A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

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Accepted Article

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To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.202015077

Link to VoR: https://doi.org/10.1002/anie.202015077

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RESEARCH ARTICLE

β-Diazocarbonyl compounds: synthesis and their Rh(II)-catalyzed 1,3 C-H insertions

Liyin Jiang[a], Zhaofeng Wang[a], Melanie Armstrong[a], and Marcos G. Suero[a]*

Dedicated to the memory of Professor Kilian Muñiz

[a] Dr. L. Jiang, Dr. Z. Wang, M. Armstrong, Prof. M. G. Suero
Institute of Chemical Research of Catalonia (ICIQ), Barcelona Institute of Science and Technology
Av. Països Catalans 16 – 43007 Tarragona (Spain)
E-mail: mgsuero@icig.es

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Abstract: Herein, we describe the first electrophilic diazomethylation of ketone silyl enol ethers with diazomethyl-substituted hypervalent iodine reagents that gives access to unusual β-diazocarbonyl compounds. The potential of this unexplored class of diazo compounds for the development of new reactions was demonstrated by the discovery of a rare Rh-catalyzed intramolecular 1,3 C–H carbene insertion that led to complex cyclopropanes with excellent stereocontrol.

Introduction

Since Curtius reported the synthesis of ethyl diazoacetate for the first time in 1883,[1] α-diazocarbonyl compounds have found broad applications in chemical synthesis,[2] chemical biology[3] as well as in the directed evolution of enzymes (Scheme 1a).[4] The long-lasting success of α-diazocarbonyl reagents has been underpinned by the discovery and development of general and efficient synthetic routes for their preparation.[2e],[5]

A key feature of α-diazocarbonyl compounds is their ability to generate reactive free carbenes or transition-metal-carbene(carbenoid) species, upon thermal, photonic or transition-metal catalyst activation. Some of the most important advances in the field of C–H functionalization rely on the use of dirhodium paddlewheel complexes and α-diazocarbonyl compounds to catalytically generate Rh-carbene species, which showed efficient site- and stereoselective C–H functionalization of simple and complex molecules.[6]

In contrast, β-diazocarbonyl compounds have been underexplored and overlooked for years, mainly due to the lack of synthetic procedures (Scheme 1a). In fact, to the best of our knowledge, only one synthetic protocol has been reported by Barluenga, López and co-workers in 2011 and is based on a Cu(II)-catalyzed oxidative rearrangement of vinyl diazo derivatives with iodosylbenzene (Scheme 1b).[7] The products obtained are functionalized with an ester group at the β position, which enables stability to the diazo function. The method is particularly efficient in the synthesis of β-diazocarbonyl compounds unsubstituted in alfa position. However, lower yields or no reaction is observed for the synthesis of mono or disubstituted derivatives, respectively. In addition, an study of the functional group tolerance of the process and the synthesis of β-diazocarbonyl compounds from complex natural products as starting materials was not reported. The authors also showed that this diazo compound class can be used in classic intermolecular Rh(II)-catalysed carbene transfer reactions for alkene cyclopropanation, O–H insertion, as well as arylation with phenyl boronic acid.

Taking into account the impact of α-diazocarbonyl compounds in chemical science and the potential untapped synthetic applications of β-diazocarbonyl derivatives, we sought to develop a general strategy relying on the coupling of ketones, via the corresponding enol/enolate, with an electrophilic diazomethyl source (Scheme 1c). In contrast to the Barluenga strategy that relied in vinyl diazo derivatives, the disconnection proposed would be convergent and conceptually the simplest possible. It would rely on the use of ketone building blocks, which are one of the most structurally diverse, useful and commercially available starting materials. If successful, this simple protocol would give immediate access to unexplored β-diazocarbonyl compounds to the broad synthetic community working in reaction discovery and development, natural product synthesis and (bio)catalysis.

Recently, our group reported the synthesis of a new class of cyclic and pseudocyclic hypervalent iodine reagents substituted with diazomethyl groups and exploited them in photocatalytic arene C–H bond diazomethylations via diazomethyl radicals;[8] and in the catalytic cleavage of C–C double bonds with Rh-carbynoids.[9],[10] In 1994, the group of Weiss reported the synthesis of the parent linear hypervalent iodine derivate and demonstrated its ability to react with nucleophiles such as sulfides, phosphines or amines.[11] More recently, the groups of Bonge-Hansen[12] and Gaunt[13] demonstrated applications of the linear hypervalent iodine reagents in nucleophilic halogenations and in a methionine bioconjugation of peptides and proteins, respectively.[14]

Considering that this unusual class of hypervalent iodine reagents can serve as an electrophilic diazomethyl source, we anticipated that silyl enol ethers derived from ketones could be suitable nucleophiles. In fact, silyl enol ethers are known to react with hypervalent iodine reagents and deliver α-substituted carbonyl compounds.[15] Herein, we present the successful execution of this concept for a new synthesis of β-diazocarbonyl compounds. The synthetic method is general, simple to perform, relatively fast, occurs at room temperature and does not require a transition-metal catalyst (Scheme 1d). In addition, we found that β-diazocarbonyl compounds can be converted into cyclopropanes

