Account/Revue

The anionic chemistry of ynamides: A review

La chimie anionique des ynamides : une revue

Gwilherm Evano[*], Bastien Michelet, Chunyang Zhang

Laboratoire de chimie organique, Service de chimie et physicochimie organiques, Université libre de Bruxelles (ULB), avenue Franklin D. Roosevelt 50, CP160/06, 1050 Brussels, Belgium

A B S T R A C T

Ynamides have recently evolved as remarkably reactive and versatile building blocks for chemical synthesis. The development of efficient and robust methods for their preparation combined with their recent commercialization have facilitated both the design of an ever-growing number of original methods based on their unique reactivity and their use in other areas such as medicinal chemistry. One crucial aspect of the reactivity of these building blocks is based on their anionic chemistry, which has been extensively studied during the last decade and enabled not only the design and development of remarkably efficient and original reactions but also brought general answers to long-standing problems in organic chemistry and contributed to the emergence of new synthetic paradigms. In this short review, the anionic chemistry of ynamides is overviewed.

© 2016 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.

R É S U M É

Les ynamides ont récemment émergé comme une nouvelle classe de briques élémentaires particulièrement réactives. Le développement de méthodes générales et efficaces pour leur synthèse ainsi que leur commercialisation a permis la mise au point d'un nombre croissant de nouvelles méthodes basées sur leur réactivité unique ainsi que leur utilisation dans d'autres domaines tels que la chimie médicinale. Un des aspects majeurs de leur réactivité repose sur leur chimie anionique, particulièrement étudiée ces dix dernières années, qui a non seulement facilité le développement de nouvelles réactions originales et redoutablement efficaces, mais qui a également permis d'apporter des solutions générales à des problèmes ouverts de chimie organique et l'émergence de nouveaux paradigmes. La chimie anionique des ynamides est présentée dans cet article de revue.

© 2016 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.

1. Ynamides: a brief introduction

Ynamides **1**, stable surrogates of the more labile ynamines [1], have emerged as remarkably useful building blocks during the last two decades [2]. The nitrogen atom directly connected to the alkyne strongly activates and

* Corresponding author.
 *E-mail address:* gevano@ulb.ac.be (G. Evano).

polarizes the triple bond, whereas the electron-withdrawing group ensures the stability of these building blocks and can also act as a directing group and/or a chiral auxiliary (Fig. 1a). Various classes of electron-deficient ynamines have been developed based on the nature of this electron-withdrawing group, which can be an amide, a carbamate, urea, an imide [3], a sulfonamide, a phosphoramidate [4], a phosphorodiamidate [4] or a hydrazide [5] (Fig. 1b), all corresponding stabilized nitrogen-substituted alkynes falling under the general denomination "ynamides", which is therefore not restricted anymore to *N*-alkynyl-amides. Other stable equivalents of ynamines in which the delocalization of the nitrogen lone pair into the alkyne is also restricted because of electronic or geometrical reasons have been reported more recently: they include *N*-alkynylated N-containing arenes, ynimines [6], yne-sulfoximines [7], yne-sulfonimidamide [8] and *N*-alkynyl-triazenes [9].

The key to the success met by these building blocks was the development of efficient, reliable and broadly applicable methods for their preparation. They can indeed be prepared, on multigram scales, by an array of synthetic methods [10] mostly based on the direct alkynylation of nitrogen nucleophiles with hypervalent alkynyliodonium salts [11], copper acetylides [12], trichloroethylene [13] or copper-catalysed alkynylation with bromoalkynes [14], terminal alkynes [15], *gem*-dibromoalkenes [16], propiolic acids [17] and potassium alkynyltrifluoroborates [18]. Some of them being now even commercially available, their chemistry was extensively studied, which resulted in the design of an ever-growing number of original methods based on their unique reactivity. Over the years, they have indeed been shown to be remarkable starting materials in a broad range of transformations, which have been recently reviewed [2,19]. They have also been shown to be ideal substrates in metal-mediated [20], pericyclic [21], radical [22], cationic [23] and anionic chemistry, their use in anionic processes being the core of this article.

The enthusiasm generated by the use of ynamides in various anionic processes is actually easily understandable

(a) Ynamides and their resonance structures
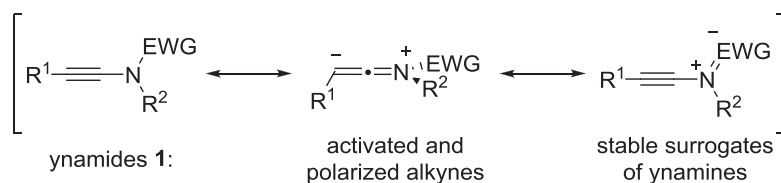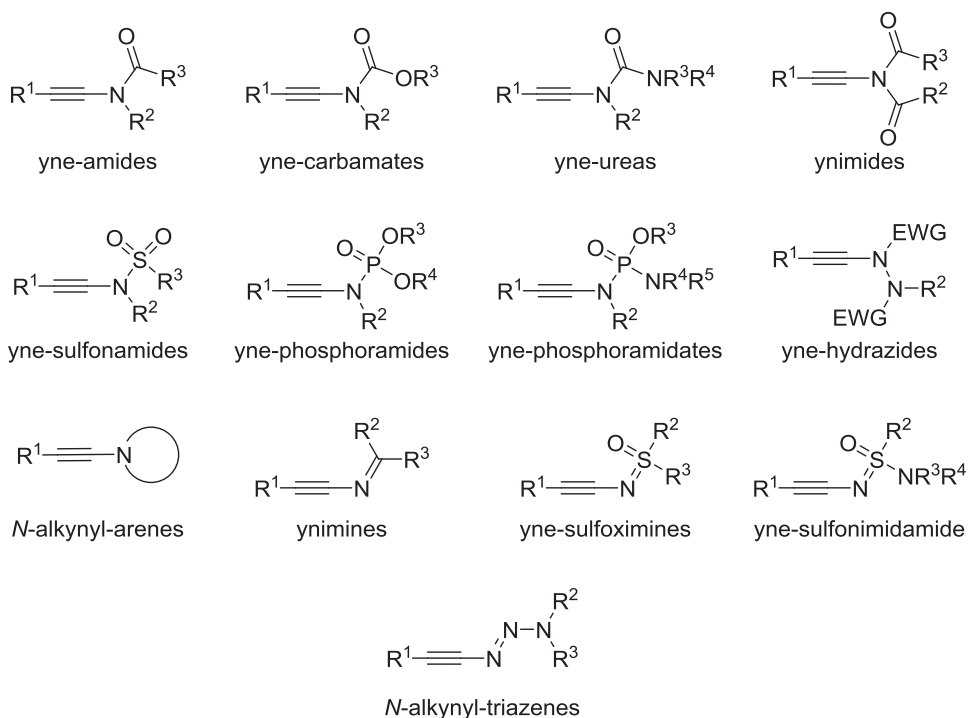

(b) Main classes of ynamides

Fig. 1. Ynamides: resonance structures and main classes.

and stands in the nature itself of these reagents, which possess various sites that can be used for the development of anionic reactions. These include the polarized alkyne, which can be used in carbometallation and related processes, the electron-withdrawing group, which can control their regioselectivity and can also be used, depending on its nature, for nucleophilic additions or metallations initiating further transformations, as well as the propargylic position or the acetylenic position in terminal ynamides, which possesses acidic protons (Fig. 2). Although the propargylic metallation of ynamides has not been reported to date, the polarization of the alkyne and the presence/reactivity of the electron-withdrawing group have been exploited for the development of new reactions based on the anionic reactivity of ynamides. ***These reactions will be overviewed in this review article, which will cover the "anionic" chemistry of ynamides in a broad sense*** (reactions such as carbopalladations and even some radical processes have been incorporated, mostly for comparison purposes) and they will be classified according to the type of anionic transformation (carbometallation, nucleophilic addition and deprotonation) and its nature (inter- or intra-molecular), starting with processes based on the intermolecular carbometallation of ynamides and related reactions, which will be covered in the following section.

2. Intermolecular carbometallation of ynamides and related processes: useful entries to polysubstituted enamides and new approaches in asymmetric synthesis

2.1. Intermolecular carbometallation of ynamides and related processes: a straightforward and regioselective entry to highly substituted enamides

The carbometallation reaction of ynamides is probably one of the best examples illustrating that ynamides are more than stable surrogates of the more labile ynamines [24]. Indeed, although the carbocupration of ynamines **2** was shown in the early 1970s to strictly follow the inherent polarization of the triple bond affording a transient β-amino-vinylcopper **3**, which was then reacted with a series of electrophiles to provide enamines **4** (Scheme 1a) [25], Marek and colleagues demonstrated some 30 years later that the presence of the electron-withdrawing group in

ynamides **1** overcomes the polarization of the alkyne, the carbocupration being now directed by chelation of copper by the electron-withdrawing group to afford an intermediate α-amino-vinylcopper **5**, which upon trapping with a series of electrophiles then affords enamides **6** resulting from a *syn*-carbocupration (Scheme 1b) [26]. As a note, the synthesis of the organocopper/cuprate reagents is not strictly required, because a copper-catalysed carbomagnesiation was also shown to be operative.

