RESEARCH ARTICLE doi.org/10.1002/adsc.202200824 Advanced Synthesis & Catalysis

"Back-to-Front" Indole and Carbazole Synthesis from *N,N*-Bis-(2-bromoallyl)amines by Combining Carbolithiation Reactions with Gold-Catalysis

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Manuscript received: July 26, 2022; Revised manuscript received: September 13, 2022;
Version of record online: October 21, 2022

Dedicated to Professor Joan Bosch on the occasion of this 75th birthday.

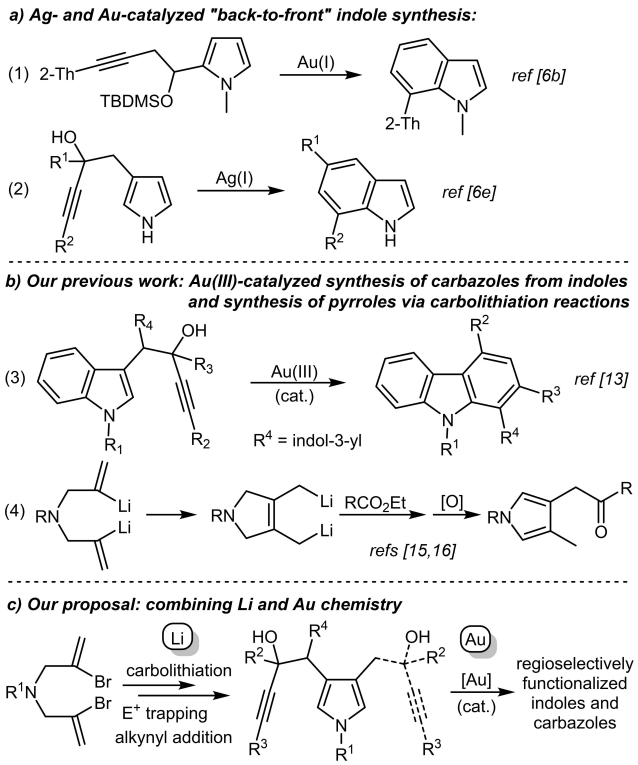
Supporting information for this article is available on the WWW under https://doi.org/10.1002/adsc.202200824

Abstract: The combination of organolithium chemistry with gold catalysis has enabled the development of a synthetic strategy for accessing polysubstituted indoles and carbazoles from readily available starting materials. This method is based on a "back-to-front" approach from ketopyrroles, generated by intramolecular carbolithiation of *N,N*-bis-(2-lithioallyl)amines that evolve into 3,4-bis(lithiomethyl)dihydropyrrole intermediates capable of reacting with carboxylic esters and Weinreb amides. These ketopyrroles have demonstrated to be excellent precursors of mono or bis(alkynols)pyrroles that, under gold-catalysis, experience a benzannulation reaction providing access to regioselectively substituted indoles or carbazoles.

Keywords: carbolithiation; gold; homogeneous catalysis; nitrogen heterocycles; organolithiums

Introduction

Indole and carbazole heteroaromatic scaffolds play a privileged role in organic chemistry as they are the core constituent in a plethora of biologically relevant molecules.[1] In addition, fused indoles and carbazoles possess interesting electronic and optoelectronic properties that make them useful in the field of materials chemistry.[2] So, the development of efficient and versatile methods for synthesizing these compounds, mainly with a defined substitution pattern, continues to be a hot research topic for organic chemists.[3] Most of the reported methods for the indole construction employ nitrogen-functionalized benzene derivatives building the hetereocyclic ring from them ("front-to-back" approach). However, this extensively used approach typically requires substrate pre-functionalization or the use of non-general reactions for subsequent functionalization, with regiochemical issues that need to be considered, to prepare regioselectively functionalized substrates.[4] Surprisingly, fewer strategies are known for generating the indole core from functionalized pyrroles ("back-to-front" approach). This underdeveloped strategy, the benzannulation on the pyrrole, has important advantages for the regioselective functionalization of C4-7 positions.[5] In this area, transition metal-catalyzed annulations, both intramolecular[6] or intermolecular,[7] are the most studied processes, although some metal catalyst-free cyclizations have also been reported (Scheme 1a).[8] In contrast, the benzannulation of properly designed (indolyl)butynols is a well-established methodology for accessing carbazoles from functionalized indoles ("indole-to-carbazole" approach),[9] mainly under transition metal-



Scheme 1. Previous work and proposed indole and carbazole synthesis from *N,N*-bis-(2-bromoallyl)amines.

