Palladium-Catalyzed Cyclization of *o*-Alkynyltrifluoroacetanilides with Allyl Esters. A Regioselective Synthesis of 3-Allylindoles

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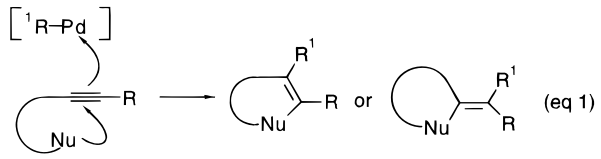
Received July 8, 1997

The reaction of readily available *o*-alkynyltrifluoroacetanilides **1** with allyl esters provides a valuable new route to 3-allylindoles **3**. Three basic procedures have been developed: a stepwise method based on the isolation of the *N*-allyl derivative **4** and its subsequent cyclization to **3** (procedure a), a one-pot reaction omitting the isolation of **4** (procedure b), and a procedure which most probably leads to the formation of **3** through a mechanism not involving the intermediacy of **4** (procedure c). In the presence of the electron-rich sterically encumbered ligand tris(2,4,6-trimethoxyphenyl)-phosphine (ttmpp) the reaction exhibits remarkable regioselectivity and almost exclusive formation of 3-allylindoles with the indolyl moiety bound to the less substituted allyl terminus is usually observed. However, some loss of olefin geometry is observed.

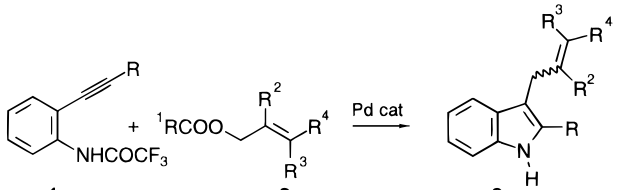
Introduction

The cyclization of terminal and internal alkynes containing proximate nucleophiles, promoted by organopalladium complexes, is expanding into one of the most effective strategies for ring construction. It provides in fact a straightforward approach to the synthesis of functionalized carbo- and heterocycles through the regio- and stereoselective addition of a nucleophile and of an unsaturated carbon unit across the carbon−carbon triple bond (eq 1).



R^1 = η³-allyl, σ-aryl, σ-vinyl, σ-alkynyl, σ-allenyl, σ-acyl
R = H, alkyl vinyl, aryl
Nu = C, O, N

Most of this chemistry, however, deals with the utilization of σ-organopalladium complexes.[1−4] Reports of cyclization reactions promoted by η^3-allylpalladium complexes are limited to the pioneering synthesis of γ-(*E*)-alkylidene-γ-butyrolactones from pentynoic acid and allyl acetates (or from pentynoic acid allyl esters) described by Tsuda, Saegusa et al.[5] and to the synthesis of α-substituted-γ-methylene-γ-butyrolactones from pentynoic acid derivatives described by Mandai, Tsuji et al.[6] Our continuing interest in the application of this chemistry to the synthesis of heterocycles[1a−c,g−i,2b] and the attractiveness of widening the scope of the methodology to include the vastly important class of nitrogen heterocycles led us to investigate the utilization of η^3-allylpalladium complexes as promoters of cyclization reactions of alkynes containing nitrogen nucleophiles. In particular, because of the intense interest in indole-based biologically active molecules[1e,7] and, consequently, in the selective syntheses of the indole nucleus,[1a,i,2b,8] our efforts were devoted to the development of a new approach to the preparation of indole derivatives. *o*-Alkynyltrifluoroacetanilides **1**, previously employed by us in new syntheses of variously substituted indoles,[1i,2b] were selected as the acetylenic building blocks that might participate in a new cyclization process leading to 3-allylindoles **3** (eq 2).



R^1 = Me, EtO, MeO

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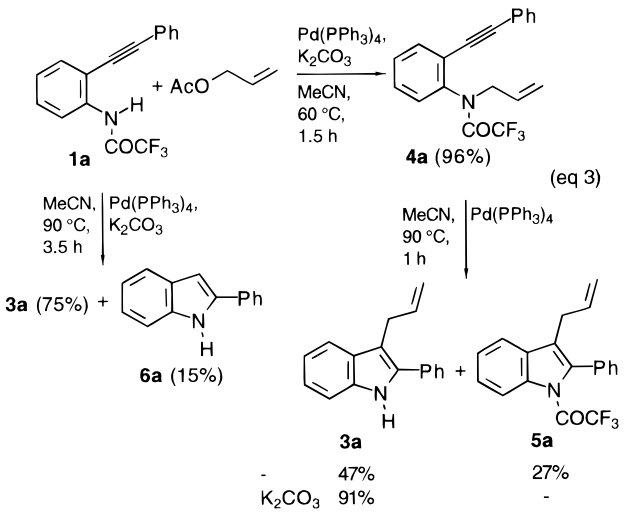
S0022-3263(97)01237-1 CCC: $15.00
Published on Web 02/05/1998

The preparation of 3-allylindoles has previously been described by Utimoto.[9] His approach is based on the cyclization of N-(methoxycarbonyl)-*o*-alkynylanilines and allyl chlorides in the presence of a palladium(II) catalyst not containing σ-carbon−palladium bonds, $PdCl_2(MeCN)_2$. The reaction was presumed to proceed via trapping of the σ-indolylpalladium intermediate, generated in situ, with the allyl chloride, which has to be used in large excess (10 equiv). The new carbon−carbon bond is generated regioselectively at the γ-position in an S_N2' fashion. We surmised that our procedure might employ a limited excess of the allylating agent and, more significantly, might provide a chance to synthesize 3-allylindoles not available by means of the $PdCl_2$-catalyzed cyclization/allylation sequence.

Hereafter we report our observations on the scope of the reaction, the influence of the ligands on the regiochemical outcome, and a few mechanistic insights.

