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3-(*o*-Trifluoroacetamidoaryl)-1-propargylic esters: common intermediates for the palladium-catalyzed synthesis of 2-aminomethyl-, 2-vinylic, and 2-alkylindoles

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ABSTRACT

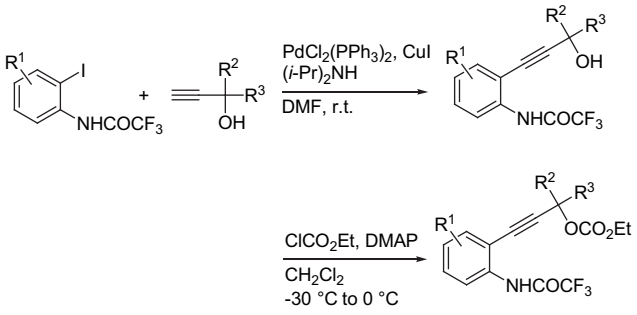
3-(*o*-Trifluoroacetamidoaryl)-1-propargylic esters have been used as common synthetic intermediates for the preparation of a variety of 3-unsubstituted 2-substituted indoles. Treating ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates unsubstituted or containing an aryl substituent at the propargylic carbon with piperazines and $Pd(PPh_3)_4$ in THF at 80 °C affords 2-(piperazin-1-ylmethyl)-indoles in excellent yields. Good to excellent yields of 2-aminomethylindoles are also obtained with other secondary amines. Ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates bearing an alkyl substituent at the propargylic carbon and ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic acetates disubstituted at the propargylic carbon give 2-vinylic indoles with the $Pd(OAc)_2/PPh_3$ combination and Et_3N in THF at 80 °C. Formation of 2-vinylic indoles is quite stereoselective, generating *trans* vinylic derivatives, at least with the substrates that we have investigated. In the presence of formic acid, Et_3N, and $Pd(PPh_3)_4$ in MeCN at 80 °C, ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates afford 2-alkylindoles in good to excellent yields.

1. Introduction

The indole nucleus is prevalent in a vast array of biologically active natural and unnatural compounds. In view of this, the development of efficient and versatile methods for the construction of this structural unit is a subject of great interest in drug discovery and palladium catalysis has provided an almost unique tool to develop a wide range of synthetic strategies.[1] In attempting to further extend our palladium-catalyzed alkyne-based synthesis of indoles,[2] we observed and previously communicated that ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates **1**[3] could be used as precursors of 2-aminomethyl-[4] and 2-alkylindoles[5] via trapping of π-allylic palladium intermediates generated in situ with amines and formate anions, respectively. We wish at this time to report full details on this very useful new synthetic approach to indoles, including its extension to the preparation of 2-vinylic indoles.

2. Results and discussion

Ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates **1** were prepared from *o*-(iodo)trifluoroacetanilides via Sonogashira cross-coupling with propargylic alcohols followed by an esterification step (Scheme 1). This protocol was typically used with neutral or electron-rich *o*-(iodo)trifluoroacetanilides. Alternatively, particularly when the preparation of ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates containing electron-poor aromatic rings was required, they were synthesized from *o*-iodoanilines via Sonogashira cross-coupling with the THP derivatives of propargylic alcohols followed by treatment of the resultant cross-coupling products with trifluoroacetic anhydride and deprotection and esterification steps (Scheme 2).



Scheme 1.

2.1. Synthesis of 2-aminomethylindoles

Initial studies were directed toward finding a general set of reaction conditions that could be applied to the conversion of a wide

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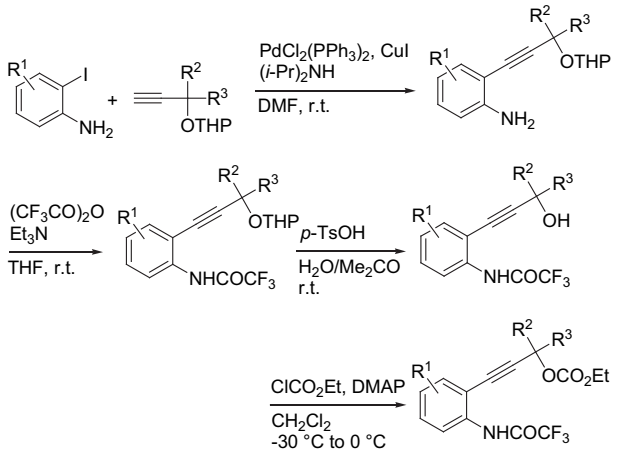
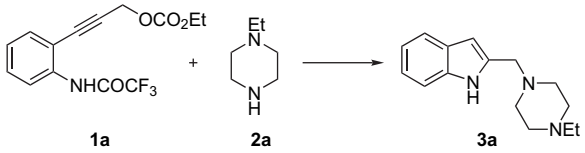


Scheme 2.

range of ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates into the corresponding 2-aminomethylindoles. Compound **1a** and *N*-ethylpiperazine **2a** were selected as the model system. Reactions were carried out at 80 °C and the following reaction variables were closely examined: the source of Pd(0) species, the nature of the ligands, and solvents. Some results of our screening study are summarized in Table 1.

Table 1
Optimization of reaction conditions[a]



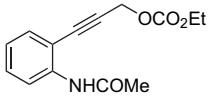
1a **2a** **3a**

Entry	Precatalyst	Solvent	Time (h)	Yield % of **3a**[b]
1	$Pd(OAc)_2/PPh_3$	THF	6	52[c]
2	$Pd_2(dba)_3/PPh_3$	THF	6	58[d]
3	$PdCl_2(2\text{-furyl})_2$	THF	24	33
4	$Pd_2(dba)_3$/dppe	THF	24	50[e]
5	$Pd_2(dba)_3$/dppf	THF	6	85[e]
6	$Pd(PPh_3)_4$	THF	1.5	91
7	$Pd(PPh_3)_4$	MeCN	6	57
8	$Pd(PPh_3)_4$	DMF	6	54

[a] Unless otherwise stated, reactions were carried out on a 0.159 mmol scale in 1 mL of solvent under argon at 80 °C by using 1 equiv of **1a**, 3 equiv of **2a**, 0.05 equiv of [Pd].
[b] Yields are given for isolated products.
[c] 0.2 equiv of PPh_3.
[d] 0.1 of PPh_3.
[e] 0.05 equiv of bidentate phosphine ligand.

The desired indole derivative was isolated in low to moderate yields using $Pd(OAc)_2$ and $Pd_2(dba)_3$ with PPh_3 as ligand (Table 1, entries 1 and 2) or $PdCl_2(2\text{-furyl})_2$ (Table 1, entries 3) in THF. The $Pd_2(dba)_3$/dppe [1,3-bis(diphenylphosphino)ethane] combination gave a similar yield (Table 1, entry 4). Switching to $Pd_2(dba)_3$ and dppf [1,1′-bis(diphenylphoshino)ferrocene] allowed for the isolation of **3a** in high yield (Table 1, entry 5) but the best result in terms of yield and reaction time was obtained with $Pd(PPh_3)_4$ in THF (Table 1, entry 6). Lower yields and longer reaction times were observed when the same precatalyst system was used in MeCN or DMF (Table 1, entries 7 and 8) as well as when the corresponding less reactive propargylic acetate was used as the starting alkyne [50% yield; $Pd(PPh_3)_4$, THF, 80 °C, 24 h]. A slightly higher yield (67%) was obtained at 100 °C after 9 h, but still significantly lower than with **1a**.

As observed in our previous studies on the aminopalladation/reductive elimination route to indoles,[6] the acidity of the nitrogen–hydrogen bond was found to play a crucial role. Treatment of ethyl 3-(*o*-acetamidophenyl)-1-propargyl carbonate **4**, containing a less acidic nitrogen–hydrogen bond, with 4-ethylpiperazine under the conditions shown in Table 1, entry 6 afforded a complex reaction mixture and the indole product was formed only in trace amounts, if any.



4

Interestingly, the reaction gives excellent results using a monodentate phosphine ligand such as PPh_3, although it has been reported that π-propargylic palladium complexes (which are likely intermediates in this chemistry, vide infra) are formed in a more stable manner in the presence of bidentate ligands, particularly with dppe,[7] and that the best ligands for the palladium-catalyzed reaction of propargylic halides[8] and carbonates[9] with soft nucleophiles are the bidentate ligands.

Using the optimized conditions [$Pd(PPh_3)_4$, THF, 80 °C], we next explored the scope and generality of the reaction. As indicated in Table 2, a large number of 2-(piperazin-1-ylmethyl)-indoles were prepared in excellent yields. Piperazines were selected as nitrogen nucleophiles because they are (as indoles themselves) privileged structures[10] and 2-(piperazin-1-ylmethyl)-indoles, which exhibit important biological activities, have attracted considerable attention in organic, medical, and pharmaceutical chemistry.[11] Only with **2j** (Table 2, entry 10) the corresponding indole product was isolated in moderate yield, very likely because of the low nucleophilicity of the nitrogen derivative due to steric effects.

The reaction can be applied to other secondary amines and yields are usually good to high (Table 3, entries 1–3). The moderate yield obtained with diisopropylamine (Table 3, entry 4) was attributed again to the involvement of steric effects. With primary amines the efficiency of the reaction is flawed by the occurrence of side reactions. For example, with benzylamine and butylamine complex reaction mixtures of unidentified products were obtained, presumably containing indole derivatives generated via N-allylation of the initially formed 2-aminomethylindoles.

The extension of the reaction to propargylic carbonates substituted at the propargylic carbon was next examined. The phenyl-containing propargylic carbonate **1b** was initially used and its treatment with a variety of secondary amines under standard conditions afforded the desired products in moderate to excellent yields (Table 4). Interestingly, moderate to high yields were in this case obtained with primary amines as well (Table 4, entries 7 and 8). Very likely, steric effects due to the presence of the phenyl group may play a role in preventing 2-aminomethylindoles from undergoing a subsequent N-allylation reaction.

However, when the reaction was extended to the ethyl derivative **1c** no formation of the corresponding 2-aminomethylindole was observed upon treatment with **2a**, the main product being 2-(propen-1-yl)indole **5a**, isolated in 70% yield as an approximately 80:20 *E*/*Z* mixture (Scheme 3). Apparently, the corresponding π-allylic palladium intermediate (vide infra), containing an adjacent carbon–hydrogen bond, is more prone to undergo an elimination reaction[12] than a nucleophilic attack.

