Media-Driven Pd-Catalyzed Reaction Cascades with 1,3-Diynamides Leading Selectively to Either Indoles or Quinolines

Illia Lenko,[a] Alexander Mamontov,[a] Carole Alayrac,*[a] Rémi Legay,[a] and Bernhard Witulski,*[a]

[a] I. Lenko, Dr. A. Mamontov, Dr. C. Alayrac, Dr. R. Legay, Prof. Dr. B. Witulski,
Laboratoire de Chimie Moléculaire et Thio-organique
CNRS UMR 6507, ENSICAEN & UNICAEN, Normandie Univ.
6 Bvd Maréchal Juin, 14050 Caen (France)
E-mail: carole.witulski-alayrac@ensicaen.fr; E-Mail:Bernhard.witulski@ensicaen.fr

Supporting information for this article is given via a link at the end of the document.

Abstract: Divergent Pd-catalyzed reaction cascades with various 1,3-diynamides yielding either 2-amino-3-alkynylindoles or 2-amino-4-alkenylquinolines were established. Omitting or adding TBAF (tetrabutylammonium fluoride) to the reaction of *N*,*N*-(2-iodophenyl)(4-toluenesulfonyl)-1,3-diynamides with secondary or primary amines in the presence of KOH in THF and catalytic amounts of $Pd(PPh_3)_4$ completely changed the outcome of the reaction. In the absence of TBAF, 2-amino-3-alkynylindoles were the sole products, while the presence of TBAF switched the product formation to 2-amino-4-alkenylquinolines. Deuterium labeling proceeded selectively at the C3 and C11 positions of the 2-amino-4-alkenylquinoline products and this suggests the unprecedented formation of [4]cumulenimines from 1,3-diynamides as reactive key intermediates.

Ynamides are inspiring building blocks for the construction of heterocycles relevant to pharmaceutical, agrochemical, and materials chemistry.[1] Their key reactivity is stirred by an electronically tunable nitrogen atom necessitating an adjacent electron-rich and polarized carbon-carbon triple bond being best described by the mesomeric forms A and A' in Figure 1. The electron-withdrawing group (EWG) attached to the ynamide nitrogen is guaranteeing sufficient stability and tunable reactivity.[1,2] Further activation of ynamides often relies on their reaction with Brønsted[3] or transition metal π-acids[4] to form keteniminium ions[1a,5] providing superb reactivity within addition and/or annulation processes. Such approaches were particularly realized in the emerging gold catalysis of ynamides[6] leading to indoles[7,8] and quinolines[9,10] with different substitution pattern. Protocols aiming at generating reactive neutral ketenimines[11] from ynamides have been less explored.[12] They encompass the *N*→*C* 1,3-tosyl group transfer of an *N*-(4-toluenesulfonyl)ynamide carboxylic ester (Figure 1a)[13] and the *N*→*C* allyl shift *via* aza-Claisen rearrangement (Figure 1b).[8e,14] Decarboxylative allyl rearrangements were also reported to involve ketenimine intermediates that were designed to undergo a second Pd-guided [3,3] sigmatropic rearrangement (Figure 1c).[15] Last but not least, the saponification of ynamides under strong basic conditions provided ketenimines that were trapped in subsequent transformations[16] such as the addition of indoles,[16a] or the Imino-Staudinger reaction (Figure 1d).[16d]

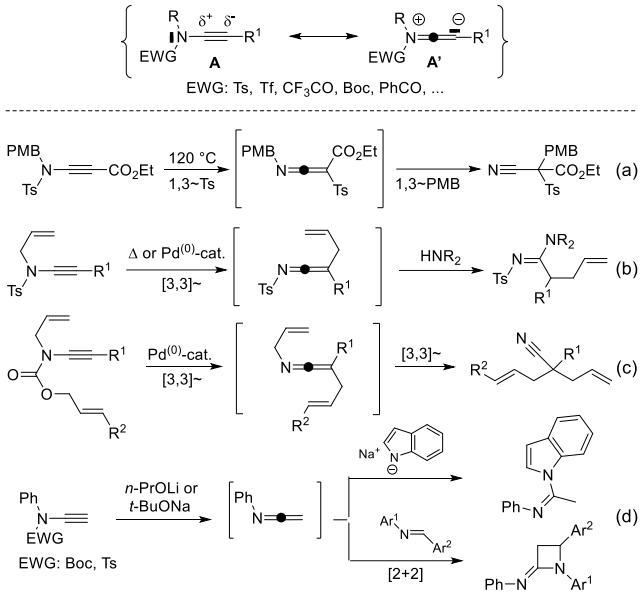
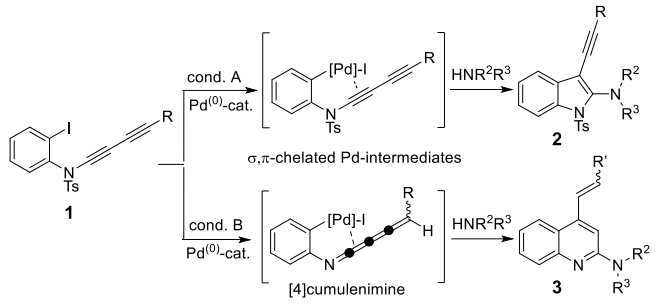


Figure 1. Resonance structures **A/A'** of ynamides; and ynamides as precursors of *in situ* generated ketenimine intermediates (a-d).