catalysis.[10] In addition, the Au-catalyzed cyclization of alkyne-tethered pyrroles has been shown to be a useful method for synthesizing different *N*-heterocycles.[11] In this field, and following our interest in the functionalization of indoles via gold-catalyzed reactions,[12] we have described efficient access to 1-(indol-3-yl)carbazoles from α-bis(indol-3-yl)methyl alkynols involving an unexpected and selective 1,2-alkyl vs. 1,2-alkenyl migration, which has also been supported by DFT calculations (Scheme 1b, eq 3).[13]

On the other hand, functionalized organolithiums are versatile intermediates for accessing value-added molecules.[14] In this context, our group reported a novel intramolecular carbolithiation of lithiated double bonds. This interesting transformation allows access to bis-(3,4-lithiomethyl)dihydropyrroles from easily available *N,N*-bis-(2-bromoallyl)amines by their simple treatment with *t*-BuLi.[15] Studying the reactivity of these dianions, we found that their reaction with carboxylic esters at low temperatures selectively afforded, after oxidation, pyrrol-3-ylmethyl ketones (Scheme 1b, eq 4).[16]

At this point, we envisaged that combining the synthesis of α-pyrrolylmethyl ketones, via organolithiums, with the gold-catalyzed cyclization of π-excedents heterocycles bearing an appropriate alkynol moiety, may trigger benzannulation processes leading to regioselectively functionalized indoles or carbazoles (Scheme 1c).

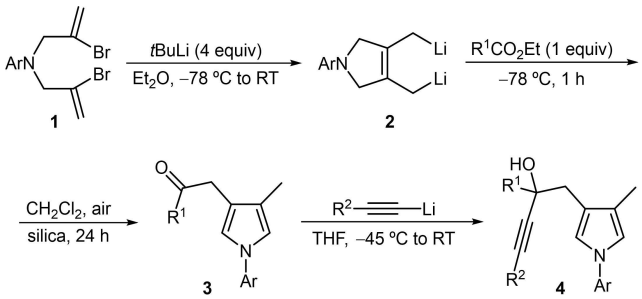
Results and Discussion

As we have previously established, *N,N*-bis(2-lithioallyl)amines, generated by double bromine-lithium exchange from readily available *N,N*-bis(2-bromoallyl)amines **1**, undergo an unexpected intramolecular carbolithiation of a lithiated double bond leading, after allylic rearrangement, to 3,4-bis(lithiomethyl)dihydropyrrole derivatives **2** (see Table 1). Their treatment with 1 equiv. of selected carboxylic esters at low temperature, and subsequent air-oxidation, gave rise to 3-carbonylmethyl-4-methyl pyrroles **3** in moderate to good yields (Table 1). Alkynylation of these ketopyrroles was easily accomplished by reaction of **3** with alkynyl lithium or magnesium reagents leading to the corresponding alkynols **4** in high yields (Table 1). Regarding the carboxylic ester, primary, secondary (*c*)-alkyl groups, or aryl groups are tolerated as R^1 substituents as well as a bromo-functionalized alkyl chain. For the alkynol formation, metallated alkynes bearing (hetero)aromatic (entries 1, 2, 10–15 and 20), (*c*)-alkyl (entries 3, 4, 16, 17 and 21), alkenyl (entries 5 and 18), or even oxygen-functionalized substituents (enries 6 and 7) could be successfully employed as well as simple acetylene ($R^2 = H$) (entries 8 and 19). The terminal alkynol **4aah** could be employed for subsequent functionalization by Sonogashira coupling (entry 9). In this way, a wide variety of alkynol-functionalized pyrroles **4** were synthesized in high yields (Table 1).[17]

Gratifyingly, using our previous reported conditions for synthesizing indolylcarbazoles,[13] the treatment of alkynol-functionalized pyrroles **4** with catalytic amounts of $NaAuCl_4 \cdot 2H_2O$ delivers 5,7-disubstituted-3-methylindoles **5** in high yields (Table 2). The reaction shows good compatibility regarding the substituents that could be introduced at C-5 and C-7 positions of the indole nucleus. In this sense, a wide selection of regioselectively functionalized indoles **5** were prepared, in which the C5-substituent (R^1) was determined by the carboxylic ester employed in the trapping of the corresponding bis-(3,4-lithiomethyl)dihydropyrrole **2**, and the C7 group (R^2) was fixed by the substituent of the alkyne used for the alkynol preparation. Interestingly, indole derivative **5aaa** could be prepared at gram-scale in 83% yield (0.803 g from 1.018 g of **4aaa**).

Looking for further decoration of the indole moiety, we took advantage of the fact that after the reaction of dianion **2a** with 1 equiv. of a carboxylic ester the monoanion **I** is generated, which upon addition of THF undergoes lithium translocation giving rise to a more stable lithium enolate like **II**, likely favored by an increase of basicity of anion **I** due to the higher polar

Table 1. Synthesis of ketopyrrole derivatives **3** and alkynols **4**.