Table 2
Palladium-catalyzed synthesis of 2-(piperazin-1-ylmethyl)indoles **3** from ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargyl carbonate **1a** and piperazines **2**[a]

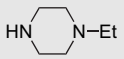
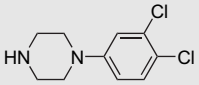
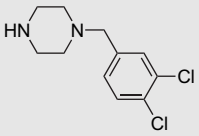
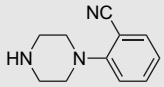
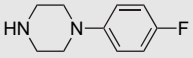
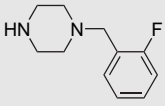
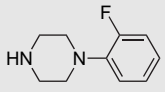
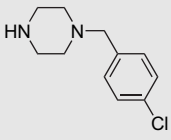
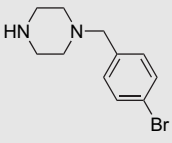
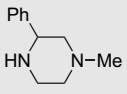
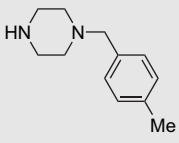
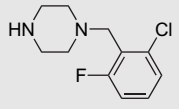
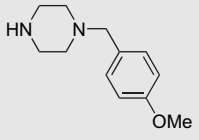
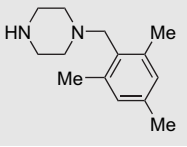
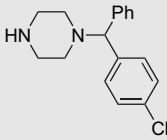
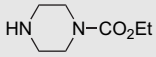
Entry	Piperazine **2**		Time (h)	Yield % of **2**[b]
1		**2a**	1.5	**3a** (91)
2		**2b**	2	**3b** (96)
3		**2c**	24	**3c** (80)
4		**2d**	3	**3d** (98)
5		**2e**	6	**3e** (96)
6		**2f**	6	**3f** (98)
7		**2g**	2.5	**3g** (97)
8		**2h**	3	**3h** (92)
9		**2i**	3	**3i** (94)
10		**2j**	6	**3j** (58)
11		**2k**	4	**3k** (85)
12		**2l**	12	**3l** (78)
13		**2m**	4	**3m** (81)
14		**2n**	4	**3n** (80)

Table 2 (*continued*)

Entry	Piperazine **2**		Time (h)	Yield % of **2**[b]
15		**2o**	8	**3o** (92)
16		**2p**	20	**3p** (88)

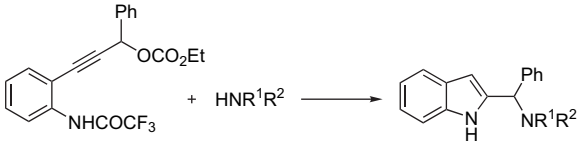
[a] Reactions were carried out on a 0.159 mmol scale in 1 mL of THF under argon at 80 °C by using 1 equiv of **1a**, 3 equiv of **2**, 0.05 equiv of $Pd(PPh_3)_4$.
[b] Yields are given for isolated products.

Table 3
The palladium-catalyzed reaction of ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargyl carbonate **1a** with secondary amines[a]

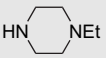
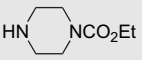
Entry	Amine	Time (h)	Yield % of **3**[b]
1		1	**3q** (94)[c]
2		1	**3r** (98)
3	Et_2NH	2	**3s** (60)[d]
4	$(i\text{-}Pr)_2NH$	4	**3t** (45)

[a] Unless otherwise stated, reactions were carried out on a 0.159 mmol scale in 1 mL of THF under argon at 80 °C by using 1 equiv of **1a**, 3 equiv of secondary amine, 0.05 equiv of $Pd(PPh_3)_4$.
[b] Yields are given for isolated products.
[c] The indole product **3q** was isolated in 84% yield in the presence of 0.0125 equiv of $Pd_2(dba)_3$ and 0.05 equiv of PPh_3 after 6 h and in 73% yield with 0.025 equiv of $Pd_2(dba)_3$, omitting PPh_3, after 24 h.
[d] With 5 equiv of amine.

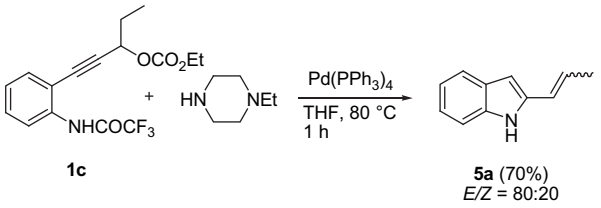
Table 4
The palladium-catalyzed synthesis of 2-aminomethylindoles from of **1b**[a]



1b **2** **3**

Entry	Amine	Time (h)	Yield % of **3**[b]
1		1	**3u** (92)
2		2	**3v** (90)
3		1	**3w** (94)
4		1	**3x** (98)
5	Et_2NH	2	**3y** (60)
6	$(i\text{-}Pr)_2NH$	4	**3z** (45)
7	NH_2CH_2Ph	4	**3za** (54)
8	$n\text{-}NH_2Bu$	5	**3zb** (80)

[a] Reactions were carried out on a 0.159 mmol scale in 2 mL of THF under argon at 80 °C by using 1 equiv of **1b**, 3 equiv of **2**, 0.05 equiv of $Pd(PPh_3)_4$.
[b] Yields are given for isolated products.

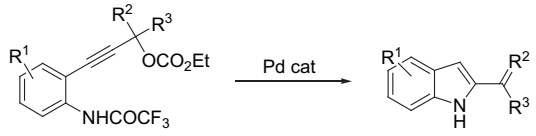


1c **5a** (70%) *E*/*Z* = 80:20

Scheme 3.

2.2. Synthesis of 2-vinylic indoles

Although we did not obtain the desired indole derivative, we were attracted by the possibility to develop this reaction into a general method for the synthesis of 2-vinylic indoles (Scheme 4). These compounds are useful synthetic intermediates.[13] The 2-vinylic indole motif is also diffused among molecules exhibiting interesting biological activities.[14] Therefore, we decided to optimize the conditions of this type of reaction.

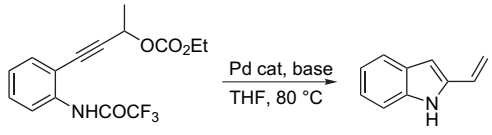


1 **5**

Scheme 4.

Using the methyl derivative **1d** as the model system, a few representative bases and palladium precatalysts were tested (Table 5). The best result was obtained with Et_3N in the presence of 0.05 equiv of $Pd(OAc)_2$ and 0.2 equiv of PPh_3 (Table 5, entry). Interestingly, the $Pd(OAc)_2/PPh_3$ combination gave excellent results in this reaction whereas $Pd(PPh_3)_4$ was found to be superior in the reaction of ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargyicl carbonate **1a** with *N*-ethylpiperazine **2a**.

Table 5
Optimization of reaction conditions[a]



1d **5b**

Entry	Precatalyst	Base	Time (h)	Yield % of **5b**[b]
1	$Pd(PPh_3)_4$	—	24	—
2	$Pd(PPh_3)_4$	K_2CO_3	1	40
3	$Pd(PPh_3)_4$	Et_3N	4	53
4	$Pd(OAc)_2/(PPh_3)_2$	K_2CO_3	2	70
5	$Pd(OAc)_2/(PPh_3)_2$	Et_3N	0.5	90
6	$Pd(OAc)_2/(PPh_3)_2$	Styrene oxide	12	80

[a] Reactions were carried out on a 0.32 mmol scale in 2 mL of THF under argon at 80 °C by using 1 equiv of **1d**, 0.05 equiv of [Pd], 0.2 equiv of PPh_3 (when added), and 3 equiv of base.
[b] Yields are given for isolated products.

The conditions shown in Table 5, entry 5 were then used when the procedure was extended to include other propargylic substrates containing one and two alkyl groups on the propargylic carbon.

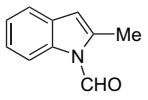
With the latter, propargylic acetates were needed as the starting material. Indeed, the preparation of carbonates via esterification of tertiary propargylic alcohols with ethyl chlorocarbonate and a variety of amine bases in CH_2Cl_2 failed to give the desired products. Good results were instead obtained by using acetic anhydride and 4-dimethylaminopyridine (DMAP).

The results obtained in the synthesis of 2-vinylic indoles from ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates and acetates are summarized in Table 6. The process is quite general and a variety of substituents can be accommodated both on the aniline fragment and on the propargylic carbon. Interestingly, high yields of 2-vinylic indoles were obtained even with propargylic esters bearing electron-withdrawing substituents on the anilide fragment (Table 6, entries 16–18), although electron-withdrawing substituents might be expected to decrease the nucleophilicity of the nitrogen atom and consequently hamper the cyclization step. Most noteworthy from the synthetic viewpoint is the essentially 100% stereoselective formation of *trans* vinylic derivatives under the 'optimal' conditions used, at least with the substrates that we have investigated (Table 6, entries 1, 3, 7).

2.3. Synthesis of 2-alkylindoles

During our early studies on this chemistry,[4] we had the occasion to observe that subjecting ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates to formate anions in the presence of a palladium catalyst could form 2-alkylindoles. Consequently, we became interested even in the utilization of these substrates as precursors of free NH 3-unsubstituted 2-alkylindoles **6** (Scheme 5). Despite the interest for 3-unsubstituted 2-alkylindoles as synthetic intermediates,[15] the number of available routes to this class of compounds is indeed quite limited[16] and the development of new straightforward procedures is desirable.

Some of the results of our screening study using **1a** as the model system are summarized in Table 7. Utilization of HCOOH in the presence of Et_3N proved to be superior to HCOOK (Table 7, compare entry 1 with entry 2) and, as found in the synthesis of 2-aminomethylindoles, $Pd(PPh_3)_4$ gave better results than the $Pd(OAc)_2/(PPh_3)_2$ combination (Table 7, compare entry 3 with entry 4). Under a variety of conditions the main byproduct was the *N*-formylindole **7a**, which in some cases was isolated in significant yields (Table 7, entries 4–6).



7a

The highest yield of **6a** was obtained using $Pd(PPh_3)_4$, HCOOH, and Et_3N in MeCN (Table 8, entry 8) and these conditions were applied when the synthetic scope of the reaction was examined. As shown by the results listed in Table 8, 2-alkylindoles were isolated in good to high yields with a wide range of ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargylic carbonates. The presence of one alkyl or aryl substituent on the propargylic carbon is tolerated (Table 8, entries 2–5, 14–18).

With propargylic esters containing two alkyl groups on the propargylic carbon, however, a competition between the reduction to 2-alkylindoles and the elimination to 2-vinylic indoles is observed.

