RESEARCH ARTICLE

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Tandem indium(III)-catalyzed cyclization and intermolecular hydrofunctionalization of 1,6-enynes

Raquel Pérez-Guevara, [iD] Diego Folgueira-Iravedra, [iD] Lorena Alonso-Marañón, [iD] M. Montserrat Martínez [iD] and José Pérez Sestelo [iD] *

A tandem indium(III)-catalyzed cyclization and intermolecular hydrofunctionalization of 1,6-enynes for the stereoselective synthesis of functionalized carbo- and heterocycles is reported. The synthetic transformation involves a regio- and stereoselective 5-*exo-dig* 1,6-enyne cyclization followed by intermolecular nucleophilic addition of alcohols (including water), carboxylic acids, arenes and trimethylsilyl azide. Remarkably, the reaction proceeds under mild reaction conditions with low catalyst loading using inexpensive commercial indium(III) halides, affording good yields with broad chemoselectivity and high regio- and stereoselectivity.

Introduction

Metal-catalyzed 1,*n*-enyne cyclizations provide an efficient and atom-economical method for the synthesis of architecturally complex cyclic frameworks, with generally good levels of regio- and stereoselectivity and reasonable versatility.[1] In addition, tandem processes in which a nucleophilic addition occurs after the cyclization step provide direct access to more elaborate chemical structures in a single operation.[2] This chemical transformation starts with the electrophilic activation of the alkyne (π-acid catalysis), although the reaction mechanism varies depending on the metal catalyst.[3] Usually, catalysis is associated with precious transition metals such as palladium, platinum, and gold due to their unique chemical properties.[4] However, some main group elements, particularly post-transition metals such as indium, gallium and bismuth have been postulated as valuable and economical alternatives, although their reactivity and synthetic utility are still underexplored.[5]

Indium(III) is a low-cost Group 13 element with attractive chemical properties for catalysis.[6] Its larger size compared to boron or aluminum renders it as a softer Lewis acid with oxophilic and carbophilic character, enabling dual catalytic activity. Over the years, indium(III) has proven to be an effective σ-Lewis acid in fundamental organic transformations such as Diels–Alder cycloadditions or carbonyl additions, and more recently as a π-acid in the electrophilic activation of C–C unsaturated bonds, mostly alkynes.[7] Interestingly, the alkynophilicity can be tuned through ligand modification, although only a small number of synthetic examples have been developed to
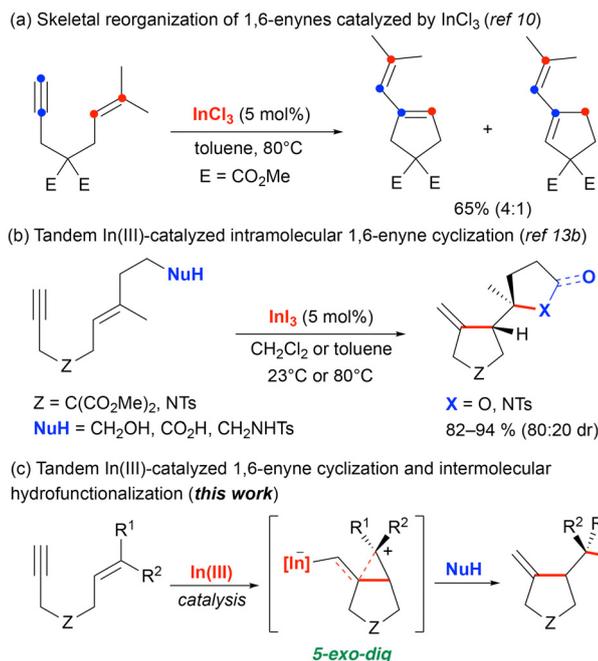
date.[8] In this field of research, we have recently shown indium(III) iodide as a particularly efficient π-acid catalyst in intramolecular alkyne hydroarylation, hydroalkoxylation and hydroamination reactions.[9] The cycloisomerization reaction of enynes under indium(III) catalysis was first studied by Chatani,[10] showing that 1,6-enynes react with 5-*exo-dig* regioselectivity, affording a variable mixture of cyclopentene dienes through a metathesis skeletal rearrangement (Scheme 1a).[11] The power of indium(III) catalysis, particularly cationic indium(III) iodide, in enynic cyclizations was highlighted by Corey in the synthesis of polycyclic structures through cascade polyenyne cyclization reactions.[12] In addition, our group has also reported In(III)-catalyzed enyne cyclizations such as the regio-, stereoselective and stereospecific synthesis of tricyclic frameworks by tandem indium-catalyzed cyclization/hydroarylation of aryl 1,5-enynes and 1,6-enynes with excellent chemoselectivity (Scheme 1b).[13] Herein, we disclose the first tandem 1,6-enyne cyclization and intermolecular nucleophilic addition under indium(III) catalysis. This approach demonstrates the feasibility of trapping the cycloisomerization intermediate with an external nucleophile under In(III) catalysis, broadening the synthetic utility of main group metals in the electrophilic activation of C–C unsaturated bonds under π-acid catalysis. Although these synthetic transformations have been reported under transition metal catalysis, this communication uncovers the first such examples using main group element catalysis.[2]