Some time ago, we reported the synthesis of 2-aminoindoles from *N*-alkynyl-2-haloanilides by a Pd-catalyzed heteroannulation reaction.[8m] This diversity oriented approach encompassed the activation of ynamides through *in situ* formed σ,π-chelated palladium intermediates facilitating the addition of various primary and secondary amines to give 2-aminoindoles after reductive elimination.

As a part of our current efforts in the synthesis and application of 1,3-diynamides,[17] the extension of this 2-aminoindole approach was investigated aiming to unravel the ethynylogous reactivity of 1,3-diynamides and gaining access to versatile functionalized 2-amino-3-alkynylindoles **2** (Scheme 1). However, by exploring this annulation sequence we realized that by increasing the basicity of the reaction medium an unprecedented reactivity mode of 1,3-diynamides was observed: *Instead of the expected indoles **2** now 2-amino-4-alkenylquinolines **3** were produced – most likely via [4]cumulenimine intermediates*[18,19].



Scheme 1. Pd-catalyzed transformation of 1,3-diynamides **1** to 2-amino-3-alkynylindoles **2** and its unprecedented reaction to give 2-amino-4-alkenylquinolines **3** via [4]cumulenimines.

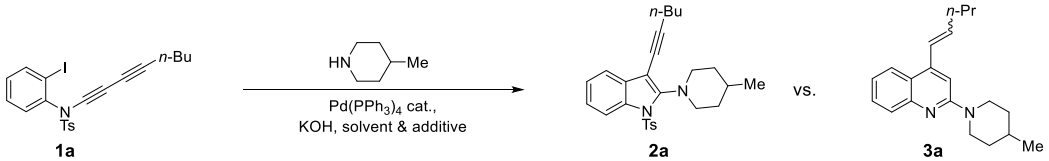
In view of the significance of indoles[20] and quinolines[21] as privileged molecular platforms for drug discovery, divergent syntheses to these heterocyclic motifs allowing a great extent of structural diversity are important. Here, we report that the outcome of the reaction between 1,3-diynamide **1** and nucleophilic amines can be steered from the formation of 2-amino-3-alkynyl-indoles **2** to the selective construct of functionalized 2-amino-4-alkenyl-quinolines **3** by just adding TBAF to the reaction medium while keeping all other reagents and conditions identical.

As a first experiment, the reaction of 1,3-diynamide **1a** with 4-methylpiperidine, pre-catalyst $Pd(PPh_3)_4$ (10 mol%) and K_2CO_3 in THF was run at 70 °C for 12 h (Table 1, entry 1). The expected indole **2a** was readily produced and isolated in 74% yield. With KOH as the base (solid KOH in THF) the reaction was faster and full conversion was reached after 2 h at 70 °C (76% yield; Table 1, entry 2). Switching the solvent to ethanol, in order to improve the solubility of KOH in the reaction medium, led to the full conversion of **1a** after 1 h (reaction monitored by TLC). However, now a new compound - different from indole **2a** - was formed selectively and isolated in 65% yield. It was identified as the 2-amino-4-alkenylquinoline **3a** (Table 1, entry 3; for 2D NMR analysis, see supporting information). Moreover, now the indole **2a** was not found.

Optimization favouring the formation of quinoline **3a** was taken on: Small amounts of EtOH in THF sufficiently increased the solubility of KOH and promoted the formation of **3a** (71% yield) during 1h at 70 °C (Table 1, entry 4). When THF was replaced by toluene the reaction was slowed down and the yield dropped to 55% (Table 1, entry 5). The effect of TBAF as additive aiming to improve the solubility of hydroxide anions in THF through counter ion exchange (Bu_4NOH instead of KOH) was investigated. Gratifyingly, the reaction of **1a** run in the presence of TBAF (10 equiv) in THF furnished **3a** in 80% yield after 1 h at 70 °C (Table 1, entry 6). Clearly, the presence of TBAF boosted the formation of the 2-aminoquinoline **3a** - and even 2.5 equivalents of TBAF with respect to substrate **3a** were sufficient to promote the quinoline formation (Table 1, entry 7). It is noteworthy to mention, that the synthesis of **3a** proceeded even at room temperature in the presence of TBAF, albeit with a lower yield of 49% (Table 1, entry 8).