The reaction of the model compound **1r** under standard conditions gave a 91% yield of an approximately 88:12 mixture of **6u** and **5p** (Scheme 6). Changing some reaction parameters in the attempt to suppress the formation of the vinylic product (mixtures of these indole derivatives are difficult to separate) met with failure. Worse results were usually obtained both in terms of yields and selectivity. For example, using $n\text{-}Bu_4NO_2CH$ as reducing agent in the absence of tertiary amines (they might favor the formation of the vinylic product through a base promoted elimination of the elements HPdX[17]) gave a complex mixture of products that we have not identified. With the $Pd_2(dba)_3$/dppb precatalyst system,

Table 6
Palladium-catalyzed heterocyclization of ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargylic esters **1** to 2-vinylic indoles **5**[a]

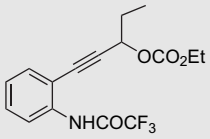
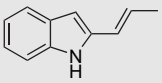
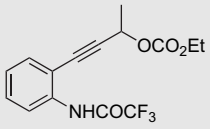
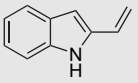
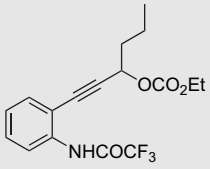
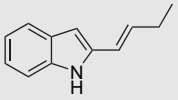
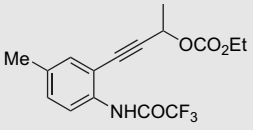
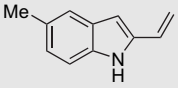
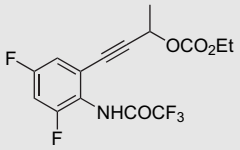
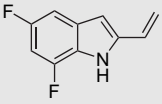
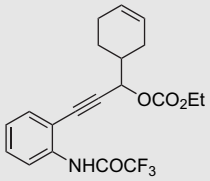
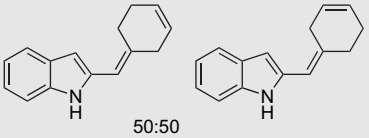
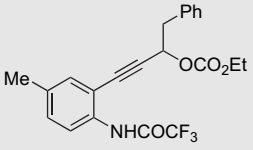
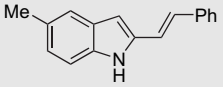
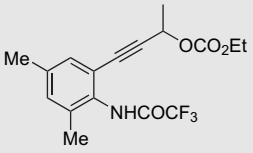
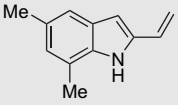
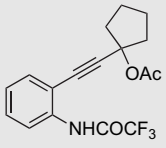
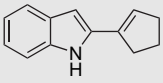
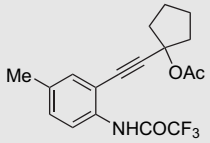
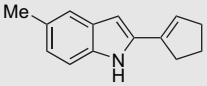
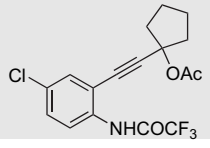
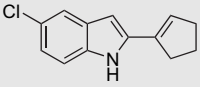
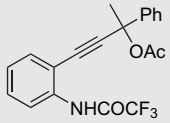
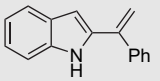
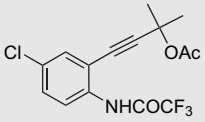
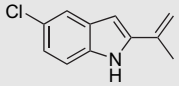
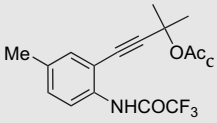
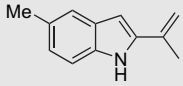
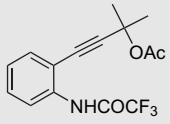
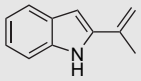
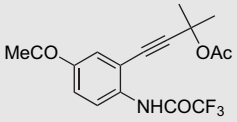
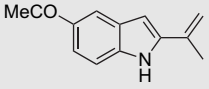
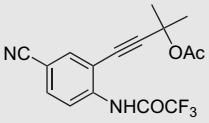
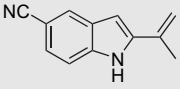
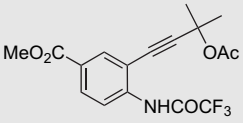
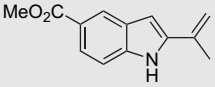
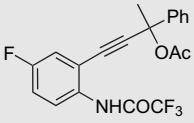
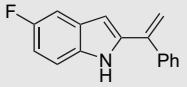
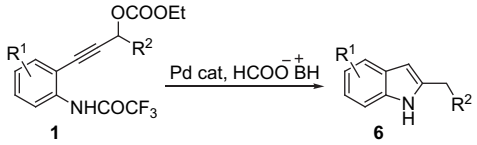
Entry	Ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic esters **1**		Time (h)	2-Vinylic indole **5**[b]		Yield[c] %
1		**1c**	1		**5a**	95
2		**1d**	0.5		**5b**	90
3[b]		**1e**	1		**5c**	83
4		**1f**	2		**5d**	63
5		**1g**	2		**5e**	82
6		**1h**	1	 50:50	**5f**	76
7		**1i**	0.5		**5g**	85
8		**1j**	1		**5h**	87
9		**1k**	8		**5i**	77
10		**1l**	7		**5j**	75
11		**1m**	7		**5k**	85

Table 6 (*continued*)

Entry	Ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic esters **1**		Time (h)	2-Vinylic indole **5**[b]		Yield[c] %
12		**1n**	6		**5l**	78
13		**1o**	2		**5m**	85
14		**1p**	3		**5n**	84
15		**1q**	1		**5o**	80
16		**1r**	1		**5p**	91
17		**1s**	1		**5q**	83
18		**1t**	2		**5r**	87
19		**1u**	1		**5s**	68

[a] Reactions were carried out on a 0.32 mmol scale in 2 mL of THF under argon at 80 °C by using 1 equiv of **1**, 3 equiv of Et_3N, 0.05 equiv of $Pd(OAc)_2$, and 0.2 equiv of PPh_3.
[b] Single *E*-isomers were obtained when not otherwise stated.
[c] Yields are given for isolated products.



Scheme 5.

a quantitative conversion of **1r** was observed: **6u** and **5p** were isolated in 99% yield. However, a dramatic worsening of the selectivity led to an approximately 55:45 mixture.

A possible solution to the reduction/elimination competition observed with this type of propargylic esters is converting them into 2-vinylic indoles, a reaction that usually occurs in high to excellent yields (Table 6), and reducing the carbon–carbon double bond by

Table 7
Palladium precatalysts, formate anions, solvents, and temperature in the cyclization of ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargyl carbonate **1a** to 2-methylindole **6a**[a]

Entry	Palladium precatalyst	Reducing agent	Base	Solvent	Time (h)	**6a** yield[b] %	**7a** yield[b] %
1	$Pd(OAc)_2/PPh_3$[c]	HCOOK	—	DMF	4	24	—
2	$Pd(OAc)_2/PPh_3$[d]	HCOOH	Et_3N	DMF	4	38	7
3	$Pd(OAc)_2/PPh_3$[d]	HCOOH	Et_3N	THF	3	48	5
4	$Pd(PPh_3)_4$	HCOOH	Et_3N	THF	1.5	62	12
5	$Pd(PPh_3)_4$	HCOOH	Et_3N	Dioxane	1	56	10
6	$Pd(PPh_3)_4$	HCOOH	Et_3N	Toluene	3	48	19
7	$Pd(PPh_3)_4$	HCOOH	Et_3N	Dioxane[e]	1	69	8
8	$Pd(PPh_3)_4$	HCOOH	Et_3N	MeCN	1	91	5
9	$Pd_2(dba)_3$/dppe	HCOOH	Et_3N	MeCN	1	84	—

[a] Reactions were conducted under argon at 80 °C on a 0.317 mmol scale using 1 equiv of **1a**, 2 equiv of HCOOH, 3 equiv of Et_3N in 2 mL of solvent.
[b] Yields are given for isolated products.
[c] $Pd(OAc)_2$:PPh_3=1:4.
[d] $Pd(OAc)_2$:PPh_3=1:2.
[e] In the presence of 1 equiv of H_2O.

Table 8
Palladium-catalyzed reductive heterocyclization of ethyl 3-(*o*-trifluoroacetamidophenyl)-1-propargylic carbonates **1** to 2-alkylindoles **6**[a]

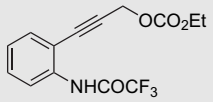
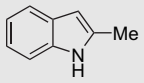
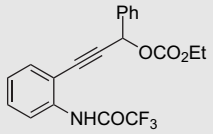
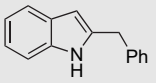
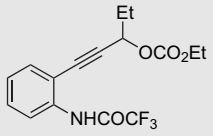
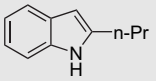
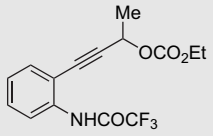
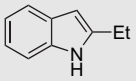
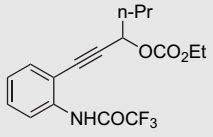
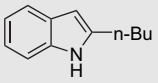
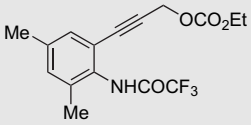
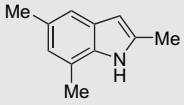
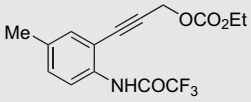
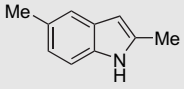
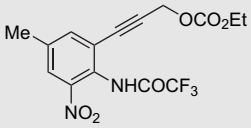
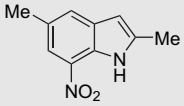
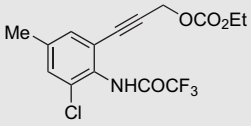
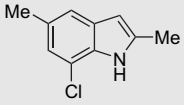
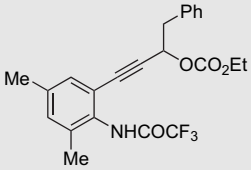
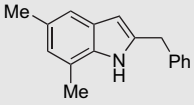
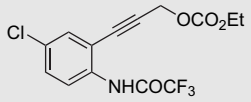
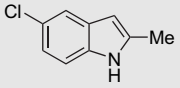
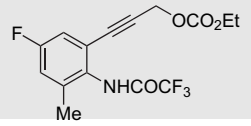
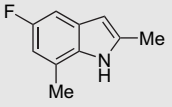
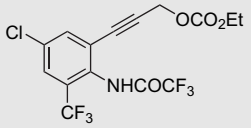
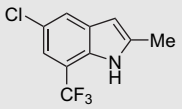
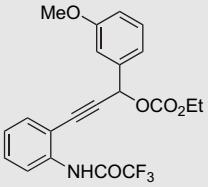
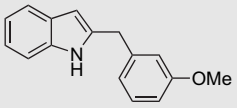
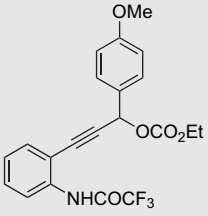
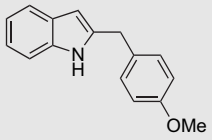
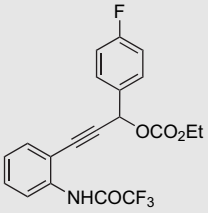
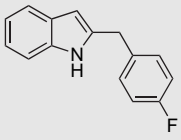
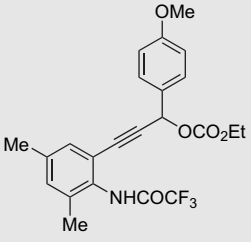
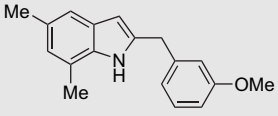
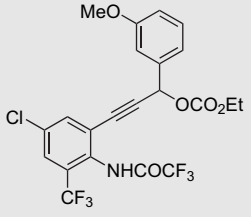
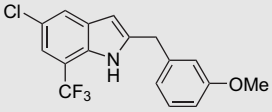
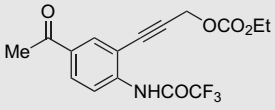
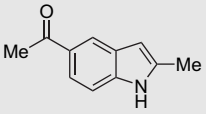
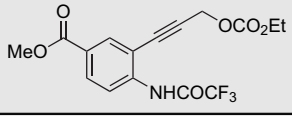
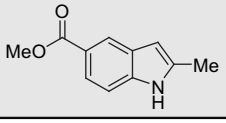
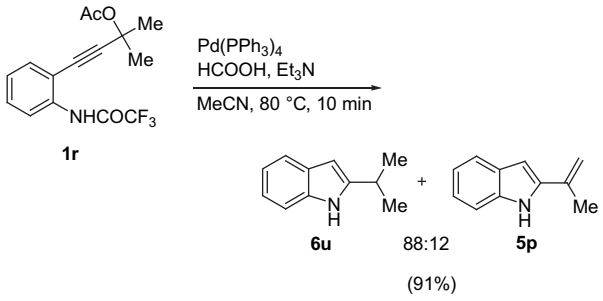
Entry	Ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonate **1**		Time (h)	2-Alkylindole **6**		Yield[b] %
1		**1a**	1		**6a**	91
2		**1b**	3		**6b**	75
3		**1c**	2		**6c**	70
4		**1d**	1		**6d**	70
5		**1e**	1		**6e**	67
6		**1w**	1		**6f**	99
7		**1x**	0.5		**6g**	80
8		**1y**	2		**6h**	78
9		**1z**	2		**6i**	51
10		**1aa**	1		**6j**	50
11		**1ab**	0.5		**6k**	60
12		**1ac**	1		**6l**	65