Results and discussion

According to our previous experience,[13b] our research started by exploring the indium(III)-catalyzed 1,6-enyne cycloisomeriza-

CICA – Centro Interdisciplinar de Química e Bioloxía and Departamento de Química, Universidade da Coruña, 15071 A Coruña, Spain. E-mail: sestelo@udc.es

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(a) Skeletal reorganization of 1,6-enynes catalyzed by InCl₃ (ref 10)

(b) Tandem In(III)-catalyzed intramolecular 1,6-enyne cyclization (ref 13b)

Z = C(CO₂Me)₂, NTs
NuH = CH₂OH, CO₂H, CH₂NHTs

X = O, NTs
82–94 % (80:20 dr)

(c) Tandem In(III)-catalyzed 1,6-enyne cyclization and intermolecular hydrofunctionalization (**this work**)

Scheme 1 Previous and current research on In(III)-catalyzed 1,6-enyne cycloisomerization reactions.

tion of **1** in the presence of methanol as an external nucleophile with the aim to trap the proposed zwitterionic cyclopropyl-like intermediate formed during the cycloisomerization (Scheme 2). Interestingly, the treatment of **1** with 5 mol% InI₃ in toluene (0.035 M) and MeOH (5 equiv.) at 80 °C afforded the methoxycyclization product **3a** in 56% isolated yield in just 3 h along with cycloisomerization product **1a** (entry 1, Table 1). The reaction also proceeded using CH₂Cl₂ as the solvent at 23 °C with the same chemical yield and short reaction time (entry 2). However, increasing the concentration (0.1 M in CH₂Cl₂) at 23 °C only produced a mixture of cycloisomerization products (**1a** and **1b**) (entry 3). On the other hand, a larger excess of methanol inhibited the catalytic reaction at 23 °C even with 20 mol% InI₃ (entry 4), while 10 equiv. of MeOH and InI₃ in CH₂Cl₂ at 23 °C gave **3a** in 72% yield (entry 5). Catalysis using the indium diiodonium cation (InI₂⁺) generated by treatment of InI₃ (5 mol%) with AgSbF₆ (5 mol%) provided **3a** in a modest 32% yield (entry 6). On the other hand, In(OTf)₃ or In(NTf₂)₃ (5 mol%) produced a complex mixture of products (entries 7 and 8). Finally, we found that setting up the reaction at −20 °C and slowly warming up to 23 °C prevents the skeletal rearrangement, giving rise to the desired product **3a** in 80% isolated yield in just 4 h (entry 10).

With the optimal reaction conditions in hand, we explored the versatility of the protocol by employing other organic nucleophiles and 1,6-enynes (Scheme 2). Starting from alcohols, we were delighted that the alkoxycyclization of **1** could be extended to the allylic alcohol 3-methyl-2-buten-1-ol, or phenol which were regioselectively incorporated with good yields (**3b–d**, 47–86%). In addition, the hydroxycyclization was successfully achieved using tap water as a nucleophile, giving rise to the corresponding alcohol **3e** (84%). These results demonstrate the synthetic utility of indium(III) catalysis in hydroxy- and hydroalkoxylations of 1,6-enynes, providing novel examples uncovered under transition metal catalysis. Encouraged by these results, we tested carboxylic acids as nucleophiles for a selective hydroacyloxylation reaction which has been elusive using transition metal catalysis. Gratifyingly, following the previous experimental protocol developed, we found that indium(III) iodide catalyzed this tandem intermolecular transformation efficiently with a variety of novel aromatic and aliphatic carboxylic acids such as benzoic acid, cyclohexane carboxylic acid, 3,3-dimethylacrylic acid or pivalic acid, giving rise to a novel set of esters (**3f–i**) in moderate yields (45–53%). The compatibility of indium(III) catalysis with the carboxylic acid functional group is highly remarkable.