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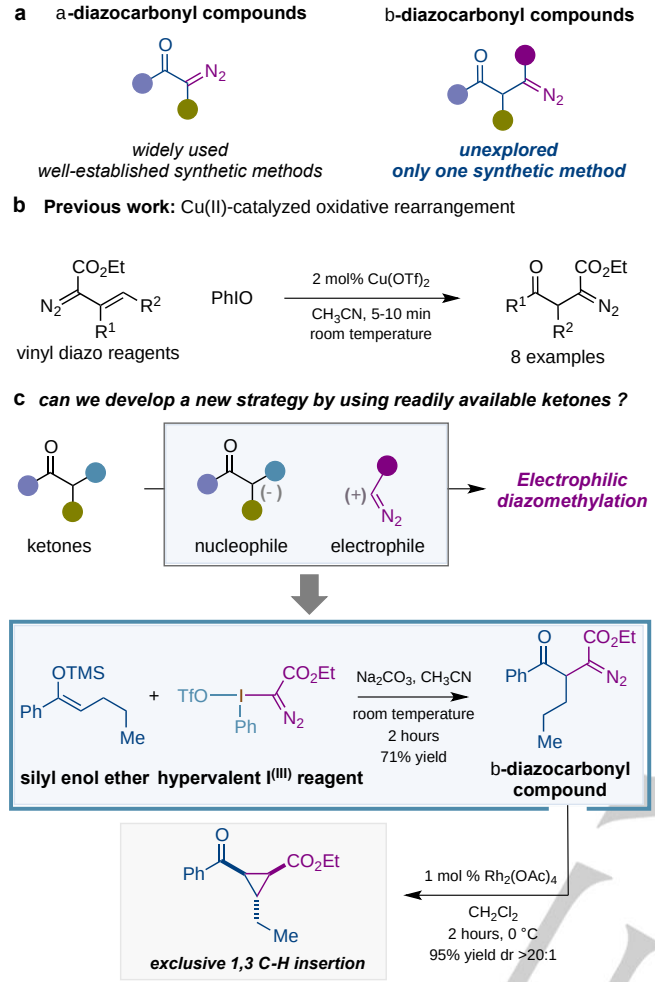
by an unusual diastereoselective 1,3 C–H carbene insertion with Rh(II) catalysis.



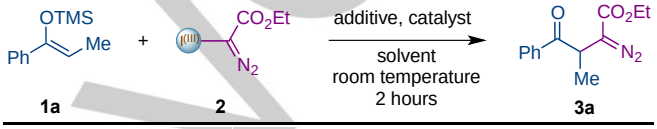
Scheme 1. General synthesis of β-diazocarbonyl compounds by electrophilic diazomethylation and their use in cyclopropane synthesis by Rh_2-catalyzed 1,3 C–H carbene insertion (**a-c**).

Results and Discussion

The feasibility of the envisaged coupling was initially evaluated with propiophenone silyl enol ether **1a** (1.25 equiv.) with benziodoxolone-based hypervalent iodine reagent **2a** (1 equiv.) in acetonitrile at room temperature and sodium benzoate (1 equiv.) was added as additive to quench TMSOTf sub-product (Table 1). After 2 hours, conversion to **3a** was not observed and longer reaction times conducted to decompositions of the silyl enol ether **1a** (entry 1). It is well-known that the electrophilicity of benziodoxolone-based reagents can be enhanced with Lewis acid catalysts.[10e] In fact, we reported that $Zn(NTf_2)_2$ catalyst had a crucial role in our photocatalytic arene C–H bond diazomethylation with **2a**.[8] However, we did not observe any conversion to **3a** when using zinc catalysts as well as with scandium or rhenium catalysts (entry 2-5). Then, we turned our efforts to evaluate whether the structural nature of the hypervalent iodine core would be key in the reaction. Neither benziodoxole-based reagent **2b** nor pseudo-cyclic derivative **2c** were successful (entries 6,7). In contrast, we observed a promising 38% ^{1}H-NMR yield when using the more electrophilic linear reagent **2d** (entry 8).

After this, we observed a significant increment on efficiency by degasifying the reaction mixture (entry 9) and among the solvents screened, CH_3CN was the best so far (entry 10-17). We then screened a range of carboxylate, phosphate or carbonate additives (entry 18-25) and found that Na_2CO_3 provided better yields (entry 25). Control experiments showed the necessity of using an additive in the reaction (entry 26), since we proved in a control experiment that TMSOTf decomposed the diazo product **3a**. Finally, we observed a positive effect in the efficiency of the reaction when we scaled-up from 0.20 mmol to 0.60 mmol of **2d**. **3a** was obtained in 81% isolated yield after purification by flash chromatographic column (entry 27).[16]

Table 1. Optimization studies.[a]