Table 8 (*continued*)

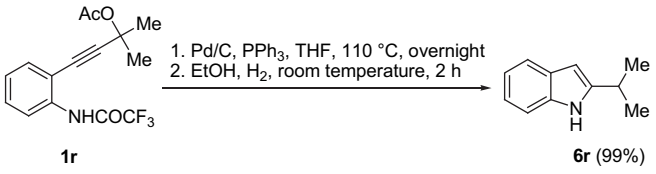
Entry	Ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonate **1**		Time (h)	2-Alkylindole **6**		Yield[b] %
13		**1ad**	1		**6m**	86
14		**1ae**	1		**6n**	75
15		**1af**	1		**6o**	70
16		**1ag**	1		**6p**	85
17		**1ah**	2		**6q**	72
18		**1ai**	0.5		**6r**	85
19		**1aj**	0.66		**6s**	73
20		**1ak**	1		**6t**	70

[a] Reactions were conducted under argon at 80 °C on a 0.2–0.3 mmol scale using 1 equiv of **1**, 2 equiv of HCOOH, 3 equiv of Et_3N in 2 mL of MeCN.
[b] Yields are given for isolated products.



Scheme 6.

palladium-catalyzed hydrogenation. To make this overall approach more attractive from a synthetic standpoint, we explored a process that would omit the isolation of 2-vinylic indole intermediates. After some experimentation, we were pleased to find that excellent results could be obtained treating **1r** with palladium on charcoal in the presence of PPh_3, evaporating the volatile material after completion of the indole formation process (no 2-alkylindole formation was observed when the evaporation step was omitted), and adding ethanol and a hydrogen atmosphere (balloon). Under these conditions, **6u** was prepared in 99% overall isolated yield (Scheme 7).



Scheme 7.

Although the mechanistic details of this new approach to the construction of the indole skeleton are not clear, a possible rationale considers the basic steps described in Scheme 8. The initial reaction of the palladium complex with the starting propargylic derivative (via a S_N2' reaction), affords the σ-allenylic palladium complex **8** which would be in equilibrium with the π-propargylic palladium intermediate **9**.[18] The intramolecular nucleophilic attack of the nitrogen at the central carbon of the allenylic/propargylic palladium complex[3,19,20] generates the carbene **10**, which is subsequently protonated to give the π-allylic palladium complex **11**. In the presence of formic acid and triethylamine, this intermediate is converted into the formate derivative **12** from which the 2-alkylindole product **6** is formed by concerted decarboxylation and hydride transfer to one of the allylic termini.[21] With primary and secondary amines the π-allylic palladium complex **11** undergoes a regioselective intermolecular nucleophilic attack of the nitrogen nucleophile at the exocyclic allylic terminus to afford the 2-aminomethylindole **3**. If the π-allylic palladium complex **11** is unable to undergo a nucleophilic attack by the nitrogen nucleophile, an elimination reaction can take place and a 2-vinylic indole **5** is formed.

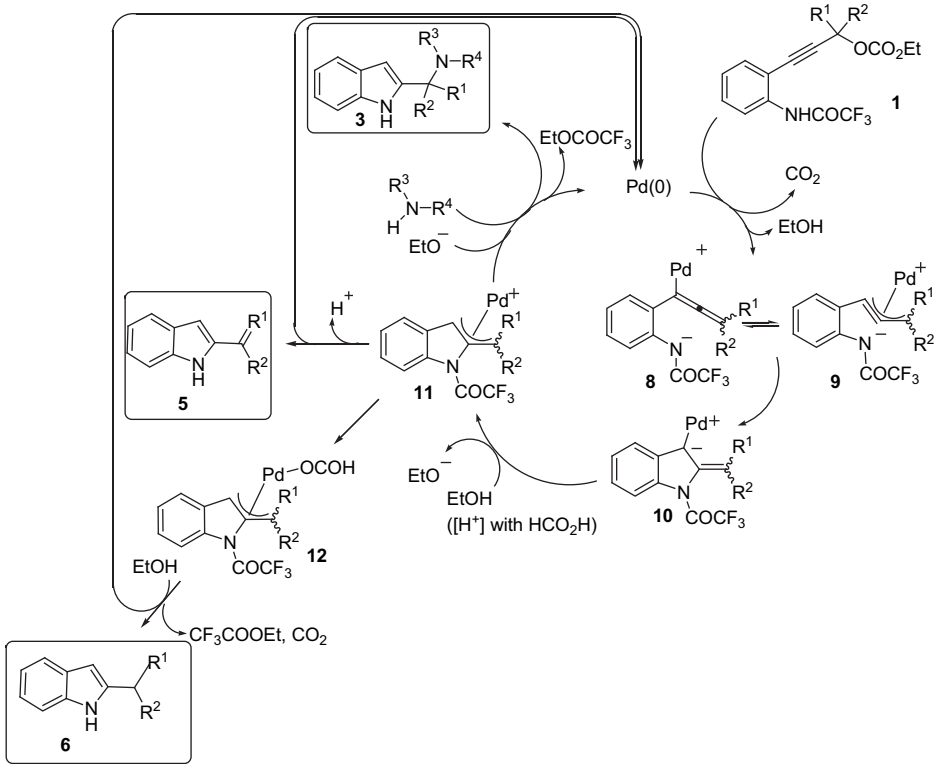
3. Conclusions

In summary, we have developed a convenient straightforward approach for the construction of the functionalized pyrrole ring incorporated into the indole system from 3-(*o*-trifluoroacetamidoaryl)-1-propargylic esters. In particular, these compounds have been shown to be useful common synthetic intermediates for the preparation of a variety of 3-unsubstituted 2-substituted indoles. Depending on reaction conditions and the substitution pattern, they can be converted into 2-aminomethylindoles, 2-vinylic indoles, and 2-alkylindoles usually in good to excellent yields.

4. Experimental

4.1. General

Melting points were determined with a Büchi apparatus and are uncorrected. All of the reagents and solvents are commercially available and were used as purchased, without further purification.



Scheme 8.

Compounds **1a** and **1b**, 2-vinylic indoles **5**, and 2-alkylindoles **6** were purified on axially compressed columns, packed with SiO_2 25–40 μm (Macherey Nagel), connected to a Gilson solvent delivery system and to a Gilson refractive index detector, and eluting with *n*-hexane/AcOEt mixtures. 2-Aminomethylindoles were purified by flash chromatography, using basic Al_2O_3 Brockmann activity II (Fluka) as stationary phase, eluting with *n*-hexane/AcOEt mixtures. ^1H NMR (400.13 MHz) and ^{13}C NMR (100.6 MHz) and ^{19}F NMR (376.5 MHz) spectra were recorded with a Brüker Avance 400 spectrometer. Infrared (IR) spectra were recorded on a JASCO FT/IR-430 spectrophotometer. Mass spectra were determined with a QP2010 Gas Chromatograph Mass spectrometer (EI ion source).

4.2. Preparation of (1a)

o-Iodoaniline (1.50 g, 6.85 mmol), $PdCl_2(PPh_3)_2$ (0.072 g, 0.103 mmol), and CuI (0.020 g, 0.103 mmol) were added to 2.5 mL of DMF and 5.0 mL of Et_2NH and the mixture was stirred under argon for 15 min. Then, tetrahydro-2-(2-propynyloxy)-2*H*-pyran (1.15 g, 1.15 mL, 8.22 mmol) was added dropwise in 5 min and the resulting reaction mixture was stirred at 60 °C for 12 h. After cooling, the reaction mixture was diluted with diethyl ether, washed twice with NH_4Cl solution, dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was dissolved in 10 mL of THF containing Et_3N (6.85 mmol, 0.95 mL) and cooled at 0 °C. Then, trifluoroacetic anhydride (13.7 mmol, 1.93 mL) was added dropwise in 10 min and the resultant solution was stirred at room temperature for 2 h. After this time, the solution was diluted with diethyl ether, washed twice with a saturated $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in 12 mL of an acetone/water 1:1 solution and *p*-toluensulfonic acid hydrate (1.30 g, 6.85 mmol) was added. The resulting solution was heated at 40 °C and stirred for 6 h. After cooling, the reaction mixture was diluted with diethyl ether, washed twice with $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated under reduced pressure. The final crude mixture was dissolved in 7 mL of CH_2Cl_2, Et_3N (10.3 mmol, 1.427 mL) was added and, subsequently, ethyl chloroformate (8.22 mmol, 0.78 mL) was added dropwise at 0 °C. The resulting solution was stirred at room temperature for 2 h. Then, the reaction mixture was diluted with diethyl ether, washed twice with a saturated NaCl solution, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography (SiO_2, 140 g; *n*-hexane/ethyl acetate 90/10 v/v) to give 1.73 g (80% overall yield) of **1a**: mp: 69–70 °C; ^1H NMR ($CDCl_3$) δ 8.73 (br s, 1H), 8.36 (d, J=8.3 Hz, 1H), 7.51–7.44 (m, 2H), 7.20 (t, J=7.6 Hz, 1H), 5.01 (s, 2H), 4.27 (q, J=7.1 Hz, 2H), 1.35 (t, J=7.1 Hz, 3H); ^{13}C NMR (CDCl3) δ 154.7 (q, J=37.6 Hz), 154.6, 136.8, 132.3, 130.5, 125.5, 119.9, 115.6 (q, J=288.8 Hz), 112.2, 91.3, 81.1, 64.8, 55.4, 14.3; ^{19}F NMR ($CDCl_3$) δ −75.8; IR (KBr): 3319, 2987, 1748, 1713, 1379 cm^{-1}; Anal. Calcd for $C_{14}H_{12}F_3NO_4$: C, 53.34; H, 3.84; N, 4.44. Found: C, 53.21; H, 3.85; N, 4.40.