Next, we focused our attention on the tandem intermolecular addition using arenes as external nucleophiles. We were pleased to find that the tandem intermolecular cyclization/hydroarylation reaction using 1,3,5-trimethoxybenzene afforded **3j** in 61% yield and the reaction with N-methylindole gave the corresponding product **3k** in 92% yield. Our efforts to perform the hydroamination reaction using amines resulted in poor yields, but the versatile azide functional group was introduced using TMSN₃ and 10 mol% InI₃ (**3l**, 60%, Scheme 2).[14] Overall, we demonstrate that the tandem indium(III)-catalyzed

Table 1 In(III)-catalyzed methoxycyclization of 1,6-enyne **1**

Entry	InX₃ [a]	T (°C)	Solvent	MeOH[b]	t [c] (h)	Yield[d]
1	InI₃	80	Toluene	5	3	56
2	InI₃	23	CH₂Cl₂	5	3	56
3	InI₃	23	CH₂Cl₂ [e]	5	24	—
4	InI₃	23	CH₂Cl₂	50	72	nr
5	InI₃	23	CH₂Cl₂	10	24	72
6	InI₃ [f]	23	CH₂Cl₂	5	4	32
7	In(OTf)₃	23	CH₂Cl₂	5	24	—
8	In(NTf₂)₃	23	CH₂Cl₂	5	24	—
9	InI₃	−20	CH₂Cl₂	5	24	nr
10	InI₃	−20–23	CH₂Cl₂	5	4	80

[a] 5 mol% except entries 4 (20 mol%) and 5 (10 mol%). [b] Equivalent amount with respect to 1,6-enyne. [c] Monitored by TLC. [d] Isolated yield (%). [e] 0.1 M CH₂Cl₂. [f] Using AgSbF₆ (5 mol%) as a cocatalyst.