Besides organocopper, organocuprates and Grignard reagents, organozinc halides and diorganozincs can also be used for the carbometallation of ynamides, the main advantage being the high functional group tolerance of these reagents. Organozinc derivatives being unable to perform the carbozincation of ynamides themselves, a catalyst is required in this case, as demonstrated by Lam and colleagues who reported in 2009 the stereoselective synthesis of multisubstituted enamides **6** via a rhodium-catalysed carbozincation of ynamides **1** [27]. In the presence of 5 mol % of Rh(cod)(acac), a series of organozinc halides and diorganozincs could be smoothly added across the triple bond of yne-lactams, yne-oxazolidinones and yne-imidazolidinones with high levels of regio- and stereoselectivity, providing fully substituted enamides **6** after further reaction with an electrophile (Scheme 2a). In addition, intermediate vinylzinc **7** can participate in a Negishi cross-coupling, affording conjugated enamides **8** (Scheme 2b). Although acyclic ynamides such as yne-carbamates or yne-sulfonamides failed to undergo the carbozincation, an interesting observation was made upon investigating the effect of the ligand. Indeed, the use of diethylzinc in the presence of 2.5 mol % of [Rh(cod)Cl]$_2$ and 10 mol % of tris-(2-furyl)phosphine completely altered the reaction course to favour a clean hydro-zincation yielding *Z*-enamides **9** (Scheme 2c) [27b]. The carbozincation could be further extended to the preparation of α,β-dehydroamino acids **10**, which could be readily obtained by a copper-catalysed carbozincation with dialkylzinc reagents under an atmosphere of carbon dioxide, the former being chemically compatible with the latter (Scheme 2d) [28]. Compared with other methods available for the preparation of α,β-dehydroamino acids, which often suffer from a lack of stereoselectivity, this formal alkylative carboxylation of ynamides is clearly an excellent alternative.
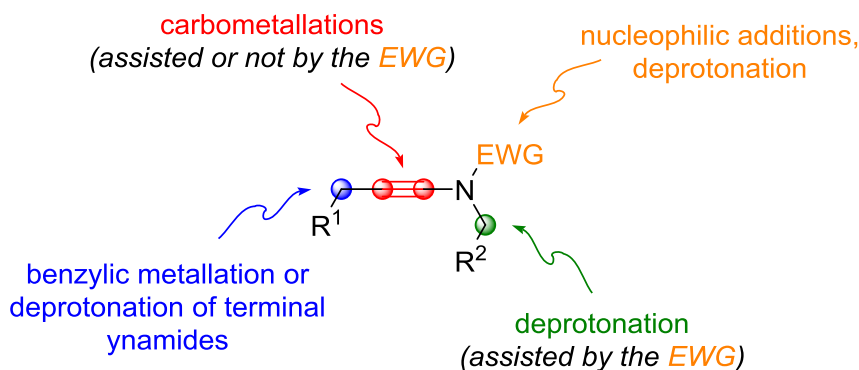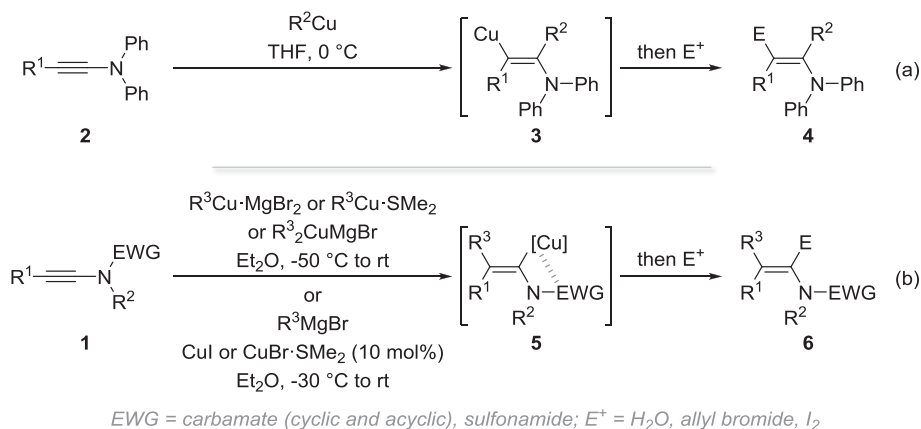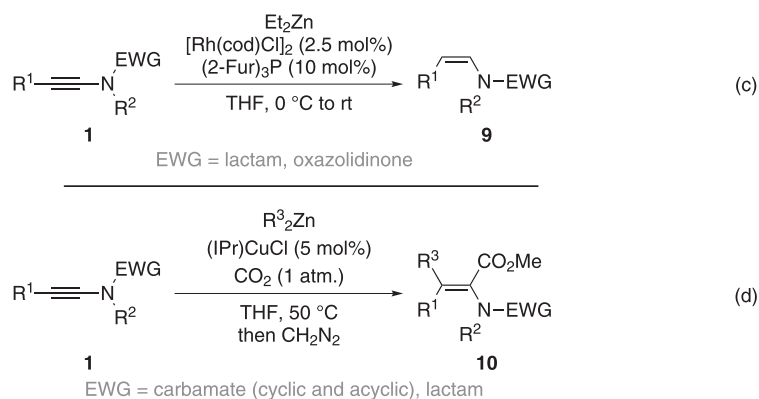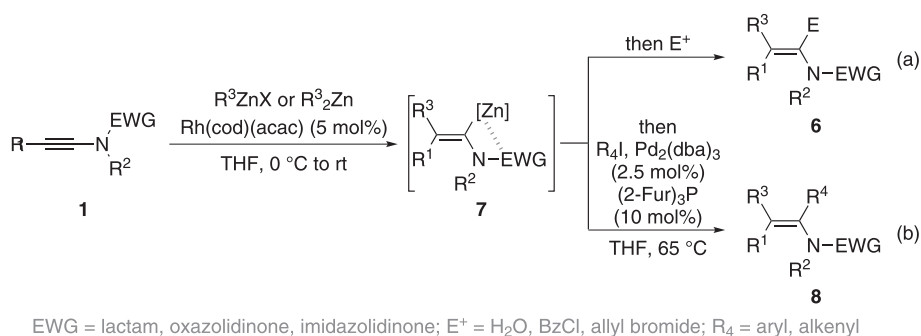

Fig. 2. Ynamides: ideal substrates for anionic chemistry.

EWG = carbamate (cyclic and acyclic), sulfonamide; E⁺ = H₂O, allyl bromide, I₂

Scheme 1. Carbocupration and copper-catalysed carbomagnesiation of ynamines and ynamides: inherent polarization of the alkyne vs chelation with the electron-withdrawing group.

EWG = lactam, oxazolidinone, imidazolidinone; E⁺ = H₂O, BzCl, allyl bromide; R₄ = aryl, alkenyl

EWG = lactam, oxazolidinone

EWG = carbamate (cyclic and acyclic), lactam

Scheme 2. Rhodium- and copper-catalysed carbozincation of ynamides.

The synthetic potential of the regio- and stereo-controlled access to multisubstituted enamides [29] based on the carbometallation of ynamides was further demonstrated by Gourdet and Lam who reported an efficient and innovative total synthesis of (+)-taniko-lide **17**, an antifungal lactone possessing a chiral tertiary alcohol (Scheme 3) [30]. Capitalizing on the method they developed for the synthesis of multisubstituted enam-ides, the synthesis began with the preparation of yna-mide **13** using the Hsung procedure from bromoalkyne **11** and oxazolidinone **12** and its further rhodium-

catalysed carbozincation using functionalized alkylzinc bromide **14**. The corresponding disubstituted enamide **15**, obtained as a single regioisomer and diastereoisomer resulting from a directed *syn*-carbozincation, was next subjected to an asymmetric Sharpless dihydroxylation, yielding enantioenriched diol **16** after reduction of the intermediate aminal with sodium borohydride. Further saponification of the ester followed by lactonization provided the desired target molecule **17** with an excellent overall yield, further highlighting the efficiency of the regio- and stereoselective synthesis of enamides—which
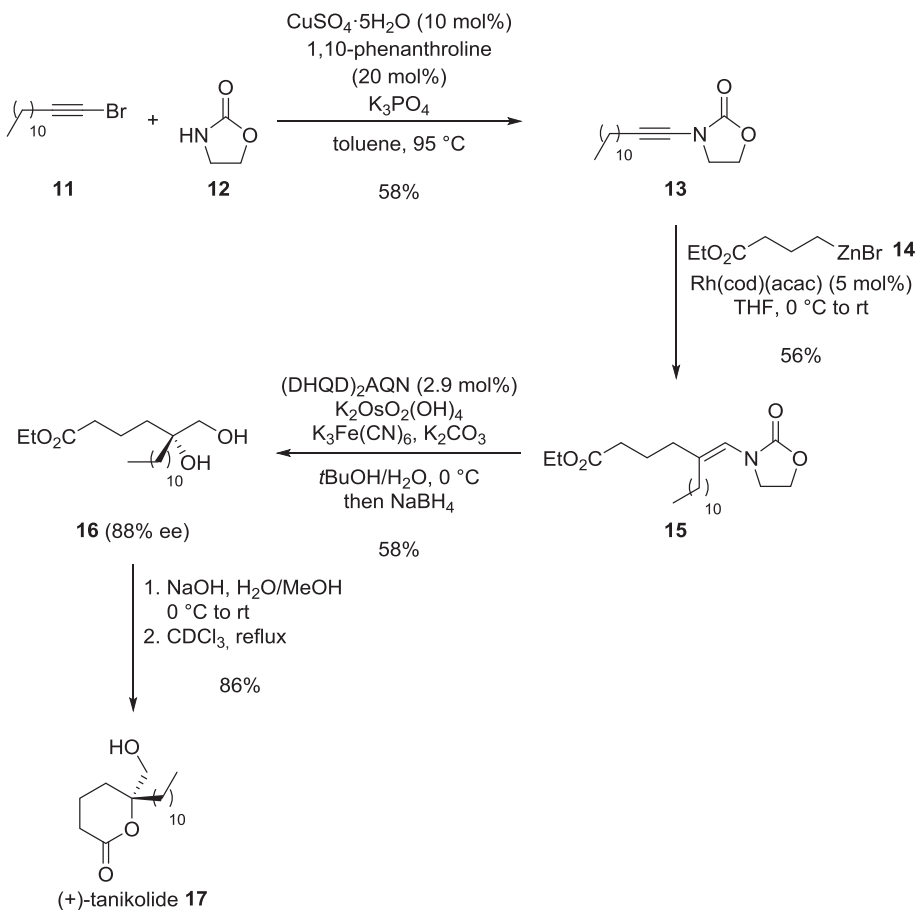
Scheme 3. Total synthesis of (+)-tanikolide: highlighting the synthetic efficiency of the carbometallation of ynamides.

are not that trivial to prepare—by carbometallation of ynamides.

Organoboron reagents such as aryl/alkenyl-boronic acids, arylboronates and triarylboroxines were also shown to be suitable reaction partners, in combination with a rhodium catalyst, for the carbometallation of ynamides, which represent an interesting alternative to the use of the corresponding aryl copper, magnesium and zinc reagents because of their greater availability (Scheme 4) [31]. The reaction is performed in a mixture of tetrahydrofuran (THF) and water under microwave irradiation and, as in the previous cases, enables the regio- and stereocontrolled synthesis of β,β′-disubstituted enamides **6** from the corresponding ynamides **1**.
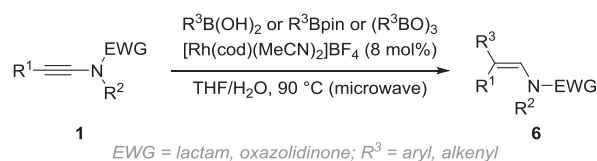
Scheme 4. Rhodium-catalysed carbometallation of ynamides with organoboron reagents.

Although they clearly do not fall into the classification of anionic transformations, a series of procedures have been reported for the intermolecular carbopalladation of ynamides: they clearly deserve to be mentioned, at least for comparison purposes. One of the major differences between carbopalladations involving ynamides and the other carbometallations described above is the shift in regioselectivity observed in most cases. Indeed, although carbocuprations and carbozincations proceed to favour the formation of an α-metallated enamide analogous to **18**, which benefits from chelation of the metal by the electron-withdrawing group, carbopalladations are less sensitive to directing effects and preferably follow the inherent polarization of ynamides **1** to afford intermediate β-palladated enamides **19** (Scheme 5). The presence of the amino group β to the palladium can in addition facilitate the E–Z isomerization to **21**, presumably via a palladium carbene **20**, which renders the stereoselectivity of the overall carbopalladation process dependent on the steric properties of the substituent on the starting ynamide.

