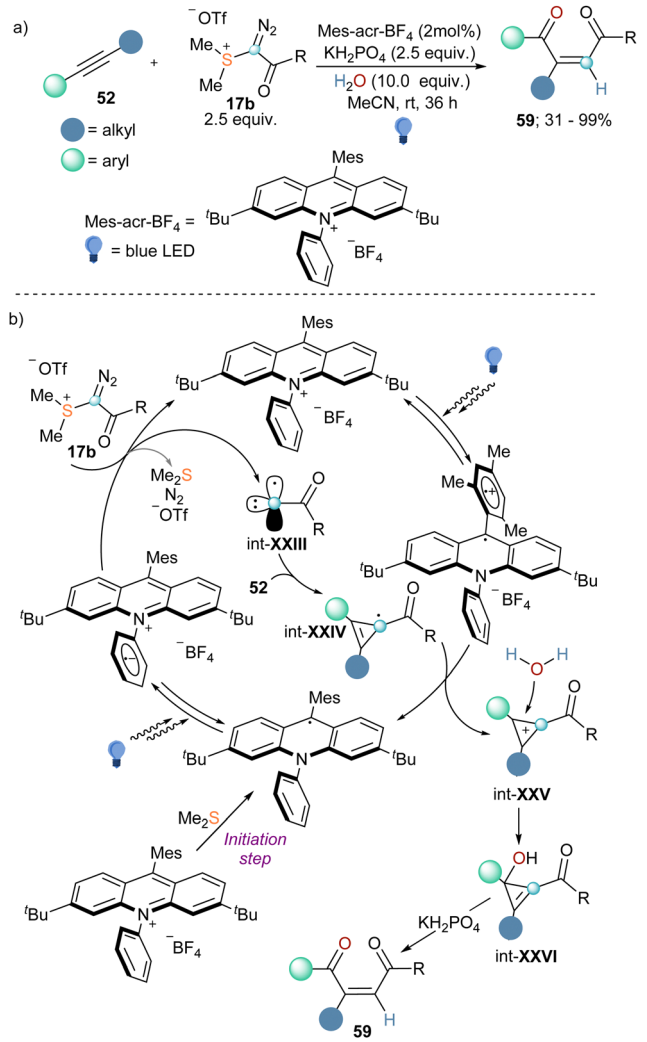

Scheme 17 (a) Rh-catalysed carbyne transfer with alkenyl carboxylic acids. (b) Proposed mechanism for the formation of a Fisher-type carbene with follow up intramolecular alkene cyclopropanation.




Scheme 18 (a) Photoredox catalysed 1-amino-1,2,3-triazole formation by α-diazo sulfonium salts and hydrazones. (b) Proposed mechanism of the 1-amino-1,2,3-triazole formation. (c) Utility as mesoionic 1-amino-1,2,3-triazol-4-ylidene ligands.

also able to obtain the corresponding 1-dialkylamino-1,2,3-triazolium salts **57**. These compounds were later used as mesoionic carbene precursors, and the corresponding Rh and Pd-complexes were prepared (Scheme 18c).[17,44]

Finally, in 2022 the group of Wang published the coupling of internal alkynes **52** with α-diazo sulfonium triflate **17b** in the presence of water to afford 1,4-dicarbonyl *Z*-alkenes (Scheme 19a).[45] Reagent **17b** had been first published by Weiss while studying the reactivity of compound **4a**, but it was not employed for any synthetic porpoise since then.[11] To understand how the reaction proceeds Wang and co-workers also conducted a variety of mechanistic investigations. The use of $^{18}O$-labelled and deuterated water as coupling partners in the reaction suggested that both the oxygen atom and the hydrogen one derived from water. Interestingly, when reagent **5a** was employed no conversion was detected, whereas the addition of $Me_2S$ to that reaction promoted the conversion of **52** into **59**, albeit in low yield. This observation together with cyclic voltammetry analyses and fluorescent quenching experiments indicate that $Me_2S$, which is generated *in situ* during the progression of the reaction, is needed for an initial single-electron reduction of the photo catalyst that initiates the catalytic cycle. The reduced photocatalyst can be excited once more and undergoes single-electron transfer with reagent **17b**, resulting in the formation of radical carbyne intermediate int-**XXIII**. By addition of this species into the C–C triple bond of the alkyne substrate, int-**XXIV** is formed, which is oxidized by