Results

The Reaction of *o*-(Phenylethynyl)trifluoroacetanilide 1a with Allyl Acetate. Our initial attempt explored the reaction of *o*-(phenylethynyl)trifluoroacetanilide **1a** with allyl acetate (1.2 equiv) under conditions similar to those employed by us for the cyclization of **1** promoted by σ-vinyl- and σ-arylpalladium species [Pd(PPh_3)$_4$ (0.05 equiv), K_2CO_3 (5.0 equiv), MeCN, 60 °C].[1i] However, the nucleophilic attack of the nitrogen on the η^3-allylpalladium intermediate derived from allyl acetate and palladium proved to be faster than the desired organopalladium-promoted cyclization. Only the corresponding *N*-allyl derivative **4a** was isolated in 96% yield after 1.5 h (eq 3). Nonetheless, because of the contemporary presence of the aryl and trifluoroacetyl groups on the nitrogen atom of **4a**, we thought that under suitable reaction conditions it might undergo a palladium-promoted ionization of the N−C_{allyl} bond and generate an η^3-allylpalladium complex which, by taking advantage of the proximity of the π-electrons of the carbon−carbon triple bond, could in turn promote the desired heterocyclization to the indole nucleus. We were pleased to find that heating **4a** in MeCN at 90 °C for 1 h in the presence of Pd(PPh_3)$_4$ (0.05 equiv) afforded 2-phenyl-3-allylindole **3a** and its *N*-trifluoroacetyl derivative **5a** in 47 and 27% yield, respectively (eq 3). Complete conversion into **3a** (91% isolated yield) was achieved by allowing **4a** to react under the same conditions in the presence of K_2CO_3 (5.0 equiv).



The reaction of **1a** with allyl acetate at higher temperature (90 °C; 3.5 h), but otherwise keeping all other parameters the same, also produced **3a** in good yield, although lower than the overall yield of the two-step protocol (75 vs 87%) (eq 3). The lower yield appears to be mainly associated with the formation of 2-phenylindole, **6a**, very likely arising from a palladium-catalyzed reaction. It was in fact generated only in trace amounts when the reaction was carried out with the omission of the Pd(PPh_3)$_4$.

The best result was obtained by treating **1a** with allyl acetate (1.2 equiv) at 60 °C in MeCN in the presence of Pd(PPh_3)$_4$ (0.05 equiv) and K_2CO_3 (5 equiv) for 1.5 h (after which time it is completely converted into **4a**) and then raising the reaction temperature to 90 °C (2 h): **3a** was isolated in 81% yield. However, the application of these conditions to substituted allyl acetates such as 2-hexen-

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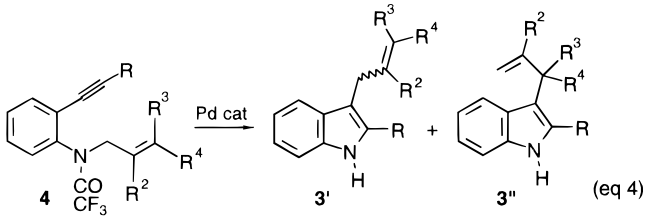
1-yl and 1-octen-1-yl acetates met with failure. For example, neither 3-(2-hexen-1-yl)indole nor the corresponding *N*-(2-hexen-1-yl) derivative was discernible when **1a** was treated with 2-hexen-1-yl acetate (1.2 equiv) for 24 h [MeCN, 60 °C, $Pd(PPh_3)_4$ (0.05 equiv), K_2CO_3 (5 equiv); **1a** was recovered in 76% yield].

N−Allylation of *o*-Alkynyltrifluoroacetanilides 1 with Allyl Carbonates 2. Because allyl carbonates have been reported to be very reactive substrates, more prone to undergo a number of reactions difficult to achieve with allyl acetates under mild conditions,[10] we decided to investigate their utilization in the present reaction. Taking into account our results with allyl acetates, we started this part of the study by exploring each of the two steps of the process separately. We initially tried the N-allylation of **1a** with ethyl 2-hexen-1-yl carbonate, **2b**, and $Pd(PPh_3)_4$ (0.05 equiv) in MeCN (60 °C, 24 h) but omitting K_2CO_3.[10] Under these conditions, **1a** was allylated to afford **4b** as one regioisomer in 33% yield. A remarkable increase in yield to 80% (of approximately an 86:14 *E:Z* mixture) was achieved in THF (60 °C, 5 h). Even faster reaction and higher yield were observed in the presence of $Pd_2(dba)_3$ and dppb [1,4-bis(diphenylphosphino)butane] in THF (60 °C, 1.5 h): **4b** was isolated in 87% yield (∼88:12::*E:Z*). The use of dppp [1,3-bis(diphenylphosphino)propane] was found equally effective (87% yield, ∼ 86:14::*E:Z*, 1.5 h) whereas adding dppe [1,2-bis(diphenylphosphino)ethane] to the reaction mixture resulted in the isolation of **4b** in a sparing 27% yield (48 h) along with 2-phenylindole (45% yield).

Cyclization of *o*-Alkynyl-*N*-allyltrifluoroacetanilides 4. We next investigated the cyclization step (eq 4). *o*-(Phenylethynyl)-N-(2-hexen-1-yl)trifluoroacetanilide **4b** (R = Ph, $R^2 = R^3 = H$, $R^4 = Pr^n$) was selected as the model system, and the effect of temperature and a variety of ligands and solvents on the product distribution was examined.



(eq 4)

The use of the same ligand that gives the highest yields in the N-allylation, dppb, led to acceptable results only in DME or DMSO at 100 °C (Table 1, entries 1−4). Similar overall yields and higher **3′b**:**3″b** ratios were obtained with dppp and dppe (Table 1, entries 5 and 6). The popular $Pd(PPh_3)_4$ led to the cyclization derivative in good yield (Table 1, entries 21 and 22), but the best result with regard to both yield and regioselectivity was observed upon going to $Pd_2(dba)_3$ and an electron-rich sterically encumbered ligand, tris(2,4,6-trimethoxyphenyl)phosphine (ttmpp),[11] in a 1:6 Pd:ligand ratio (Table 1, entry 11). Decreasing the amount of ligand relative to palladium resulted in incomplete conversion (Table 1, entries 9 and 10). Notably, regioisomeric distribution remains unchanged moving from a 1:2 to a 1:6 Pd:ligand ratio. The less electron-rich, but equally crowded tris(2,6-dimethoxyphenyl)phosphine (tdmpp),[11] showed the same regioselectivity,[12] but it was less rewarding in terms of yield (Table 1, entries 12 and 13). The ligand effect on the stereoselectivity appears to be minor because, with the exception of a slightly greater loss of olefin geometry with dppe (Table 1, entry 6), *E:Z* ratios change little upon switching from electron-withdrawing to electron-donating or from monodentate to bidentate ligands. Solvent effects (as well as temperature effects), while affecting the reaction rate and yields, do not seem to play a significant role in the regio- and stereoselectivity.