1a   1b
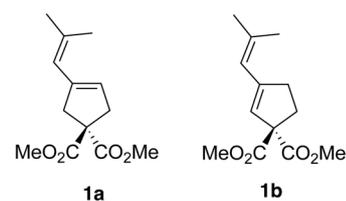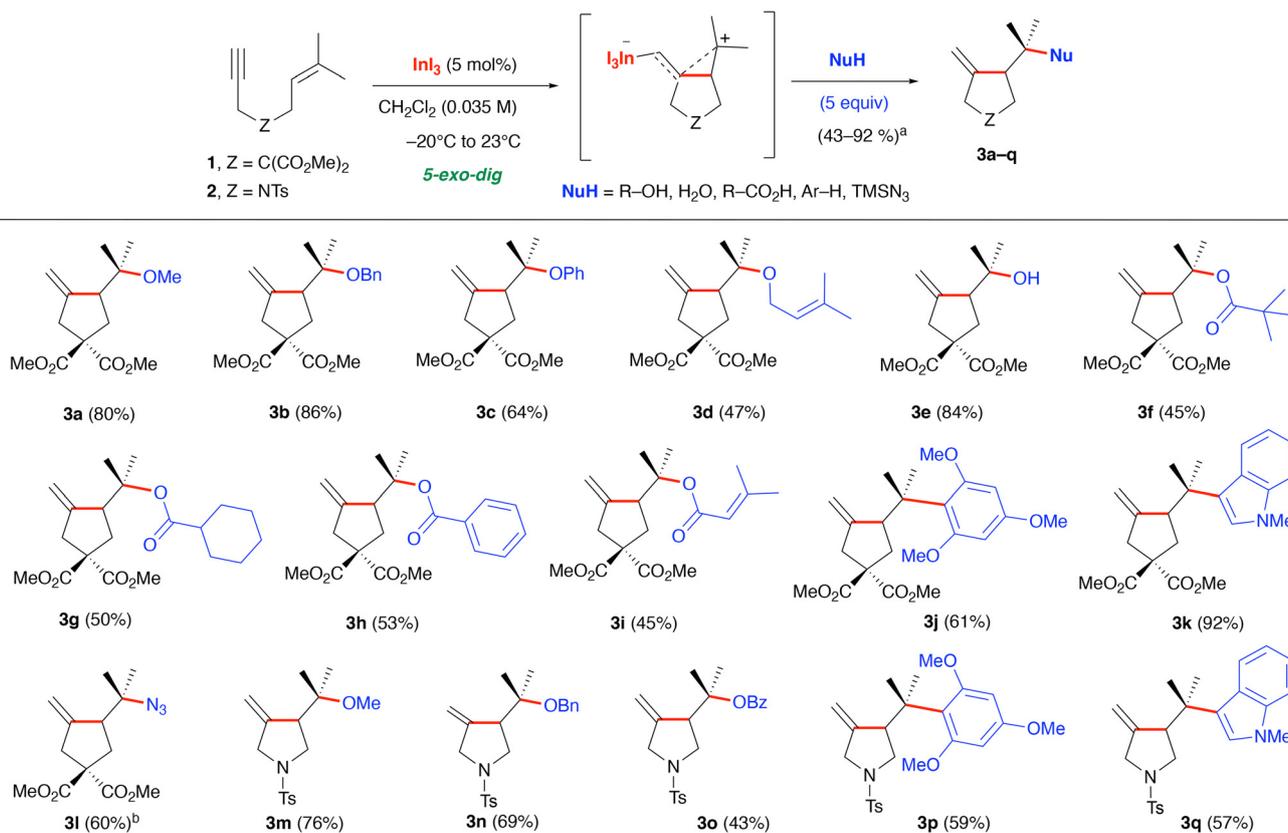
Scheme 2 Indium(III)-catalyzed cyclization/intermolecular hydrofunctionalization reactions of 1,6-enynes **1** and **2**. [a]Isolated yields; [b]10 mol% catalyst employed.

cyclization of 1,6-enynes and intermolecular nucleophilic addition can be performed with alcohols, carboxylic acids, arenes or the azide ion regioselectively (5-*exo-dig*) with good yields. As the next step, we planned to extend this methodology to other 1,6-enynes like **2** bearing an *N*-tosyl group as the 1,6-enyne bridge. As previously, the tandem reaction also took place efficiently with 5-*exo-dig* regioselectivity with a variety of oxygenated nucleophiles such as methanol or benzyl alcohol, carboxylic acids such as benzoic acid, or arenes such as 1,3,5-trimethoxybenzene or *N*-methylindole, affording the corresponding pyrrolidines **3m–q** in 43–76% yields.

To explore the synthetic scope and stereoselectivity of this novel tandem indium(III)-catalyzed intermolecular nucleophilic addition to 1,6-enynes, we tested the styryl 1,6-enyne **4** presenting a 1,2-disubstituted alkene. Under the previously optimized reaction conditions, we found that the treatment of (*E*)-**4** with InI$_3$ (5 mol%) and benzyl alcohol (5 equiv.) in CH$_2$Cl$_2$ at 23 °C gave the desired benzyloxycyclization product **5a** in 75% isolated yield as a single diastereoisomer.[15] Analogously, the reaction of benzoic acid also provided the diastereomerically pure benzoate **5b** in 62% yield. In addition, the reaction using *N*-methylindole or 1,3,5-trimethoxybenzene as nucleophiles afforded the expected cyclopentenes **5c** and **5d** stereoselectively in 88 and 78% isolated yields with complete diastereoselectivity. Furthermore, the

reaction using TMSN$_3$ also gave the azide **5e** derivative in 80% yield.