Entry	2	catalyst	solvent	Additive	Yield **3a** [%][b]
1	**2a**	-	CH_3CN	NaO_2CPh	0
2	**2a**	$Zn(OTf)_2$	CH_3CN	NaO_2CPh	0
3	**2a**	$Zn(NTf_2)_2$	CH_3CN	NaO_2CPh	0
4	**2a**	$Sc(OTf)_3$	CH_3CN	NaO_2CPh	0
5	**2a**	ReO_3Me	CH_3CN	NaO_2CPh	0
6	**2b**	-	CH_3CN	NaO_2CPh	0
7	**2c**	-	CH_3CN	NaO_2CPh	0
8	**2d**	-	CH_3CN	NaO_2CPh	38
9	**2d**	-	CH_3CN	NaO_2CPh	59[c]
10	**2d**	-	CH_2Cl_2	NaO_2CPh	19[c]
11	**2d**	-	THF	NaO_2CPh	27[c]
12	**2d**	-	acetone	NaO_2CPh	32[c]
13	**2d**	-	DMF	NaO_2CPh	20[c]
14	**2d**	-	Et_2O	NaO_2CPh	23[c]
15	**2d**	-	EtOAc	NaO_2CPh	0[c]
16	**2d**	-	toluene	NaO_2CPh	0[c]
17	**2d**	-	MeOH	NaO_2CPh	23[c]
18	**2d**	-	CH_3CN	NaO_2CCH_2Ph	24[c]
19	**2d**	-	CH_3CN	$NaO_2CC_6H_4$(*p*-OH)	48[c]
20	**2d**	-	CH_3CN	NaOAc	57[c]
21	**2d**	-	CH_3CN	KOAc	27[c]
22	**2d**	-	CH_3CN	K_3PO_4	44[c]
23	**2d**	-	CH_3CN	K_2CO_3	69[c]
24	**2d**	-	CH_3CN	Cs_2CO_3	0[c]
25	**2d**	-	CH_3CN	Na_2CO_3	72[c]
26	**2d**	-	CH_3CN	-	24[c]
27	**2d**	-	CH_3CN	Na_2CO_3	85(81)[c],[d]

[a] Reaction conditions: **1a** (0.25 mmol), **2a-d** (0.20 mmol), additive (0.20 mmol), catalyst (10 mol %), solvent (1 mL). [b] ^{1}H-NMR yields calculated using mesitylene as internal standard. [c] the reaction mixture was degassed under

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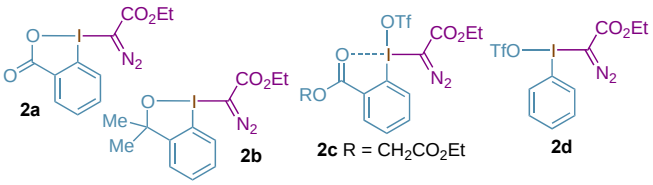
argon. [d] Yield of the isolated product **3a** using **1a** (0.60 mmol), **2d** (0.50 mmol), Na_2CO_3 (0.60 mmol), CH_3CN (2 mL).



With the optimized reaction conditions, we evaluated the scope of the electrophilic diazomethylation using non-terminal ketone silyl enol ethers and reagent **2d** (Table 2). We were delighted to find that our protocol permitted access to β-diazocarbonyl compounds substituted in α position with simple alkyl chains (**3b-e**) as well as with a range of useful functionalities, including alkene, alkyne, phenyl, alcohol, chlorine and esters (**3f-l**). The use of tetrasubstituted silyl enol ethers led to the formation of β-diazocarbonyl compounds which are doubly-substituted at α position (**3m-q,3s**). In addition, cyclic silyl enol ethers derived from benzocyclopentanone were well tolerated (**3r,s**). It is worth highlighting that compound **3s** exemplifies the ability of this method to reach diazo compounds α-substituted with all-carbon quaternary stereogenic centers. Such structural motifs are hardly inaccessible by classical or modern diazo synthesis.[17]

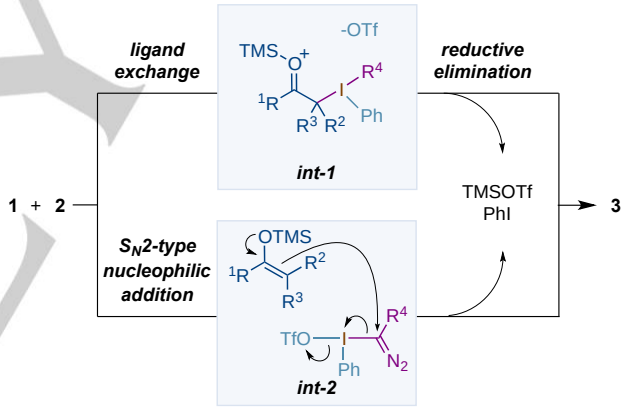
On the other hand, the substitution of the aromatic ring of the silyl enol ether in (**3t-w**) or the use of heterocycles such as furane (**3z**) did not influence the efficiency of the electrophilic diazomethylation. Terminal silyl enol ethers worked well (**3y-ah**) and β-diazocarbonyl compounds from acetone, 3-pentanone and cyclohexanone could be obtained albeit in lower yields (**3ai**, **3aj,3ak**). Unfortunately, silyl enol ethers derived from esters or aldehydes did not work under the optimized reaction conditions. However, we were able to introduce the versatile Donohoe pentamethylphenyl (Ph*) acyl protecting group (**3x**), which could be derivatized into esters, aldehydes, alcohols, amides, carboxylic acids or aldehydes under relative mild conditions.[18]

