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Modular Access to Substituted Germales by Intramolecular Germylzincation

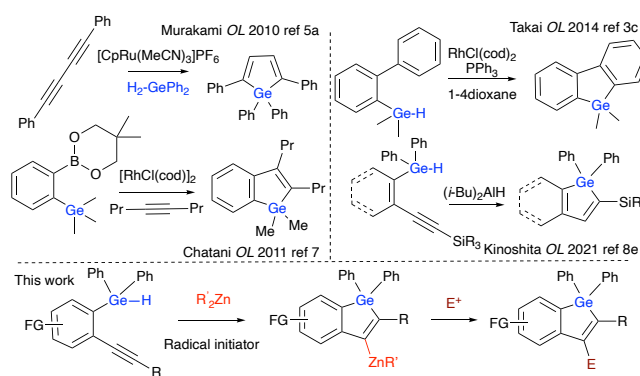
Seydou Kassamba,^a Alejandro Perez-Luna,^b Franck Ferreira^b and Muriel Durandetti^{*a}

Intramolecular alkyne germylzincation giving access to a wide range of germales is achieved from triarylgermanes in the presence of diethylzinc and AIBN as radical initiator. The reaction proceeds through activation of the Ge—H bond, leading to a heteroarylzinc intermediate after cyclisation, which can then be involved in a post-functionalisation reaction. Our results show that only 5-endo-dig cyclizations occur, benzogermoles being exclusively obtained.

Metalloles, five-membered heterocyclic derivatives of cyclopentadiene bearing a heteroatom and a diene moiety, are very important scaffolds for their luminescence properties. They are associated with low energy LUMO levels, resulting from the stabilization of the π -system of the diene via interaction with the σ^* orbitals of the heteroatom and the diene π^* orbitals ($\sigma^*-\pi^*$ conjugation).¹ As a result, they are among the n-type organic materials possessing low barrier to electron injection and transport a negative charge efficiently.¹ Due to their luminescence properties, siloles and germales are incorporated in electroluminescent organic materials.² So, 9-germafluorenes are key components for new functional organic materials, including solar cells, thin-film transistors and host materials for electroluminescent devices.³ The synthetic chemistry of organogermanium compounds is less developed than organosilicon compounds,⁴ in spite of their interesting photochemical properties, which can exceed those of siloles⁵ and their lower toxicity.^{5c} Germales can be obtained through C—Ge bond formation processes that require a transition-metal catalyst such as palladium,^{2b,6} ruthenium,^{5a} or rhodium^{3c,7} which are in turn based on the activation of Ge—H, or Ge—C(sp³) bonds (Scheme 1, top). As the Ge—H bond is quite easy to activate, the intermolecular addition of Ge—H to an alkyne is one of the most commonly used methods to synthesise vinylgermanes.⁸ An intramolecular version developed very recently by Kinoshita using (*i*-Bu)₂AlH gives efficiently germales (Scheme 1).^{8e}

Our group has been engaged in research devoted to the synthesis of group-14 heterocycles by intramolecular cyclisation

reactions such as anionic rearrangements,⁹ C—H activation of a methyl of a TMS¹⁰ or *syn*-silapalladation of alkynes.¹¹ As part of this work, we reasoned that radical cyclisation reactions of germanium-centered radicals on alkynes could be used to construct original germales. Such a prospect has not been considered so far despite that intermolecular radical addition of germanium-centered radicals across alkynes is an established process.^{8b,12} We also anticipated that such radical cyclisation reactions would be advantageously combined with radical alkylzinc group-transfer chemistry in an intramolecular variant of the alkyne radical germylzincation reactions developed by some of us.¹³ Such approach could deliver zincated germales intermediates for which the C(sp²)—Zn bond could be used as handle for subsequent functionalization in one-pot. In this communication, we disclose the application of this strategy to the construction of germales from *o*-alkynyl aryldiphenylgermanes (Scheme 1, bottom).



Scheme 1 Synthesis of germales.