Scheme 19 (a) Formation of 1,4-dicarbonyl *Z*-alkenes by coupling of alkynes, α-diazo sulfonium triflate, and water under photoredox catalysis. (b) Proposed mechanism for the three-compound reaction towards 1,4-dicarbonyl *Z*-alkenes.

the excited photocatalyst to the corresponding cyclopropenium cation (int-**XXV**). This step also delivers the reduced form of the photocatalyst, closing the catalytic cycle. Subsequent attack of water to int-**XXV** followed by $KH_2PO_4$ assisted ring-opening of the corresponding cyclopropanol intermediate furnishes the *Z*-configurated 1,4-dicarbonyl alkenes **59** (Scheme 19b).[45]

## 5. Summary and outlook

α-Diazo-$\lambda^3$-iodanes combine on the same carbon atom two exceptionally versatile functionalities from a synthetic point of view; namely, an excellent leaving group and a masked carbene moiety. For this reason, it results difficult to understand why for the first 20 years after their introduction they were considered just curiosities, and practically ignored by the synthetic community. The answer to this question can be found in their reactive nature. Probably, the difficulty to control the reactivity of the first synthesized species of this type discouraged synthetic chemists from using them. It has not been until the change from the iodobenzene scaffold to the benziodoxolone one, and the subsequent development of the more stable α-diazo sulfonium salts that synthetic applications of these reagents have flourished. Nowadays, it is possible to selectively make react each of the two functionalities by controlling the reaction conditions. Especially useful in this regard has been the use of photocatalytic conditions to generate diazoalkyl radicals and the use of Rh catalysts able to transfer a carbene bearing an excellent leaving group as substituent. Just by gearing these two modes of reactivity we predict these compounds to find new applications in areas such as late-stage functionalization or (hetero)cycle editing. In addition, there are still several challenges ahead that deserve to be explored, such as the combination of (photochemically generated) diazoalkyl radicals with C–H activation strategies, the enantioselective transfer of the diazoalkyl or carbyne groups, or the design of stable and easy to handle "nitrene"-analogues of these reagents.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

Support from the European Research Council (ERC CoG 771295) and the University of Göttingen is gratefully acknowledged.

## Notes and references

1 A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire and M. A. McKervey, *Chem. Rev.*, 2015, **115**, 9981–10080.
2 (*a*) H.-U. Reissig and R. Zimmer, *Chem. Rev.*, 2003, **103**, 1151–1196; (*b*) H. Lebel, J.-F. Marcoux, C. Molinaro and A. B. Charette, *Chem. Rev.*, 2003, **103**, 977–1050.
3 (*a*) H. M. L. Davies and R. E. J. Beckwith, *Chem. Rev.*, 2003, **103**, 2861–2904; (*b*) H. M. L. Davies and S. J. Hedley, *Chem. Soc. Rev.*, 2007, **36**, 1109–1119; (*c*) M. P. Doyle, R. Duffy, M. Ratnikov and L. Zhou, *Chem. Rev.*, 2010, **110**, 704–724; (*d*) H. Lu and X. P. Zhang, *Chem. Soc. Rev.*, 2011, **40**, 1899–1909.
4 (*a*) S.-F. Zhu and Q.-L. Zhou, *Acc. Chem. Res.*, 2012, **45**, 1365–1377; (*b*) D. Gillingham and N. Fei, *Chem. Soc. Rev.*, 2013, **42**, 4918–4931.
5 J. Fink and M. Regitz, *Synthesis*, 1985, 569–585.
6 (*a*) T. V. Baiju and I. N. N. Namboothiri, *Chem. Rec.*, 2017, **17**, 939–955; (*b*) M. Breugst and H.-U. Reissig, *Angew. Chem., Int. Ed.*, 2020, **59**, 12293–12307.
7 A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648–5652.
8 (*a*) F. Weigend and R. Alrichs, *Phys. Chem. Chem. Phys.*, 2005, **7**, 3297–3305; (*b*) F. Weigend, *Phys. Chem. Chem. Phys.*, 2006, **8**, 1057–1065.
9 Calculations were performed using Gaussian16, Revision A.03.; M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scal-mani, V. Barone, G. A. Petersson, H. Nakatsuji, *et al.*, *Gaussian 16 Rev. A.03*, Wallingford, CT, 2016.
10 S. P. Green, K. M. Wheelhouse, A. D. Payne, J. P. Hallett, P. W. Miller and J. A. Bull, *Org. Process Res. Dev.*, 2020, **24**, 67–84.
11 R. Weiss, J. Seubert and F. Hampel, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1952–1953.
12 (*a*) V. V. Zhdankin and J. D. Protasiewicz, *Coord. Chem. Rev.*, 2014, **275**, 54–62; (*b*) S. V. Kohlhepp and T. Gulder, *Chem. Soc. Rev.*, 2016, **45**, 6270–6288; (*c*) S. Alazet, J. Preindl, R. Simonet-Davin, S. Nicolai, A. Nanchen, T. Meyer and J. Waser, *J. Org. Chem.*, 2018, **83**, 12334–12356.