Then, we explored the scope of the linear hypervalent iodine reagents **2**. We successfully demonstrated the introduction of alternative alkyl substituents in the ester group such as benzyl, *t*-butyl, 2,2,2-trichloroethyl and (–)-menthyl [**3al-n**,(±)-**3ao**]. Importantly, we were able to synthesize β-diazocarbonyl compounds substituted with ketone, phosphonate, trifluoromethyl and sulphonate groups (**3ap-au**). These results clearly underline the high modularity of our approach to the synthesis of β-diazocarbonyl compounds.

In 2018, our group demonstrated the late-stage radical C–H bond diazomethylation of drug molecules/natural products and its application in the construction of chiral centers, by exploiting a broad range of known catalytic carbene insertion reactions.[8] The installation of a substituted diazomethyl group at the β position of complex ketone derivatives may be of utility for streamlining the synthesis of libraries of analogues.[19] Here we show four examples of an electrophilic diazomethylation reaction using flavanone, testosterone, jasmone and donezepil derivative (**3av-ay**).

Our methodology in comparison with the Barluenga rearrangement of vinyl diazo compounds demonstrated to be a more general approach.[7] Our new process surpasses the main limitations of the Barluenga protocol with regards to the (1) generality, (2) substitution patterns, (3) functional group tolerance, (4) late-stage functionalization of natural products and drug molecules. The key for success has been basically due to the convergent coupling strategy based on the unique reactivity of the diazomethyl-substituted hypervalent iodine reagents and the employment of ketone silyl enol ethers as nucleophiles. Furthermore, the diversity and availability of the latter reagents, that can be made by robust synthetic protocols, is in sharp contrast with vinyl diazo compounds.[2e]

Two possible mechanisms can be envisaged for the diazomethylation reaction of silyl enol ethers (Scheme 2). The first possibility could involve a ligand exchange of the triflate anion with the silyl enol ether to form ***int-1*** and then a subsequent reductive elimination would form the product and iodobencene. This possibility is aligned with a widely accepted mechanism for coupling of nucleophiles and hypervalent iodine reagents.[10] The second mechanism would involve a S_N2-type nucleophilic reaction of the silyl enol ether at the diazo carbon via ***int-2*** with concomitant elimination of PhI and triflate.[12] We proposed also this possibility based on the DFT calculations performed by the group of Bonge-Hansen with the same class of linear hypervalent iodine reagents and neutral or charged nucleophiles. The calculations showed that the nucleophilic addition can occur directly at the diazo carbon by a S_N2-type mechanism (with Me_2S and Et_3N) or by a carbonyl-like addition−elimination reaction (with bromide).[20] At present, we do not have any evidence that support one of the above mentioned mechanisms.[21]



Scheme 2 Mechanism proposals

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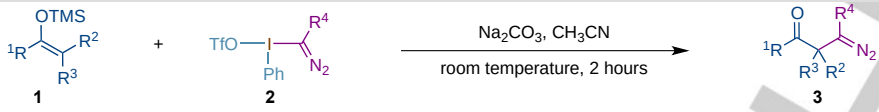
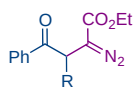
Table 2. Scope of the electrophilic diazomethylation of ketone silyl enol ethers **1** with hypervalent iodine reagents **2**.[a]

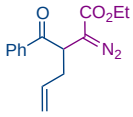


1 **2** **3**

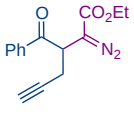
enol ether scope



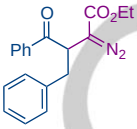
3b R = Et, 88%
3c R = *n*-propyl, 71%
3d R = *iso*-propyl, 65%
3e R = *iso*-pentyl, 79%



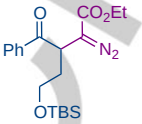
3f 61%



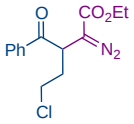
3g 70%



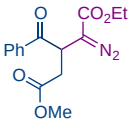
3h 66%



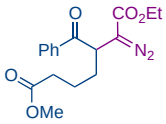
3i 74%



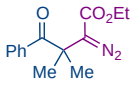
3j 64%



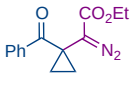
3k 71%



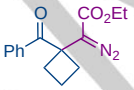
3l 60%



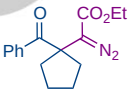
3m 66%



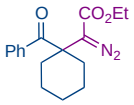
3n 74%



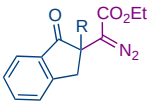
3o 84%



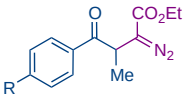
3p 64%



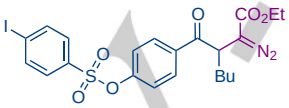
3q 62%



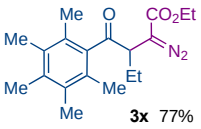
3r R = H, 84%
3s R = Me, 76%



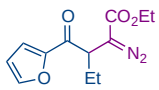
3t R = OMe, 75%
3u R = Me, 78%
3v R = Cl, 77%