Furthermore, the stereochemical outcome of this diastereoselective 1,6-enyne cyclization was explored using (*Z*)-1,6-enyne **4**. Under the same experimental conditions, (*Z*)-**4** showed lower reactivity than (*E*)-**4**, and an increase in the temperature up to 60 °C and extension of the reaction time (24 h) were necessary for a complete conversion. Interestingly, the tandem reaction using different organic nucleophiles such as benzyl alcohol, benzoic acid, 1,3,5-trimethoxybenzene or trimethylsilyl azide also gave the expected reaction products **5a–e** as single diastereoisomers in 25–75% yields (Scheme 3). Distinct from the indium-catalyzed intramolecular sequence (Scheme 1b),[13b] this transformation was stereoconvergent, probably due to the thermal isomerization of the chiral intermediate during the 1,6-enyne cyclization through an open carbocation structure, as deduced by monitoring the reaction of (*Z*)-**4** with 1,3,5-trimethoxybenzene at different temperatures using ^{1}H NMR (see the SI). This behaviour contrasts with the stereospecific outcome observed under platinum(II) or gold(I) catalysis.[2a,j]

To shed light on the mechanism of this tandem process, some experiments with deuterated 1,6-enyne **1** and nucleophiles were performed. Under the previously developed reaction conditions, the reaction of **1** with deuterated methanol gave (*E*)-**3a**-d_4 as a single stereoisomer in 74% yield

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Scheme 3 Diastereoselective In(III)-catalyzed cyclization/intermolecular hydrofunctionalization reactions using 1,6-enynes (E)-**4** and (Z)-**4**. [a]Reactions set up at −20 °C and heated to 60 °C in DCE.

Scheme 4 In(III)-catalyzed cyclization/intermolecular hydrofunctionalization reactions using deuterated methanol-d_4 and 1,6-enyne **1**-d_1.

(Scheme 4a).[16] In addition, the reaction of 1,6-enyne deuterated at the terminal alkyne **1**-d_1 (91% D) with non-deuterated methanol, under the same reaction conditions, gave (Z)-**3a**-d_1 in 65% yield and identical deuterium percentage (91% D, Scheme 4b). These overall results are in accordance with a *trans*-attack of the alkene on the (η^2-alkyne)-indium complex and demonstrate that the carbon–deuterium bond is not broken throughout the cyclization process.

Scheme 5 Mechanistic proposal.

According to our previous experimental and computational studies on indium(III)-catalyzed alkyne hydrofunctionalization, and 1,6-enyne cycloisomerization reactions,[13b] we postulate a stepwise reaction mechanism initiated by the formation of an (η^2-alkyne)-indium complex (**I**) that promotes the cyclization. Then, the enyne cyclization occurs with 5-*exo-dig* regioselectivity and *anti*-stereoselectivity, giving rise to a chiral zwitterionic transition state that involves an indium-stabilized homoallylic cationic species (**II**). Finally, the stereoselective nucleophilic addition affords an indium organometallic species (**III**) which undergoes a protodemetalation to give the corresponding cyclization product (Scheme 5).

Conclusions

In summary, herein we report the first tandem indium(III)-catalyzed 1,6-enyne cyclization and intermolecular nucleophilic addition for the synthesis of carbo- and heterocyclic structures. The reaction takes place under mild conditions using InI$_3$ (5 mol%) with good yields. Remarkably, indium(III) catalysis exhibits high chemoselectivity, enabling the incorporation of a variety of carbon, oxygen and nitrogen nucleophiles such as alcohols, water, carboxylic acids, arenes and azides, allowing the formation of C–C, C–O and C–N bonds in a wide number of functionalized carbo- and heterocyclic compounds. Furthermore, the synthetic transformation is highly regioselective (5-*exo-dig*) and stereoselective, proving the synthetic potential of indium(III) catalysis and opening the possibility of developing novel applications in organic synthesis and enantioselective transformations using other 1,n-enynes.

Author contributions

J. P. S. conceived the project and wrote the manuscript with contributions of all authors. R. P.-G., D. F.-I., and L. A.-M. per-

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formed the experimental work. M. M. M. and J. P. S. supervised the experimental work. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: experimental procedures and copies of the NMR spectra for all compounds prepared. See DOI: **https://doi.org/10.1039/d5qo01388g**.

Acknowledgements

References

1 For a comprehensive review, see: (*a*) V. Michelet and P. Knochel, *Noble Metal-Catalyzed Enyne Cycloisomerizations and Related Reactions. Comprehensive Organic Synthesis II*, Elsevier Ltd, 2014, vol. 5, pp. 1483–1536. For other reviews, see: ; (*b*) J.-X. Liu, S.-Q. Xu, Y.-P. Han and Y.-M. Liang, Recent Advances in Cyclization Reactions of 1,6-Enynes, *Adv. Synth. Catal.*, 2024, **366**, 1220; (*c*) V. Michelet, P. Y. Toullec and J.-P. Genêt, Cycloisomerization of 1,n-Enynes: Challenging Metal-Catalyzed Rearrangements and Mechanistic Insights, *Angew. Chem., Int. Ed.*, 2008, **47**, 4268–4315.