As observed with 4-methylpiperidine as the nucleophile, the presence or absence of the additive TBAF prompted a switch in the reaction of **1a** with primary and secondary amines. Without TBAF the 2-amino-3-alkynylindoles **2a-m** were the exclusively formed products (Scheme 2). Morpholine, 1-benzylpiperazine, acyclic dialkyl amines or *N*-methylanilines led to the corresponding indoles **2b-i** in yields up to 98%. Conversion of **1a** into the corresponding indoles **2a-h** required 2-3 h heating (70 °C) with 10 mol% of $Pd(PPh_3)_4$ as the catalyst source and solid KOH as the base in THF. Notably, the unprotected alcohol function of **1c** was tolerated and the indoles **2k** and **2l** were obtained in 83% and 99% yield with respectively morpholine and 2,2-dimethoxy-*N*-methylethanamine. Finally, the latter gave the 2-amino-3-alkynylindole **2m** (93% yield) in the reaction with **1b** ($R^1 = (CH_2)_3OBn$).

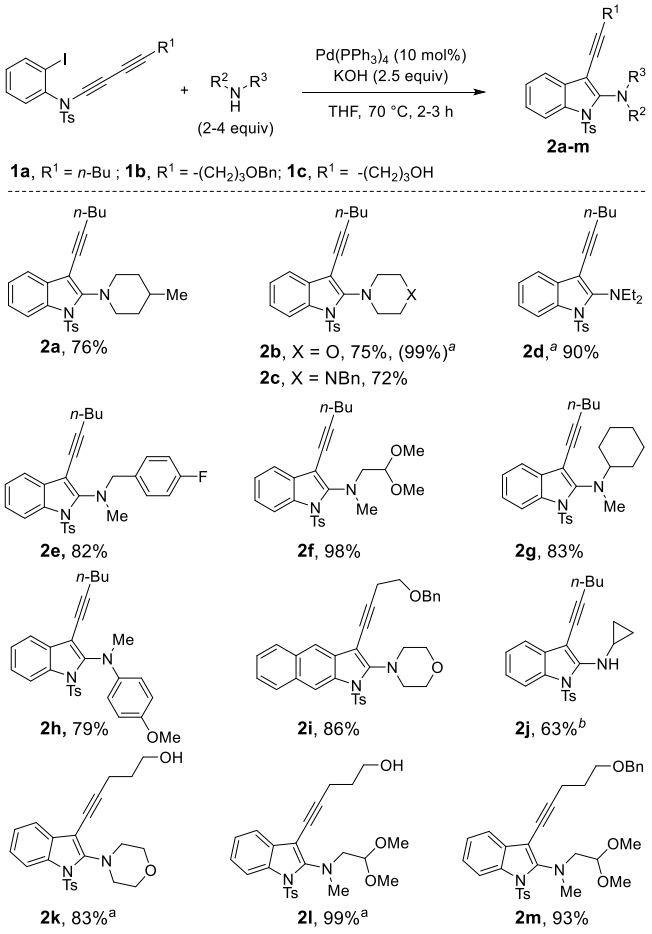
Table 1. Optimization of the synthesis of 2-amino-3-alkynylindole **2a** and 2-amino-4alkenylquinoline **3a**[a]



1a **2a** **3a**

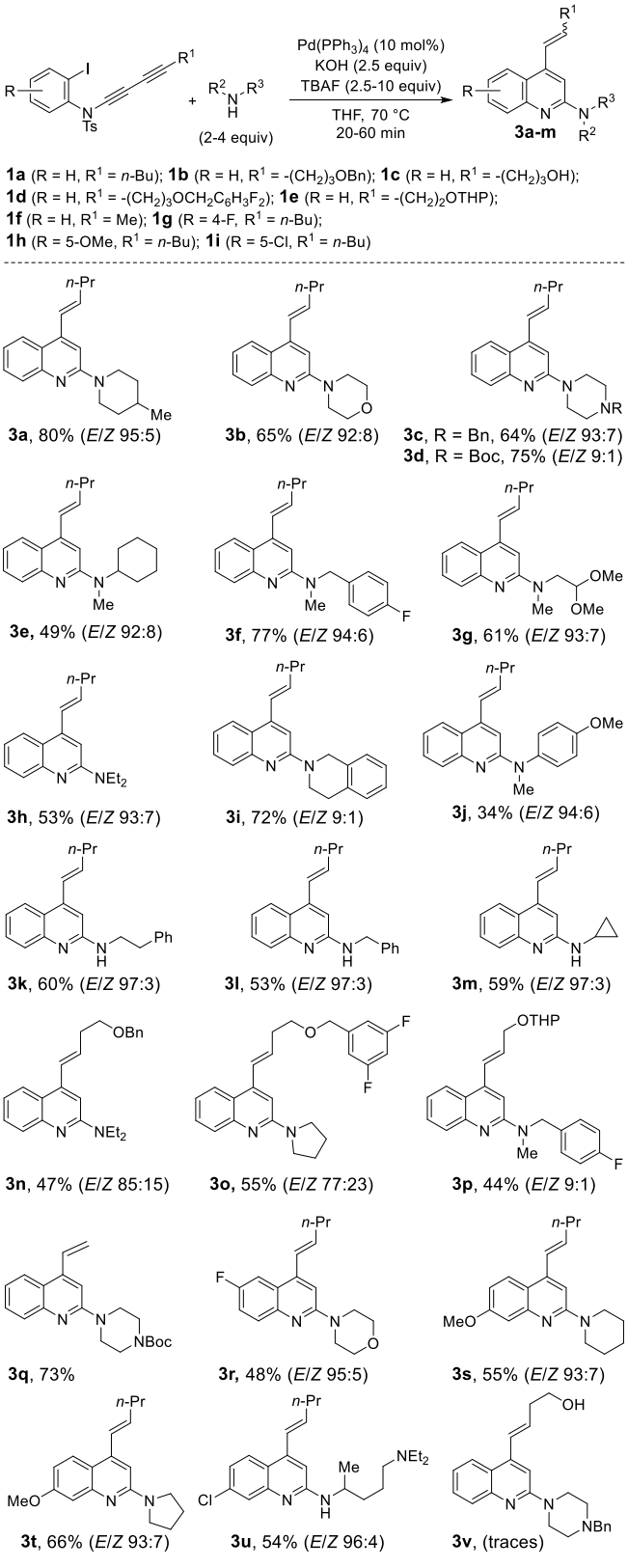
Entry[a]	Solvent	Additive (equiv)	Amine (equiv)	t [°C]	Time [h]	**2a** Yield [%][b]	**3a** Yield [%][b]	**3a** (*E*) / (*Z*)[c]
1[d]	THF	K_2CO_3 (2.5)	2	70	12	74	--	--
2	THF	none	2	70	2	76	--	--
3	EtOH	none	5	70	1	--	65	93 : 7
4	THF	EtOH (10)	5	70	1	--	71	92 : 8
5	Toluene	EtOH (10)	5	70	1	--	55	88 : 12
6	THF	TBAF (10)	2	70	1	--	80	95 : 5
7	THF	TBAF (2.5)	2	70	1	--	74	94 : 6
8	THF	TBAF (5)	2	25	1	--	49	88 :12