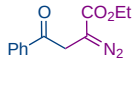
3w 53% [*x-ray*]



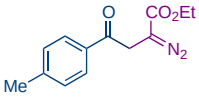
3x 77%



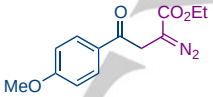
3y 63%



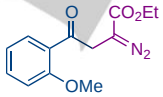
3z 79% (71%)[b]



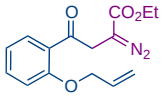
3aa 81%



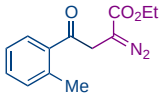
3ab 75%



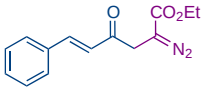
3ac 85%



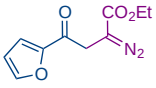
3ad 69%



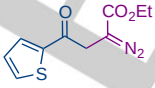
3ae 77%



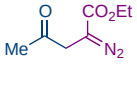
3af 88%



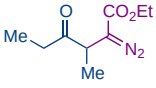
3ag 70%



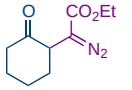
3ah 73%



3ai 60%

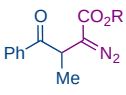


3aj 44%

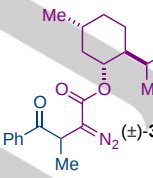


3ak 25%

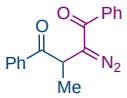
reagent scope



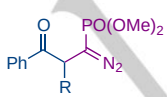
3al R = CO_2Bn, 82%
3am R = CO_2tBu, 81%
3an R = $CO_2CH_2CCl_3$, 67%



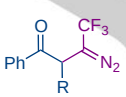
(±)-**3ao** 84% (1:1)



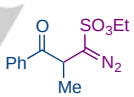
3ap 92%



3aq R = Me, 91%
3ar R = Pr, 87%

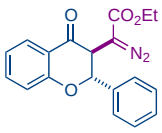


3as R = Me, 82%
3at R = Pr, 77%

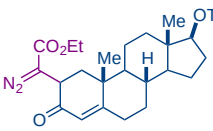


3au 71%

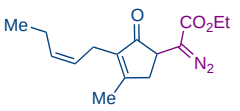
late-stage functionalization



3av 62% (8:1) from flavanone



(±)-**3aw** 44% (1:1) from testosterone



3ax 33% from jasmone

3ay 27% from donezepil

[a] Reaction conditions: silyl enol ether **1** (0.50 mmol), reagent **2d** (0.60 mmol), Na_2CO_3 (0.60 mmol), CH_3CN (2 mL), room temperature, 2 hours. Reported yields are of isolated product after purification by flash chromatographic column with silica gel. [b] Yield in parenthesis of isolated product using 1.4 grams of acetophenone trimethylsilyl enol ether and 2.8 grams of **2d.**

10.1002/anie.202015077

The intramolecular carbene C–H insertion with diazo compounds catalyzed by paddlewheel dirhodium carboxylate catalysts has been of great importance in the effective construction of complex carbocycles.[2] Diazo compounds substituted with a free-rotation linear carbon chain often conduct to five-membered rings via 1,5 C–H insertion.[22] We wondered whether the β-diazocarbonyl compounds **3** could be transformed in complex cyclopentanes using Rh_2 catalysis. To our surprise, when we performed a reaction using **3c** and simple $Rh_2(OAc)_4$ in dichloromethane at 0 ºC, we found the exclusive formation of cyclopropane **4a** with excellent yield and as a single diastereoisomer via 1,3 C–H insertion (Table 3A, 95% yield, >20:1). Interestingly, a similar outcome was observed when we used more electrophilic catalysts such as $Rh_2(TFA)_4$ (TFA = trifluoroacetate) or the bulkier $Rh_2(TPA)_4$ (TPA = triphenylacetate).

The 1,3 C–H carbene insertion is a rare behavior and has only been observed in structurally rigid diazo compounds,[23] and to the best of our knowledge, only one report is described for a freely rotating chain system.[24] We believe that formation of cyclopropane **4a** as single isomer where both carbonyl functions are in *cis* disposition, may involve the generation of the reacting conformation ***int-3***, where the ester at C1 and the propyl substituent at C3 are displayed in pseudo-axial and pseudo-equatorial, respectively, to prevent steric clashes. In conformation ***int-3*** the Rh-carbene and the pseudo-equatorial C–H bond at C3 are in close proximity and that could be explaining the excellent levels of regio and diastereoselectivity.