The palladium-catalysed addition of aryl- and alkenyl-boronic acids to ynamides is a remarkable illustration of the reversal of both regio- and stereoselectivities that can be observed with the carbopalladation of ynamides
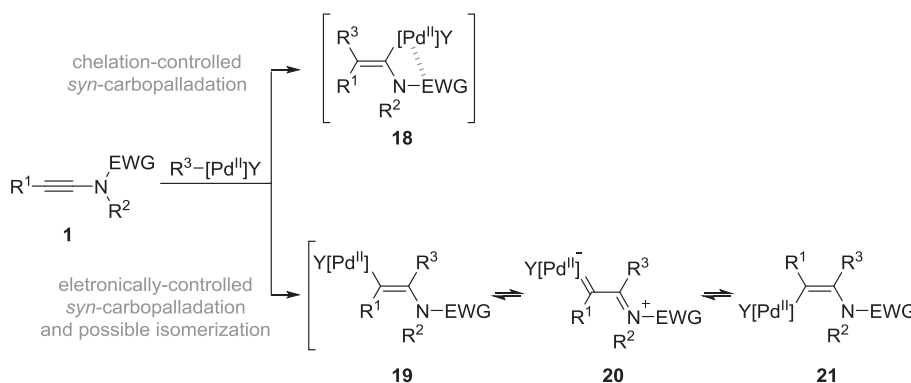
Scheme 5. Possible reversal of regio- and stereoselectivity in the carbopalladation of ynamides.

(Scheme 6a). Indeed, the reaction of ynamides **1** with boronic acids in the presence of catalytic amounts of palladium acetate and tris(3-tolyl)phosphine in ethanol at 70 °C gave conjugated enamides **22** resulting from an overall *trans* addition across the triple bond in which the newly introduced substituent R³ is placed at the α-position, which can be explained by an intermediate vinylpalladium species such as **21** (Scheme 5) [32]. The dramatic influence of the nature of the substituents on the starting ynamide was also noted by the Reddy group who, in continuation of previous studies by the Zhu group [33], examined in detail the selectivity of the palladium-catalysed hydro-alkynylation of ynamides [34]. Although the regiose-lectivity observed in all cases was consistent with an electronically controlled carbopalladation placing the palladium β to the nitrogen, the stereoselectivity observed

was found to be strongly influenced by the nature of both the electron-withdrawing groups and the substituent on the alkyne. Indeed, although small electron-withdrawing groups such as oxazolidinones, β-lactam and indoles fav-oured the formation of the *E*-ynenamides **23** (via an in-termediate such as **19** in Scheme 5), more sterically demanding sulfonamides were found to mostly induce the selective formation of either *E*-ynenamides **23** when starting from yne-sulfonamides bearing a small R¹ sub-stituent such as an alkyl chain or *Z*-ynenamides **24** (via isomerization of intermediate **19** to **21** to avoid steric clash) when this R¹ substituent was replaced by a bulkier aryl group (Scheme 6b). A similar preference was observed starting from a *N*-Boc-ynamine.

In addition to their carbometalation, which allows for the selective introduction of a carbon substituent to the
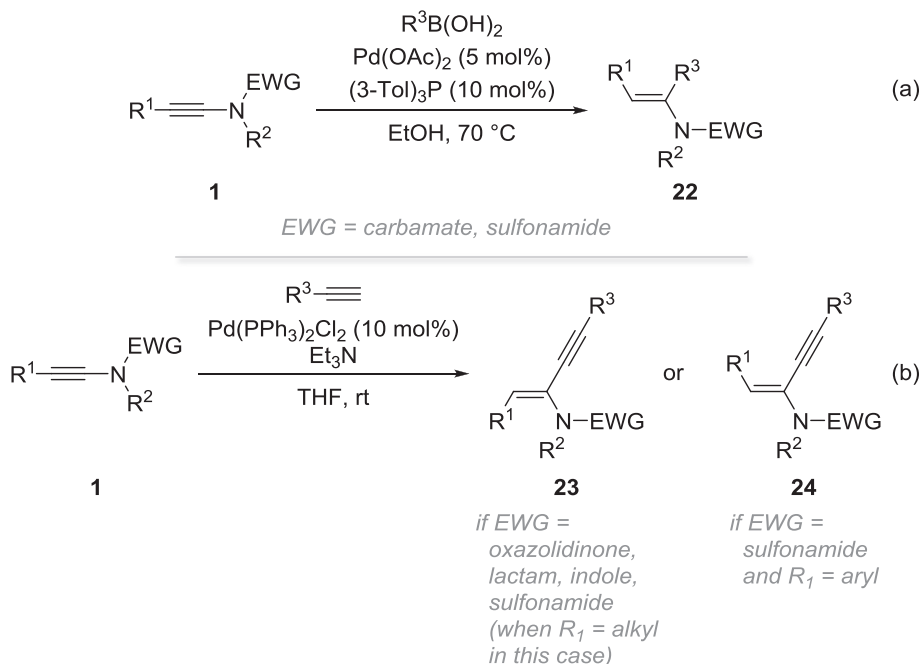
Scheme 6. Reactions involving an intermolecular carbopalladation of ynamides.

starting ynamide, related processes enabling the intro-duction of heavier group 14 elements such as silicon and tin as well as a boron substituent have been reported. They provide a straightforward access to functionalizable enamides and they will be briefly overviewed in the following section.

2.2. Intermolecular silyl-, stannyl- and boryl-metallation of ynamides: an efficient entry to functionalizable enamides

The first example of a silylcupration of an ynamide was reported in 2008 by the Yorimitsu and Oshima group [35]. Using a large excess of silylcopper reagents in a mixture of THF and hexamethylphosphoramide at −60 °C, phenyl-substituted yne-sulfonamides **25** were found to readily undergo a silylcupration yielding, after hydrolysis or trap-ping with allylbromide, the corresponding β-silylated enamides **26** obtained with good, although not complete, regio- and stereoselectivities (Scheme 7a). In collaboration with the Riant group [36], we reported a catalytic version of this reaction based on a copper-catalysed silylcupration with Suginome's silylboronates. Upon reaction with these reagents and methanol in THF at room temperature in the presence of copper(I) fluoride tris(triphenylphosphine), a range of ynamides **1** were found to undergo a smooth silylcupration. This reaction, which tolerates various func-tional groups, affords a straightforward and efficient entry to the corresponding β-silyl-enamides **27** that were formed with high levels of regio- and stereoselectivities (Scheme 7b). This silylmetallation, which was found to be highly E-selective, can also be performed through a silylzincation
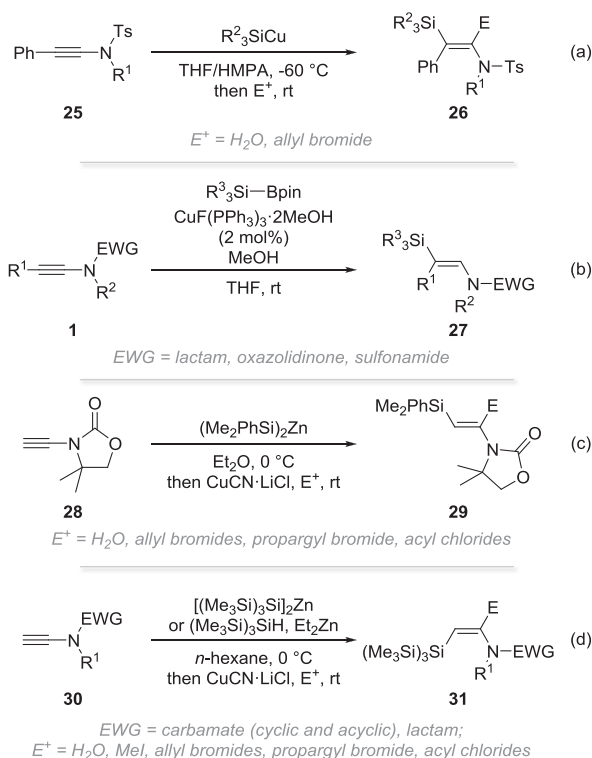
starting from terminal ynamide **28**, which upon reaction with (Me$_2$PhSi)$_2$Zn, followed by transmetallation with CuCN·LiCl and reaction with an electrophile provides the corresponding E-enamides **29** in fair to good yields (Scheme 7c) [37]. An interesting and quite remarkable reversal of selectivity, which was attributed to a switch from a polar to a radical-chain mechanism, was observed when starting from [(Me$_3$Si)$_3$Si]$_2$Zn, which was proposed to be more susceptible to undergo homolytic cleavage of the silicon−zinc bond. The Z-enamides **31** could indeed be obtained through a trans-selective radical silylzincation of terminal ynamides **30** using this reagent in combination with diethylzinc as an additive or by using directly (Me$_3$Si)$_3$SiH with an excess of diethylzinc (Scheme 7d) [37,38].

The only examples of stannylmetallation of ynamides reported to date involve palladium catalysis. As mentioned in the previous section, palladium being less sensitive to chelation, the regioselectivity of the syn-stannylpalladation is controlled by the polarization of the triple bond, which provides E-α-stannyl-enamides **32**, although the regiose-lectivity decreases when starting from terminal and aryl-substituted yne-oxazolidinones or yne-sulfonamides (Scheme 8) [39]. The stannylpalladation is not limited to a formal hydrostannylation because replacing tributyltin hy-dride by Bu$_3$SnSnBu$_3$, Me$_3$SnSnMe$_3$ or Bu$_3$SnSiMe$_3$ enables clean bis-stannylation or stannylsilylation reactions [39a,b].

Finally, it ought to be mentioned that the bor-ylmetallation of ynamides has also been investigated using either bis(pinacolato)diboron in combination with a copper catalyst (Scheme 9a) [40] or Suginome's reagent in com-bination with a palladium catalyst (Scheme 9b) [41]. In the former case, Z-enamides **33** are isolated, their formation being rationalized by a borylcupration yielding an inter-mediate β-boryl-enamide—whose formation is actually quite surprising because it involves a complete reversal of regioselectivity compared with most cupration reactions involving ynamides—followed by a transmetallation with the copper alkoxide catalyst and final protonolysis. In the latter case, α-silyl-β-boryl-enamides **34** are obtained, the regioselectivity being consistent with the silylborylation proceeding through preferential insertion of the triple bond to the Pd−B σ bond formed after oxidative addition of Suginome's reagent to palladium(0), which, however, in-volves a chelation-controlled borylpalladation that is in sharp contrast with the regioselectivity observed for car-bopalladations (see Scheme 6).