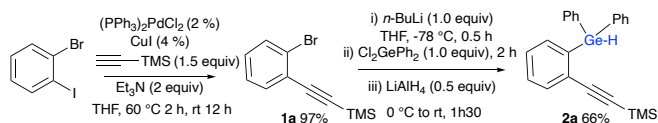
At the outset of our study, we focused on the germylzincation reaction on germane **2a**, easily accessible from 2-bromoiodobenzene: after Sonogashira cross-coupling, the lithium-halogen exchange gives an aryllithium, which is then trapped with dichlorodiphenylgermane, followed by a mono reduction step with LiAlH₄, leading to germane **2a** (Scheme 2).

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Electronic Supplementary Information (ESI) available.

With germane **2a** in hands, optimization of the germalzincation reaction was performed as reported in Table 1.



Scheme 2 Synthesis of germane **2a**.

Table 1 Optimization of the intramolecular germalzincation of **2a**.^a

Entry	R ₂ Zn	Solvent ^b	Conditions	2a ^c	3a/4a ^c
1	Me ₂ Zn	Hexane/Toluene 4/1	1 h, 100 °C	96	4/0
2	Et ₂ Zn	Hexane	1 h, 100 °C	57	7/36
3	<i>i</i> -Pr ₂ Zn	Hexane/Toluene 4/1	1 h, 100 °C	27	7/66
4	Cy ₂ Zn	Hexane/Et ₂ O 2/1	1 h, 100 °C	32	13/55
5	Et ₂ Zn	Hexane	2 h, 80 °C, AIBN ^d	0	92/8
6	Cy ₂ Zn	Hexane/Et ₂ O 2/1	2 h, 80 °C, AIBN ^d	0	43/57
7	<i>i</i> -Pr ₂ Zn	Hexane/Toluene 4/1	2 h, 80 °C, AIBN ^d	8	10/82
8	-	Hexane	1 h, 80 °C, AIBN ^d	0	47/0 ^e
9	-	Hexane	1 h, 100 °C	95	5/0

^aReactions were performed using 0.5 mmol of **2a** and 1.5 equiv of R₂Zn. ^bMixture of solvents due to the commercial solutions of dialkylzinc reagents. ^cThe amount of **2a**, **3a** and **4a** were determined by ¹H NMR analysis on the crude mixture. ^dAIBN 0.15 equiv. ^eDegradation occurred.

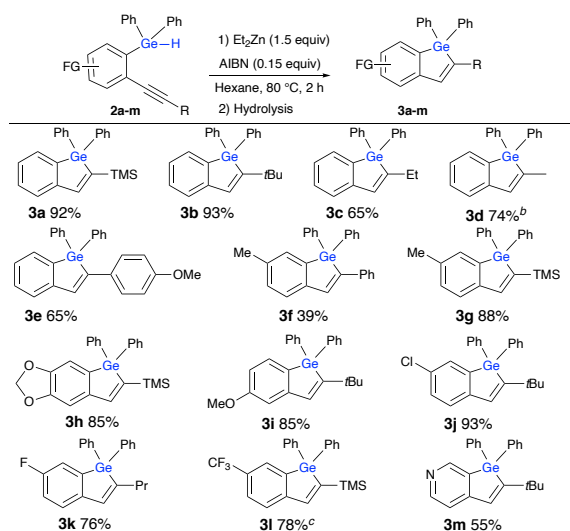
Treatment of **2a** with different dialkylzinc reagents at 100 °C for 1 h resulted in non-complete conversion, and the expected product **3a** was only detected as minor product (4–13%, Table 1, entries 1–4). By contrast, germanol **4a** was recovered in considerable amounts. Based on a literature precedent,¹⁴ we assume that **4a** results from the oxidation during work-up of a germalzinc intermediate formed by reaction between the dialkylzinc species and triarylhydrogermane **3a**.