This 1,3 C–H insertion also occurred in β-diazocarbonyl compounds substituted with shorter carbon chains and the cyclopropanes were generally obtained with high efficiency and excellent diasteroselectivities (**4b-f**). However, we observed that compound **3e** substituted with a longer carbon chain led to an equimolecular ratio of 1,3 and 1,5 C–H insertion products (**4g,5**). We rationalized that the use of a bulkier catalysts may hamper the 1,5 C–H insertion and in consequence favors the 1,3 C–H insertion. In this sense, when we used $Rh_2(TPA)_4$, we were delighted to see a dramatic increment of the ratio in favor of the 1,3 C–H insertion and efficiency of the process (82%, **4f:5** 12:1).[25]

After this, we explored substrates containing functionalities that could potentially intercept the corresponding electrophilic Rh_2-carbene intermediate through well-known transformations such as alkene cyclopropanation, Buchner reaction, arene C–H insertions or ylide generation by carbonyl addition. However, we were glad to not observe those processes and instead, the exclusive formation of cyclopropanes **4h-j**. The latter results clearly suggest that those processes are unfavored due to the reacting conformations analogous to ***int-3*** that favors the 1,3 C–H insertion process. In addition, the use of β-diazocarbonyl compounds substituted with trifluoromethyl and phosphate group conducted to valuable cyclopropane rings **4k,l**.

On the other hand, β-hydride migration is a well-known process observed for α-alkyl-substituted α-diazo compounds under Rh_2 catalysis that conducts to olefins. β-hydride migration can be generally suppressed by the use of sterically demanding carboxylate ligands in the Rh_2 catalyst and low reaction temperatures (–78 ºC).[26] We generally did not observe β-hydride migration and this might be due to the electron-withdrawing character of the carbonyl group in **3**. It is worth mentioning that Barluenga did not observed β-hydride migration in classic Rh-catalyzed transformations showed for β-diazocarbonyl compounds. In our case, the only example that showed such migration from the β-diazocarbonyl compounds tested is **3a** (Table 3C) with $Rh_2(OAc)_4$ as catalyst. We found that the reaction led to cyclopropane **4m** and to olefin **6** in significant yield. The β-hydride migration in ***int-4*** can now be observed probably because the 1,3 C–H insertion occurs in the less reactive methyl C–H bond. However, we were able to mitigate the β-hydride migration pathway by using $Rh_2(TPA)_4$ at –60 ºC. Olefin **6** was formed in 4% yield and cyclopropane **4m** was obtained with even higher efficiency.

On the other hand, another competitive pathway found to the 1,3 C–H insertion was the 1,2-alkyl shift rearrangement. Benzocyclopentane **3s** conducted to spirocycle **4m** as the minor product when $Rh_2(OAc)_4$ was used. The major product found was naphtol **7** formed by a cyclopentane ring-expansion in ***int-5*** via selective 1,2-migration of the carbonyl group. This migration was fully suppressed by using $Rh_2(TPA)_4$ and **4m** was obtained as the only reaction product. In contrast to this, no 1,3 C–H insertion was observed when using derivative **3n**. Both catalysts, $Rh_2(OAc)_4$ and $Rh_2(TPA)_4$, enabled the synthesis of cyclobutene **8** by a well-known cyclopropyl carbene ring-expansion of ***int-6***.[27]

The new stereoselective cyclopropane synthesis represents a new strategy to construct cyclopropane cores from α & β C–H bonds in aliphatic ketones.[28] The use of two C–H bonds as functional groups for the synthesis of this privileged core is relative unusual.[29] This is in sharp contrast with the large variety of synthetic methods based on metal-catalyzed C–H bond functionalization that access larger cyclic molecules.[30]

Cyclopropanes **4** show a *cis* disposition of the carbonyl function from the ketone with the electron-withdrawing group (ester, CF_3, phosphate) alfa to the diazo functionality, and that relative configuration has been confirmed by single-crystal x-ray diffraction analysis (**4i,k**; Table 3). Our process complement more direct cyclopropane synthesis substituted with two electron-withdrawing groups from α,β-unsaturated carbonyls via Corey-Chaykovsky processes as well as with diazo compounds.[31] Interestingly, those strategies generally conduct to *trans* isomer cyclopropane with the exception of the Macmillan cyclopropanation, which lead to *cis* cyclopropanes via enantioselective organocatalysis.[31b] Recently, Rovis developed a Rh(III)-cyclopropanation reaction using *N*-enoxyphthalimides able to reach also *cis* cyclopropane isomers from moderate to high diastereomerio ratios.[29c],[29f]