2 For selected references, see: (*a*) M. Méndez, M. P. Muñoz and A. M. Echavarren, Platinum-Catalyzed Alkoxy- and Hydroxycyclization of Enynes, *J. Am. Chem. Soc.*, 2000, **122**, 11549–11550; (*b*) M. Méndez, M. P. Muñoz, C. Nevado, D. J. Cárdenas and A. M. Echavarren, Cyclizations of Enynes Catalyzed by PtCl₂ or Other Transition Metal Chlorides: Divergent Reaction Pathways, *J. Am. Chem. Soc.*, 2001, **123**, 10511–10520; (*c*) C. Nevado, L. Charrault, V. Michelet, C. Nieto-Oberhuber, M. P. Muñoz, M. Méndez, M.-N. Rager, J.-P. Genêt and A. M. Echavarren, On the Mechanism of Carbohydroxypalladation of Enynes. Additional Insights on the Cyclization of Enynes with Electrophilic Metal Complexes, *Eur. J. Org. Chem.*, 2003, 706–713; (*d*) L. Charruault, V. Michelet, R. Taras, S. Gladiali and J.-P. Genêt, Functionalized Carbo- and Heterocycles via

Pt-catalyzed Asymmetric Alkoxycyclization of 1,6-Enynes, *Chem. Commun.*, 2004, 850–851; (*e*) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, Gold (I)-Catalyzed Cyclizations of 1,6-Enynes: Alkoxycyclizations and exo/endo Skeletal Rearrangements, *Chem. – Eur. J.*, 2006, **12**, 1677–1693; (*f*) E. Genin, L. Leseurre, P. Y. Toullec, J.-P. Genêt and V. Michelet, Gold-Catalyzed Hydroxy- and Alkoxycyclization of Functionalized Enynes, *Synlett*, 2007, 1780–1784; (*g*) C. Bartolomé, Z. Ramiro, P. Pérez-Galán, C. Bour, M. Raducan, A. M. Echavarren and P. Espinet, Gold(I) Complexes with Hydrogen-Bond Supported Heterocyclic Carbenes as Active Catalysts in Reactions of 1,6-Enynes, *Inorg. Chem.*, 2008, **47**, 11391–11397; (*h*) C. Bartolomé, Z. Ramiro, D. García-Cuadrado, P. Pérez-Galán, M. Raducan, C. Bour, A. M. Echavarren and P. Espinet, Nitrogen Acyclic Gold(I) Carbenes: Excellent and Easily Accessible Catalysts in Reactions of 1,6-Enynes, *Organometallics*, 2010, **29**, 951–956; (*i*) P. Y. Toullec, E. Genin, L. Leseurre, J.-P. Genêt and V. Michelet, Room-Temperature AuI-Catalyzed C–C Bond Formation through a Tandem Friedel–Crafts-Type Addition/Carbocyclization Reaction, *Angew. Chem., Int. Ed.*, 2006, **45**, 7427–7430; (*j*) C. H. M. Amijs, V. López-Carrillo, M. Raducan, P. Pérez-Galán, C. Ferrer and A. M. Echavarren, Gold(I)-Catalyzed Intermolecular Addition of Carbon Nucleophiles to 1,5- and 1,6-Enynes, *J. Org. Chem.*, 2008, **73**, 7721–7730.

3 (*a*) G. C. Lloyd-Jones, Mechanistic Aspects of Transition Metal Catalysed 1,6-Diene and 1,6-Enyne Cycloisomerisation Reactions, *Org. Biomol. Chem.*, 2003, **1**, 215–236; (*b*) A. Fürstner and P. W. Davies, Catalytic Carbophilic Activation: Catalysis by Platinum and Gold π Acids, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410–3449; (*c*) A. Fürstner, From Understanding to Prediction: Gold- and Platinum-Based π-Acid Catalysis for Target Oriented Synthesis, *Acc. Chem. Res.*, 2014, **47**, 925–938.