Stepwise Preparation of 3-Allylindoles 3 (Procedure a). Having established satisfactory conditions for the N-allylation of **1** [$Pd_2(dba)_3$, dppb, THF, 60 °C] and the subsequent cyclization of the corresponding *o*-alkynyl-*N*-allyltrifluoroacetanilide **4** [$Pd_2(dba)_3$, ttmpp, DME, 100 °C or $Pd(PPh_3)_4$, K_2CO_3, MeCN, 90 °C], the stepwise protocol was applied to the synthesis of some 3-allylindoles. Our preparative results are summarized in Table 2. No attempts have been made to optimize the N-allylation and cyclization conditions for any example. Thus, further improvement for a particular case of importance appears likely. Nevertheless, $Pd(PPh_3)_4$ has been successfully employed in the cyclization of allylic derivatives generating symmetric η^3-allylpalladium complexes and even when the two allylic termini are markedly different from a steric point of view (Table 2, entries 1−7, 10−12, 15, 17−21). The $Pd_2(dba)_3$/ttmpp combination has been found to be the catalyst of choice when steric differences between the two allylic termini are small, as it is the case of 2-hexen-1-yl and 1-octen-1-yl carbonates (Table 2, entries 8, 9, 13).

One-Pot Preparation of 3-Allylindoles 3 (Procedure b). To keep the procedure as simple as possible, we turned our attention to the development of a protocol not involving the isolation of **4**. We explored the effect on the reaction outcome of temperature and of a variety of ligands and solvents and arrived at the following one-pot protocol: $Pd(PPh_3)_4$ in THF at 60 °C till the disappearance of **1**, addition of K_2CO_3, and then raising the reaction temperature to 80 °C. The results obtained are summarized in Table 3.

The Reaction of *o*-Alkynyltrifluoroacetanilides 1 with Allyl Carbonates 2 in the Presence of $Pd_2(dba)_3$ and Tris(2,4,6-trimethoxyphenyl)phosphine (ttmpp) (Procedure c). When the development of a one-pot protocol to **3** was attempted, the utilization of ttmpp in the reaction of *o*-alkynyltrifluroacetanilides with allyl carbonates was evaluated first. The aim was to find conditions allowing the employment of this ligand and $Pd_2(dba)_3$ in both steps, so as to evolve a simplified protocol with the beneficial effect of ttmpp on the regiochemistry of the new carbon−carbon bond. To this end, the reaction of **1a** with ethyl 2-hexen-1-yl carbonate **2b**, our model system, was reexamined in the presence of $Pd_2(dba)_3$ and ttmpp in THF at 60 °C (procedure c). Surprisingly, under these conditions **1a** was found to undergo a rapid (3 h) conversion into the corresponding indole derivative, isolated in 76% yield (**3′b**:**3″b** = 97:3). The use of a 1:6 Pd:ligand ratio proved to be crucial for the

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(12) Tris(2,6-dimethoxyphenyl)phosphine has been described to play an important role in the regioselective addition of terminal alkynes to either terminal or activated internal alkynes: Trost, B. M.; Sorum, M. T.; Chan, C.; Harms, A. E.; Rûhter, G. *J. Am. Chem. Soc.* **1997**, *119*, 698. Trost, B. M.; McIntosh, M. C. *J. Am. Chem. Soc.* **1995**, *117*, 7255.

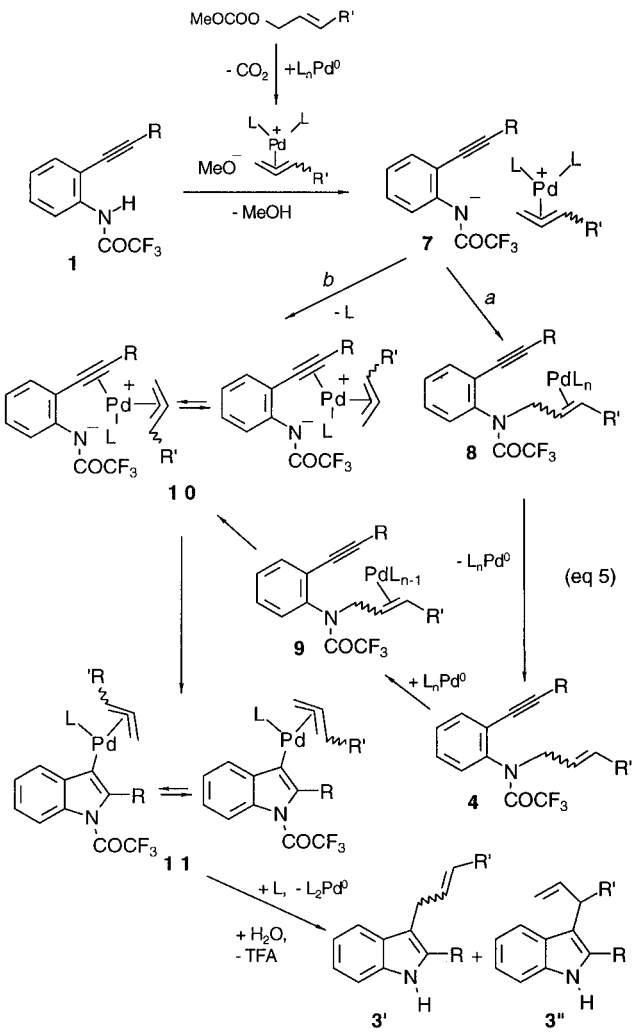
success of the reaction (decreasing the Pd:ligand ratio to 1:2 resulted in the isolation of the indole derivative in 15% yield; **1a** was recovered in 73% yield and 2-phenylindole was isolated in 11% yield). No *N*-allyl intermediate, **4b**, however, was discernible in the reaction mixture. Furthermore, **4b** was recovered in 78% yield when allowed to react under the same conditions [$Pd_2(dba)_3$, ttmpp, THF, 60 °C] for 10 h, and the indole derivative was isolated in 16% yield only. On the other hand, the cyclization of **4b** in the presence of $Pd_2(dba)_3$ and ttmpp took about 15 h in DME at 100 °C to reach completion (Table 1, entry 11). The results obtained by using procedure c are summarized in Table 4.

Discussion

Mechanistically, the present synthesis of 3-allylindoles is likely to proceed as outlined in eq 5. Path a, typical of stepwise and one-pot protocols, consists of the following four basic phases: (1) the nucleophilic attack of the nitrogen atom on the allylic portion of the η^3-allylpalladium complex **7** to give **4** (only *N*-allyl derivatives bearing the nitrogen fragment on the less substituted allyl terminus have been isolated); (2) the formation of **10**, resulting from the ionization of the η^2-olefinpalladium complex **9** (η^2-olefinpalladium complexes are usually believed to be the first intermediates in the palladium-catalyzed allylations)[13] and the displacement of one ligand to the palladium by the carbon−carbon triple bond (that may be favored by the proximity of the acetylenic moiety to the metal and that may also take place before ionization); (3) the intramolecular nucleophilic attack of the nitrogen atom across the activated carbon−carbon triple bond to afford **11**; (4) the reductive excision of Pd(0) through the transfer of the indolyl fragment to the allyl group in a cis fashion,[14] which produces the indole derivative and regenerates the active catalytic species.