4.3. Preparation of (1b)

o-Iodoaniline (1.50 g, 6.85 mmol), $PdCl_2(PPh_3)_2$ (0.072 g, 0.103 mmol), and CuI (0.020 g, 0.103 mmol) were added to 2.5 mL of DMF and 5.0 mL of Et_2NH and the mixture was stirred under argon for 15 min. Then, 1-phenylprop-2-yn-1-ol (1.08 g, 8.22 mmol) was added dropwise and the resulting reaction mixture was stirred at room temperature for 6 h. After this time, the reaction mixture was diluted with diethyl ether, washed twice with NH_4Cl solution, dried over Na_2SO_4 and concentrated under reduced pressure. Then, trifluoroacetic anhydride (13.7 mmol, 1.93 mL) was added dropwise in 10 min and the resultant solution was stirred at room temperature for 2 h. After this time, the solution was diluted with diethyl ether, washed twice with a saturated $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated under reduced pressure. The final crude mixture was dissolved in 7 mL of CH_2Cl_2, Et_3N (10.3 mmol, 1.427 mL) was added and, subsequenty, ethyl chloroformate (8.22 mmol, 0.78 mL) was added dropwise at 0 °C. The resulting solution was stirred at room temperature for 2 h. Then, the reaction mixture was diluted with diethyl ether, washed twice with a saturated NaCl solution, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography (SiO_2, 140 g; *n*-hexane/ethyl acetate 90/10 v/v) to give 1.44 g (78% yield) of **1b**: mp: 89–91 °C; ^1H NMR ($CDCl_3$) δ 8.69 (br s, 1H), 8.35 (d, J=8.3 Hz, 1H), 7.50–7.40 (m, 2H), 7.19 (t, J=7.6 Hz, 1H), 4.96 (s, 2H), 2.15 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.1, 154.6 (q, J=37.7 Hz), 136.7, 132.1, 130.4, 125.5, 119.9, 113.3 (q, J=288.8 Hz), 112.4, 91.9, 80.5, 52.3, 20.6; ^{19}F NMR ($CDCl_3$) δ −75.8; IR (KBr): 3319, 2987, 1748, 1713, 1379 cm^{-1}. Anal. Calcd for $C_{13}H_{10}F_3NO_3$: C, 54.74; H, 3.53; N, 4.91. Found: C, 54.59; H, 3.51; N, 4.88.

4.4. Typical procedure for the preparation of 2-(aminomethyl)indoles

A Carousel Tube Reactor (Radley Discovery), equipped with a magnetic stirrer, was charged with **1a** (0.050 g, 0.159 mmol), *N*-ethylpiperazine (0.055 g, 0.477 mmol), and $Pd(PPh_3)_4$ (0.009 g, 0.00795 mmol) in 1.0 mL of dry THF under argon. The mixture was warmed at 80 °C and stirred for 1.5 h. After cooling, the reaction mixture was dried under reduced pressure and the residue was purified by flash chromatography (Al_2O_3, 50 g; *n*-hexane/ethyl acetate 70/30 v/v) to give 0.035 g of **3a**: 90% yield; oil; ^1H NMR ($CDCl_3$) δ 8.64 (br s, 1H), 7.56 (d, J=8.3 Hz, 1H), 7.33 (d, J=8.3 Hz, 1H), 7.16–7.07 (m, 2H), 6.37 (s, 1H), 3.67 (s, 2H), 2.54–2.41 (m, 10H), 1.09 (t, J=8.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 136.2, 135.8, 128.4, 121.6, 120.2, 119.6, 110.7, 101.7, 55.9, 53.3, 52.8, 52.3, 12.0; IR (neat): 3404, 2935, 2816, 1454 cm^{-1}. Anal. Calcd for $C_{15}H_{21}N_3$: C, 74.03; H, 8.70; N, 17.27. Found: C, 74.01; H, 8.68; N, 17.25.

*4.4.1. 2-[(4-Ethylpiperazin-1-yl)(phenyl)methyl]-1H-indole (**3u**)*

92% yield; mp: 107.3–10.8.6 °C; ^1H NMR ($CDCl_3$) δ 8.53 (br s, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.48 (d, J=8.0 Hz, 2H), 7.36 (m, 3H), 7.28 (m, 1H), 7.17 (m, 1H), 7.09 (m, 1H), 6.41 (s, 1H), 4.66 (s, 1H), 2.48 (m, 10H), 1.13 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 139.1, 139.0, 136.0, 128.5, 128.5, 128.4, 127.6, 121.6, 120.4, 119.7, 110.8, 101.6, 69.2, 53.2, 52.3, 51.2, 12.0; IR (KBr): 3405, 3058, 2967, 2811, 1683, 1600, 1454 cm^{-1}. Anal. Calcd for $C_{21}H_{25}N_3$: C, 78.96; H, 7.89; N, 13.15. Found: C, 78.92; H, 7.83; N, 13.10.

*4.4.2. 2-[(4-Ethoxycarbonylpiperazin-1-yl)(phenyl)methyl]-1H-indole (**3v**)*

90% yield; mp: 159.0–160.3 °C; ^1H NMR ($CDCl_3$) δ 8.56 (br s, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.48 (d, J=8.0 Hz, 2H), 7.38 (m, 4H), 7.28 (m, 1H), 7.18 (m, 1H), 7.11 (m, 1H), 6.42 (s, 1H), 4.68 (s, 1H), 4.13 (s, 2H), 3.35 (m, 4H), 2.42 (m, 4H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 155.5, 138.7, 138.4, 136.2, 128.7, 128.5, 128.3, 127.8, 121.8, 120.4, 119.8, 110.9, 101.9, 69.2, 61.4, 51.0, 43.9, 51.2, 12.0; IR (KBr): 3413, 2919, 2362, 1683, 1600, 1455 cm^{-1}. Anal. Calcd for $C_{22}H_{25}N_3O_3$: C, 72.70; H, 6.93; N, 11.56. Found: C, 72.64; H, 6.87; N, 11.50.

*4.4.3. 2-[(Butylamino)(phenyl)methyl]-1H-indole (**3zb**)*

80% yield; oil; ^1H NMR ($CDCl_3$) δ 8.62 (br s, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.46 (d, J=8.0 Hz, 2H), 7.34 (m, 4H), 7.18 (m, 1H), 7.10 (m, 1H), 6.33 (s, 1H), 5.06 (s, 1H), 3.38 (m, 1H), 2.65 (m, 2H), 1.55 (m, 4H), 0.93 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 142.3, 135.7, 128.6, 128.5, 127.6, 127.3, 121.5, 120.3, 119.6, 110.8, 100.2, 61.5, 47.7, 32.3, 20.4, 13.6; IR (neat): 3399, 3058, 2958, 2929, 2362, 1712, 1681, 1455 cm^{-1}. Anal. Calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06. Found: C, 81.93; H, 7.94; N, 10.00.

4.5. Typical procedure for the cyclization of ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates (1) to 2-vinylic indoles (5)

A Carousel Tube Reaction (Radley Discovery), equipped with a magnetic stirrer, was charged with THF (2.0 mL), **1c** (0.100 g, 0.291 mmol), $Pd(OAc)_2$ (0.003 g, 0.014 mmol), PPh_3 (0015 g, 0.0584 mmol) Et_3N (0.088 g, 0.873 mmol), under argon. The mixture was stirred at 80 °C for 1 h. After cooling, the reaction mixture was concentrated under reduced pressure and the crude was purified by chromatography (SiO_2, 35 g; *n*-hexane/AcOEt 92/8 v/v) to give 0.044 g of **5a**: 95% yield; mp: 316.0–317.3 °C; ^{1}H NMR ($CDCl_3$) δ 8.05 (br s, 1H), 7.63 (d, J=8.0 Hz, 1H), 7.37 (d, J=8.0 Hz, 1H), 7.23 (m, 1H), 7.10 (m, 1H), 6.44 (d, J=16.0 Hz, 1H), 6.08 (m, 1H), 2.76 (m, 2H), 1.95 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.5, 129.0, 124.9, 122.2, 122.1, 120.4, 120.0, 110.5, 101.3, 18.5; IR (KBr): 3409, 2956, 2923, 1685, 1455 cm^{-1}; MS *m*/*z* (relative intensity) 157 (M^+, 4), 130 (29), 117 (13), 87 (6), 74 (36), 63 (100). Anal. Calcd for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found: C, 84.10; H, 7.00; N, 8.86.

4.5.1. 2-Vinyl-1H-indole (**5b**)

90% yield; mp: 80.1–81.3 °C, lit.[22] mp: 83–85 °C; ^{1}H NMR ($CDCl_3$) δ 8.19 (br s, 1H), 7.61 (d, J=8.0 Hz, 1H), 7.36 (d, J=8.0 Hz, 1H), 7.23 (m, 1H), 7.13 (m, 1H), 6.76 (m, 1H), 6.53 (s, 1H), 5.59 (d, J=16.0 Hz, 1H), 5.31 (d, J=16.0 Hz, 1H), 4.19 (m, 1H), 2.75 (m, 2H), 2.45 (m, 2H), 1.96 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 134.6, 131.2, 128.2, 122.3, 121.7, 120.9, 120.6, 119.8, 111.6, 101.0; IR (KBr): 3429, 2948, 2837, 1454 cm^{-1}; MS *m*/*z* (relative intensity) 143 (M^+, 100), 115 (57), 89 (44), 63 (49). Anal. Calcd for $C_{10}H_9N$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.86; H, 6.30; N, 9.72.

4.5.2. (E)-2-(But-1-enyl)-1H-indole (**5c**)

83% yield; mp: 342.2–343.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.08 (br s, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.33 (d, J=8.0 Hz, 1H), 7.18 (t, J=8.0 Hz, 1H), 7.07 (t, J=8.0 Hz, 1H), 6.46 (s, 1H), 6.13 (m, 1H), 2.32 (m, 2H), 1.15 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 136.5, 131.7, 122.2, 120.4, 119.9, 119.94, 110.5, 101.3, 26.1, 13.6; IR (KBr): 3421, 2962, 2927, 1454 cm^{-1}; MS *m*/*z* (relative intensity) 171 (M^+, 5), 130 (26), 117 (22), 89 (33), 77 (26), 63 (57), 51 (61), 41 (100). Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.11; H, 7.60; N, 8.14.

4.5.3. 5-Methyl-2-vinyl-1H-indole (**5d**)

63% yield; mp: 153.5–154.7 °C; ^{1}H NMR ($CDCl_3$) δ 8.12 (br s, 1H), 7.63 (d, J=8.0 Hz, 1H), 7.37 (d, J=8.0 Hz, 1H), 7.24 (m, 1H), 7.15 (m, 1H), 6.77 (m, 1H), 6.55 (s, 1H), 5.60 (d, J=16.0 Hz, 1H), 5.33(d, J=16.0 Hz, 1H), 4.20 (m, 1H), 2.75 (m, 2H), 2.46 (m, 2H), 2.55 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.4, 135.0, 129.3, 129.0, 127.8, 124.5, 120.5, 111.8, 110.4, 102.8, 21.5; IR (KBr): 3392, 3010, 2917, 1454 cm^{-1}; MS *m*/*z* (relative intensity) 157 (M^+, 6), 130 (8), 104 (12), 89 (17), 78(8), 63 (62). Anal. Calcd for $C_{10}H_9N$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.86; H, 6.30; N, 9.72.