4 (*a*) D. J. Gorin and F. D. Toste, Relativistic Effects in Homogeneous Gold Catalysis, *Nature*, 2007, **446**, 395–403; (*b*) Y. Yamamoto, From σ- to π-Electrophilic Lewis Acids. Application to Selective Organic Transformations, *J. Org. Chem.*, 2007, **72**, 7817–7831.

5 (*a*) P. P. Power, Main-Group Elements as Transition Metals, *Nature*, 2010, **463**, 171–177; (*b*) R. L. Melen, Frontiers in Molecular p-Block Chemistry: From Structure to Reactivity, *Science*, 2019, **363**, 479–484; (*c*) M. E. De Orbe, M. Zanini, O. Quinonero and A. M. Echavarren, Gold- or Indium-Catalyzed Cross-Coupling of Bromoalkynes with Allylsilanes through a Concealed Rearrangement, *ACS Catal.*, 2019, **9**, 7817–7822; (*d*) J. Tian, Y. Chen, M. Vayer, A. Djurovic, R. Guillot, R. Guermazi, S. Dagorne, C. Bour and V. Gandon, Exploring the Limits of π-Acid Catalysis Using Strongly Electrophilic Main Group Metal Complexes: The Case of Zinc and Aluminium, *Chem. – Eur. J.*, 2020, **26**, 12831–12838; (*e*) R. Wang, S. Martínez, J. Schwarzmann, C. Z. Zhao, J. Ramler, C. Lichtenberg and Y.-M. Wang, Transition Metal Mimetic π-Activation by Cationic Bismuth

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(III) Catalysts for Allylic C-H Functionalization of Olefins Using C=O and C=N Electrophiles, *J. Am. Chem. Soc.*, 2024, **146**, 22122–22128.

6 (*a*) S. R. Pathipati, A. Van Der Werf and N. Selander, Indium(III)-Catalyzed Transformations of Alkynes: Recent Advances in Carbo- and Heterocyclization Reactions, *Synthesis*, 2017, 4931–4941; (*b*) J. Pérez Sestelo, L. A. Sarandeses, M. M. Martínez and L. Alonso-Marañón, Indium(III) as π-Acid Catalyst for the Electrophilic Activation of Carbon-Carbon Unsaturated Systems, *Org. Biomol. Chem.*, 2018, **16**, 5733–5747; (*c*) P. Brandão, A. J. Burke and M. Pineiro, A Decade of Indium-Catalyzed Multicomponent Reactions (MCRs), *Eur. J. Org. Chem.*, 2020, 5501–5513.

7 (*a*) S. Dagorne and R. Wehmschulte, Recent Developments on the Use of Group 13 Metal Complexes in Catalysis, *ChemCatChem*, 2018, **10**, 2509–2520; (*b*) D. J. Cabrera, R. D. Lewis, C. Díez-Poza, L. Álvarez-Miguel, M. E. G. Mosquera, A. Hamilton and C. J. Whiteoak, Group 13 Salphen Compounds (In, Ga and Al): A Comparison of Their Structural Features and Activities as Catalysts for Cyclic Carbonate Synthesis, *Dalton Trans.*, 2023, **52**, 5882–5894; (*c*) H.-J. Jung, Y. Cho, D. Kim and P. Mehrkhodavandi, Cationic Aluminum, Gallium, and Indium Complexes in Catalysis, *Catal. Sci. Technol.*, 2021, **11**, 62–91.

8 S. Yang, A. Alix, C. Bour and V. Gandon, Alkynophilicity of Group 13 MX₃ Salts: A Theoretical Study, *Inorg. Chem.*, 2021, **60**, 5507–5522.