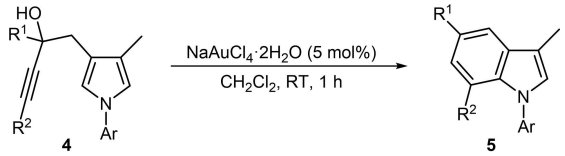
entry	**1**	Ar	R^1	**3**	yield [%][a]	R^2	**4**	yield [%][b]
1	**1a**	*p*Tol	*i*Pr	**3aa**	67[c]	Ph	**4aaa**	92[d]
2	**1a**	*p*Tol	*i*Pr			3-Th	**4aab**	85
3	**1a**	*p*Tol	*i*Pr			*n*Bu	**4aac**	87
4	**1a**	*p*Tol	*i*Pr			cC_3H_5	**4aad**	84
5	**1a**	*p*Tol	*i*Pr			cC_6H_9	**4aae**	90
6	**1a**	*p*Tol	*i*Pr			$(4\text{-}ClC_6H_4)OCH_2$	**4aaf**	80
7	**1a**	*p*Tol	*i*Pr			$(4\text{-}MeOC_6H_4)OCH_2$	**4aag**	75
8	**1a**	*p*Tol	*i*Pr			H[e]	**4aah**	89
9	**1a**	*p*Tol	*i*Pr			$2\text{-}NO_2C_6H_4$	**4aai**[f]	63
10	**1a**	*p*Tol	Me	**3ab**	60	Ph	**4aba**	87
11	**1a**	*p*Tol	Et	**3ac**	56	Ph	**4aca**	93
12	**1a**	*p*Tol	cC_3H_5	**3ad**	57	Ph	**4ada**	84
13	**1a**	*p*Tol	$5\text{-}Br(CH_2)_4$	**3ae**	66	Ph	**4aea**	85
14	**1a**	*p*Tol	Ph	**3af**	60	Ph	**4afa**	85
15	**1b**	$4\text{-}MeOC_6H_4$	*i*Pr	**3ba**	59	Ph	**4baa**	96
16	**1b**	$4\text{-}MeOC_6H_4$	*i*Pr			*n*Bu	**4bac**	92
17	**1b**	$4\text{-}MeOC_6H_4$	*i*Pr			cC_3H_5	**4bad**	87
18	**1b**	$4\text{-}MeOC_6H_4$	*i*Pr			cC_6H_9	**4bae**	94
19	**1b**	$4\text{-}MeOC_6H_4$	*i*Pr			H[e]	**4bag**	89
20	**1c**	$4\text{-}ClC_6H_4$	*i*Pr	**3ca**	67	Ph	**4caa**	87
21	**1c**	$4\text{-}ClC_6H_4$	*i*Pr			*n*Bu	**4cac**	77

[a] Yield of isolated product **3** referred to the corresponding *N,N*-bis-(2-bromoallyl)amine **1**. Reactions conducted with 2 mmol of **1**.
[b] Yield of isolated product **4** referred to the corresponding ketone **3**. Reactions conducted with 0.5 mmol of **3**.
[c] Reaction carried out with 1.04 g of **1a** afforded 60% of **3aa**.
[d] Reaction carried out with 0.86 g of **3aa** afforded 88% of **4aa**.
[e] The acetylide addition was performed with ethynylmagnesium bromide.
[f] Prepared from **4aah** by a Sonogashira coupling with 2-bromonitrobenzene.

character of THF (Scheme 2). So, the addition of selected electrophiles, such as allylic, benzylic, or propargylic halides, provided access, after air dehydrogenation, to ketopyrroles **6** with an additional substituent (R^3). The addition of lithium phenylacetylide gave rise to the corresponding alkynols **7** in high yields and variable diastereoselectivities (Scheme 2).

Similarly, when ethyl 5-bromovalerate was used as carboxylic ester, the addition of THF, and subsequent oxidation, led to 2-(pyrrol-3-yl)cyclohexanone **8**, which upon alkynylation with two different lithium acetylides gave rise to alkynylcyclohexanols **9a**,**b**, isolated as mixtures of diastereoisomers (Scheme 2). In this case, the trapping of the corresponding intermediate enolate **II** takes place intramolecularly. In addition, other *N,N*-bis-(2-bromoallyl)amines, like *N*-2-bromoallyl-*N*-2-bromocinnamyl *p*-toluidine (**1d**), is also able to undergo the intramolecular carbolithiation leading to dianion **2d**. In this case, its reaction with selected carboxylic esters at low temperature was not completely selective, giving rise, after oxidation, to regioisomeric ketones **10** and **11**, although those derived from the attack of the benzylic organolithium were the major, or even the only, products (Scheme 2).[18] Interestingly, pyrrolyl ketones **10** possess a phenyl group at R^3 position, which could not be introduced by the enolate route that provided related ketones **6**. Subsequent alkynylation with lithium phenylacetylide afforded pyrrolylalkynols **12**, as mixtures of diastereoisomers, and **13** in high yields (Scheme 2).