As previously observed for the intermolecular reactions,¹³ we reasoned that the presence of AIBN would facilitate the germalzincation process. We therefore added 0.15 equiv. of AIBN, in the presence of 1.5 equiv. of diethylzinc, and we were pleased to obtain total conversion of **2a**, providing 92% yield of the desired 5-*endo-dig* cyclized product **3a** (Table 1, entry 5). Replacing Et₂Zn by other dialkylzinc reagents still led to a good conversion of **2a**, but higher amounts of the side product **4a** were formed (Table 1, entries 6–7). Carrying out the reaction without Et₂Zn, in presence of AIBN alone, delivered (still with full conversion), a moderate amount of germole **3a**, but above all, significant amounts of degradation products that could not be characterized. Simply heating the reaction mixture in the absence of R₂Zn and AIBN resulted in a very small amount (5%) of germole **3a** (Table 1, entry 9). From these results we can

propose the coexistence of two competitive pathways, occurring in presence of germane **2a**, organozinc, AIBN and heat. The first process corresponds to the expected radical germalzincation initiated by AIBN leading (after aqueous work-up) to the 5-*endo-dig* cyclisation product **3a**. The second to the zincation of the hydrogermane leading to a Ge–Zn intermediate which ultimately produces germanol **4a** by oxidation. Using Et₂Zn as dialkylzinc reagent, the reaction can be steered towards the cyclisation pathway almost exclusively.¹⁵

With optimal conditions in hands, various germanes were prepared, following the methodology employed for compound **2a** (overall yield between 46% and 81% for **2a–e** starting from 2-bromiodobenzene). We next synthesized arylgermanes **2f–l** in order to study the influence of electron-donating or withdrawing groups on the aromatic ring (overall yield between 39% and 56%). These germanes were engaged using the optimal germalzincation conditions *i.e.* Et₂Zn (1.5 equiv), AIBN (0.15 equiv) and heating at 80 °C for 2 h before being hydrolyzed with aqueous NH₄Cl. The results are reported in Table 2.

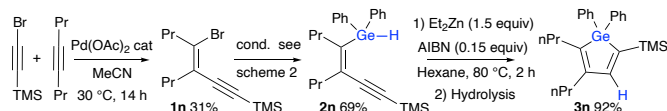
Table 2 Scope of the intramolecular germalzincation of aryl germanes **2a–m**.^a



^aReaction conditions: **2a–k** (0.5 mmol), Et₂Zn (1.5 equiv), AIBN (0.15 equiv), hexane (1.5 mL), 80 °C, 2 h. Yields of isolated products. ^bReaction time: 3 h, 85% of conversion. ^cReaction time: 4 h.

Treatment of **2a–m** with 1.5 equiv. of Et₂Zn, in the presence of AIBN, triggered intramolecular 5-*endo-dig* germalzincation and led to the expected germoles **3a–m** in 39–93% isolated yields (Table 2). It should be noted that in all cases a small amount (5–10%) of germanol (**4a–m**) was obtained. The substitution of the triple bond did not seem to affect the cyclisation, as the reaction was effective irrespective of the nature of R that can be a silyl- (**3a**), alkyl- (*t*Bu, Et, Me **3b–d**) or aryl (**3e–f**) moiety. Cyclisation did not appear to be substituent dependent either; good isolated yields were obtained with both electron-donating (**3f–i**) or withdrawing (**3j–l**) groups on the aromatic ring. We then decided to extend the scope to pyridine germane **2m** which is obtained in two steps from 3-bromo-4-iodo-pyridine. The cyclisation gave the pyridine germole **3m** in 55% yield. To further increase the synthetic potential of this