[a] Reaction conditions: **1a** (0.1 mmol), 4-methylpiperidine (2 equiv), $Pd(PPh_3)_4$ (10 mol%), KOH (2.5 equiv), Solvent (1mL). [b] Yield of isolated product after chromatography. [c] Isomer ratio determined from the ^1H NMR spectrum by integration of the olefinic proton signals assigned to the (*E*) and (*Z*) isomers. [d] reaction run without KOH.



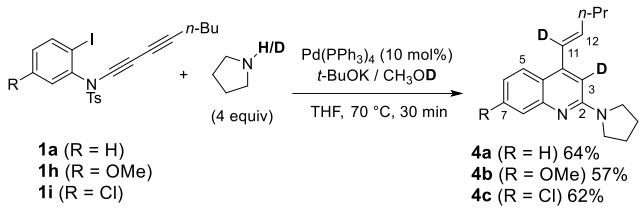
Scheme 2. Synthesis of indoles **2a-m**. [a]K_2CO_3 (2.5 equiv), 12 h at 70 °C. [b]Cs_2CO_3 (2.5 equiv) and 10 equiv cyclopropylamine, 4 h at 80 °C.

The scope of the 2-amino-4-alkenylquinoline-(**3**)-synthesis promoted by adding TBAF to the reaction medium was surveyed: Defined reaction conditions (10 mol% of $Pd(PPh_3)_4$, 2.5 equiv KOH, reaction temperature 70 °C) were applied to all transformations of 1,3-diynamide **1a** (0.1 mmol in 1 mL of a commercially available 1M TBAF/THF solution) with various amines. Both, cyclic and acyclic secondary amines led to the corresponding 2-amino-4-alkenylquinolines **3a-i** in 49 to 80% yield (Scheme 3). In all cases the major isomer had (*E*) configuration. The reaction proceeded also with the weaker nucleophilic *N*-methyl-*para*-methoxyaniline to afford the quinoline **3j** in 34% yield. Furthermore, it was successful with primary amines to give the functionalized 2-amino-4-alkenylquinolines **3k-m** (53-60% yield). The scope was further extended through variations in the 1,3-diynamide substrate - by substituents on the 1,3-diyne or the phenyl moieties. For example, the *O*-benzyl, *O*-3,5-difluorobenzyl, or *O*-THP substituted 1,3-diynamide substrates **1b**, **1d**, and **1e** effectively underwent this reaction to give the quinolines **3n-p** with 2-diethylamine, 2-pyrrolidine, and 2-(4-fluorobenzyl)methylamine, in 47, 55 and 44% yield respectively. The methyl group bearing 1,3-diynamide **1f** and *N*-Boc-piperazine gave 2-amino-4-vinylquinoline **3q** in 73% yield. Substitution of the phenyl ring of 1,3-diynamides by an electron-withdrawing or electron-donating group did not affect the efficiency of the synthesis as exemplified by the obtained 2-amino-4-alkenylquinolines **3r-u** (48-66% yield). The 1,3-diynamide **1c** with its non-protected hydroxy moiety, however, yielded only trace amounts of **3v** with decomposition of the starting 1,3-diynamide.



Scheme 3. Synthesis of quinolines **3a-u.** The *E/Z*- ratio was determined via ^1H NMR spectroscopy by integration of the corresponding olefinic proton signals.