Table 2. Synthesis of 5,7-disubstituted-3-methylindoles **5**.[a]



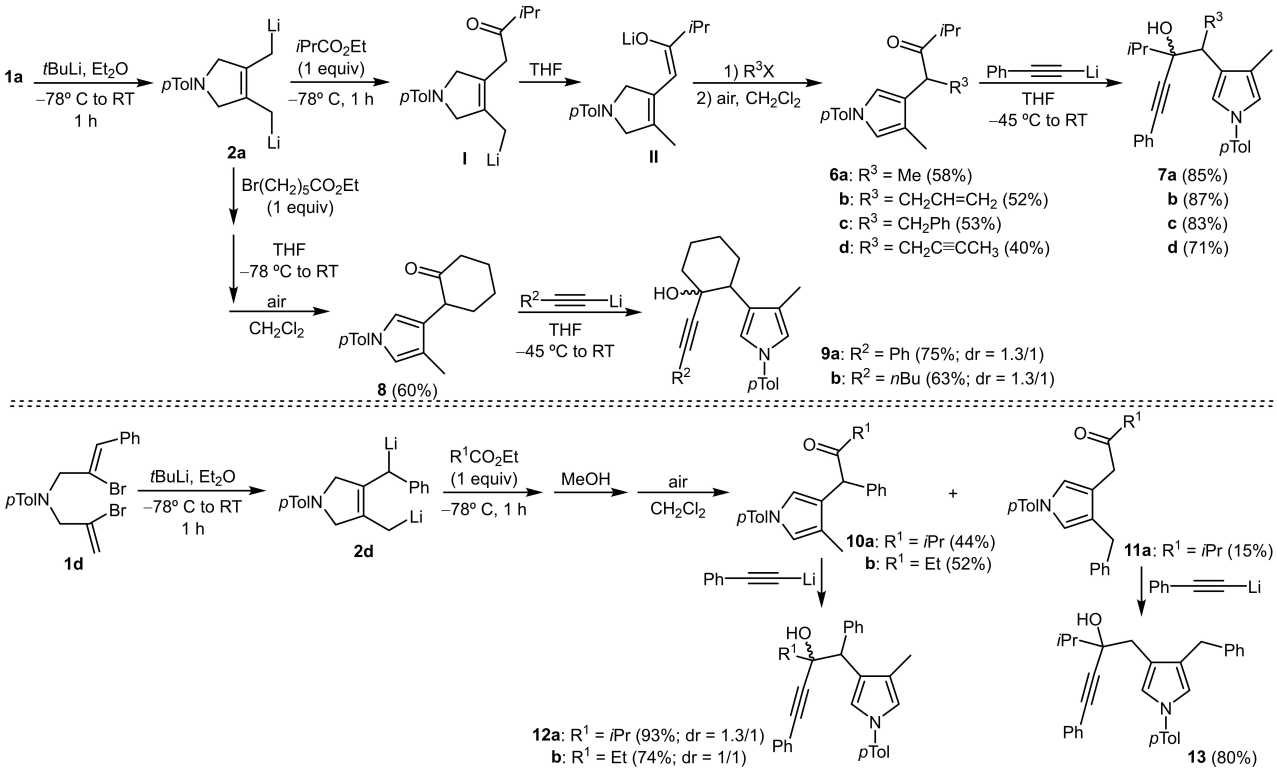
ent	4	Ar	R^1	R^2	5	yield [%][b]
1	**4aaa**	*p*Tol	*i*Pr	Ph	**5aaa**	88[c]
2	**4aab**	*p*Tol	*i*Pr	3-Th	**5aab**	88
3	**4aac**	*p*Tol	*i*Pr	*n*Bu	**5aac**	94
4	**4aad**	*p*Tol	*i*Pr	cC_3H_5	**5aad**	85
5	**4aae**	*p*Tol	*i*Pr	cC_6H_9	**5aae**	91
6[d]	**4aaf**	*p*Tol	*i*Pr	Ar^1OCH_2	**5aaf**	83
7[e]	**4aag**	*p*Tol	*i*Pr	Ar^2OCH_2	**5aag**	80
8	**4aah**	*p*Tol	*i*Pr	H	**5aah**	95
9	**4aai**	*p*Tol	*i*Pr	$2\text{-}NO_2C_6H_4$	**5aai**	70
10	**4aba**	*p*Tol	Me	Ph	**5aba**	84
11	**4aca**	*p*Tol	Et	Ph	**5aca**	88
12	**4ada**	*p*Tol	cC_3H_5	Ph	**5ada**	79
13	**4aea**	*p*Tol	$5\text{-}Br(CH_2)_4$	Ph	**5aea**	78
14	**4afa**	*p*Tol	Ph	Ph	**5afa**	81
15	**4baa**	$4\text{-}MeOC_6H_4$	*i*Pr	Ph	**5baa**	94
16	**4bac**	$4\text{-}MeOC_6H_4$	*i*Pr	*n*Bu	**5bac**	92
17	**4bad**	$4\text{-}MeOC_6H_4$	*i*Pr	cC_3H_5	**5bad**	76
18	**4bae**	$4\text{-}MeOC_6H_4$	*i*Pr	cC_6H_9	**5bae**	92
19	**4baf**	$4\text{-}MeOC_6H_4$	*i*Pr	H	**5baf**	91
20	**4caa**	$4\text{-}ClC_6H_4$	*i*Pr	Ph	**5caa**	90
21	**4cac**	$4\text{-}ClC_6H_4$	*i*Pr	*n*Bu	**5cac**	90