9 (*a*) L. Alonso-Marañón, M. M. Martínez, L. A. Sarandeses and J. Pérez Sestelo, Indium-Catalyzed Intramolecular Hydroarylation of Aryl Propargyl Ethers, *Org. Biomol. Chem.*, 2015, **13**, 379–387; (*b*) L. Alonso-Marañón, M. M. Martínez, L. A. Sarandeses, E. Gómez-Bengoa and J. Pérez Sestelo, Indium(III)-Catalyzed Synthesis of Benzo[*b*] furans by Intramolecular Hydroalkoxylation of *ortho*-Alkynylphenols: Scope and Mechanistic Insights, *J. Org. Chem.*, 2018, **83**, 7970–7980; (*c*) L. Alonso-Marañón, L. A. Sarandeses, M. M. Martínez and J. Pérez Sestelo, Synthesis of Fused Chromenes by the Indium(III)-Catalyzed Cascade Hydroarylation/Cycloisomerization Reactions of Polyyne-Type Aryl Propargyl Ethers, *Org. Chem. Front.*, 2018, **5**, 2308–2312; (*d*) R. Pérez-Guevara, L. A. Sarandeses, M. M. Martínez and J. Pérez Sestelo, Indium-Catalyzed Synthesis of Benzannulated Spiroketals by Intramolecular Double Hydroalkoxylation of *ortho*-(Hydroxyalkynyl)benzyl Alcohols, *Org. Chem. Front.*, 2022, **9**, 6894–6901; (*e*) A. Da

Lama, J. Pérez Sestelo, L. A. Sarandeses and M. M. Martíez, Indium(III)-Catalyzed Synthesis of Pyrroles and Benzo[*g*] Indoles by Intramolecular Cyclization of Homopropargyl Azides, *J. Org. Chem.*, 2024, **89**, 16015–16021.

10 Y. Miyanohana and N. Chatani, Skeletal Reorganization of Enynes Catalyzed by InCl₃, *Org. Lett.*, 2006, **8**, 2155–2158.

11 (*a*) L. Zhuo, J. Zhang and Z. Yu, Mechanisms of the InCl₃-Catalyzed Type-I, II, and III Cycloisomerizations of 1,6-Enynes, *J. Org. Chem.*, 2014, **79**, 3809–3820; (*b*) L.-G. Zhuo, J.-J. Zhang and Z.-X. Yu, DFT and Experimental Exploration of the Mechanism of InCl₃-Catalyzed Type II Cycloisomerization of 1,6-Enynes: Identifying InCl₂⁺ as the Catalytic Species and Answering Why Nonconjugated Dienes Are Generated, *J. Org. Chem.*, 2012, **77**, 8527–8540.

12 (*a*) K. Surendra, W. Qiu and E. J. Corey, A Powerful New Construction of Complex Chiral Polycycles by an Indium (III)-Catalyzed Cationic Cascade, *J. Am. Chem. Soc.*, 2011, **133**, 9724–9726; (*b*) K. Surendra and E. J. Corey, Diiodoindium(III) cation, InI₂⁺, a Potent Yneophile. Generation and Application to Cationic Cyclization by Selective π-Activation of C≡C, *J. Am. Chem. Soc.*, 2014, **136**, 10918–10920.

13 (*a*) R. E. Millán, J. Rodríguez, L. A. Sarandeses, E. Gómez-Bengoa and J. Pérez Sestelo, Indium(III)-Catalyzed Stereoselective Synthesis of Tricyclic Frameworks by Cascade Cycloisomerization Reactions of Aryl 1,5-Enynes, *J. Org. Chem.*, 2021, **86**, 9515–9529; (*b*) R. Pérez-Guevara, L. A. Sarandeses, R. Alvarez, M. M. Martínez and J. Pérez Sestelo, Stereospecific Indium(III)–Catalysed Tandem Cycloisomerization of Functionalized 1,6−enynes: Scope and Mechanistic Insights., *Adv. Synth. Catal.*, 2024, **366**, 852–861.

14 This result suggests the presence of trace amounts of water in the reaction mixture, probably from the solvent. For an example of using TMSN₃ as a nucleophile in enyne cyclizations, see: A. Franchino, A. Martí and A. M. Echavarren, H-Bonded Counterion-Directed Enantioselective Au(I) Catalysis, *J. Am. Chem. Soc.*, 2022, **144**, 3497–3509.

15 Y. Tang, I. Benaissa, M. Huynh, L. Vendier, N. Lugan, S. Bastin, P. Belmont, V. César and V. Michelet, An Original L-Shape, Tunable N-Heterocyclic Carbene Platform for Efficient Gold(I) Catalysis, *Angew. Chem., Int. Ed.*, 2019, **58**, 7977–7981.

16 The (*E*)-**3a**-*d₄* stereochemistry was assigned by ¹H NMR comparison according to the literature by the signal absence of the *trans* hydrogen (ref. 2c, see the SI for details).

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