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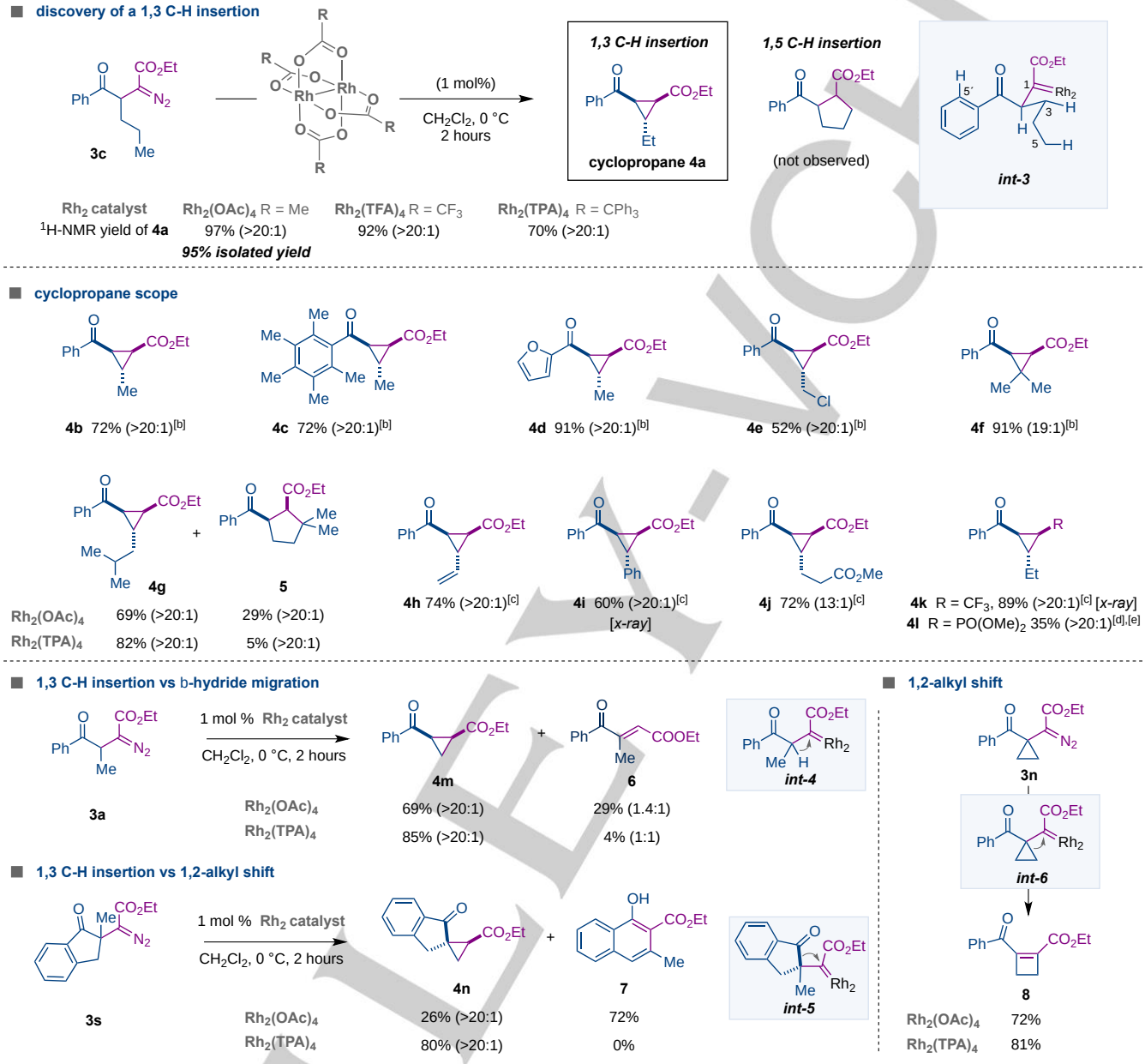
Table 3. Rh-catalyzed stereoselective 1,3 C−H insertion of β-diazocarbonyl compounds **3**.[a]



[a] See Supporting Information for experimental details. Diastereomeric ratios are shown in parenthesis and were determined by ^{1}H NMR analysis of the crude reaction mixture. [b] $Rh_2(OAc)_4$ was used. [c] $Rh_2(TPA)_4$ was used. [d] $Rh_2(TFA)_4$ was used. [e] 40% of **3ar** was recovered.

After this, we wondered whether we could develop a one-pot protocol for the synthesis of cyclopropanes **4** from the electrophilic diazomethylation reaction of silyl enol ethers and the Rh-catalyzed stereoselective 1,3 C−H insertion. If successful, this process would avoid the isolation and purification of the corresponding diazo compound, and that may be of utility when dealing with sensitive diazo derivatives. We explored this possibility with silyl enol ether **1c** and reagent **2d** and found that cyclopropane **4d** could in fact be obtained with excellent efficiency considering that isolation of diazo intermediate **3c** was avoided (Scheme 3a). For the one-pot protocol, we had to increase the Rh catalyst loading (2 mol%) and the reaction time in the C–H insertion process (12 hours) to enable conversion of **3c**. This might be due to the fact that the reaction is carried out in CH_3CN (instead of CH_2Cl_2), which is known to formed $Rh_2(OAc)_4(CH_3CN)_2$ complexes.[32] Finally, we wanted to exploit the utility of the Donohoe acyl protecting group in cyclopropane **4c**. By using the reported protocol for the synthesis of amides,[18h] we were pleased to find that **4c** could be transformed into cyclopropyl amide **8** in a reasonable good yield. (Scheme 3b). The latter result further illustrates the versatility of our new approach for the synthesis of cyclopropane rings.