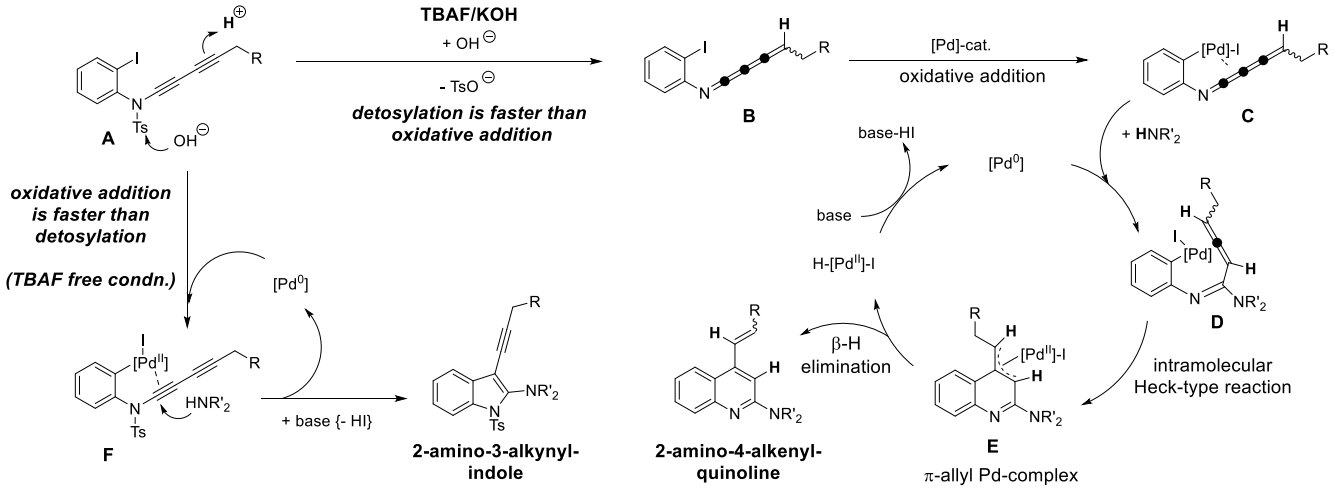
Deuterium labelling experiments were helpful to provide mechanistic insights into the conversion of 1,3-diynamides into 2-amino-4-alkenylquinolines. These experiments were performed with *t*-BuOK in CH_3OD/THF to promote efficient H/D exchange with the amine NH proton and to exclude other proton sources that are obvious when using KOH as the base. Deuterium incorporation experiments with the 1,3-diynamides **1a, 1h,** and **1i** provided the deuterated quinolines **4a-c** in yields of 64%, 57%, and 62% respectively (Scheme 4).



Scheme 4. Deuterium labelling experiment with *in situ* prepared *N*-deuterated pyrrolidine. Yields are given for the mixture of 3,11-bis- and the two mono-deuterated products with a ratio of approx. 8:2 respectively.

The deuterium was selectively incorporated into the C3 and C11 positions of the quinoline product and this was evidenced by a very significant intensity decrease/disappearance of the corresponding ^{1}H-NMR signals at δ = 6.58 (s, H-3) and 6.91 (broad d, H-11) for product **4b** in comparison to the non-deuterated product **3t** (for further details on the deuterium labelling experiments, see supporting information).

By considering the above deuterium labelling experiments, the mechanism outlined in Scheme 5 is proposed. Saponification of the 1,3-diynamide **A** with TBAF/KOH in THF gives the [4]cumulenimine **B** that after oxidative addition of the Pd(0)-catalyst to the chelated Pd-species **C** facilitates amine addition to give the allene derived intermediate **D**. Intramolecular Heck-type reaction furnishes the annulated π-allyl-palladium species **E**.[22,23] The latter undergoes β-hydrogen elimination to produce the 2-amino-4-alkenylquinoline product. However, when the oxidative addition of the palladium catalyst to the iodophenyl moiety of the 1,3-diynamide (**A**→**F**) is faster than its detosylation (**A**→**B**) the σ,π-chelated palladium species **F** is formed activating the ynamide carbon-carbon triple bond and facilitating amine addition along the 2-amino-3-alkynylindole formation.



Scheme 5. Proposed mechanism for the synthesis of 2-amino-4-alkenylquinolines involving the [4]cumulenimine **B** and the TBAF-free pathway to 2-amino-3-alkynylindoles. H atoms (bold) indicate the positions identified by deuterium incorporation experiments.

In conclusion, we have developed divergent Pd-catalyzed reaction cascades for the selective synthesis of either 2-amino-3-alkynylindoles or 2-amino-4-alkenylquinolines from 1,3-diynamides and primary or secondary amines. Starting from identical or similar substrates the outcome of the reaction giving either indole or quinoline motifs can be switched respectively by the absence or presence of TBAF. The *in situ* generation of [4]cumulenimine intermediates is proposed as a key step of the 2-amino-4-alkenylquinoline synthesis. This was supported by selective deuterium incorporation into the C3 and C11 positions of the quinoline products. Thus, a new reaction mode – the *in situ* transformation of 1,3-diynamides into [4]cumulenimines – was revealed and this will open new exciting opportunities for the development of the chemistry of ynamides and [n]cumulenimines.