As hopefully evidenced by all examples described, the carbo-, silyl-, stannyl- and borylmetallation of ynamides represent remarkably useful entries to highly functional-ized and functionalizable enamides, which can be prepared

Scheme 7. Silylcupration and silylzincation of ynamides.
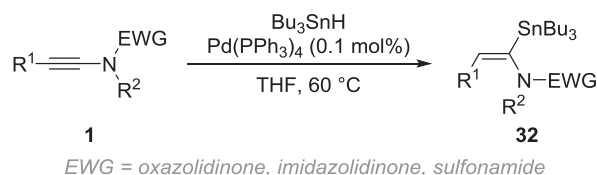
Scheme 8. Stannylpalladation of ynamides.
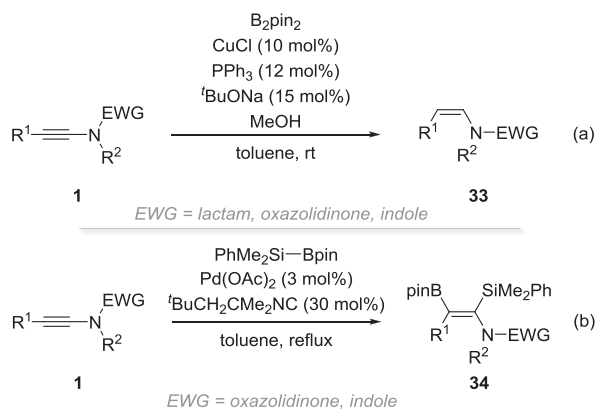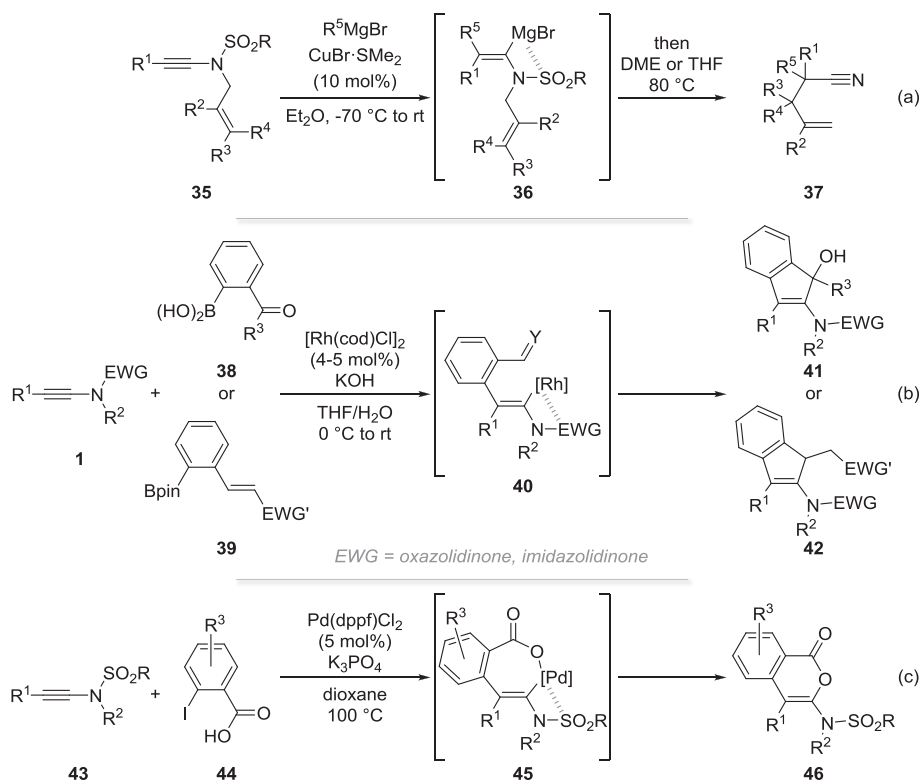
Scheme 9. Borylmetallation of ynamides.

with excellent control, at least in most cases, of the regio- and stereoselectivities. The choice of the metal is crucial for these reactions, which can be controlled either by chelation or by the polarization of the triple bond. These reactions are not limited to the synthesis of enamides because the incorporation of such metallation reactions in cascade processes in which the intermediate metallated enamide further reacts with a substituent judiciously incorporated in the starting ynamide enables the preparation of other building blocks and molecular scaffolds; they will be briefly described in the following section.

2.3. Cascade reactions involving an intermolecular carbometallation of ynamides: efficient access to useful building blocks

The first example of a cascade reaction involving metallation of an ynamide was reported by Yorimitsu and Oshima group in the course of their studies of the copper-catalysed carbomagnesiation of ynamides [35,42]. When starting from *N*-allyl-ynamides **35** and heating the intermediate vinyl Grignard reagent **36** at 80 °C after addition of 1,2-dimethoxyethane or THF, an aza-Claisen rearrangement occurred, which after elimination of a magnesium sulfinate (which can also proceed before the sigmatropic rearrangement) produced homoallylic nitriles **37** (Scheme 10a).

In continuation to their studies on the rhodium-catalysed carbometallation of ynamides with organoboron reagents, the Lam group reported in 2010 an interesting annulation of ynamides starting from arylboron reagents possessing an electrophilic functional group *ortho* to the boronic acid/boronate such as in **38** or **39** [43]. In this case, the carbometallation yielding **40** is followed by nucleophilic addition to an aldehyde/ketone or a 1,4-addition to an α,β-unsaturated aldehyde, ketone or ester, yielding 2-aminoinden-1-ols **41** or 2-aminoindenes **42** (Scheme 10b).

In a similar vein, the group of Wang and Chang reported another annulation of yne-sulfonamides **43** based on their palladium-catalysed reaction with *ortho*-iodo-benzoic


Scheme 10. Cascade reactions involving an intermolecular carbometallation of ynamides.

acids **44**. In this case, the carbopalladation was found to be chelation-controlled, yielding intermediate **45**, which after further reductive elimination furnishes 3-amino-iso-coumarins **46** (Scheme 10c) [44].

Last, but definitely not least, especially elegant and remarkably efficient one-pot sequences involving an intermolecular carbocupration of chiral ynamides were reported in a series of publication by Marek and colleagues. Capitalizing on the high levels of regio- and stereo-selectivities observed for the carbocupration of ynamides,

including chiral ones such as **47**, they had earlier studied (Scheme 1b), they envisioned that the resulting vinyl-copper **48** could be further exploited in a series of trans-formations performed in a one-pot sequence to access aldol products possessing all-carbon quaternary stereo-centres, products that cannot be accessed through classical asymmetric aldolization reactions because of the lack of stereocontrol observed for the generation of the enolates that would be required (Scheme 11). In this perspective, Marek and colleagues first envisioned a homologation of
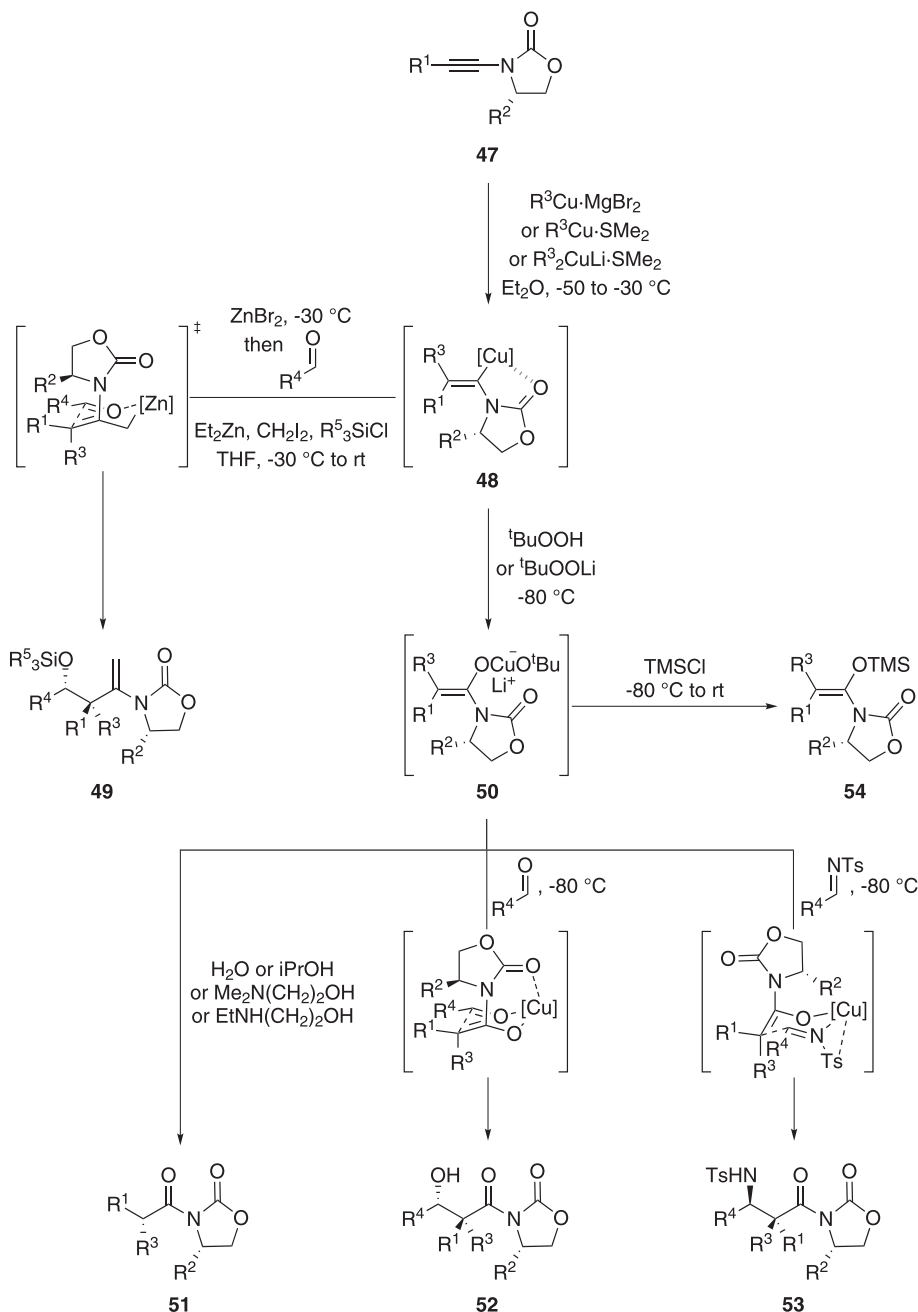
Scheme 11. Unique approaches to aldol products possessing all-carbon quaternary stereogenic centres through carbocupration of chiral ynamides.

48 with in situ generated ICH$_2$ZnCH$_2$I yielding an intermediate chiral allylzinc. Further reaction of this allylzinc with an aldehyde provided, through a Zimmerman–-Traxler transition state, adduct **49**, which after a two-step cleavage of the chiral oxazolidinone enables an efficient and highly stereoselective access to the corresponding formal aldol adducts [45]. Although this sequence was found to be remarkably efficient and stereoselective, the main limitation relies on the two-step cleavage of the chiral auxiliary. To address this drawback, they reported 3 years later that the zinc carbenoid used for the homologation of the intermediate vinylcopper **48** could be replaced by an oxenoid generated in situ from equimolar amounts of *tert*-butylhydroperoxide and *n*-butyllithium. Although counter-intuitive, the use of this oxenoid turned out to be remarkably well-thought because it was demonstrated to enable a clean and stereoselective generation of fully substituted enolate **50**, which was next shown to react smoothly with a series of electrophiles including protic sources, aldehydes and imines to afford, with high levels of diastereoselectivity, chiral imides **51**, aldol **52** and Mannich **53** adducts, respectively [46]. In addition, intermediate copper enolate **50** was shown to be an excellent precursor of stereodefined disubstituted ketene aminals **54**, which can be generated upon trapping **50** with trimethylsilyl chloride [47]. These ketene aminals, which were shown to be excellent reaction partners for the Mukaiyama aldol reaction (by reaction with an aldehyde in the presence of titanium tetrachloride to give aldol adducts **52**), being rather sensitive in the presence of copper, the addition of copper scavengers such as 1,10-phenanthroline before the work up was found to increase the yields.