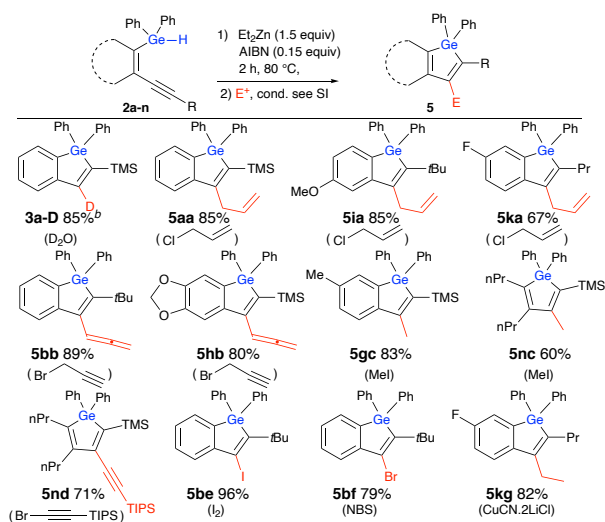
reaction, we decided to prepare germylated enyne **2n** in order to evaluate the methodology on acyclic substrates. The desired germane **2n** was isolated in 69% yield after the germylation step of bromoenyne **1n** (Scheme 3). The germylzincation under the same conditions successfully led to the expected monocyclic germole **3n** in an excellent 92% yield.



Scheme 3 Synthesis and germylzincation of germane **2n**.

Subsequently, we wanted to take full advantage of this new cyclisation methodology by exploiting the synthetic potential of the heteroarylzinc intermediate arising from the cyclisation. To demonstrate the availability of the C(sp²)-Zn bond for further functionalization, the reaction was first quenched with D₂O. The D-labeled germole **3a-D** was isolated in 85% yield, confirming the formation of the organozinc intermediate. We next investigated the reactivity of the latter in tandem reactions with classical electrophiles, using copper(I) catalysis (Table 3).

Table 3 Preparation of 3-substituted germoles **5** through tandem intramolecular germylzincation/copper(I)-mediated electrophilic substitution.^a

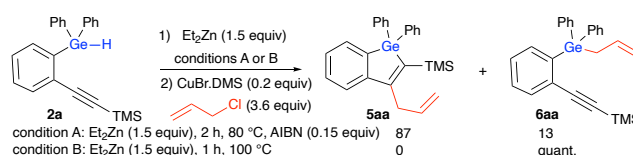


^aYields of isolated products. ^b96% D incorporation

The expected products were obtained in good yields whatever the electrophile added following the 5-*endo-dig* cyclisation process. However, traces of products **6**, resulting from electrophilic substitution of the Ge-Zn side-products, were generally observed in the mixture (Scheme 4). Alkylation of the heteroarylzinc intermediate was efficiently performed (67–85% isolated yields) using allyl chloride in the presence of CuBr.SMe₂ (Table 3, compounds **5aa**, **5ia** and **5ka**). Propargyl bromide, using CuCN.2LiCl as catalyst, gave 89% and 80% respectively of compounds **5bb** and **5hb**, following S_N2' propargylic substitution. Applying the same procedure to methyl iodide led to the expected compounds **5gc** and **5nc** in 83% and 60% yields respectively. We then sought to extend this

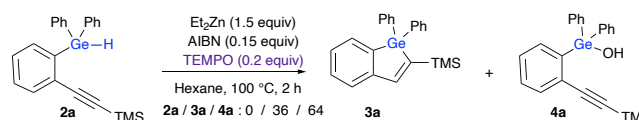
coupling process to alkynyl halides and obtained substituted germole **5nd** in 71% yield. Extension to halogenation reactions led to iodide **5be** and bromide **5bf** in 96% and 79% yields, from I₂ or NBS as electrophiles. Interestingly, when the reaction was run without electrophiles by adding CuCN.2LiCl alone after the germylzincation step, the ethyl compound **5kg** was isolated in 82% yield. Note that **5kg** was never detected in the other cases.