[a] *Reaction conditions*: **4** (0.3 mmol), $NaAuCl_4 \cdot 2H_2O$ (5 mol%), CH_2Cl_2 (3 mL), RT, 1 h.
[b] Yield of isolated product referred to the corresponding alkynol **4**.
[c] Reaction carried out with 1.018 g of **4aaa** afforded 83% of **5aaa**.
[d] $Ar^1 = 4\text{-}ClC_6H_4$.
[e] $Ar^2 = 4\text{-}MeOC_6H_4$.

Next, we essayed the benzannulation of these new alkynols under gold-catalysis (Table 3). Again, the indole formation took place in high yields leading to regioselectively functionalized indoles **14**. Using this strategy, the C-4 position of the indole nucleus could be functionalized with methyl, allyl, benzyl, or phenyl groups (**14a–c,f,g**; entries 1–3 and 7–8), although not with a propargyl substituent (entry 4), probably due to competitive pathways arising from the presence of two different alkynes in **7d**. Interestingly, tetrahydrobenzo[*e*]indoles **14d,e** could be synthesized from pyrrolylalkynols **9** (entries 5 and 6). Finally, a 3-benzylindole derivative **14h** could also be prepared from alkynol **13** (entry 9).[19]

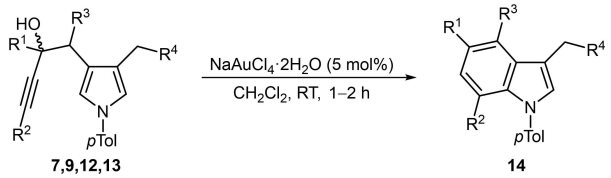
Regarding the mechanism, an initial attack of the pyrrole onto the activated alkyne is expected to take place (Scheme 3). However, it is not clear if the attack involves C-2 activation leading to intermediate **III**, as pyrroles are more nucleophilic through this position, or C-3, giving rise to spirocyclic intermediate **IV**, as it has been recently reported based on DFT studies performed on the related Ag(I)-catalyzed reaction.[6e] In the first case, protodeauration and water elimination provide the indole derivative, whereas in the second case, a selective 1,2-migration should occur prior to proto-demetallation and aromatization.

At this point, and taking advantage of the potential of dianions **2**, we decided to test its reaction with Weinreb amides to access pyrroles keto-functionalized at both 3- and 4-positions. Gratifyingly, diketones **15** were obtained in moderate to good yields, after treatment of **2** with a selection of Weinreb amides and subsequent oxidation (Scheme 4). Furthermore, a diketone with additional substituents, such as **15e**, was prepared from **15d** through regioselective enolization and trapping with allyl bromide. In addition, besides *N*-aryl pyrroles **15a–f**, *N*-benzyl derivatives **15g,h** could also be synthesized from *N*-benzyl *N,N*-bis-(2-bromallyl)amine (**1e**), although longer reaction times were required for the carbolithiation process that affords dianion **2e**. Further alkynylation of these diketopyrrole derivatives **15** with lithium acetylides took place efficiently, leading to the corresponding



Scheme 2. Synthesis of pyrrolyl alkynols **7**, **9**, **12** and **13**.