Acknowledgements

This work was supported by the CNRS, Normandie Université, the Conseil Régional de Normandie, and the Fonds Européen de Développement Régional (FEDER).

Keywords: ynamides • indoles • quinolines • cumulenes • homogeneous catalysis

[1] For reviews on the chemistry of ynamides, see: a) Y.-C. Hu, Y. Zhao, B. Wan, Q.-A. Chen, *Chem. Soc. Rev.* **2021**, *50*, 2582-2625; b) C. C. Lynch, A. Sripada, C. Wolf, *Chem. Soc. Rev*. **2020**, *49*, 8543-8583; c) C. Mahe, K. Cariou, *Adv. Synth. Catal*. **2020**, *362*, 4820-4832; d) T.-D. Tan, Z.-S. Wang, P.-C. Qian, L.-W. Ye, *Small Methods* **2021**, *5*,

2000673; e) B. Reinus, S. M. Kerwin, *Molecules* **2019**, *24*, 422; f) B. Zhou, T.-D. Tan, X.-Q. Zhu, M. Shang, L.-W. Ye, *ACS Catal.* **2019**, *9*, 6393-6406; g) B. Prabagar, N. Ghosh, A. K. Sahoo, *Synlett* **2017**, *28*, 2539-2555; h) A. M. Cook, C. Wolf, *Tetrahedron Lett*. **2015**, *56*, 2377-2392; i) G. Evano, A. Coste, K. Jouvin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2840-2859; j) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064-5106.

[2] a) B. Witulski, T. Stengel, *Angew. Chem. Int. Ed.* **1998**, *37*, 489-492; b) B. Witulski, M. Gößmann, *Chem. Commun*. **1999**, 1879-1880.

[3] a) Y.-B. Chen, P.-C. Qian, L.-W. Ye, *Chem. Soc. Rev.* **2020**, *49*, 8897-8909; b) W. Hu, F. Zhang, C. Chen, T. Qi, Y. Shen, G. Qian, Z. Rong, *Chem. Commun*. **2021**, *57*, 6995-6998; c) L. Xu, P. Yang, L. Wang, *Org. Chem. Front*. **2018**, *5*, 1854-1858; d) M. Lecomte, G. Evano, *Angew. Chem. Int. Ed.* **2016**, *55*, 4547-4551; e) C. Theunissen, B. Métayer, N. Henry, G. Compain, J. Marrot, A. Martin-Mingot, S. Thibaudeau, G. Evano, *J. Am. Chem. Soc.* **2014**, *136*, 12528-12531; f) S. Nayak, N. Ghosh, B. Prabagar, A. K. Sahoo, *Org. Lett.* **2015**, *17*, 5662-5665; g) N. Ghosh, S. Nayak, A. K. Sahoo, *Chem. Eur. J.* **2013**, *19*, 9428-9433; g) Y. Yamaoka, T. Yoshida, M. Shinozaki, K.-i. Yamada, K. Takasu, *J. Org. Chem.* **2015**, *80*, 957-964; h) Y. Zhang, R. P. Hsung, X. Zhang, J. Huang, B. W. Slafer, A. Davis, *Org. Lett.* **2005**, *7*, 1047-1050.

[4] a) F.-L. Hong, L.-W. Ye, *Acc. Chem. Res*. **2020**, *53*, 2003-2019; b) for Pd- and Pt-mediated divergent annulations utilizing *N*-alkynylindoles, see: K. Alam, S. W. Hong, K. H. Oh, J. K. Park, *Angew. Chem. Int. Ed*. **2017**, *56*, 13387-13391.

[5] a) G. Evano, M. Lecomte, P. Thilmany, C. Theunissen, *Synthesis* **2017**, *49*, 3183-3214; b) C. Madelaine, V. Valerio, N. Maulide, *Chem. Asian J.* **2011,** *6*, 2224-2239.

[6] a) D. Campeau, D. F. León Rayo, A. Mansour, K. Muratov, F. Gagosz, *Chem. Rev*. **2021**, *121*, 8756-8867; b) X. Zhao, M. Rudolph, A. M. Asiri, A. S. K. Hashmi, *Front. Chem. Sci. Eng*. **2020**, *14*, 317-349; c) F. Pan, C. Shu, L.-W. Ye, *Org. Biomol. Chem.* **2016**, *14*, 9456-9465; d) Z. Tong, O. L. Garry, P. J. Smith, Y. Jiang, S. J. Mansfield, E. A. Anderson, *Org. Lett*. **2021**, *23*, 4888-4892.