As overviewed with all examples discussed up to this point in this article, the carbometallation of ynamides has recently evolved from a simple curiosity to a remarkably efficient reaction enabling the preparation of a wide array of building blocks. Indeed, it does not only provide efficient accesses to highly substituted stereodefined enamides but also to an impressive number of building blocks and molecular scaffolds derived from the intermediate metallated enamides. Importantly enough to be mentioned, this simple carbometallation reaction also facilitated the emergence of new synthetic paradigms, notably in asymmetric

synthesis as exemplified by the work emphasized above by Marek and colleagues.

The carbometallation of ynamides is not limited to its intermolecular version and has also been recently studied and elegantly exploited in its intramolecular version, which will be overviewed in the next section.

3. Intramolecular carbometallation of ynamides: a remarkably useful reaction for heterocyclic synthesis

In addition to benefiting from the polarization of the ynamide triple bond or directing effect of the electron-withdrawing group, the intramolecular carbometallation of ynamides is of course also favoured by entropy effects. Depending on the relative position of the metal and the alkyne, the nitrogen atom being either in between these two functional groups (such as in **55**) or not (such as in **59**), the intramolecular reaction can be exploited for the synthesis of nitrogen heterocycles **56**–**58** or amino-cycles **60**–**62** (Scheme 12). Both the regio- and stereoselectivity of the intramolecular carbometallation have to be considered and fully controlled for the reaction to be of any synthetic usefulness. Although endo-dig cyclizations yielding **56** or **60** have to proceed through a non-classical *anti*-carbometallation, their exo-dig counterparts proceed in most cases via *syn*-carbometallations yielding vinylmetal species such as **57** or **61**, although *anti*-carbometallations have also been reported in some cases. The parameters governing the regio- and stereoselectivity are multiple and include the size of the ring formed [48], the nature of the metal and reagents used (one should keep in mind e.g., that halogen–lithium exchanges can proceed through polar or radical mechanisms), as well as the nature of the electron-withdrawing group, which has been shown to have a dramatic effect.

Intrigued and motivated by the possibility of accessing heterocyclic scaffolds for which there were only limited options for their synthesis, we became interested in 2012 in the intramolecular carbometallation of ynamides. In this perspective, we could successfully demonstrate that lithiated *N*-allyl-ynamides **64**, readily generated by deprotonation of the corresponding *N*-allyl-ynamides **63** with *s*-butyllithium in the presence of *N*,*N*,*N'*,*N'*-tetramethylethylenediamine, underwent a smooth and extremely rapid
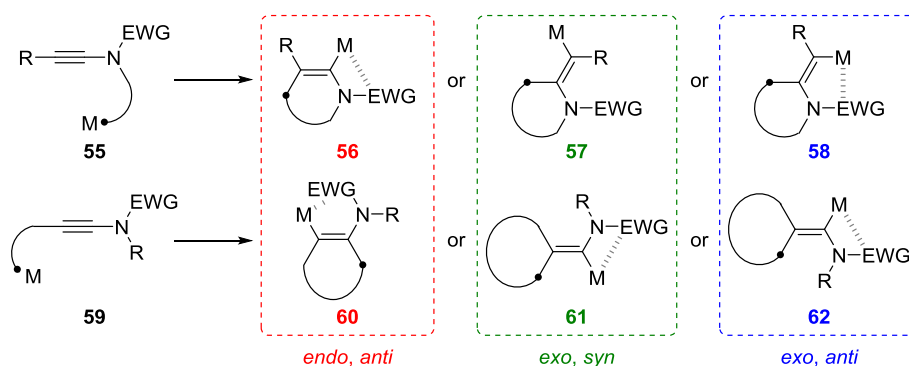

Scheme 12. Overall picture of the possibilities for the intramolecular carbometallation of ynamides.

metallotropic equilibrium followed by an unprecedented anionic 6-endo-dig cyclization to afford the corresponding 1,4-dihydropyridines **67** in good to excellent yields (Scheme 13a) [49]. Besides providing an efficient access to 1,4-dihydropyridines non-stabilized by the presence of an electron-withdrawing group at C3, which is strictly required in most syntheses of such molecules, we could also demonstrate that by simply replacing the final hydrolysis by a workup under acidic and oxidizing conditions, the corresponding polysubstituted pyridines **68** could be obtained (Scheme 13b). The efficiency of this anionic cyclization could then be further demonstrated in a formal synthesis of the anti-dyskinesia agent sarizotan **69** for which the 3,5-disubstituted pyridine core could be readily prepared by intramolecular carbolithiation of the corresponding suitably functionalized ynamide [50].

The success of this intramolecular carbolithiation led us to investigate related systems, and we reported later on other nitrogen heterocycles, such as indoles, which could also be obtained using a similar strategy. Indeed, we could demonstrate that polyfunctionalized indoles **72** could be readily obtained by carbocupration starting from ynamides such as **70**, the related carbolithiation being inoperative in this case (Scheme 14a) [51]. A similar cyclization using either a carbocupration or a copper-catalysed carbomagnesiation after a bromine−magnesium exchange (**73** → **75**, Scheme 14b) was reported by Knochel and colleagues who also extended it to the synthesis of azaindoles **78** and pyrrolopyrimidines **83** starting from the corresponding N-(pyridin-3-yl)- and N-(pyrimidin-4-yl)-ynamides **76** and **81**, respectively (Scheme 14c,e) [52]. Capitalizing on the acidity of the proton at C4 in **76** and on

the possibility of a directed metallation, they in addition reported a divergent carbocupration based on a direct deprotonation yielding **80** (after transmetallation/carbocupration) instead of the halogen−lithium exchange (Scheme 14d) [52a]. In all cases, a single regioisomer resulting from a 5-endo-dig cyclization was observed.

The intramolecular carbopalladation of suitably functionalized ynamides was also demonstrated to be quite efficient for the synthesis of a range of heterocycles, ranging from simple azacycles to complex polycyclic systems. In all cases, regardless of the size of the heterocycle formed, the carbopalladation seems to follow the inherent polarization of the triple bond and the electron-withdrawing group on the starting ynamides does not seem to have any directing effect on these cyclizations, which is in accordance with results previously discussed, in the intermolecular series, in Section 2. The first example of an intramolecular carbopalladation of ynamides was actually reported in 2004 by Meyer, Cossy and colleagues who reported an efficient access to methylene-isoindolinones **85** based on a carbopalladation of ynamides **84** in the presence of an arylboronic acid, which traps the vinylpalladium(II) species formed after the oxidative addition/carbopalladation sequence (Scheme 15a) [53]. The efficiency of this cyclization, in which the boronic acid can be replaced by ammonium formate to replace the aryl group by a hydrogen atom in the final cyclized product, was later on used as a key step in a remarkably efficient and short total synthesis of lennoxamine **86** [54]. Capitalizing on the success of this intramolecular carbopalladation, Anderson and colleagues reported later a similar cyclization starting from bromoenynamides **87**. As in the previous case, the
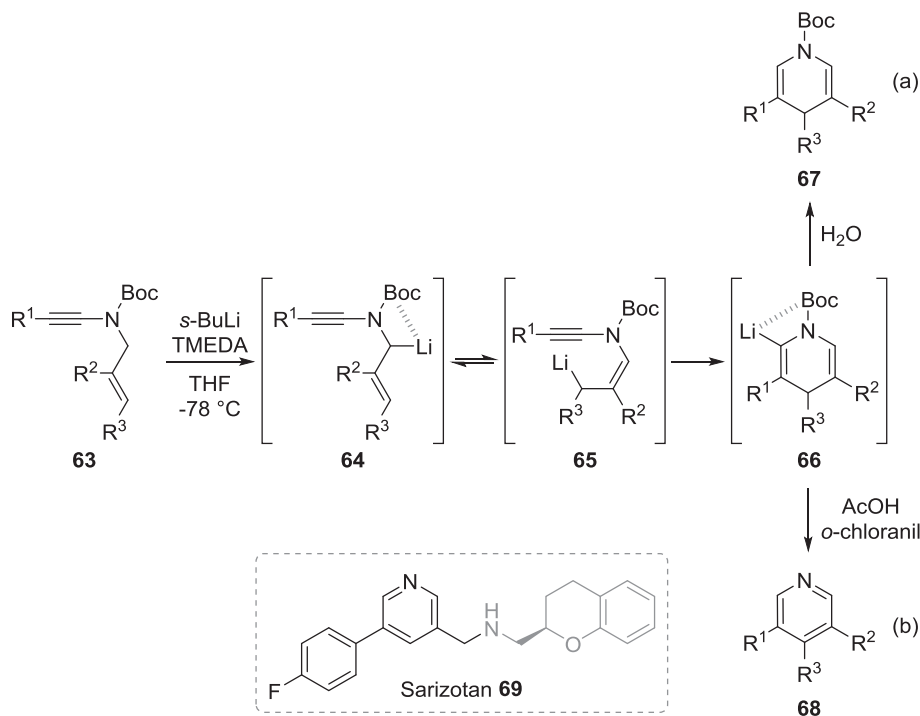
Scheme 13. Synthesis of 1,4-dihydropyridines and pyridines by intramolecular carbolithiation of ynamides.
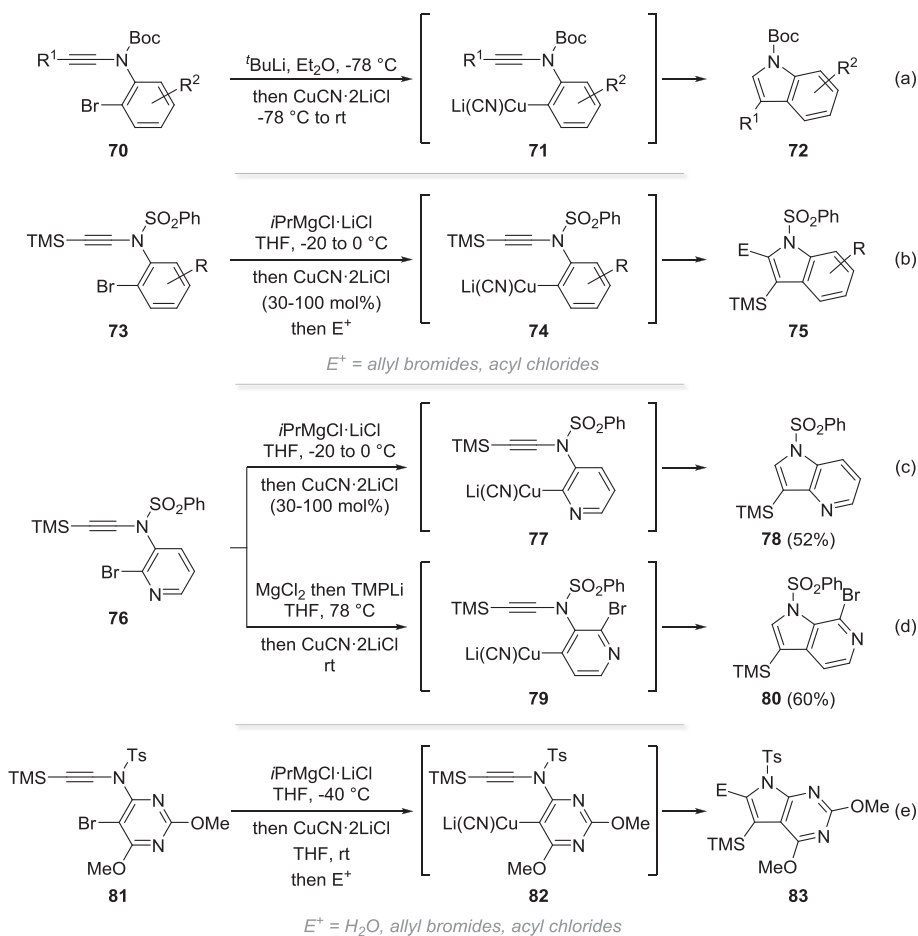
**Scheme 14.** Synthesis of indoles and related heterocycles by intramolecular carbocupration of ynamides.

intermediate vinylpalladium **88** resulting from the oxidative addition/carbopalladation could either be reduced with ethanol, yielding simple cyclized product **89** (Scheme 15b) or used to transmetallate a vinyltin or vinylboron derivative present in the reaction mixture to furnish, after 6π-electrocyclization, polycyclic azacycles **90** (Scheme 15c) [55]. In the presence of an additional triple bond suitably placed on the starting ynamide such as in **91**, a remarkable cascade polycyclization involving consecutive carbopalladations was found to occur, yielding tricycles **92** in good to excellent yields (Scheme 15d) [56].