Table 3. Synthesis of 3,4,5,7-tetrasubstituted indole derivatives **14**.[a]

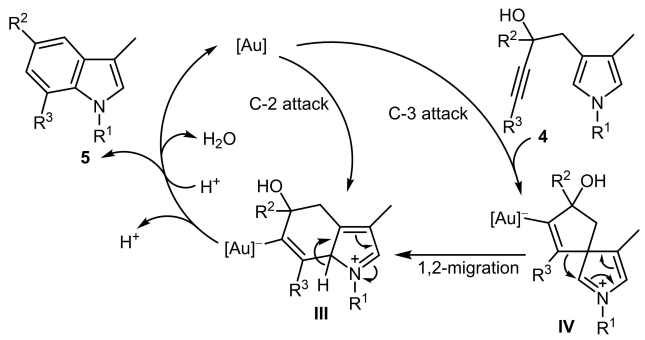


entry	Alkynol	R^1	R^3	R^2	R^4	**14**	yield [%][b]
1	**7a**	*i*Pr	Me	Ph	H	**14a**	83
2	**7b**	*i*Pr	$CH_2CH{=}CH_2$	Ph	H	**14b**	92
3	**7c**	*i*Pr	CH_2Ph	Ph	H	**14c**	90
4	**7d**	*i*Pr	$CH_2C{\equiv}CCH_3$	Ph	H	–	–
5	**9a**	$-(CH_2)_4-$		Ph	H	**14d**	77
6	**9b**	$-(CH_2)_4-$		*n*Bu	H	**14e**	70
7	**12a**	*i*Pr	Ph	Ph	H	**14f**	70
8	**12b**	Et	Ph	Ph	H	**14g**	82
9	**13**	*i*Pr	H	Ph	Ph	**14h**	84

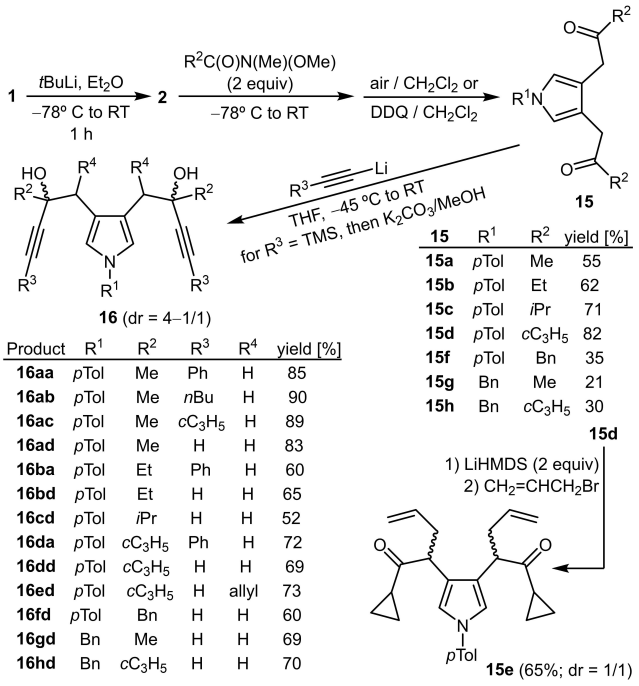
[a] *Reaction conditions*: starting alkynol (0.3 mmol), $NaAuCl_4 \cdot 2H_2O$ (5 mol%), CH_2Cl_2 (3 mL), RT, 1–2 h.
[b] Yield of isolated indole referred to the corresponding starting alkynol.

bisalkynols **16** in good yields and as variable mixtures of diastereoisomers (Scheme 4).

In order to synthesize carbazole derivatives **17** through a double benzannulation process, 3,4-bis(alkynol)pyrroles **16** were treated with catalytic amounts of $NaAuCl_4 \cdot 2H_2O$ (Table 4). Starting substrates bearing a methyl group as R^2 substituent or a hydrogen atom as R^3 group efficiently underwent the expected double cyclization affording symmetrically functionalized 1,3,4,5,6,8,9-substituted carbazoles **17** in good yields (entries 1–4, 6–7, 9–13). However, bisalkynols **16** possessing the propargylic group R^2 bigger than methyl and the alkyne substituent R^3 different from hydrogen, such as **16ba** and **16da**, did



Scheme 3. Mechanistic proposal.