[7] For indole syntheses based on Au-catalysis with ynamides, see: a) X. Tian, L. Song, K. Farshadfar, M. Rudolph, F. Rominger, T. Oeser, A. Ariafard, A. S. K. Hashmi, *Angew. Chem. Int. Ed*. **2020**, *59*, 471-478; b) X. Tian, L. Song, M. Rudolph, F. Rominger, T. Oeser, A. S. K. Hashmi, *Angew. Chem. Int. Ed*. **2019**, *58*, 3589-3593; c) X. Tian, L. Song, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Org. Lett*. **2019**, *21*, 4327-4330; d) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794-797; e) C. Shu, Y.-H. Wang, B. Zhou, X.-L. Li, Y.-F. Ping, X. Lu, L.-W. Ye, *J. Am. Chem. Soc*. **2015**, *137*, 9567-9570; f) Y. Tokimizu, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2014**, *16*, 3138-3141; g) S. Kramer, K. Dooleweerdt, A. T. Lindhardt, M. Rottländer, T. Skrydstrup, *Org. Lett*. **2009**, *11*, 4208-4211.

[8] For indole syntheses based on ynamides, see: a) J. Zhang, Y. Li, C. Zhang, X.-N Wang, J. Chang, *Org. Lett*. **2021**, *23*, 2029-2035; b) Z.-S. Wang, Y.-B. Chen, K. Wang, Z. Xu, L.-W. Ye, *Green Chem*. **2020**, *22*, 4483-4488; c) Z.-S. Wang, Y.-B. Chen, H.-W. Zhang, Z. Sun, C. Zhu, L.-W. Ye, *J. Am. Chem. Soc*. **2020**, *142*, 3636-3644; d) Y. H. Kim, H. J. Yoo, S. W. Youn, *Chem. Commun*. **2020**, *56*, 13963-13966; e) R. Su, X.-H. Yang, M. Hu, Q.-A. Wang, J.-H. Li, *Org. Lett*. **2019**, *21*, 2786-2789; f) S. E. Kiruthika, P. T. Perumal, *Org. Lett*. **2014**, *16*, 484-487; g) A. Frischmuth, P. Knochel, *Angew. Chem. Int. Ed*. **2013**, *52*, 10084-10088; h) T. Y. Lam, Y.-P. Wang, R. L. Danheiser, *J. Org. Chem.* **2013**, *78*, 9396-9414; i) J. Cao, Y. Xu, Y. Kong, Y. Cui, Z. Hu, G. Wang, Y. Deng, G. Lai, *Org. Lett*. **2012**, *14*, 38-41; j) N. Saito, T. Ichimaru, Y. Sato, *Org. Lett.* **2012**, *14*, 1914-1917; k) K. Dooleweerdt, T. Ruhland, T. Skrydstrup, *Org. Lett.* **2009**, *11*, 221-224; l) P.-Y. Yao, Y. Zhang, R. P. Hsung, K. Zhao, *Org. Lett.* **2008**, *10*, 4275-4278; m) B. Witulski, C. Alayrac, L. Tevzadze-Saeftel, *Angew. Chem. Int. Ed.* **2003**, *42*, 4257-4260.

[9] For quinoline synthesis based on Au-catalysis, see: a) X. Zhao, X. Song, H. Jin, Z. Zeng, Q. Wang, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Adv. Synth. Catal.* **2018**, *360*, 2720-2726; b) Z. Zeng, H. Jin, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed*. **2018**, *57*, 16549-16553; c) N. D. Rode, A. Arcadi, A. Di Nicola, F. Marinelli, V. Michelet, *Org. Lett.* **2018**, *20*, 5103-5106; d) R. Vanjari, S. Dutta, M. P. Gogoi, V. Gandon, A. K. Sahoo, *Org. Lett.* **2018**, *20*, 8077-8081; e) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed*. **2016**, *55*, 12688-12692.

[10] For quinoline syntheses based on ynamides, see: a) K. H. Oh, J. G. Kim, J. K. Park, *Org. Lett*. **2017**, *19*, 3994-3997; b) T. Wezeman, S. Zhong, M. Nieger, S. Bräse, *Angew. Chem. Int. Ed*. **2016**, *55*, 3823-3827; c) T. P. Willumstad, P. D. Boudreau, R. L. Danheiser, *J. Org. Chem.* **2015**, *80*, 11794-11805; d) M. Movassaghi, M. D. Hill, O. K. Ahmad, *J. Am. Chem. Soc*. **2007**, *129*, 10096-10097.

[11] For reviews on ketenimines, see: a) P. Lu, Y. Wang, *Chem. Soc. Rev.* **2012**, *41*, 5687-5705; b) G. R. Krow, *Angew. Chem. Int. Ed*. **1971**, *10*, 435-449.

[12] R. H. Dodd, K. Cariou, *Chem. Eur. J.* **2018**, *24*, 2297-2304.

[13] M. Bendikov, H. M. Duong, E. Bolanos, F. Wudl, *Org. Lett.* **2005**, *7*, 783-786.