Although in all examples mentioned above, the nitrogen atom is located between the triple bond and the site where the metallation occurs, which provides efficient entries to a broad variety of nitrogen heterocycles, a different connectivity enables the synthesis of nitrogen-substituted cyclic systems. This strategy was explored by Durandetti, Maddaluno and colleagues who investigated the intramolecular carbolithiation of a series of ynamides **93**: although a chelation-driven 5-exo-dig *anti*-carbolithiation yielding aminomethylene-dihydrobenzofuran derivatives **94** was observed in most cases, a complete switch in regioselectivity in favour of a 6-endo-dig cyclization to **95** was observed starting from an yne-

phosphoramide, irrespective of the organolithium species used to trigger the iodine–lithium exchange (Scheme 16) [57]. If Density Functional Theory calculations revealed that the unusual *anti*-carbolithiation could be explained by the affinity of the electron-withdrawing group in the starting ynamides for the lithium cation, the peculiar behaviour of the yne-phosphoramide could not be rationalized.

As evidenced by all results described in this section, the intramolecular carbometallation of ynamides provides effective accesses to numerous heterocyclic systems. Efficient reactions could be designed based on such a step, provided that the parameters controlling both the reactivity and the selectivity are carefully understood. The nature of the metal and the electron-withdrawing group on the starting ynamides clearly have a strong influence on the outcome of intramolecular carbometallations, and there is now clearly enough experimental data—although still not fully understood—for the design and development of other processes based on the unique reactivity of ynamides towards carbometallations.

If such reactions clearly constitute the corner stone of the anionic chemistry of ynamides, other reactions based on the unique reactivity of ynamides and related building
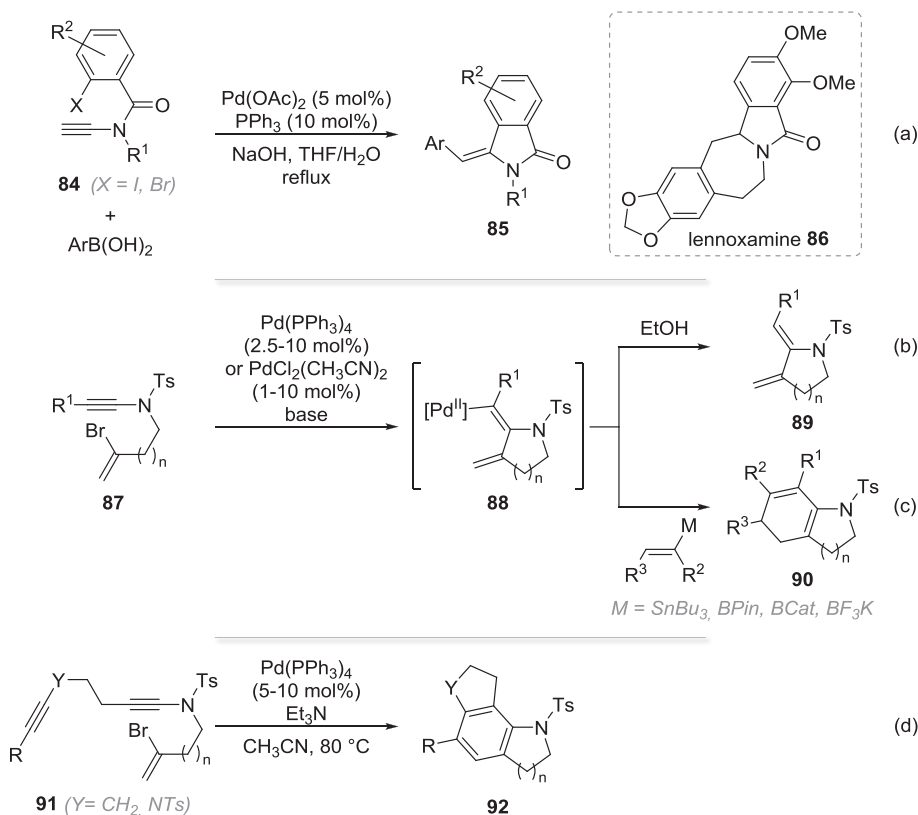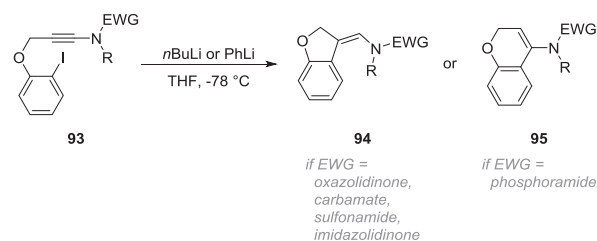
Scheme 15. Intramolecular carbopalladation of ynamides from isoindolinones to polycylic nitrogen heterocycles.

blocks under anionic conditions have been reported. They include reactions triggered by deprotonation or nucleophilic addition to the electron-withdrawing group, which will be overviewed in the following section.

4. Deprotonation/nucleophilic addition to the electron-withdrawing group of ynamides: efficient generation of otherwise hardly accessible reactive intermediates

Reactions involving the anionic chemistry of the electron-withdrawing group of ynamides are actually rather scarce, which is fairly logical because this group usually serves as a protecting group responsible for the

stability of ynamides. Playing around with this group might therefore result in a total loss of stability and it might therefore seem safer not to fool around with strong bases or nucleophiles that might react with this electron-withdrawing group.

For a while, the only example of a reaction involving metallation of the electron-withdrawing group was indeed limited to the metallation at the 2-position of N-alkynyl-imidazoles **96** followed by trapping of the resulting anion, in which the stability brought to the nitrogen-substituted alkyne by delocalization into the imidazole ring is intact, with various electrophiles (Scheme 17) [58]. Everything therefore happens as in the absence of the nitrogen-substituted alkyne, which does not react under the reaction conditions and is not affected by the metallation of the imidazole.

The synthetic usefulness of a reaction sequence involving an anionic reaction at the electron-withdrawing

Scheme 16. Dramatic effect of the electron-withdrawing group in the intramolecular carbolithiation of ynamides.
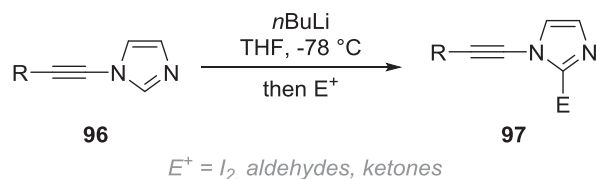
Scheme 17. Metallation of N-alkynyl-imidazoles at C2.

group of ynamides was actually reported in 2014 only when we observed that ynimines such as **98** and **110** were excellent precursors of otherwise hardly accessible metallated ketenimines **100** and **112** (Scheme 18) [59]. We could indeed demonstrate that the addition of an organolithium reagent to ynimine **98** regioselectively took place on the imine moiety and that the resulting metallated ketenimine **100** could then be trapped by an alkyl halide, generating a transient unstable ketenimine **101**, which after homolytic fragmentation and recombination provided highly substituted alkanenitriles **105** in modest to good yields (Scheme 18a). Introduction of a trimethylsilyl group on the starting ynimine resulted in a higher stability of the lithiated ketenimine, which could also be trapped by an alkyl halide, the resulting trimethylsilyl-ketenimine **106** being now perfectly stable (Scheme 18b). Alternatively, trapping the 2-lithio-2-silyl-ketenimine **100** with an aldehyde triggered a Peterson-type elimination generating an intermediate cumulene **108**, which upon hydrolysis gave α,β-conjugated amide **109** (Scheme 18c).

Alternatively, we could also show that metallated ketenimines **112** could be generated by deprotonation of the imine in ynimines such as **110** with potassium

bis(trimethylsilyl)amide rather than by nucleophilic addition of an organolithium. Further hydrolysis then afforded a transient ene-ketenimine **113** whose radical rearrangement gave allylic nitriles **114** (Scheme 18d).

It finally ought to be mentioned that related metallated ketenimines have been postulated as intermediates in the reaction between indole and ynamides [60]. In this case, sodium *tert*-butoxide has been postulated to, surprisingly, deprotect the starting ynamide **1**, generating an intermediate sodium ketenimine **115**, which would be protonated by indole **116**. Further addition of the deprotonated indole **117** to the ketenimine **118** and final protonation would account for the formation of acylated indole **119** (Scheme 19).