According to this scheme, the nitrogen atom intervenes in the process as nucleophile in the N-allylation step and as leaving group[15,16] in the cyclization step. Such an ambivalent behavior of amino groups has previously been described.[17] However, while in the present reaction the reversible formation of the nitrogen−carbon bond does not involve any change in the nature of the amino group, known applications of this chemistry use free amino groups in the preparation of *N*-allylamines, and allylammonium salts, generated in situ through protonation of the allylamines, in the formation of η^3-allylpalladium complexes.

Stepwise and one-pot protocols gave good results with a variety of *o*-alkynyltrifluoroacetanilides and allylic derivatives. The presence of a substituent on the central carbon atom of the allylic system seems to be tolerated



(Table 2, entries 5 and 6; Table 3, entry 3) whereas substitution at both termini (Table 2, entry 3) or sterically encumbered substituents at one end of the alkyne moiety (Table 2, entry 11) hamper the cyclization reaction. The examples reported in entries 18-21 (Table 2) and 4, 5 (Table 3) illustrate the compatibility of both electron-donating and electron-withdrawing substituents.

Path b differs from path a in the way **10** is generated from **7**. It entails the coordination of the carbon−carbon triple bond to the palladium of the η^3-allylpalladium fragment of **7** being faster than the nucleophilic attack of the nitrogen on the allylic portion of the complex, and **10** is generated without the intermediacy of **4**. The existence of path b is supported by the absence of the *N*-allyl derivative **4b** as intermediate when **1a** and ethyl 2-hexen-1-yl carbonate **2b** were subjected to $Pd_2(dba)_3$ and ttmpp: none of **4b** was detected under these conditions. The observation that the reaction of **1a** with **2b** in the presence of $Pd_2(dba)_3$ and ttmpp to afford the indole nucleus is much faster than the cyclization of **4b** in the presence of the same catalytic system also argues in favor of a reaction mechanism not involving the N-allylation step. In fact, it rules out the possibility that **4b** reacts as it is formed, thus making detection impossible. In practice, the use of ttmpp completely changes the course of the reaction providing an alternative, straightforward route to 3-allylindoles.

This route, however, does not invalidate procedures a and b. Its scope, in fact, has been briefly investigated,

(13) Trost, B. M.; Van Vranken, D. L. *Chem. Rev. (Washington, D.C.)* **1996**, *96*, 395. Williams, J. M. J. *Synlett* **1996**, 705.

(14) Kurosawa, H.; Shiba, K.; Hirako, K.; Kakiuchi, K.; Ikeda, I. *J. Chem. Soc., Chem. Commun.* **1994**, 1099; Trost, B. M.; Weber, L.; Strege, P. E.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3416.

(15) For the utilization of trialkylallylammonium salts as precursors of η^3-allylpalladium complexes, see: Doi, T.; Yanagisawa, A.; Miyazawa, M.; Yamamoto, K. *Tetrahedron Asymmetry* **1995**, *6*, 389; Hunter, R.; Simon, C. D. *Tetrahedron Lett.* **1988**, *29*, 2257.

(16) For the utilization of 3-vinylaziridines as precursors of η^3-allylpalladium complexes, see: Spears, G. W.; Nakanishi, K.; Ohfune, Y. *Synlett* **1991**, 91.

(17) Lemaire-Audoire, S.; Savignac, M.; Dupuis, C.; Genet, G. P. *Bull. Soc. Chim. Fr.* **1995**, *132*, 1157. Garro-Helion, F.; Merzouk, A.; Guibé, F. *J. Org. Chem.* **1993**, *58*, 6109.

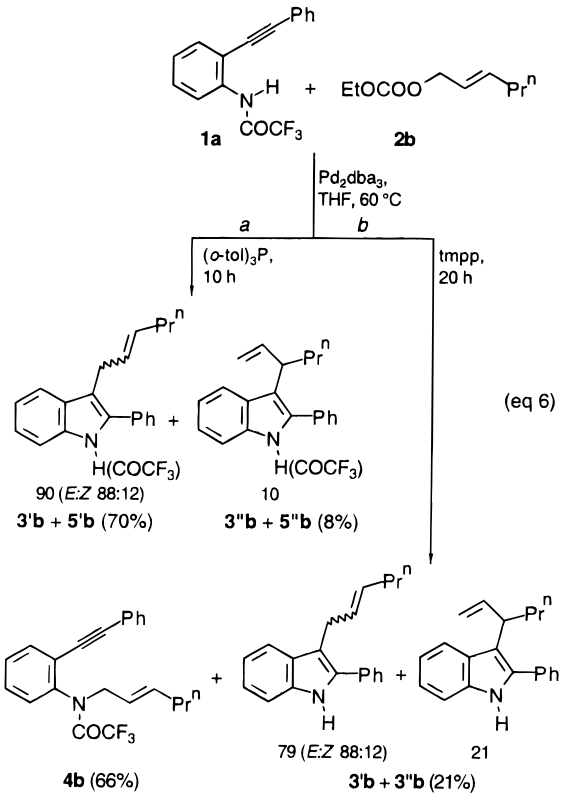
Table 1. Ligands, Solvent, Time and Temperature Studies in the Palladium-Catalyzed Cyclization of *o*-(Phenylethynyl)-*N*-(hex-2-en-1-yl)trifluoroacetanilide 4b[a]