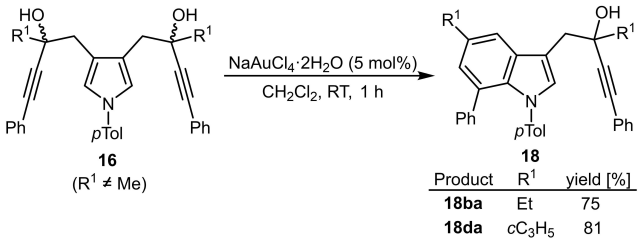
Product	R^1	R^2	R^3	R^4	yield [%]
16aa	*p*Tol	Me	Ph	H	85
16ab	*p*Tol	Me	*n*Bu	H	90
16ac	*p*Tol	Me	cC_3H_5	H	89
16ad	*p*Tol	Me	H	H	83
16ba	*p*Tol	Et	Ph	H	60
16bd	*p*Tol	Et	H	H	65
16cd	*p*Tol	*i*Pr	H	H	52
16da	*p*Tol	cC_3H_5	Ph	H	72
16dd	*p*Tol	cC_3H_5	H	H	69
16ed	*p*Tol	cC_3H_5	H	allyl	73
16fd	*p*Tol	Bn	H	H	60
16gd	Bn	Me	H	H	69
16hd	Bn	cC_3H_5	H	H	70

15	R^1	R^2	yield [%]
15a	*p*Tol	Me	55
15b	*p*Tol	Et	62
15c	*p*Tol	*i*Pr	71
15d	*p*Tol	cC_3H_5	82
15f	*p*Tol	Bn	35
15g	Bn	Me	21
15h	Bn	cC_3H_5	30

Scheme 4. Synthesis of 3,4-bis(carbonylmethyl)pyrroles **15** and 3,4-bis(alkynols)pyrroles **16**.

not afford the expected carbazole derivatives **17** (entries 5 and 8).

A detailed analysis of the reactions of these bisalkynols **16** led us to the conclusion that the first benzannulation takes place in the expected way giving rise to indoles **18**, C-3 functionalized with an alkynol moiety, which could be isolated in high yields after 1 hour (Scheme 5). Disappointingly, prolonged reaction times led to decomposition. It seems that the presence of a C-7 substituent on the indole moiety of **18** could interact with the *N*-substituent disfavoring the second benzannulation.



Product	R^1	yield [%]
18ba	Et	75
18da	cC_3H_5	81

Scheme 5. Synthesis of 3-alkynol-functionalized indoles **18**.

Conclusion

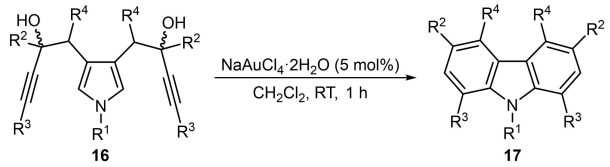
In summary, we have developed a convenient methodology to synthesize regioselectively substituted indoles and carbazoles from pyrrolynol precursors in a "back-to-front" manner. The benzannulation processes are catalyzed by a commercially available gold salt, $NaAuCl_4 \cdot 2H_2O$. Starting alkynol-functionalized pyrroles are prepared from readily simple materials such as *N,N*-bis-(2-bromoallyl)amines by using organolithium chemistry, with the key step involving the intramolecular carbolithiation of *N,N*-bis-(2-lithioallyl)amines and subsequent trapping with carboxylic esters and Weinreb amides. This strategy reveals the usefulness of combining organolithium chemistry with gold-catalyzed reactions to prepare regioselectively functionalized heterocyclic compounds from very simple starting materials.

Experimental Section

General Procedure for the Synthesis of Pyrroles 3 and 4 (Table 1)

Under a nitrogen atmosphere, *t*BuLi (8 mmol, 4.7 mL of a 1.7 M solution in pentane) was added slowly to a solution of the corresponding amine **1** (2 mmol) in anhydrous Et_2O (15 mL) at −78 °C. The resulting mixture was allowed to stir 30 min at this temperature. Then, the cooling bath was removed, and the reaction was allowed to reach room temperature for 1 h. After that, the mixture was re-cooled to −78 °C and the corresponding carboxylic ester (2 mmol) was added. The reaction was allowed to stir at −78 °C for 1 h. Thereafter, and without raising the temperature, it was quenched with MeOH (10 mL). The residue was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated at reduced pressure. The corresponding obtained dihydropyrrole was dissolved in CH_2Cl_2 (40 mL) in an open flask. The mixture was allowed to stir vigorously under air overnight. The oxidation of the pyrrole is typically accompanied by a colour change, from light yellow to dark red. After that, the residue was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated at reduced pressure. The pyrroles **3** were purified by column chromatography (hexane:EtOAc). Ethynylmagnesium bromide (1.55 mmol, 3.1 mL of a 0.5 M solution in THF) or the previously prepared lithium acetylide reagent (1.55 mol) was added to a solution of the corresponding pyrrole