Finally, we could recently demonstrate that organolithium reagents could react in a highly chemoselective manner with yne-oxazolidinones **120** to afford the ring-opened acyclic yne-amides **121**, useful building blocks for chemical synthesis whose synthesis is still rather challenging and often low yielding, without competitive carbolithiation or propargylic lithiation (Scheme 20) [61].
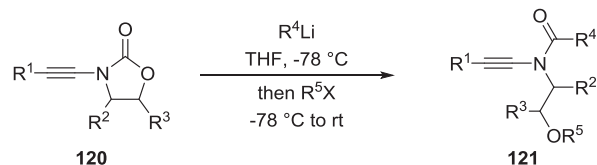
Although the anionic transformations involving nucleophilic addition or deprotonation of the electron-withdrawing
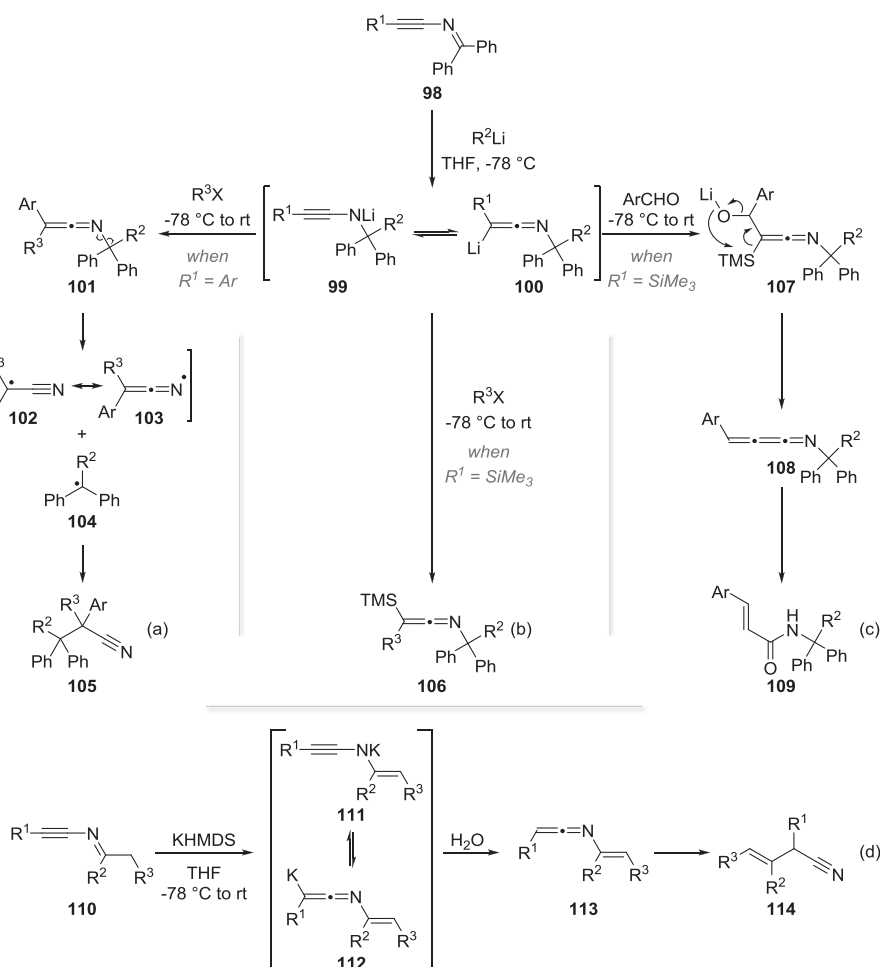
Scheme 18. Ynimines: useful precursors of metallated ketenimines.

EWG = amide, carbamate, sulfonamide
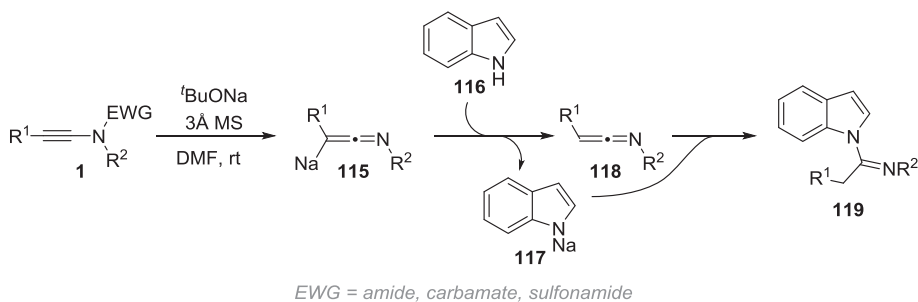
Scheme 19. Generation of sodium ketenimines by deprotection of ynamides.

**Scheme 20.** Ring-opening of yne-oxazolidinones to acyclic yne-amides.

group of ynamides are still quite underdeveloped to date, there is no doubt that this area of the anionic chemistry of ynamides will be the focus of further investigations because it clearly has a strong synthetic potential, both for the generation of anionic intermediates that are still challenging to prepare or to explore new pathways in carbanionic chemistry.

Before ending this review article, reactions involving metallated terminal ynamides will be covered in the final section.

5. Reactions involving metallated terminal ynamides: a straightforward entry to functionalized ynamides

The last area of the anionic chemistry of ynamides is indeed based on the trapping of metallated terminal

ynamides with a series of electrophiles, which enables the synthesis of complex ynamides from simpler ones (Scheme 21). If metallated ynamides **124** can of course be prepared by direct deprotonation of terminal ynamides **30** [62], although the deprotonation that can be performed with a series of strong bases is usually not as simple as it seems [62a], they can also be prepared in situ from different precursors. Indeed, β,β-halo- [62a,63] and α,β-dichloro- [13] enamides **122** and **123** were found to be excellent precursors of metallated ynamides **124**, which are generated depending on the nature of the halogen through deprotonation/elimination/lithium–halogen exchange (for chlorinated enamides) or lithium–halogen exchange/Fritsch–Buttenberg–Wiechell rearrangement/deprotonation (for brominated enamides) sequences. The metallated ynamides **124** generated in situ can then be trapped by a broad range of electrophiles including alkyl halides, chlorosilanes, epoxides, aldehydes, ketones, enones, anhydrides, chloroformates, CO_2, isocyanates, imines, sulfinylimines, disulfides or chlorophosphates, although the list might not be exhaustive [13,62,63]. Further transmetallation with zinc bromide also enables the synthesis of aryl-substituted ynamides **126** via a Negishi coupling [64]. As a note, it should also be mentioned that copper acetylides derived from terminal ynamides, usually generated under catalytic
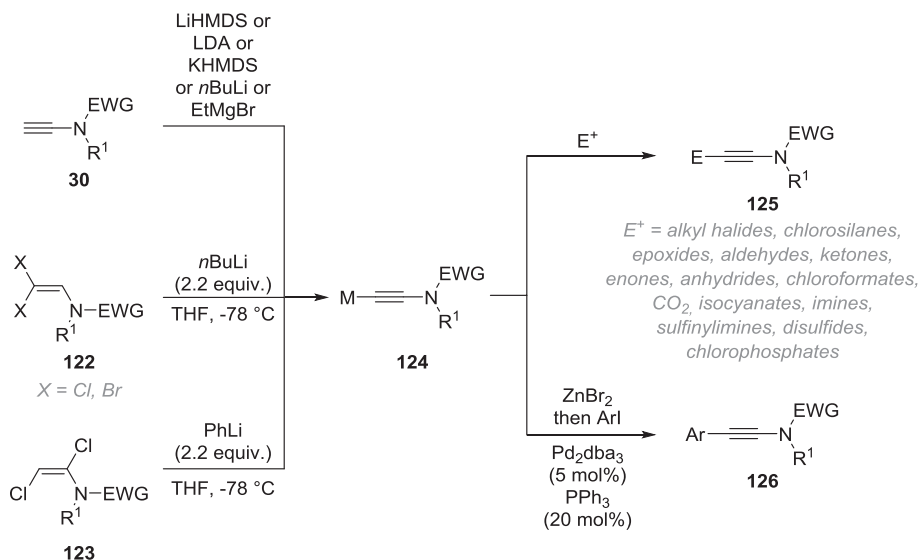
Scheme 21. Generation and functionalization of metallated terminal ynamides.

conditions, can also be used for the Glaser−Hay dimerization of terminal ynamides [64b,65], their Cadiot−Chodkiewicz cross-coupling with bromoalkynes [66], or for their addition to activated electrophiles such as acyl chlorides and *N*-acyl-pyridinium salts [67] and that Carreira's enantioselective addition of terminal alkynes to aldehydes was recently extended to the use of terminal ynamides [68].

6. Conclusions and outlook

As evidenced by all examples overviewed in this article, the anionic chemistry of ynamides has proven over the years to be extremely fruitful and productive. The development of efficient and robust methods for their preparation have facilitated the design of an ever-growing number of original methods based on their unique reactivity under anionic conditions. All together, these studies enabled not only the design and development of remarkably efficient and original reactions but also brought general answers to long-standing problems in organic chemistry and the emergence of new synthetic paradigms. Considering the number of reactive sites that can be used to trigger anionic transformations in ynamides, they can clearly be considered as unique building blocks in anionic chemistry provided that their reactivity can be finely understood, tuned and controlled. There is now clearly enough data, most of them being summarized in this article, to predict the anionic reactivity of ynamides, even if further developments will certainly be, at least in part, based on new, unpredictable and unforeseen reactivities. Let us wait and see.

References

[1] For reviews on ynamines, see: (a) J. Ficini, Tetrahedron 32 (1976) 1449;
(b) G. Himbert, in: H. Kropf, E. Schaumann (Eds.), Methoden Der Organischen Chemie (Houben-Weyl), Georg Thieme, Stuttgart, 1993, p. 3267.
[2] For reviews on ynamides, see: (a) G. Evano, A. Coste, K. Jouvin, Angew. Chem., Int. Ed. 49 (2010) 2840;
(b) K.A. DeKorver, H. Li, A.G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R.P. Hsung, Chem. Rev. 110 (2010) 5064;
(c) G. Evano, C. Theunissen, M. Lecomte, Aldrichimica Acta 48 (2015) 59.
[3] T. Sueda, A. Oshima, N. Teno, Org. Lett. 13 (2011) 3996.
[4] K.A. DeKorver, M.C. Walton, T.D. North, R.P. Hsung, Org. Lett. 13 (2011) 4862.
[5] R.E. Beveridge, R.A. Batey, Org. Lett. 14 (2012) 540.
[6] (a) A. Laouiti, M.M. Rammah, M.B. Rammah, J. Marrot, F. Couty, G. Evano, Org. Lett. 14 (2012) 6;
(b) A. Laouiti, K. Jouvin, F. Bourdreux, M.M. Rammah, M.B. Rammah, G. Evano, Synthesis 44 (2012) 1491.
[7] L. Wang, H. Huang, D.L. Priebbenow, F.-F. Pan, C. Bolm, Angew. Chem., Int. Ed. 52 (2013) 3478.
[8] G.C. Nandi, S.R. Kota, T. Naicker, T. Govender, H.G. Kruger, P.I. Arvidsson, Eur. J. Org. Chem. (2015) 2861.
[9] F.G. Perrin, G. Kiefer, L. Jeanbourquin, S. Racine, D. Perrotta, J. Waser, R. Scopelliti, K. Severin, Angew. Chem., Int. Ed. 54 (2015) 13393.