					3-allylindole		
entry	catalyst	solvent	reaction temp (°C)	reaction time (h)[b]	overall yield %[c,d]	**3′b/3″b**[c]	*E*:*Z* ratio for **3′b**
1	$Pd_2(dba)_3$/dppb	THF	80	24	– (84)	–	–
2	$Pd_2(dba)_3$/dppb	MeCN	90	24	35 (34)[f]	64/36	88:12
3	$Pd_2(dba)_3$/dppb	DME	100	24	64	65/35	88:12
4	$Pd_2(dba)_3$/dppb	DMSO	100	3.5	62	71/29	88:12
5	$Pd_2(dba)_3$/dppb	DME	100	24	52	75/25	88:12
6	$Pd_2(dba)_3$/dppe	DME	100	24	60	81/19	78:22
7	$Pd_2(dba)_3/(^iPrO)_3P$	MeCN	90	24	– (92)	–	–
8	$Pd_2(dba)_3/^nBu_3P$	DME	100	24	83	71/29	86:14
9	$Pd_2(dba)_3$/ttmpp[g,h]	DME	100	6	42 (31)	97/3	83:17
10	$Pd_2(dba)_3$/ttmpp[g,i]	DME	100	11	69 (18)	97/3	83:17
11	$Pd_2(dba)_3$/ttmpp[g,j]	DME	100	15	84	97/3	83:17
12	$Pd_2(dba)_3$/tdmpp[k,l]	DME	100	6	25 (69)	97/3	87:17
13	$Pd_2(dba)_3$/tdmpp[k,m]	DME	100	15	71 (12)	97/3	84:16
14	$Pd_2(dba)_3$/tmpp[n]	DME	100	6.5	85	81/19	86:14
15	$Pd_2(dba)_3/(p\text{-tol})_3P$	DME	100	8	68	65/35	86:14
16	$Pd_2)dba)_3/(o\text{-tol})_3P$	DME	100	24	– (86)[o]		
17	$Pd_2(dba)_3/Ph_3P$	DME	100	8	63	57/43	86:14
18	$Pd_2(dba)_3/(p\text{-Cl-}C_6H_4)_3P$	DME	100	24	44 (53)	54/46	87:13
19	$Pd_2(dba)_3/(C_6F_5)_3P$	DME	100	24	– (98)		
20	$Pd_2(dba)_3/(PhO)_3P$	DME	100	24	– (75)[p]		
21	$Pd(PPh_3)_4$	THF	80	20	73	65/35	88:12
22	$Pd(PPh_3)_4$	MeCN	90	4	71	66/34	88:12
23	$Pd(PPh_3)_4$	DME	100	2.5	64	66/34	86:14

[a] All of the reactions were carried out under an argon atmosphere, in the presence of 0.05 equiv of the palladium catalyst, 0.1 equiv of the phosphorus ligand (when added), and 5 equiv of K_2CO_3. [b] In most cases, monitoring by TLC or HPLC showed that the reaction ceased after less time than the time alloted. [c] Yields are given for isolated products and refer to single runs. [d] Figures in parentheses refer to the recovered starting alkyne **4b**. [e] Relative percentages were calculated by NMR analysis. [f] 2-Phenylindole was isolated in 15% yield. [g] ttmpp = tris[2,4,6-$(MeO)_3$-C_6H_2]$_3$P. [h] Pd:ttmpp = 1:2. [i] Pd:ttmpp = 1:4. [j] Pd:ttmpp = 1;6. [k] tdmpp = tris[2,6-$(MeO)_2$-C_6H_3]$_3$P. [l] Pd:tdmpp = 1:2. [m] Pd:tdmpp = 1:6. [n] tmpp = tris(*p*-MeO-C_6H_4)$_3$P. [o] A similar result was obtained by using a 1:6 Pd:(*o*-tol)$_3$P ratio. [p] 2-Phenylindole was isolated in 14% yield.

and the examples examined have shown that the reaction suffers from some limitations that can be overcome by using procedures a and b. For example, the reaction of **1e** (R = *n*-C_5H_{11}) with 2-hexen-1-yl and cinnamyl carbonates failed to afford the corresponding indole derivatives **3′l** and **3′v** (Table 4, entries 6 and 7) whereas they were isolated in 69 and 75% overall yield, respectively, by using the stepwise and one-pot protocols (Table 2, entry 13 and Table 3, entry 6). In effect, the presence of an aryl substituent on the alkyne moiety appears to be crucial for the success of procedure c. The substitution pattern of the allylating agents also plays a role. Despite the presence of the phenyl group, no indole derivative, **3f**, was isolated when **1a** was allowed to react with isobutenyl carbonate, **2f**, bearing a substituent on the central carbon of the allylic system (Table 4, entry 4). Conversely, the stepwise protocol gave **3f** in an overall 89% yield (Table 2, entry 5).

We explored the question of whether the effect of ttmpp on the reaction mechanism is dependent on steric or electronic factors. Therefore, as model, we examined the employment of $Pd_2(dba)_3$ in the presence of a sterically demanding ligand, P(*o*-tol)$_3$, and of an electron-rich ligand that does not exhibit steric bulk, tris(*p*-methoxyphenyl)-phosphine (tmpp). Using **1a** and **2b** as substrates, we exposed them to $Pd_2(dba)_3$ and P(*o*-tol)$_3$ [Pd:P(*o*-tol)$_3$ = 1:6] and found that the reaction gave the indole nucleus in 78% overall yield (eq 6a). None of the *N*-allyl intermediate was discernible. Subjection of **1a** and **2b** to the $Pd_2(dba)_3$/tmpp combination [Pd:tmpp = 1:6] resulted instead in the isolation of the *N*-allyl derivative, **4b**, in 66% yield and of the indole derivative in 21% yield, with the latter arising largely if not exclusively from **4b** (eq 6b). Strong support for this view is provided by the observation that monitoring the reaction showed that no indole was present before **4b** was formed, but that the amount of the indole derivative increased with time after **4b** became a component of the reaction mixture.

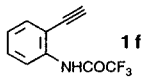
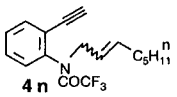
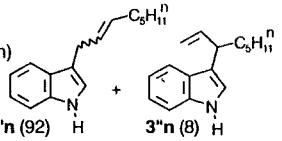
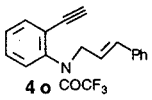
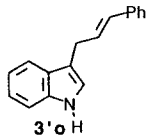
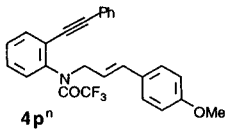
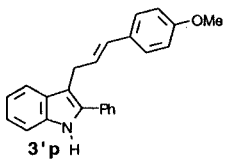
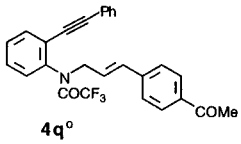
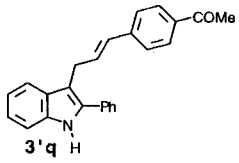
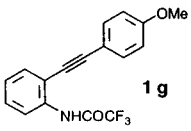
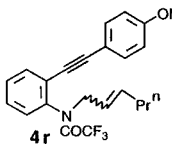
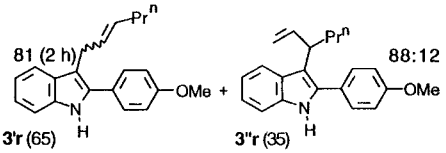
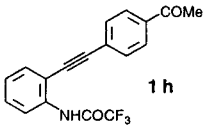
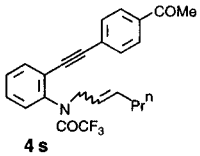
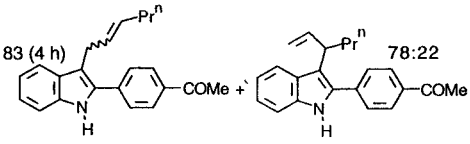