To gain insight into the reaction mechanism, the electrophilic trapping was considered under conditions of germylzincation (in presence of AIBN) and zincation (without AIBN). On reaction with allyl chloride and catalytic CuBr.SMe₂ (Scheme 4), while the substituted germole **5aa** was obtained as a main product when the first step was carried out in the presence of AIBN (conditions A), only product **6aa** arising from the direct germanium functionalisation was recovered when the first step was conducted without AIBN (conditions B). This result proves that the direct reaction of **2a** with Et₂Zn leads to full zincation of the Ge-H bond and that cyclisation from the Ge-Zn intermediate thus produced does not occur.



Scheme 4 Influence of AIBN in coupling products with allyl chloride.

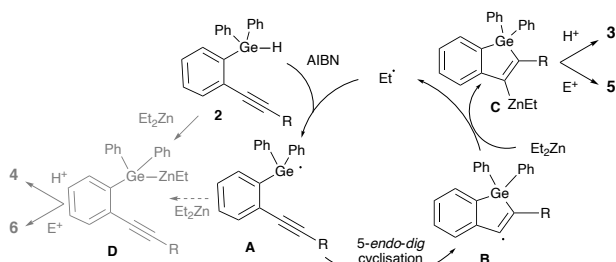
To assess the radical character of the intramolecular germylzincation, two experiments were performed in the presence of TEMPO, as radical inhibitor. When the germylzincation reaction was carried out, under the previously optimized conditions (Et₂Zn and AIBN), in the presence of sub-stoichiometric amounts of TEMPO, germane **2a** was totally consumed, and the by-product **4a** was obtained as a major product (64%), along with the desired germole **3a** (36%) (Scheme 5). This result is in sharp contrast with the reaction outcome in the absence of TEMPO (Table 1, entry 5; 92% of **3a**). On the contrary, TEMPO had no influence when the reaction was conducted without AIBN, since a **3a/4a** ratio of 9/38 was obtained, compared to the ratio of 7/36 obtained without TEMPO (Table 1, entry 2), as well as 53% of the starting product **2a**. While the use of TEMPO as radical probe needs to be taken with caution when Et₂Zn is involved because the analysis might be blurred by the reaction of TEMPO with Et₂Zn,¹⁶ the distinctive impact on the reaction outcome with or without AIBN lends clear evidence for the involvement of a radical chain in the former and not in the latter.



Scheme 5 Influence of TEMPO.

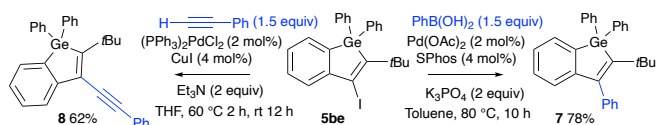
These observations led us to propose a plausible mechanism for the successful cyclisation using Et₂Zn with a catalytic amount

of AIBN (Scheme 6). Initiation of the radical chain is likely to proceed as for radical alkyne hydrogermylation reactions by H-atom abstraction from germane **2** promoted by AIBN.^[12a] The germyl radical intermediate **A** produced then reacts with the triple bond and delivers cyclised radical **B**, following a 5-*endo-dig* cyclisation. Et₂Zn undergoes homolytic substitution at the zinc atom by radical **B**, which leads to heteroarylzinc **C** and the formation of radical Et· which propagates the radical chain.¹³ A competitive pathway, which occurs in the absence of AIBN, involves the direct reaction of Et₂Zn with **2**, releasing germylzinc **D**, which does not undergo cyclisation.



Scheme 6 Plausible Mechanism.

Since the iodide **5be** we have prepared can participate in other cross-coupling reactions, we decided to end up this work by further modifying the obtained germyles (Scheme 7). Thus, **5be** was engaged in Suzuki and Sonogashira reactions, leading to germyles **7** and **8** in 78% and 62% yields respectively.



Scheme 7 Functionalization of **5be**.

In conclusion, this paper described an efficient method to prepare substituted germyles, based on an intramolecular alkyne germylzincation reaction, followed by post-functionalization of the heteroarylzinc reagents produced by electrophilic substitution with various electrophiles. This transformation allows in one step to access highly efficiently a large variety of germyles in a modular way.

The authors declare no conflict of interest.

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