13 L. Jiang, Z. Wang, M. Armstrong and M. G. Suero, *Angew. Chem., Int. Ed.*, 2021, **60**, 6177–6184.
14 (*a*) V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, M. S. Formaneck and J. T. Bolz, *Tetrahedron Lett.*, 1994, **35**, 9677–9680; (*b*) A. P. Krasutsky, C. J. Kuehl and V. V. Zhdankin, *Synlett*, 1995, 1081–1082; (*c*) Y. Kita, S. Akai, T. Okuno, M. Egi, T. Takada and H. Tohma, *Heterocycles*, 1996, **42**, 47; (*d*) V. V. Zhdankin, A. P. Krasutsky, C. J. Kuehl, A. J. Simonsen, J. K. Woodward, B. Mismash and J. T. Bolz, *J. Am. Chem. Soc.*, 1996, **118**, 5192–5197; (*e*) V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2008, **108**, 5299–5358; (*f*) V. V. Zhdankin, *Hypervalent Iodine Chemistry*, John Wiley & Sons Ltd, Chichester, UK, 2013.
15 Z. Wang, A. G. Herraiz, A. M. Del Hoyo and M. G. Suero, *Nature*, 2018, **554**, 86–91.
16 T. A. Podrugina, A. S. Pavlova, D. S. Vinogradov, M. V. Shuvalov, I. D. Potapov, I. I. Levina, A. V. Mironov and R. Gleiter, *Russ. Chem. Bull.*, 2019, **68**, 284–292.
17 X. Li, C. Golz and M. Alcarazo, *Angew. Chem., Int. Ed.*, 2021, **60**, 6943–6948.
18 D. B. Cowie, G. N. Cohen, E. T. Bolton and H. de Robichin-Szulmajster, *Biochim. Biophys. Acta*, 1959, **34**, 39–46.
19 R. L. Levine, J. Moskovitz and E. R. Stadtman, *IUBMB Life*, 2000, **50**, 301–307.
20 M. T. Taylor, J. E. Nelson, M. G. Suero and M. J. Gaunt, *Nature*, 2018, **562**, 563–568.
21 C. Schnaars, M. Hennum and T. Bonge-Hansen, *J. Org. Chem.*, 2013, **78**, 7488–7497.
22 M. Regitz, *Ann. Chem. Pharm.*, 1964, **676**, 101–109.
23 H. Huang, X. Zou, S. Cao, Z. Peng, Y. Peng and X. Wang, *Org. Lett.*, 2021, **23**, 4185–4190.
24 M. A. Ansari, G. Kumar and M. S. Singh, *Org. Lett.*, 2022, **24**, 2815–2820.
25 L. Devi, P. Kumar, R. Kant and N. Rastogi, *Chem. Commun.*, 2022, **58**, 7062–7065.
26 M. A. Ansari, S. Khan, S. Ray, G. Shukla and M. S. Singh, *Org. Lett.*, 2022, **24**, 6078–6082.
27 (*a*) T. Do Minh, H. E. Gunning and O. P. Strausz, *J. Am. Chem. Soc.*, 1967, **89**, 6785–6787; (*b*) O. P. Strausz, D. M. Thap and J. Font, *J. Am. Chem. Soc.*, 1968, **90**, 1930–1931; (*c*) O. P. Strausz, G. J. A. Kennepohl, F. X. Garneau, T. DoMinh, B. Kim, S. Valenty and P. S. Skell, *J. Am. Chem. Soc.*, 1974, **96**, 5723–5732; (*d*) T. B. Patrick and G. H. Kovitch, *J. Org. Chem.*, 1975, **40**, 1527–1528; (*e*) T. B. Patrick and T.-T. Wu, *J. Org. Chem.*, 1978, **43**, 1506–1509.
28 Y. Yamaguchi and H. Schaefer, *J. Chem. Phys.*, 2004, **120**, 9536–9546.
29 X. Ma, A. Sun and K.-K. Wang, *New J. Chem.*, 2022, **46**, 6856–6859.