These data argue in favor of the idea that steric factors may play a major role on the reaction mechanism. A working hypothesis accounting for this effect envisages that the use of a sterically demanding ligand may create

Table 2. Palladium-Catalyzed N-Allylation of *o*-Alkynyltrifluoroacetanilides 1 and Cyclization of *o*-Alkynyl-*N*-allyltrifluoroacetanilides 4 (procedure a)

entry	*o*-alkynyl trifluoroacetanilide **1**	allyl ester **2**	N-allyl derivative **4**[a,b] yield % (reaction time)	*E*:*Z* ratio for **4**	cyclization conditions[c]	3-allylindole **3** overall yield %[b] (reaction time)	*E*:*Z* ratio for **3'**
1	**1a**	**2a**	**4a** 95 (1 h)		A	**3a** 91 (1 h)	
2	**1a**	**2c**	**4c** 98 (0.5 h)	100:0	A	**3'c** 91 (1.5 h)	100:0
3	**1a**	**2d**	**4d** 63 (3.0 h)		A	- (2 h)[d]	
4	**1a**	**2e**	**4e** 41 (36 h)[e]		A	**3'e** 44 (24 h)[f]	
5	**1a**	**2f**	**4f** 94 (0.5 h)		A	**3f** 95 (3 h)	
6	**1a**	**2g**	**4g** 97[g] (1.0 h)	98:2	A	**3'g** 78 (5.5 h)	67:33
7	**1b**	**2b**	**4h** 84 (1.0 h)	97:3	A	**3'h** (88) + **3"h** (12) 71 (5 h)	88:12
8	**1b**	**2b**	**4h**	"	" B	**3'h** (96) + **3"h** (4) 76 (12 h)	82:18
9	**1b**	**2h**	**4i** 93 (1.0 h)	93:7	B	**3'i** (97) + **3"i** (3) 69 (12 h)	83:17
10	**1c**	**2c**	**4j** 96 (1 h)	100:0	A	**3'j** 76 (1 h)	100:0
11	**1d**	**2b**	**4k**[h] 93 (0.5 h)	91:9	A	(12 h)[i]	
12	**1e**	**2b**	**4l** 98 (1.0 h)	92:8	A	**3'l** (81) + **3"l** (18) 66 (8 h)	81:19
13	**1e**	**2b**	**4l**	"	" B	**3'l** (97) + **3"l** (3) 69 (24 h)	85:15
14	**1e**	**2i**	**4m** 60 1.0 h)	89:11	B	**3'm** 75 (4 h)	88:12

Table 2 (Continued) Palladium-Catalyzed N-Allylation of *o*-Alkynyltrifluoroacetanilides 1 and Cyclization of *o*-Alkynyl-*N*-allyltrifluoroacetanilides 4 (procedure a)

entry	*o*-alkynyl trifluoroacetanilide **1**	allyl ester **2**	N-allyl derivative **4**[a,b] yield % (reaction time)	*E*:*Z* ratio for **4**	cyclization conditions[c]	3-allylindole **3** overall yield %[b] (reaction time)	*E*:*Z* ratio for **3'**
15	 **1f**	**2h**	 **4n** 82 (0.5 h)	90:10	A	38 (24 h)  **3'n** (92) + **3"n** (8)	89:11
16	**1f**	**2h**	**4n**	"	B	-[l]	
17	**1f**	**2c**	 **4o** 78 (1 h)	100:0	A	49 (24 h)[m]  **3'o**	100:0
18	-	-	 **4p**[n]	100:0	A	84 (1.5 h)  **3'p**	100:0
19	-	-	 **4q**[o]	100:0	A	77 (2 h)  **3'q**	100:0
20	 **1g**	**2b**	 **4r** 82 (0.5 h)	92:8	A	81 (2 h)  **3'r** (65) + **3"r** (35)	88:12
21	 **1h**	**2b**	 **4s** 93 (0.5 h)	92:8	A	83 (4 h)  **3's** (75) **3"s** (25)	78:22

[a]N-allylations were carried out in THF at 60 °C under an argon atmosphere, using the following molar ratios: **1**:**2**:$Pd_2(dba)_3$:dppb = 1:1.2:0.025:0.1.[b]Yields refer to isolated products. [c]A: (MeCN, 90 °C) **4**:$Pd(PPh_3)_4$:K_2CO_3 = 1:0.05:5. B: (DME, 100 °C) **4**:Pd_2dba_3:ttmpp = 1:0.025:0.3. [d]2-Phenylindole was isolated in 82% yield. [e]**1a** was recovered in 22% yield. [f]**4e** was recovered in 31% yield. [g]Approximately an 98:2 :: *E*:*Z* mixture. [h]Approximately an 93:7 :: *E*:*Z* mixture. [i]2-*tert*-Butylindole was isolated in 66% yield. [l]**4n** was recovered in 22% yield. [m]Indole was isolated in 31% yield. [n]Prepared from **4a** and 4-MeO-C_6H_4-I [$Pd(OAc)_2$, KOAc, K_2CO_3, DMF, 80 °C, 6 h] in 49% yield. [o]Prepared from **4a** and 4-MeCO-C_6H_4-I [$Pd(OAc)_2$, KOAc, K_2CO_3, DMF, 80 °C, 3 h] in 66% yield.

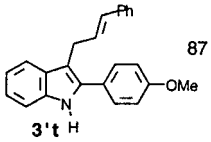
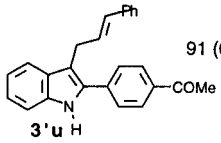
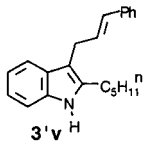
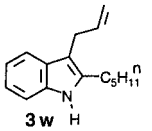
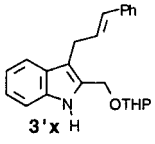
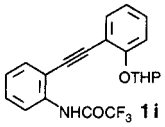
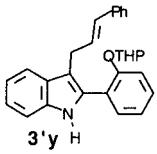
an η^3-allylpalladium complex **7** more prone to relieving steric crowding in the coordination sphere of palladium rather than allowing a nucleophilic attack by the nitrogen atom on the allylic complex. Consequently, in the presence of ttmpp [or even tdmpp or P(*o*-tol)$_3$] the ambident electrophilic part of **7** prefers to complex with the alkyne unit, generating **10**, instead of producing the η^2-olefin-palladium complex **8**.