Table 4. Synthesis of carbazole derivatives **17**.[a]



entry	**16**	R^1	R^2	R^3	R^4	**17**	yield [%][b]
1[c]	**16aa**	*p*Tol	Me	Ph	H	**17aa**	60
2[c]	**16ab**	*p*Tol	Me	*n*Bu	H	**17ab**	68
3[c]	**16ac**	*p*Tol	Me	cC_3H_5	H	**17ac**	61
4	**16ad**	*p*Tol	Me	H	H	**17ad**	80
5	**16ba**	*p*Tol	Et	Ph	H	–	
6	**16bd**	*p*Tol	Et	H	H	**17bd**	85
7	**16cd**	*p*Tol	*i*Pr	H	H	**17cd**	73
8	**16da**	*p*Tol	cC_3H_5	Ph	H	–	
9	**16dd**	*p*Tol	cC_3H_5	H	H	**17dd**	78
10[c]	**16ed**	*p*Tol	cC_3H_5	H	allyl	**17ed**	44
11	**16fd**	*p*Tol	Bn	H	H	**17fd**	72
12	**16gd**	Bn	Me	H	H	**17gd**	73
13	**16hd**	Bn	cC_3H_5	H	H	**17hd**	73

[a] *Reaction conditions*: starting bisalkynol **16** (0.3 mmol), $NaAuCl_4 \cdot 2H_2O$ (5 mol%), CH_2Cl_2 (3 mL), RT, 1 h (unless otherwise stated).
[b] Yield of isolated carbazole **17** referred to the corresponding starting material **16**.
[c] Reaction time: 16 h. An additional catalyst loading (5 mol%) was added after ca. 8 h.

derivative **3** (0.5 mmol) in anhydrous THF (2 mL), at −45 °C. The lithium acetylides were prepared from the corresponding terminal alkyne (1.65 mmol) in anhydrous THF (5 mL) by addition of *n*BuLi (1.55 mmol, 0.97 mL of a 1.6 M solution) at -45 °C and further stirring for 30 min. Once the organometallic compound was added to the pyrrole derivative, the resulting mixture was allowed to stir until the starting pyrrole **3** was consumed as determined by TLC (1–16 h). Then, the reaction was quenched by adding a saturated aqueous NH_4Cl solution and most of THF was evaporated. After that, the residue was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated at reduced pressure. The resulting alkynols **4** were purified on silica gel by column chromatography (hexane:EtOAc). Characterization data and NMR spectra are presented in the Supporting Information.

General Procedure for the Synthesis of Indoles 5 and 14 (Tables 2 and 3)

$NaAuCl_4 \cdot 2H_2O$ (6 mg, 5 mol%) was added to a solution of the corresponding pyrrolyl alkynol **4**, **7**, **9**, **12** or **13** (0.3 mmol) in CH_2Cl_2 (3 mL) at room temperature. The resulting reaction mixture was allowed to stir at room temperature until the starting pyrrole was consumed, as determined by TLC (1–2 h). The reaction was quenched by adding a few drops of a saturated NH_4Cl aqueous solution and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated at reduced pressure. The indole derivatives **5** and **14** were purified on silica gel by column chromatography (hexane:EtOAc). Characterization data and NMR spectra are presented in the Supporting Information.

Acknowledgements

We gratefully acknowledge Ministerio de Ciencia e Innovación MCIN/AEI/10.13039/501100011033 (PID2020-115789GB-C21), and Junta de Castilla y León and FEDER (BU049P20) for financial support. The project leading to these results has received funding from "la Caixa" Foundation, under the Agreement LCF/PR/PR18/51130007> (CAIXA-UBU001). M.A.M., F.M.-L., M.S. and S.S.-P. thank Junta de Castilla y León (Consejería de Educación) and Fondo Social Europeo for predoctoral (M.A.M, F.M.-L. and M.S.) and postdoctoral (S.S.-P.) contracts, respectively.

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[17] Disappointingly, when *N*-benzyl-*N*,*N*-bis-(2-bromoallyl)amine (**1 e**) was employed as starting amine for accessing a ketopyrrole derivative **3**, very low yields were obtained (~10%), thus preventing its further synthetic use. On the other hand, the carbolithiation of *N*,*N*-bis-(2-bromoallyl) *p*-toluenesulfonamide (**1 f**) was unsuccessful, as the dianion generated from the double bromine–lithium exchange proved to be unstable and evolved through β-elimination leading to *N*-allyl *p*-toluenesulfonamide (see Supporting Information for details).

[18] **10 a**/**11 a** were obtained as a ca. 3:1 mixture of regioisomers, whereas **10 b**/**11 b** were obtained as a ca. 7:1 mixture of regioisomers and **11 b** was not isolated.

[19] Using our strategy, it is not possible to prepare indoles without C3-substituent because 2-bromoallyl or 2-bromocinnamyl groups are required in the starting amines for the success of the carbolithiation reaction that affords the pyrrole scaffold.