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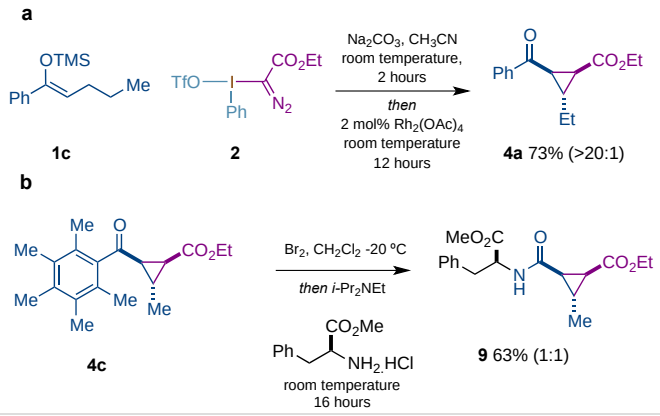

Scheme 3 One-pot synthesis of cyclopropane **4a** (**a**) and amidation of Donohoe protecting group (**b**).

Conclusion

In summary, we have developed a general synthesis of β-diazocarbonyl compounds by the coupling of readily available ketone silyl enol ether with hypervalent iodine reagents as electrophilic diazomethyl sources. The scope of our diazomethylation reaction has been demonstrated in a broad range of silyl enol ethers derived from simple ketones, natural products and drug molecules as well as from different hypervalent iodine reagents, that permitted to introduce esters, ketones, phosphate, trifluoromethyl and sulfonate groups. To date, this is the most general process for the synthesis of this diazo compound class. In addition, we have proven the synthetic utility of β-diazocarbonyl compounds by the discovery of a new cyclopropane synthesis enabled by a Rh-catalyzed intramolecular 1,3 C−H insertion, that occurs with excellent diastereoselectivity. This new synthetic strategy that construct cyclopropane cores and uses α & β C–H bonds as functional groups in aliphatic ketones, represent a complementary approach to other cyclopropanation process employing α,β-unsaturated carbonyl compounds.

Acknowledgements

We thank ICIQ and the Agencia Estatal de Investigación (AEI) of the Ministerio de Ciencia e Innovación (CTQ2016-75311-P, PID2019-104101GB-I00, FEDER-EU & Severo Ochoa Excellence Accreditation 2020-2023 -CEX2019-000925-S) for financial support. We also thank the European Union for a Marie Skłodowska-Curie Individual Fellowship (794815) (to L.J.), a Marie Curie-COFUND postdoctoral fellowship (to Z.W.) and La Caixa Foundation for a ICIQ Summer Fellowship (to M.A.). Pau Sarró is gratefully acknowledged for proofreading.

Keywords: diazo compounds • hypervalent iodine reagents • Rh-carbenes • cyclopropanes • C–H insertion

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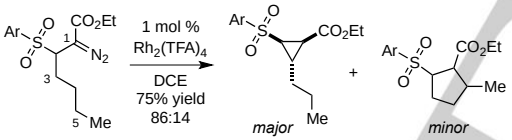

Ar = *p*Me-C_6H_4

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Entry for the Table of Contents

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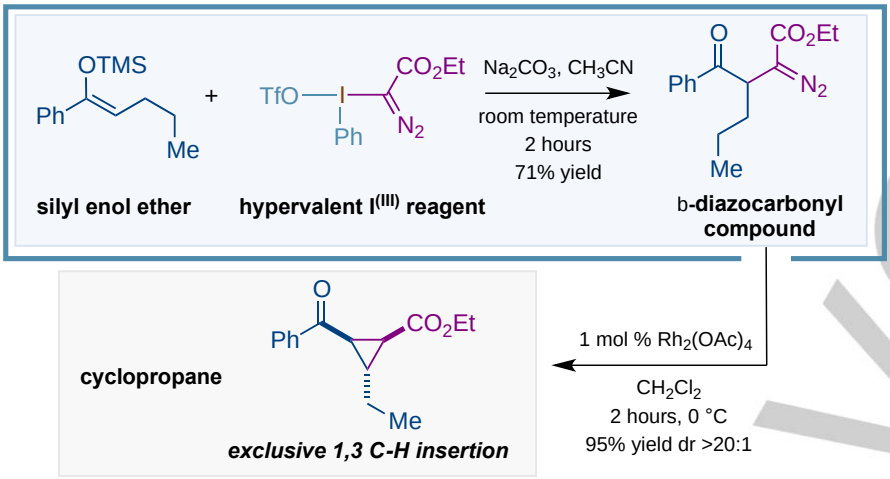

Text for Table of Contents here: A general synthesis of underexploited *β*-diazocarbonyl compounds has been developed by the electrophilic diazomethylation of silyl enol ethers. The synthetic utility of *β*-diazocarbonyl compounds was demonstrated with the discovery of a cyclopropane synthesis enabled by an unusual Rh-catalyzed intramolecular 1,3 C−H insertion.

Institute and/or researcher Twitter usernames: @MarcosGSuero