4.5.4. 5,7-Difluoro-2-vinyl-1H-indole (**5e**)

82% yield; wax; ^{1}H NMR ($CDCl_3$) δ 8.28 (br s, 1H), 7.04 (dd, J_1=4.0 Hz, J_2=8.0 Hz, 1H), 6.74 (dd, J_1=4.0 Hz, J_2=8.0 Hz, 1H), 6.55 (m, 1H), 5.66 (d, J=16.0 Hz, 1H), 5.36 (d, J=16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 158.4 (d, J=9.0 Hz), 155.9 (d, J=10.0 Hz), 149.5 (d, J=14.0 Hz), 147.12 (d, J=14.1 Hz), 142.4, 131.2 (dd, J_1=6.4 Hz, J_2=6.3 Hz), 126.9, 121.4 (d, J=21.0 Hz), 114.03, 103.6 (d, J=5.0 Hz), 102.4 (d, J=29.0 Hz), 97.8 (dd J_1=20 Hz, J_2=10.0 Hz); IR (neat): 3473, 2921, 1654, 1454 cm^{-1}; MS *m*/*z* (relative intensity) 179 (M^+, 2), 166 (5), 149 (3), 135 (2), 120 (6), 99 (11), 86 (15), 75 (38), 63 (44), 51 (100). Anal. Calcd for $C_{10}H_7F_2N$: C, 67.06; H, 3.96; N, 7.84. Found: C, 67.11; H, 3.99; N, 7.80.

4.5.5. (E)-2-(Cyclohex-3-enylidenemethyl)-1H-indole and (Z)-2-(cyclohex-3-enylidenemethyl)-1H-indole (**5f**)

76% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.98 (br s, 1H), 7.62 (d, J=8.0 Hz, 1H), 7.34 (d, J=8.0 Hz, 1H), 7.17 (m, 2H), 6.50 (d, J=8.0 Hz, 1H), 6.27 (s, 1H), 5.79 (m, 2H), 3.26 (s, 1H), 2.98 (s, 1H), 2.80 (m, 1H), 2.53 (m, 1H), 2.29 (m, 2H).

4.5.6. (E)-5-Methyl-2-styryl-1H-indole (**5g**)

85% yield; mp: 210.9–212.2 °C; ^{1}H NMR (DMSO-d_6) δ 11.2 (br s, 1H), 7.56 (d, J=8.0 Hz, 2H), 7.39 (t, J_1=8.0 Hz, J_2=8.0 Hz, 2H), 7.24 (m, 5H), 6.93 (d, J_1=8.0 Hz, 1H), 6.49 (s, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.5, 137.2, 136.2, 129.3, 129.2, 128.1, 127.9, 127.3, 126.6, 124.2, 120.2, 120.1, 111.1, 103.0, 21.7; IR (KBr): 3407, 2921, 2360, 1442, 1417 cm^{-1}; MS *m*/*z* (relative intensity) 233 (M^+, 2), 204 (7), 152 (3), 128 (7), 115 (8), 102 (22), 89 (19), 77 (61), 63 (45), 51 (100). Anal. Calcd for $C_{17}H_{15}N$: C, 87.52; H, 6.48; N, 6.00. Found: C, 87.48; H, 6.42; N, 5.96.

4.5.7. 5,7-Dimethyl-2-vinyl-1H-indole (**5h**)

85% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.96 (br s, 1H), 7.25 (s, 1H), 6.88 (s, 1H), 6.48 (s, 1H), 5.61 (d, J=16.0 Hz, 1H), 5.30 (d, J=16.0 Hz, 1H), 2.53 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.1, 134.6, 129.6, 128.6, 127.9, 125.3, 119.5, 118.1, 111.6, 103.4, 21.4, 16.7; IR (neat): 3417, 2917, 1633, 1598, 1444 cm^{-1}; MS *m*/*z* (relative intensity) 171 (M^+, 7), 156 (4), 144 (26), 130 (11), 115 (7), 89 (24), 77(25), 63 (67), 52 (100). Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.10; H, 7.60; N, 8.12.

4.5.8. 2-Cyclopentenyl-1H-indole (**5i**)

77% yield; mp: 129.3–130.6 °C; ^{1}H NMR ($CDCl_3$) δ 8.49 (br s, 1H), 7.43 (d, J=7.9 Hz, 1H), 7.30 (m, 4H), 6.06 (s, 1H), 5.95 (s, 1H), 2.75 (m, 2H), 2.45 (m, 2H), 1.96 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 142.1, 136.2, 130.7, 128.0, 124.3, 122.4, 120.1, 118.6, 110.8, 100.9, 34.5, 34.2, 23.8; IR (KBr): 3421, 2948, 2835, 1727, 1454 cm^{-1}; MS *m*/*z* (relative intensity) 183 (M^+, 17), 154 (8), 130 (6), 117 (40), 89 (12), 66 (100). Anal. Calcd for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64. Found: C, 85.15; H, 7.09; N, 85.10.

4.5.9. 2-Cyclopentenyl-5-methyl-1H-indole (**5j**)

75% yield; oil; ^{1}H NMR ($CDCl_3$) δ 8.07 (br s, 1H), 7.39 (s, 1H), 7.24 (m, 1H), 7.04 (d, J=8 Hz, 1H), 6.39 (s, 1H), 6.01 (s, 1H), 2.79 (m, 2H), 2.61 (m, 2 h), 2.48 (s, 3H), 2.39 (s, 1H), 2.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 142.1, 136.2, 130.7, 128.0, 124.3, 122.4, 120.1, 118.6, 110.8, 100.9, 34.5, 34.2, 24.9, 23.8; IR (neat): 3421, 2948, 2835, 1727 cm^{-1}; MS *m*/*z* (relative intensity) 197 (M^+, 20), 154 (8), 130 (6), 117 (40), 89 (12), 66 (100). Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.65; N, 7.10. Found: C, 85.20; H, 7.60; N, 7.00.

4.5.10. 5-Chloro-2-cyclopentenyl-1H-indole (**5k**)

85% yield; mp: 164.6–166.2 °C; ^{1}H NMR ($CDCl_3$) δ 8.13 (br s, 1H), 7.54 (s, 1H), 7.22 (d, J=8.0 Hz, 1H), 7.11 (d, J=8.0 Hz, 1H), 6.38 (s, 1H), 6.05 (s, 1H), 2.76 (m, 2H), 2.60 (m, 2H), 2.20 (s, 3H), 2.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 136.8, 134.8, 134.6, 130.0, 125.7, 125.4, 122.4, 119.8, 111.4, 100.3, 33.4, 33.05, 23.3; IR (KBr): 3426, 2919, 1571, 1444, 1062 cm^{-1}; MS *m*/*z* (relative intensity) 218 (M^+, 5), 181 (4), 151 (17), 113 (4), 87 (12), 66 (100). Anal. Calcd for $C_{13}H_{12}ClN$: C, 71.72; H, 5.56; N, 6.43. Found: C, 71.68; H, 5.50; N, 6.36.

4.5.11. 2-(1-Phenylvinyl)-1H-indole (**5l**)

78% yield; oil; ^{1}H NMR ($CDCl_3$) δ 8.14 (br s, 1H), 7.64 (d, J=8.0 Hz, 1H), 7.55 (d, J=8.0 Hz, 2H), 7.46 (m, 3H), 7.26 (d, J=8.0 Hz, 1H), 7.24 (m, 1H), 7.16 (m, 1H), 6.58 (s, 1H), 5.65 (s, 1H), 5.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 148.8, 140.3, 135.6, 128.7, 128.2, 128.0, 126.4, 122.2, 120.3, 120.1, 119.0, 111.4, 100.6; IR (neat): 3378, 2923, 1598, 1492, 1454 cm^{-1}; MS *m*/*z* (relative intensity) 219 (M^+, 24), 204 (15), 140 (5), 89 (23), 77 (61), 51 (100). Anal. Calcd for $C_{16}H_{13}N$: C, 87.64; H, 5.98; N, 6.39. Found: C, 87.56; H, 5.90; N, 6.32.

*4.5.12. 5-Chloro-2-(prop-1-en-2-yl)-1H-indole (**5m**)*

85% yield; mp: 91.6–92.3 °C; ^{1}H NMR ($CDCl_3$) δ 8.23 (br s, 1H), 7.56 (s, 1H), 7.26 (m, 2H), 7.16 (d, J=8.0 Hz, 3H), 6.50 (s, 1H), 5.14 (s, 1H), 2.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 135.2, 133.3, 130.1, 126.7, 124.2, 122.0, 119.4, 119.2, 112.5, 101.3, 22.7; IR (KBr): 3438, 1704, 1654, 1450, 1380 cm^{-1}; MS *m*/*z* (relative intensity) 191 (M^+, 21), 176 (6), 151 (11), 128 (7), 113 (9), 87 (29), 52 (100). Anal. Calcd for $C_{11}H_{10}ClN$: C, 68.93; H, 5.26; N, 7.31. Found: C, 68.88; H, 5.20; N, 7.26.

*4.5.13. 5-Methyl-2-(prop-1-en-2-yl)-1H-indole (**5n**)*

84% yield; mp: 140.0–141.2 °C; ^{1}H NMR ($CDCl_3$) δ 8.08 (br s, 1H), 7.38 (s, 1H), 7.25 (m, 1H), 7.04 (m, 1H), 6.50 (s, 1H), 5.30 (s, 1H), 5.08 (s, 1H), 2.45 (s, 3H), 2.20 (s 3H); ^{13}C NMR ($CDCl_3$) δ 138.6, 135.4, 134.9, 129.2, 124.3, 120.4, 110.3, 109.2, 100.8, 21.5, 20.6; IR (KBr): 3424, 2919, 1627, 1457, 1396 cm^{-1}; MS *m*/*z* (relative intensity) 171 (M^+, 37), 156 (11), 144 (12), 130 (20), 104 (9), 87 (15), 52 (100). Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.11; H, 7.59; N, 8.14.

*4.5.14. 2-(Prop-1-en-2-yl)-1H-indole (**5o**)*

80% yield; mp: 116.0–118.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.17 (br s, 1H), 7.63 (d, J=8.0 Hz, 1H), 7.37 (d, J=8.0 Hz, 1H), 7.22 (m, 1H), 7.12 (m, 1H), 6.59 (s, 1H), 5.34 (s, 1H), 5.11 (s, 1H), 2.20 (s 3H); ^{13}C NMR ($CDCl_3$) δ 138.6, 135.4, 134.9, 129.2, 124.3, 120.4, 110.3, 109.2, 100.8, 21.5, 20.6; IR (KBr): 3428, 2923, 1617, 1523, 1457 cm^{-1}; MS *m*/*z* (relative intensity) 158 (M^+, 9), 141 (8), 130 (26), 113 (16), 76 (26), 52 (100). Anal. Calcd for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found: C, 84.00; H, 6.98; N, 8.87.