[10] For a review on the synthesis of ynamides, see: G. Evano, K. Jouvin, A. Coste Synthesis 45 (2013) 17.
[11] For representative examples, see: (a) B. Witulski, T. Stengel, Angew. Chem., Int. Ed. 37 (1998) 489;
(b) J.D. Rainier, J.E. Imbriglio, Org. Lett. 1 (1999) 2037.
[12] K. Jouvin, J. Heimburger, G. Evano, Chem. Sci. 3 (2012) 756.
[13] S.J. Mansfield, C.D. Campbell, M.W. Jones, E.A. Anderson, Chem. Commun. 51 (2015) 3316.
[14] (a) J.R. Dunetz, R.L. Danheiser, Org. Lett. 5 (2003) 4011;
(b) Y. Zhang, R.P. Hsung, M.R. Tracey, K.C.M. Kurtz, E.L. Vera, Org. Lett. 6 (2004) 1151.
[15] T. Hamada, X. Ye, S.S. Stahl, J. Am. Chem. Soc. 130 (2008) 833.
[16] A. Coste, G. Karthikeyan, F. Couty, G. Evano, Angew. Chem., Int. Ed. 48 (2009) 4381.
[17] W. Jia, N. Jiao, Org. Lett. 12 (2010) 2000.
[18] K. Jouvin, F. Couty, G. Evano, Org. Lett. 12 (2010) 3272.
[19] For an account on our work on the chemistry of ynamides, see: G. Evano, N. Blanchard, G. Compain, A. Coste, C.S. Demmer, W. Gati, C. Guissart, J. Heimburger, N. Henry, K. Jouvin, G. Karthikeyan, A. Laouiti, M. Lecomte, A. Martin-Mingot, B. Métayer, B. Michelet, A. Nitelet, C. Theunissen, S. Thibaudeau, J. Wang, M. Zarca, C. Zhang Chem. Lett. 45 (2016) 574.
[20] For selected examples, see: (a) N. Saito, Y. Sato, M. Mori, Org. Lett. 4 (2002) 803;
(b) M.R. Tracey, J. Oppenheimer, R.P. Hsung, J. Org. Chem. 71 (2006) 8629;
(c) S. Couty, C. Meyer, J. Cossy, Angew. Chem., Int. Ed. 45 (2006) 6726.
[21] For selected examples, see: (a) J.R. Dunetz, R.L. Danheiser, J. Am. Chem. Soc. 127 (2005) 5776;
(b) M.F. Martínez-Esperón, D. Rodríguez, L. Castedo, C. Saá, Org. Lett. 7 (2005) 2213;
(c) T. Wang, D. Niu, T.R. Hoye, J. Am. Chem. Soc. 138 (2016) 7832;
(d) T. Wang, T.R. Hoye, J. Am. Chem. Soc. 138 (2016) 13870;
(e) G. Duret, R. Quinlan, R.E. Martin, P. Bisseret, M. Neuburger, V. Gandon, N. Blanchard, Org. Lett. 18 (2016) 1610.
[22] For selected examples, see: (a) F. Marion, C. Courillon, M. Malacria, Org. Lett. 5 (2003) 5095;
(b) B. Banerjee, D.N. Litvinov, J. Kang, J.D. Bettale, S.L. Castle, Org. Lett. 12 (2010) 2650.
[23] For selected examples, see: (a) J.A. Mulder, R.P. Hsung, M.O. Frederick, M.R. Tracey, C.A. Zificsak, Org. Lett. 4 (2002) 1383;
(b) H. Li, R.P. Hsung, K.A. DeKorver, Y. Wei, Org. Lett. 12 (2010) 3780;
(c) G. Compain, K. Jouvin, A. Martin-Mingot, G. Evano, J. Marrot, S. Thibaudeau, Chem. Commun. 48 (2012) 5196;
(d) H.A. Laub, G. Evano, H. Mayr, Angew. Chem., Int. Ed. 53 (2014) 4968;
(e) B. Peng, X. Huang, L.-G. Xie, N. Maulide, Angew. Chem., Int. Ed. 53 (2014) 8718;
(f) C. Theunissen, B. Métayer, N. Henry, G. Compain, J. Marrot, A. Martin-Mingot, S. Thibaudeau, G. Evano, J. Am. Chem. Soc. 136 (2014) 12528;
(g) M. Lecomte, G. Evano, Angew. Chem., Int. Ed. 55 (2016) 4547.
[24] For a review on the carbocupration of hetero-substituted alkynes, see: A. Basheer, I. Marek Beilstein J. Org. Chem. 6 (77) (2010).
[25] (a) J.F. Normant, A. Alexakis, A. Commercon, G. Cahiez, J. Villiéras, C. R. Seances Acad. Sci., Ser. C 279 (1974) 763;
(b) A. Alexakis, G. Cahiez, J.F. Normant, J. Villiéras, Bull. Soc. Chim. Fr. (1977) 693.
[26] (a) H. Chechik-Lankin, S. Livshin, I. Marek, Synlett (2005) 2098;
(b) Y. Minko, M. Pasco, H. Chechik, I. Marek, Beilstein J. Org. Chem. 9 (2013) 526.
[27] (a) B. Gourdet, H.W. Lam, J. Am. Chem. Soc. 131 (2009) 3802;
(b) B. Gourdet, M.E. Rudkin, C.A. Watts, H.W. Lam, J. Org. Chem. 74 (2009) 7849.
[28] M. Takimoto, S.S. Gholap, Z. Hou, Chem.—Eur. J. 21 (2015) 15218.
[29] For reviews on the chemistry of enamides, see: (a) D. Carbery, Org. Biomol. Chem. 6 (2008) 3455;
(b) T. Courant, G. Dagousset, G. Masson, Synthesis 47 (2015) 1799.
[30] B. Gourdet, H.W. Lam, Angew. Chem., Int. Ed. 49 (2010) 8733.
[31] B. Gourdet, D.L. Smith, H.W. Lam, Tetrahedron 66 (2010) 6026.
[32] Y. Yang, L. Wang, J. Zhang, Y. Jin, G. Zhu, Chem. Commun. 50 (2014) 2347.
[33] G. Liu, W. Kong, J. Che, G. Zhu, Adv. Synth. Catal. 356 (2014) 3314.
[34] V. Dwivedi, M.H. Babu, R. Kant, M.S. Reddy, Chem. Commun. 51 (2015) 14996.
[35] H. Yasui, H. Yorimitsu, K. Oshima, Bull. Chem. Soc. Jpn. 81 (2008) 373.

[36] S. Vercruysse, K. Jouvin, O. Riant, G. Evano, Synthesis 48 (2016) 3373.
[37] C. Fopp, E. Romain, K. Isaac, F. Chemla, F. Ferreira, O. Jackowski, M. Oestreich, A. Perez-Luna, Org. Lett. 18 (2016) 2054.
[38] E. Romain, C. Fopp, F. Chemla, F. Ferreira, O. Jackowski, M. Oestreich, A. Perez-Luna, Angew. Chem., Int. Ed. 53 (2014) 11333.
[39] (a) S. Minière, J.-C. Cintrat, Synthesis (2001) 705;
(b) S. Naud, J.-C. Cintrat, Synthesis (2003) 1391;
(c) D. Buissonneaud, J.-C. Cintrat, Tetrahedron Lett. 47 (2006) 3139.
[40] G. He, Q. Zhang, H. Huang, S. Chen, Q. Wang, D. Zhang, R. Zhang, H. Zhu, Eur. J. Org. Chem. (2013) 6979.
[41] N. Saito, K. Saito, H. Sato, Y. Sato, Adv. Synth. Catal. 355 (2013) 853.
[42] H. Yasui, H. Yorimitsu, K. Oshima, Chem. Lett. 36 (2007) 32.
[43] B. Gourdet, M.E. Rudkin, H.W. Lam, Org. Lett. 12 (2010) 2554.
[44] H. Liu, Y. Yang, J. Wu, X.-N. Wang, J. Chang, Chem. Commun. 52 (2016) 6801.
[45] J.P. Das, H. Chechik, I. Marek, Nat. Chem. 1 (2009) 128.
[46] Y. Minko, M. Pasco, L. Lercher, M. Botoshansky, I. Marek, Nature 490 (2012) 522.
[47] Z. Nairoukh, I. Marek, Angew. Chem., Int. Ed. 54 (2015) 14393.
[48] For an excellent comprehensive review on Baldwin's rules for the cyclization of alkynes, see: K. Gilmore, I.V. Alabugin Chem. Rev. 111 (2011) 6513.
[49] W. Gati, M.M. Rammah, M.B. Rammah, F. Couty, G. Evano, J. Am. Chem. Soc. 134 (2012) 9078.
[50] W. Gati, M.M. Rammah, M.B. Rammah, G. Evano, Beilstein J. Org. Chem. 8 (2012) 2214.
[51] W. Gati, F. Couty, T. Boubaker, M.M. Rammah, M.B. Rammah, G. Evano, Org. Lett. 15 (2013) 3122.
[52] (a) A. Frischmuth, P. Knochel, Angew. Chem., Int. Ed. 52 (2013) 10084;
(b) J. Nickel, M. Fernàndez, L. Klier, P. Knochel, Chem.—Eur. J. 22 (2016) 14397.
[53] (a) S. Couty, B. Liégault, C. Meyer, J. Cossy, Org. Lett. 6 (2004) 2511;
(b) S. Couty, B. Liegault, C. Meyer, J. Cossy, Tetrahedron 62 (2006) 3882.
[54] S. Couty, C. Meyer, J. Cossy, Tetrahedron Lett. 47 (2006) 767.
[55] (a) R.L. Greenaway, C.D. Campbell, O.T. Holton, C.A. Russel, E.A. Anderson, Chem.—Eur. J. 17 (2011) 14366;
(b) C.D. Campbell, R.L. Greenaway, O.T. Holton, P.R. Walker, H.A. Chapman, C.A. Russel, G. Carr, A.L. Thomson, E.A. Anderson, Chem.—Eur. J. 21 (2015) 12627.
[56] C.D. Campbell, R.L. Greenaway, O.T. Holton, H.A. Chapman, E.A. Anderson, Chem. Commun. 50 (2014) 5187.
[57] R. Lhermet, M. Ahmad, C. Hauduc, C. Fressigné, M. Durandetti, J. Maddaluno, Chem.—Eur. J. 21 (2015) 8105.
[58] (a) C. Laroche, S.M. Kerwin, Tetrahedron Lett. 50 (2009) 5194;
(b) C. Laroche, S.M. Kerwin, J. Org. Chem. 74 (2009) 9229.
[59] A. Laouiti, F. Couty, J. Marrot, T. Boubaker, M.M. Rammah, M.B. Rammah, G. Evano, Org. Lett. 16 (2014) 2252.
[60] A. Hentz, P. Retailleau, V. Gandon, K. Cariou, R.H. Dodd, Angew. Chem., Int. Ed. 53 (2014) 8333.
[61] C.S. Demmer, G. Evano, Synlett 27 (2016) 1873.
[62] For representative examples, see: (a) D. Rodríguez, M.F. Martínez-Esperón, L. Castedo, C. Saá, Synlett (2007) 1963;
(b) R. Qi, X.-N. Wang, K.A. DeKorver, Y. Tang, C.-C. Wang, Q. Li, H. Li, M.-C. Lv, Q. Yu, R.P. Hsung, Synthesis 45 (2013) 1749;
(c) X.-N. Wang, R.P. Hsung, R. Qi, S.K. Fox, M.-C. Lv, Org. Lett. 15 (2013) 2514.
[63] (a) D. Brückner, Synlett (2000) 1402;
(b) D. Brückner, Tetrahedron 62 (2006) 3809.
[64] (a) D. Rodríguez, L. Castedo, C. Saá, Synlett (2004) 783;
(b) M.F. Martínez-Esperón, D. Rodríguez, L. Castedo, C. Saá, Tetrahedron 62 (2006) 3843.
[65] D. Rodríguez, L. Castedo, C. Saá, Synlett (2004) 377.
[66] B. Witulski, T. Schweikert, D. Schollmeyer, N.A. Nemkovich, Chem. Commun. 46 (2010) 2953.
[67] P. Zhang, A.M. Cook, Y. Liu, C. Wolf, J. Org. Chem. 79 (2014) 4167.
[68] A.M. Cook, C. Wolf, Chem. Commun. 50 (2014) 3151.