It may be worth emphasizing that the result obtained in the reaction of **1a** and **2b** in the presence of $Pd_2(dba)_3$ and (*o*-tol)$_3$P (eq 6a) and the observation that the *N*-allyl derivative **4b** failed to cyclize to the corresponding indole in the presence of the same catalytic system (Table 1, entry 16), provide a further, convincing proof in favor of path b and of the notion that the ligand may have a strong directing effect on the reaction mechanism. In fact, if the reaction of **1a** and **2b** in the presence of $Pd_2(dba)_3$ and (*o*-tol)$_3$P proceeded through an N-allylation step, the *N*-allyl derivative would be recovered unreacted and no indole could be isolated.

As to the regioselectivity of the intramolecular nucleophilic attack of the indolyl carbon atom on the η^3-allyl unit,[18] several factors have been found to play a role: the nature of the allylating agent (compare, for example,

(18) Previous work on the palladium-catalyzed allylation of carbon nucleophiles (phenyl and linear vinyl fragments) which react by transfer from the palladium to the carbon[14,19] showed that the new carbon−carbon bond is generated preferentially at the more crowded allyl terminus in the presence of triphenylphosphine. This tendency has been rationalized by assuming that the sterically demanding triphenylphosphine prefers to reside trans to the bulkier allyl terminus, so as to minimize steric strain. In our case, even in the presence of triphenylphosphine, the main regioisomer contains the indolyl unit bound to the less crowded allyl terminus. This might reflect a less clear-cut differentiation between the steric requirements of the triphenylphosphine and the substituted indolyl unit.

Table 3. One-Pot Synthesis of 3-Allylindoles 3 from *o*-Alkynyltrifluoroacetanilides 1 and Allyl Esters 2 (procedure b)[a]

entry	*o*-alkynyl trifluoroacetanilide 1	allyl ester 2	3-allylindole 3	yield %[b,c]
1	**1a**	**2c**	**3'c**	91 (3 h, 1.5 h)
2	**1a**	 **2l**	**3'e**	52[d] (48 h, 2 h)
3	**1a**	**2f**	**3f**	74 (24 h, 10 h)
4	**1g**	**2c**	 **3't**	87 (1 h, 2 h)
5	**1h**	**2c**	 **3'u**	91 (0.5 h, 8 h)
6	**1e**	**2c**	 **3'v**	75 (5.5 h, 24 h)
7	**1e**	**2a**	 **3w**	74 (3.5 h, 5 h)
8	**1b**	**2c**	 **3'x**	77 (1.5 h, 1.5 h)
9	 **1i**	**2c**	 **3'y**	64 (3 h, 24 h)
10	**1c**	**2c**	**3'j**	45 (48 h, 1 h)

[a]Reactions were carried out under an argon atmosphere as follows: (THF, 60 °C): **1**: **2**: $Pd(PPh_3)_4$ = 1: 1.2: 0.05 till the disappearance of **1**, then K_2CO_3 (5 equiv.) is added and the reaction temperature is raised to 80 °C. [b]Yields refer to isolated products and are calculated on the starting *o*-alkynyltrifluoroacetanilides **1**. [c]Figures in parentheses are for the reaction times of the N-allylation and cyclization steps, respectively. [d]**1a** was recovered in 21% yield.

Table 1, entry 22 with Table 2, entry 2); steric and electronic effects exerted by the substituents on the indolyl fragment, R (Table 1, entry 17; Table 2, entries 7, 12, 15, 20, 21); the number of methylene units between the phosphorus atoms with bidentate ligands (Table 1, entries 3, 5, 6); steric (compare, for example, Table 1, entry 15 with the result reported in eq 6a) and electronic (Table 1, compare entry 14 with entry 18) effects relative to monodentate ligands. The remarkable regioselectivity exhibited by ttmpp most probably depends upon a combination of steric and electronic effects. Noteworthy, steric and electronic effects exerted by the substituent of the indolyl unit, R, which have been found to play an important role in the regiochemistry in the presence of PPh_3 (Table 1, entry 17; Table 2, entries 7, 12, 15, 20, 21), turn out to be unimportant in the presence of ttmpp.

The stereochemistry of the process reveals that it is accompanied by some loss of the olefin geometry and that this is not influenced by solvent, temperature, or ligand effects to any extent.

In conclusion, we have developed a new, highly efficient palladium-catalyzed synthesis of 2-substituted- and 2-unsubstituted-3-allyl indoles from readily available *o*-alkynyltrifluoroacetanilides and allyl esters which shows a wide structural flexibility in both the alkyne and the allyl component. In every case, almost complete regioselectivity toward the 3-allylindole bearing the indolyl unit on the less substituted allyl terminus has been achieved. The overall yields are generally high. Despite some limitations such as the partial loss of olefin geometry, the process holds promise as a useful tool for the construction of complex heterocycles containing the indole fragment.

Experimental Section

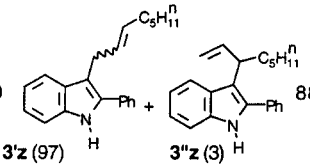
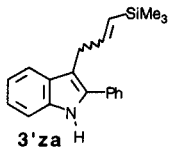
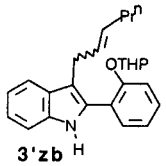
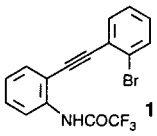
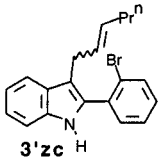
Melting points were determined with a Büchi apparatus and are uncorrected. All the starting materials (catalysts, ligands, bases, alcohols, alkynes and solvents) commercially available were used as purchased, without further purification. *o*-Ethynyltrifluoroacetanilide **1f** was prepared according to the ref 2b. Allyl esters were prepared according to standard methods. Reaction products were purified on axially compressed columns (packed with SiO_2, 25−40 nm, Macherey Nagel) connected to a Gilson solvent delivery system and to a Gilson refractive index detector. *n*-Hexane/EtOAc mixtures were used for elution. ^1H NMR spectra ($CDCl_3$, unless otherwise stated; TMS as internal standard) were recorded at 200 MHz. ^{13}C NMR spectra were recorded at 50.3 MHz.