[14] a) H. V. Adcock, E. Chatzopoulou, P. W. Davies, *Angew. Chem. Int. Ed.* **2015**, *54*, 15525-15529; b) K. A. DeKorver, R. P. Hsung, W.-Z. Song, X.-N. Wang, M. C. Walton, *Org. Lett.* **2012**, *14*, 3214-3217; c) K. A. DeKorver, R. P. Hsung, A. G. Lohse, Y. Zhang, *Org. Lett.* **2010**, *12*, 1840-1843; d) Y. Zhang, K. A. DeKorver, A. G. Lohse, Y.-S. Zhang, J. Huang, R. P. Hsung, *Org. Lett.* **2009**, *11*, 899-902.

[15] J. R. Alexander, V. I. Shchepetkina, K. S. Stankevich, R. J. Benedict, S. P. Bernhard, R. J. Dreiling, M. J. Cook, *Org. Lett.* **2021**, *23*, 559-564.

[16] a) A. Hentz, P. Retailleau, V. Gandon, K. Cariou, R. H. Dodd, *Angew. Chem. Int. Ed.* **2014**, *53*, 8333-8337; b) L. Yu, J. Cao, *Org. Biomol. Chem.* **2014**, *12*, 3986-3990; c) Y. Kong, L. Yu, Y. Cui, J. Cao, *Synthesis* **2014**, *46*, 183-188; d) E. Romero, C. Minard, M. Benchekroun, S. Ventre, P. Retailleau, R. H. Dodd, K. Cariou, *Chem. Eur. J.* **2017**, *23*, 12991-12994; e) A. C. A. D'Hollander, E. Romero, K. Vijayakumar, C. Le Houérou, P. Retailleau, R. H. Dodd, B. I. Iorga, K. Cariou, *Adv. Synth. Catal.* **2021**, *363*, 2903-2908.

[17] a) I. Talbi, C. Alayrac, J.-F. Lohier, S. Touil, B. Witulski, *Org. Lett.* **2016**, *18*, 2656-2659; b) T.-H. Doan, I. Talbi, J.-F Lohier, S. Touil, C. Alayrac, B. Witulski, *J. Mol. Struct.* **2016**, *1116,* 127-134. c) B. Witulski, T. Schweikert, D. Schollmeyer, N. A. Nemkovich, *Chem. Commun.* **2010**, *46*, 2953-2955;

[18] For [n]cumulenes, see: a) D. Wendinger, R. R. Tykwinski, *Acc. Chem. Res*. **2017**, *50*, 1468-1479; b) J. A. Januszewski, R. R. Tykwinski, *Chem. Soc. Rev*. **2014**, *43*, 3184-3203.

[19] For *in situ* azacumulene generation via reactions of terminal 1,3-diynes and azides, see: S. Ghorai, D. Lee, *Org. Lett.* **2021**, *23*, 697-701.

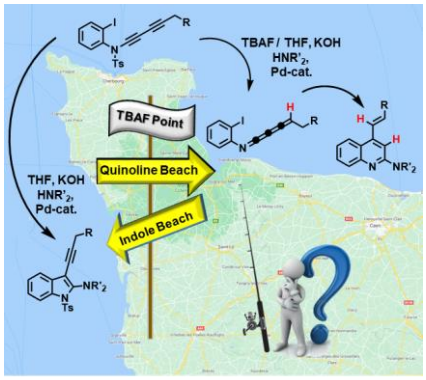
[20] a) *The Chemistry of Indoles;* (Ed.: R. J. Sundberg), Academic Press, New York, **1996**; b) *Heterocyclic Scaffolds II: Reactions and Applications of Indoles*, (Ed.: G. W. Gribble), Springer, Berlin, **2010**; pp 1-488; c) S. Kumar, Ritika, *Futur. J. Pharm. Sci.* **2020**, *6*, 121; d) D. F. Taber, P. K. Tirunahari, *Tetrahedron*, **2011**, *67*, 7195-7210; d) M. Somei, F. Yamada, *Nat. Prod. Rep*. **2005**, *22*, 73-103.

[21] a) B. S. Matada, R. Pattanashettar, N. G. Yernale, *Bioorg. Med. Chem.* **2021**, *32*, 115973; b) A. Weyesa, E. Mulugeta, *RSC Adv*. **2020**, *10*, 20784-20793; c) A. Dorababu, *ChemistrySelect* **2020**, *5*, 13902-13915.

[22] For carbopalladation of *N*-allenamides, see: a) S. Guo, J. Chen, M. Yi, L. Dong, A. Lin, H. Yao, *Org. Chem. Front.* **2021**, *8*, 1783-1788; b) X. Chen, G. Qiu, R. Liu, D. Chen, Z. Chen, *Org. Chem. Front.* **2020**, *7,* 890-895.

[23] For a review on carbopalladation, see: E.-i. Negishi, C. Copéret, S. Ma, S.-Y. Liou, F. Liu, *Chem. Rev.* **1996**, *96*, 365-394.

Entry for the Table of Contents



Which coast to take? Divergent Pd-catalyzed reaction cascades with 1,3-diynamides and primary or secondary amines result by adding or omitting TBAF. In the absence of TBAF 2-amino-3-alkynylindoles are formed – whereas the addition of TBAF leads selectively to 2-amino-4-alkenylquinolines. The latter pathway involves the unprecedented formation of [4]cumulenimines from 1,3-diynamides.