*4.5.15. 2-(Prop-1-en-2-yl)-5-acetyl-1H-indole (**5p**)*

90% yield; mp: 134.2–135.7 °C; ^{1}H NMR ($CDCl_3$) δ 8.78 (br s, 1H), 8.27 (s, 1H), 7.88 (d, J=8.0 Hz, 1H), 7.35 (d, J=8.0 Hz, 1H), 6.65 (s, 1H), 5.41 (s, 1H), 5.16 (s, 1H), 2.68 (s, 3H), 2.22 (s 3H); ^{13}C NMR ($CDCl_3$) δ 198.5, 140.3, 139.4, 134.8, 130.0, 128.4, 123.1, 122.9, 110.7, 110.6, 102.4, 26.6, 20.5; IR (KBr): 3322, 1656, 1602, 1428 cm^{-1}; MS *m*/*z* (relative intensity) 199 (M^+, 26), 184 (33), 156 (34), 144 (12), 129 (20), 100 (22), 52 (100). Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.30; H, 6.50; N, 7.00.

*4.5.16. 2-(Prop-1-en-2-yl)-5-cyano-1H-indole (**5q**)*

83% yield; mp: 122.3–123.8 °C; ^{1}H NMR ($CDCl_3$) δ 8.76 (br s, 1H), 7.92 (s, 1H), 7.42 (s, 1H), 6.60 (s, 1H), 5.43 (s, 1H), 5.21 (s, 1H), 2.21 (s 3H); ^{13}C NMR ($CDCl_3$) δ 140.9, 138.3, 134.5, 128.6, 126.1, 125.5, 120.9, 111.6, 111.5, 102.7, 101.4, 20.5; IR (KBr): 3370, 2211, 1610, 1321 cm^{-1}; MS *m*/*z* (relative intensity) 182 (M^+, 15), 154 (10), 142 (9), 127 (9), 114 (7), 100 (6), 52 (100). Anal. Calcd for $C_{12}H_{10}N_2$: C, 79.10; H, 5.53; N, 15.37. Found: C, 79.04; H, 5.47; N, 15.30.

*4.5.17. Methyl 2-(prop-1-en-2-yl)-1H-indole-5-carboxylate (**5r**)*

87% yield; mp: 143.4–144.7 °C; ^{1}H NMR ($CDCl_3$) δ 8.66 (br s, 1H), 8.37 (s, 1H), 7.92 (d, J=8.0 Hz, 1H), 7.33 (d, J=8.0 Hz, 1H), 6.63 (s, 1H), 5.38 (s, 1H), 5.14 (s, 1H), 3.95 (s, 3H), 2.21 (s 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 140.0, 139.3, 134.8, 128.4, 124.1, 123.7, 121.9, 110.5, 110.3, 102.2, 51.9, 20.5; IR (KBr): 3345, 2923, 1689, 1610, 1430 cm^{-1}; MS *m*/*z* (relative intensity) 215 (M^+, 29), 184 (19), 174 (19), 144 (19), 129 (11), 101 (12), 59 (100). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.46; H, 6.00; N, 6.48.

*4.5.18. 5-Fluoro-2-(1-phenylvinyl)-1H-indole (**5s**)*

68% yield; wax; ^{1}H NMR ($CDCl_3$) δ 8.11 (br s, 1H), 8.37 (s, 1H), 7.92 (d, J=8.0 Hz, 1H), 7.51 (m, 6H), 6.99 (m, 1H), 6.52 (s, 1H), 5.65 (s, 1H), 5.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 159.3, 156.9, 141.5, 139.8, 139.6, 133.0, 129.1, 128.9, 128.5, 128.4 113.5, 111.5, 111.4, 111.2, 110.9, 105.6, 105.4, 103.3, 103.3, 29.8; IR (neat): 3442, 3058, 2925, 1484, 1450 cm^{-1}; MS *m*/*z* (relative intensity) 237 (M^+, 24), 222 (16), 132 (5), 107 (14), 129, 50 (100). Anal. Calcd for $C_{16}H_{12}FN$: C, 80.99; H, 5.10; N, 6.90. Found: C, 80.90; H, 5.04; N, 6.84.

4.6. Typical procedure for the cyclization of ethyl 3-(*o*-trifluoroacetamidoaryl)-1-propargylic carbonates (1) to 2-alkylindoles (6)

A Carousel Tube Reaction (Radley Discovery), equipped with a magnetic stirrer, was charged with MeCN (2.0 mL), **1a** (0.100 g, 0.317 mmol), $Pd(PPh_3)_4$ (0.018 g, 0.016 mmol), Et_3N (0.096 g, 0.951 mmol), and HCOOH (0.029 g, 0.634 mmol) under argon. The mixture was stirred at 80 °C for 1 h. After cooling, the reaction mixture was concentrated under reduced pressure and the crude was purified by chromatography (SiO_2, 35 g; *n*-hexane/AcOEt 92/8 v/v) to give 0.038 g of **6a**: 91% yield; mp: 57–59 °C; lit. mp (Aldrich catalogue) 57–59 °C; ^{1}H NMR ($CDCl_3$) δ 7.76 (br s, 1H), 7.59 (d, J=7.5 Hz, 1H), 7.30 (d, J=7.6 Hz, 1H), 7.25–7.10 (m, 2H), 6.29 (s, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.1, 135.1, 129.1, 120.9, 119.6, 110.3, 100.4, 13.7 IR (KBr): 3404, 2935, 2816, 1454; MS *m*/*z* (relative intensity) 131 (M^+, 94%), 130 (100%), 77 (20%). Anal. Calcd for C_9H_9N: C, 82.41; H, 6.92; N, 10.68. Found: C, 82.50; H, 6.91; N, 10.70.

*4.6.1. 2-Benzyl-1H-indole (**6b**)*

75% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.78 (br s, 1H), 7.62 (d, J=8.0 Hz, 1H), 7.30 (m, 7H), 6.38 (s, 1H), 4.16 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.2, 135.6, 135.3, 129.0, 128.7, 128.0,125.8, 122.2, 120.9, 118.6, 111.2, 101.3, 41.0; IR (neat): 3255, 2964, 1654, 1602 cm^{-1}; MS *m*/*z* (relative intensity) 207 (M^+, 100), 178 (9), 130 (91), 77 (21), 63 (10), 44 (15). Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.98; H, 6.72; N, 6.70.

*4.6.2. 2-Propyl-1H-indole (**6c**)*

70% yield; mp: 72.1–73.6 °C; ^{1}H NMR ($CDCl_3$) δ 7.83 (br s, 1H), 7.60 (d, J=8.0 Hz, 1H), 7.33 (d, J=8.0 Hz, 1H), 7.16 (m, 2H), 6.30 (s, 1H), 2.76 (t, 2H), 1.76 (q, 2H) (t, 3H); ^{13}C NMR ($CDCl_3$) δ 136.2, 135.3, 129.3, 120.7, 119.5, 110.1, 100.2, 35.9, 24.8, 13.7; IR (KBr): 3367, 3118, 2941, 1699, 1655 cm^{-1}; MS *m*/*z* (relative intensity) 159 (M^+, 36), 130 (100), 77 (13), 50 (8). Anal. Calcd for $C_{11}H_{13}N$: C, 82.97; H, 8.23; N, 8.80. Found: C, 82.90; H, 8.23; N, 8.76.

*4.6.3. 2-Ethyl-1H-indole (**6d**)*

70% yield; wax; ^{1}H NMR ($CDCl_3$) δ 7.82 (br s, 1H), 7.59 (d, J=8.0 Hz, 1H), 7.30 (d, J=8.0 Hz, 1H), 7.15 (m, 2H), 6.43 (s, 1H), 2.81 (m, 2H), 1.38 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 141.4, 135.8, 128.8, 120.9, 119.8, 119.6, 110.3, 98.7, 21.4, 13.3; IR (neat): 3366, 3018, 2996, 1699, 1555 cm^{-1}; MS *m*/*z* (relative intensity) 145 (M^+, 54), 130 (100), 77 (13), 50 (3). Anal. Calcd for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.80; H, 7.70; N, 9.60.

*4.6.4. 2-Butyl-1H-indole (**6e**)*

67% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.89 (br s, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.29 (d, J=8.0 Hz, 1H), 7.14 (m, 2H), 6.28 (s, 1H), 2.78 (m, 2H), 1.60 (m, 2H), 1.47 (m, 2H), 1.03 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 139.9, 135.7, 128.7, 120.8, 119.6, 119.5, 110.1, 99.3, 31.2, 27.8, 22.3, 13.7; IR (neat): 3369, 3120, 2950, 1690, 1650 cm^{-1}; MS *m*/*z* (relative intensity) 174 (M^+, 5), 144 (5), 130 (100), 77 (11), 50 (4). Anal. Calcd for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. Found: C, 83.13; H, 8.67; N, 8.67.

*4.6.5. 2,5,7-Trimethyl-1H-indole (**6f**)*

90% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.91 (br s, 1H), 7.19 (s, 1H), 6.79 (s, 1H), 6.17 (s, 1H), 2.47 (s, 3H), 2.46 (s, 3H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 134.8, 133.9, 129.0, 128.9, 123.3, 119.0, 117.18, 100.5, 21.4, 16.7, 13.9; IR (neat): 3382, 2917, 1677, 1498 cm^{-1}; MS *m*/*z* (relative intensity) 131 (M^+, 94), 130 (100), 77 (20), 65 (13), 50 (8). Anal. Calcd for $C_{11}H_{13}N$: C, 82.97; H, 8.23; N, 8.80. Found: C, 82.90; H, 8.18; N, 8.73.

*4.6.6. 2,5-Dimethyl-1H-indole (**6g**)*

80% yield; mp: 110.2–11.9 °C; ^{1}H NMR ($CDCl_3$) δ 7.66 (br s, 1H), 7.37 (s, 1H), 7.20 (d, J=8.0 Hz, 1H), 7.01 (d, J=8.0 Hz, 1H), 6.19 (s, 1H),

2.50 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 135.2, 134.4, 129.4, 128.8, 122.4, 119.4, 109.9, 99.9, 21.5, 13.7; IR (KBr): 3399, 2917, 1685, 1405, 775.2 cm^{-1}; MS *m*/*z* (relative intensity) 145 (M^+, 100), 130 (16), 115 (7), 71 (9), 51 (6). Anal. Calcd for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.75; H, 7.69; N, 9.70.

4.6.7. 2,5-Dimethyl-7-nitro-1H-indole (**6h**)

78% yield; mp: 161.4–162.8 °C; ^{1}H NMR ($CDCl_3$) δ 9.56 (br s, 1H), 7.87 (s, 1H), 7.61 (s 1H), 6.28 (s, 1H), 2.52 (s, 3H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.0, 133.0, 131.7, 128.8, 128.2, 127.9, 118.6, 101.1, 21.0, 13.7; IR (KBr): 3421, 2923, 1680, 1457 cm^{-1}; MS *m*/*z* (relative intensity) 145 (M^+, 100), 130 (16), 115 (7), 71 (9), 51 (6). Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.10; H, 5.24; N, 14.64.