30 L. Liu, Y. Zhang, W. Zhao, J. Wen, C. Dong, C. Hu and J. Li, *Org. Lett.*, 2023, **25**, 592–596.
31 J.-Y. Dong, H. Wang, S. Mao, X. Wang, M.-D. Zhou and L. Li, *Adv. Synth. Catal.*, 2021, **363**, 2133–2139.
32 J. Wen, W. Zhao, X. Gao, X. Ren, C. Dong, C. Wang, L. Liu and J. Li, *J. Org. Chem.*, 2022, **87**, 4415–4423.
33 J. Li, X.-C. Lu, Y. Xu, J.-X. Wen, G.-Q. Hou and L. Liu, *Org. Lett.*, 2020, **22**, 9621–9626.
34 W.-W. Zhao, Y.-C. Shao, A.-N. Wang, J.-L. Huang, C.-Y. He, B.-D. Cui, N.-W. Wan, Y.-Z. Chen and W.-Y. Han, *Org. Lett.*, 2021, **23**, 9256–9261.
35 Z. Wang, L. Jiang, P. Sarró and M. G. Suero, *J. Am. Chem. Soc.*, 2019, **141**, 15509–15514.
36 (*a*) M. S. Baird, D. G. Lindsay and C. B. Reese, *J. Chem. Soc. C*, 1969, 1173; (*b*) P. von, R. Schleyer, G. W. van Dine, U. Schöllkopf and J. Paust, *J. Am. Chem. Soc.*, 1966, **88**, 2868–2869; (*c*) M. Fedoryński, *Chem. Rev.*, 2003, **103**, 1099–1132.
37 L. Jiang, P. Sarró, W. J. Teo, J. Llop and M. G. Suero, *Chem. Sci.*, 2022, **13**, 4327–4333.
38 H.-F. Tu, A. Jeandin and M. G. Suero, *J. Am. Chem. Soc.*, 2022, **144**, 16737–16743.
39 E. Palomo, A. K. Sharma, Z. Wang, L. Jiang, F. Maseras and M. G. Suero, *J. Am. Chem. Soc.*, 2023, **145**, 4975–4981.
40 (*a*) D. Kaiser, I. Klose, R. Oost, J. Neuhaus and N. Maulide, *Chem. Rev.*, 2019, **119**, 8701–8780; (*b*) S. I. Kozhushkov and M. Alcarazo, *Eur. J. Inorg. Chem.*, 2020, 2486–2500; (*c*) A. Péter, G. J. P. Perry and D. J. Procter, *Adv. Synth. Catal.*, 2020, **362**, 2135–2142; (*d*) L. van Dalsen, R. E. Brown, J. A. Rossi-Ashton and D. J. Procter, *Angew. Chem., Int. Ed.*, 2023, e202303104.
41 X. Li, C. Golz and M. Alcarazo, *Angew. Chem., Int. Ed.*, 2019, **58**, 9496–9500.
42 (*a*) B. Waldecker, F. Kraft, C. Golz and M. Alcarazo, *Angew. Chem., Int. Ed.*, 2018, **130**, 12718–12722; (*b*) K. Kafuta, C. J. Rugen, T. Heilmann, T. Liu, C. Golz and M. Alcarazo, *Eur. J. Org. Chem.*, 2021, 4038–4048.
43 (*a*) K. Kafuta, A. Korzun, M. Böhm, C. Golz and M. Alcarazo, *Angew. Chem., Int. Ed.*, 2020, **59**, 1950–1955; (*b*) M. H. Aukland, M. Šiaučiulis, A. West, G. J. P. Perry and D. J. Procter, *Nat. Catal.*, 2020, **3**, 163–169; (*c*) P. Xu, D. Zhao, F. Berger, A. Hamad, J. Rickmeier, R. Petzold, M. Kondratiuk, K. Bohdan and T. Ritter, *Angew. Chem., Int. Ed.*, 2020, **59**, 1956–1960; (*d*) S. Karreman, S. B. H. Karnbrock, S. Kolle, C. Golz and M. Alcarazo, *Org. Lett.*, 2021, **23**, 1991–1995.
44 Á. Vivancos, C. Segarra and M. Albrecht, *Chem. Rev.*, 2018, **118**, 9493–9586.
45 X. Wang, W.-Y. Tong, B. Huang, S. Cao, Y. Li, J. Jiao, H. Huang, Q. Yi, S. Qu and X. Wang, *J. Am. Chem. Soc.*, 2022, **144**, 4952–4965.