4.6.8. 7-Chloro-2,5-dimethyl-1H-indole (**6i**)

51% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.99 (br s, 1H), 7.28 (s, 1H), 6.98 (s, 1H), 6.20 (s, 1H), 2.47 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.0, 131.0, 130.7, 130.1, 121.7, 118.1, 115.2, 101.0, 21.3, 13.7; IR (neat): 3326, 2919, 1668, 1619, 1577, 1498 cm^{-1}; MS *m*/*z* (relative intensity) 179 (M^+, 100), 144 (57), 115 (21), 89 (10), 51 (1). Anal. Calcd for $C_{10}H_{10}ClN$: C, 66.86; H, 5.61; N, 7.80. Found: C, 66.80; H, 5.57; N, 7.76.

4.6.9. 2-Benzyl-5,7-dimethyl-1H-indole (**6j**)

50% yield; wax; ^{1}H NMR ($CDCl_3$) δ 7.64 (br s, 1H), 7.38 (d, *J*=8.0 Hz, 1H), 7.33 (m, 4H), 7.23 (s, 1H), 6.80 (s, 1H), 6.28 (s, 1H), 4.16 (s, 2H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.4, 135.8, 133.3, 129.0, 128.7, 128.0,127.8, 120.5, 120.4, 117.1, 101.5, 41.4, 25.3, 20.1; IR (neat): 3436, 2917, 1679, 1621, 1494, 1280 cm^{-1}; MS *m*/*z* (relative intensity) 235 (M^+, 100), 178 (9), 130 (91), 77 (21), 63 (10), 44 (15). Anal. Calcd for $C_{17}H_{17}N$: C, 86.77; H, 7.28; N, 6.76. Found: C, 86.70; H, 7.22; N, 6.70.

4.6.10. 5-Chloro-2-methyl-1H-indole (**6k**)

60% yield; wax; ^{1}H NMR ($CDCl_3$) δ 7.91 (br s, 1H), 7.50 (s, 1H), 7.19 (d, *J*=8.0 Hz, 1H), 7.07 (d, *J*=8.0 Hz, 2H), 6.19 (s, 1H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.7, 134.4, 125.2, 121.1, 119.0, 111.2, 100.2, 13.8; IR (neat): 3399, 2942, 1700, 1457 cm^{-1}; MS *m*/*z* (relative intensity) 131 (M^+, 94), 130 (100), 77 (20), 65 (13), 50 (8). Anal. Calcd for C_9H_8ClN: C, 65.24; H, 4.87; N, 8.46. Found: C, 65.28; H, 4.80; N, 8.40.

4.6.11. 5-Fluoro-2,7-dimethyl-1H-indole (**6l**)

65% yield; wax; ^{1}H NMR ($CDCl_3$) δ 7.78 (br s, 1H), 7.07 (d, *J*=8.0 Hz, 1H), 6.74 (d, *J*=8.0 Hz, 1H), 6.23 (s, 1H), 6.17 (s, 1H), 2.47 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 138.2 (*J*=233.1 Hz), 136.5, 132.0, 128.7 (*J*=10.7 Hz), 120.5 (*J*=9.6 Hz), 109.7 (*J*=25.7 Hz), 102.1 (*J*=23.4 Hz), 101.2 (*J*=4.6 Hz), 16.6, 13.8; IR (neat): 3372, 3072, 2933, 1685, 1492 cm^{-1}; MS *m*/*z* (relative intensity) 131 (M^+, 94), 130 (100), 77 (20), 65 (13), 50 (8). Anal. Calcd for $C_{10}H_{10}FN$: C, 73.60; H, 6.18; N, 8.58. Found: C, 73.64; H, 6.22; N, 8.53.

4.6.12. 5-Chloro-2-methyl-7-(trifluoromethyl)-1H-indole (**6m**)

86% yield; mp: 57.2–58.9 °C; ^{1}H NMR ($CDCl_3$) δ 8.29 (br s, 1H), 7.64 (s, 1H), 7.36 (s, 1H), 6.27 (s, 1H), 2.50 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.2, 133.6, 131.9, 130.0, 129.8, 127.8, 125.7, 124.7, 122.9, 118.5, 118.4, 113.9, 113.5, 113.2, 100.7, 13.7; IR (KBr): 3372, 3072, 2933, 1685, 1492 cm^{-1}; MS *m*/*z* (relative intensity) 131 (M^+, 94), 130 (100), 77 (20), 65 (13), 50 (8). Anal. Calcd for $C_{10}H_7ClF_3N$: C, 51.41; H, 3.02; N, 6.00. Found: C, 51.36; H, 3.07; N, 6.04.

4.6.13. 2-(3-Methoxybenzyl)-1H-indole (**6n**)

75% yield; wax; ^{1}H NMR ($CDCl_3$) δ 7.86 (br s, 1H), 7.60 (d, *J*=8.0 Hz, 1H), 7.28 (m, 2H), 7.13 (m, 2H), 6.85 (m, 4H), 6.37 (s, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 140.2, 137.7, 136.4, 130.1, 129.8, 129.7, 128.7, 121.4, 121.3, 120.0, 119.7, 114.7, 112.3, 112.1, 110.7, 110.6, 101.1, 55.2, 34.8; IR (neat): 3390, 2913, 2360, 1698, 1596, 1600, 1490, 1455 cm^{-1}; MS *m*/*z* (relative intensity) 237 (M^+, 46), 204 (6), 192 (7), 167 (6), 130 (100), 102 (12), 77 (26), 63 (15). Anal. Calcd for $C_{16}H_{15}NO$: C, 80.93; H, 6.37; N, 5.92. Found: C, 80.90; H, 6.33; N, 5.90.

4.6.14. 2-(4-Methoxybenzyl)-1H-indole (**6o**)

70% yield; mp: 71.6–72.8 °C; ^{1}H NMR ($CDCl_3$) δ 7.86 (br s, 1H), 7.61 (d, *J*=8.0 Hz, 1H), 7.31 (m, 2H), 7.28 (m, 2H), 7.17 (m, 3H), 6.88 (m, 3H), 6.38 (s, 1H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.2, 140.1, 137.7, 136.4, 130.1, 128.7, 124.4, 121.3, 120.3, 120.0, 119.7, 114.6, 112.3, 110.5, 101.0, 55.2, 34.8; IR (KBr): 3401, 2921, 2834, 1704, 1604, 1581 cm^{-1}; MS *m*/*z* (relative intensity) 237 (M^+, 2), 222 (4), 130 (63), 117 (10), 103 (20), 92 (38), 77 (100), 63 (92), 51 (60). Anal. Calcd for $C_{16}H_{15}NO$: C, 80.93; H, 6.37; N, 5.92. Found: C, 80.91; H, 6.33; N, 5.93.

4.6.15. 2-(4-Fluorobenzyl)-1H-indole (**6p**)

85% yield; mp: 80.3–81.9 °C; ^{1}H NMR ($CDCl_3$) δ 7.78 (br s, 1H), 7.60 (d, *J*=8.0 Hz, 1H), 7.18 (m, 5H), 7.07 (m, 2H), 6.35 (m, 1H), 4.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 163.0, 137.7, 136.4, 134.3, 134.2, 130.4, 130.3, 128.7, 121.5, 120.1, 119.9, 115.7, 115.5, 110.8, 110.6, 101.3, 33.9; IR (KBr): 3396, 3045, 2890, 1600, 1544, 1508 cm^{-1}; MS *m*/*z* (relative intensity) 225 (M^+, 87), 196 (5), 177 (2), 130 (65), 77 (14), 44 (84). Anal. Calcd for $C_{15}H_{12}FN$: C, 79.98; H, 5.37; N, 6.22. Found: C, 79.93; H, 5.33; N, 6.18.

4.6.16. 2-(3-Methoxybenzyl)-5,7-dimethyl-1H-indole (**6q**)

72% yield; oil; ^{1}H NMR ($CDCl_3$) δ 7.78 (br s, 1H), 7.27 (m, 2H), 6.84 (m, 4H), 6.30 (s, 1H), 3.81 (s, 3H), 2.44 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 159.9, 140.4, 137.3, 134.2, 129.7, 129.1, 128.5, 123.7, 121.2, 119.3, 117.5, 114.5, 112.0, 101.4, 55.2, 34.8, 21.4, 16.7; IR (neat): 3849, 2917, 2358, 1598, 1454, 1384 cm^{-1}; MS *m*/*z* (relative intensity) 265 (M^+, 44), 158 (100), 143 (16), 115 (25), 92 (21), 77 (56), 51 (27). Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.51; H, 7.28; N, 5.20.

4.6.17. 5-Chloro-2-(3-methoxybenzyl)-7-(trifluoromethyl)-1H-indole (**6r**)

85% yield; wax; ^{1}H NMR ($CDCl_3$) δ 8.26 (br s, 1H), 7.67 (s, 1H), 7.37 (s, 1H), 7.29 (m, 2H), 6.86 (m, 3H), 6.34 (m, 1H), 3.8 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.5, 137.4, 135.6, 130.6, 129.9, 127.4, 124.9, 121.3, 116.8, 114.9, 113.3, 111.3, 101.5, 55.9, 41.3; IR (neat): 3399, 2942, 1700, 1457 cm^{-1}; MS *m*/*z* (relative intensity) 304 (M^+, 94), 275 (10), 207 (34), 77 (20), 50 (8). Anal. Calcd for $C_{17}H_{13}F_3NO$: C, 67.10; H, 4.31; N, 4.60. Found: C, 67.04; H, 4.24; N, 4.56.

4.6.18. 2-Methyl-5-acetyl-1H-indole (**6s**)

73% yield; mp: 129.7–130.2 °C; ^{1}H NMR ($CDCl_3$) δ 8.65 (br s, 1H), 8.21 (s, 1H), 7.96 (s, 1H), 7.35 (s, 1H), 6.34 (s, 1H), 2.68 (s, 3H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 198.8, 139.0, 137.0, 135.6, 129.7, 128.7, 121.8, 121.5, 110.3, 101.8, 26.7, 13.8; IR (KBr): 3380, 2997, 1700, 1587 cm^{-1}; MS *m*/*z* (relative intensity) 173 (M^+, 6), 158 (16), 130 (24), 103 (16), 77 (16), 43 (100). Anal. Calcd for $C_{11}H_{11}NO$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.24; H, 6.36; N, 8.03.

4.6.19. Methyl 2-methyl-1H-indole-5-carboxylate (**6t**)

70% yield; mp: 157.1–158.0 °C; ^{1}H NMR ($CDCl_3$) δ 8.45 (br s, 1H), 8.30 (s, 2H), 7.89 (d, *J*=8.0 Hz, 1H), 7.28 (d, *J*=8.0 Hz, 1H), 7.29 (m, 2H), 6.86 (m, 3H), 3.95 (s, 3H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.5, 138.8, 136.7, 128.7, 122.5, 121.6, 109.9, 101.6, 51.8, 13.7; IR (KBr): 3328, 2950, 1698, 1436 cm^{-1}; MS *m*/*z* (relative intensity) 189 (M^+, 19), 158 (65), 130 (94), 103 (94), 77 (99), 51 (100). Anal. Calcd for $C_{11}H_{11}NO$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.79; H, 5.80; N, 7.36.

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