General Procedure for the Preparation of *o*-Alkynyltrifluoroacetanilides (1) from *o*-Iodoaniline. *o*-(Phenylethynyl)trifluoroacetanilide (1a). To a solution of 2-iodoaniline (0.850 g, 3.87 mmol) in DMF (3 mL) were added phenylacetylene (0.51 mL, 4.65 mmol), diethylamine (2.5 mL), $Pd(OAc)_2(PPh_3)_2$ (0.029 g, 0.038 mmol), and CuI (0.015 g, 0.077 mmol). The reaction mixture was stirred at room temperature under argon for 3 h and then poured into a separatory funnel containing EtOAc and water saturated with NH_4Cl. The organic layer was separated and washed with water, dried (Na_2SO_4), and concentrated under vacuum. The residue was connected to a vacuum line, kept at 1 mm/Hg for 2 h, dissolved in anhydrous THF (5 mL), and cooled in an ice bath. Trifluoroacetic anhydride (1.1 mL, 7.74 mmol) was added, and the reaction mixture was stirred under argon for 0.25 h and extracted with EtOAc and water saturated with $NaHCO_3$. The organic phase was dried (Na_2SO_4) and concentrated under vacuum. The residue was chromatographed on silica gel eluting with a *n*-hexane/EtOAc 90/10 (v/v) mixture to give 0.82 g (73% yield) of **1a**. Spectral data are in good agreement with those described in the literature.[2b]

General Procedure for the Preparation of *o*-Alkynyltrifluoroacetanilides (1) from *o*-Ethynylaniline. *o*-[(*p*-Acetylphenyl)ethynyl]trifluoroacetanilide (1h). To a stirred solution of 2-ethynylaniline (0.300 g, 2.56 mmol) in DMF (1.5 mL) were added 4-iodoacetophenone (0.757 g, 3.07 mmol), diethylamine (5 mL), $Pd(OAc)_2(PPh_3)_2$ (0.020 g, 0.025 mmol), and CuI (0.010 g, 0.051 mmol). The reaction mixture was stirred at room temperature for 3 h and extracted with

(19) Keinan, E.; Sahai, M. *J. Chem. Soc., Chem. Commun.* **1984**, 648. Temple, J. S.; Riediker, M.; Schwartz, J. *J. Am. Chem. Soc.* **1982**, *104*, 1310. Hayasi, Y.; Riediker, M.; Temple, J. S.; Schwartz, J. *Tetrahedron Lett.* **1981**, *22*, 2629.

Table 4. The Reaction of *o*-Alkynyltrifluoroacetanilides 1 with Allyl Carbonates 2 in the Presence of the $Pd_2(dba)_3$/ttmpp Combination (procedure c)[a]

entry	*o*-alkynyl trifluoroacetanilide 1	allyl ester 2	reaction time (h)	overall yield %	3-allylindoles 3	*E*:*Z* ratio for 3'
1	1a	2c	3	94	3'c	100:0
2	1a	2b	3	76	3'b (97) + 3"b (3)[b]	87:13
3	1a	2h	3	80	 3'z (97) + 3"z (3)	88:12
4	1a	2f	24	-[c]		
5	1a	2i	8	46[d]	 3'za	95:5
6	1e	2b	10	-[e]		
7	1e	2c	10	-[f]		
8	1g	2b	4	72	3'r (97) + 3"r (3)	87:13
9	1h	2b	8	67	3's (>99) + 3"s (<1)	82:18
10	1i	2b	2	96	 3'zb	82:18
11	 1j	2b	10	34[g]	 3'zc	91:9

[a]Reactions were carried out in THF at 60 °C, under an argon atmosphere, using the following molar ratios: **1**:**2**:$Pd_2(dba)_3$:ttmpp = 1:1.2:0.025:0.3. [b]2-Phenylindole was isolated in 8% yield. [c]**1a** was recovered in 63% yield and 2-*n*-pentylindole was isolated in 19% yield. [d]2-Phenylindole was isolated in 34% yield. [e]2-*n*-Pentylindole was isolated in 83% yield. [f]2-*n*-Pentylindole was isolated in 81% yield. [g]**1j** was recovered in 19% yield.

EtOAc and water saturated with NH_4Cl. The organic layer was separated and washed with water, dried (Na_2SO_4), and concentrated under vacuum. The crude coupling product was kept under vacuum (1 mm/Hg) for 2 h and dissolved in anhydrous THF (3 mL), and the resultant solution was cooled in an ice bath. Trifluoroacetic anhydride (0.71 mL, 5.12 mmol) was added and the reaction mixture was stirred under nitrogen for 0.25 h and extracted with a saturated $NaHCO_3$ solution and ethyl acetate. The organic layer was dried (Na_2SO_4) and evaporated under vacuum. The residue was chromatographed on silica gel eluting with a *n*-hexane/EtOAc 85/15 (v/v) mixture to give 0.76 g (89% yield) of **1h**: mp 135−6 °C; IR (KBr) 3303, 2212, 1712, 826, 769 cm^{-1}; ^1H NMR δ 8.83 (bs, 1 H), 8.38 (d, J = 8.0 Hz, 1 H), 7.99 (d, J = 8.3 Hz, 2 H), 7.63−7.57 (m, 3 H), 7.47 (t, J = 7.6 Hz, 1 H), 7.28−7.21 (m, 1 H), 2.64 (s, 3 H); ^{13}C NMR δ 197.3, 158.2 (q, J = 36 Hz), 137.2, 136.4, 132.1, 131.8, 130.7, 128.8, 127.6, 125.9, 120.0, 116.5 (q, J = 288 Hz), 113.1, 97.2, 86.1, 26.9; MS *m/e* (relative intensity) 331 (M^+, 68), 316 (100). Anal. Calcd for $C_{18}H_{12}F_3NO_2$: C, 65.24; H, 3.65; N, 4.23. Found C, 65.01; H, 3.66; N. 4.21.

Preparation of *o*-Ethynylaniline. To a stirred solution of *o*-iodoaniline (3.0 g, 13.70 mmol) in DMF (2 mL) and Et_2-NH (2 mL) were added (trimethylsilyl)acetylene (2.84 mL, 20.54 mmol), $Pd(PPh_3)_4$ (0.079 g, 0.068 mmol), and CuI (0.026 g, 0.137 mmol). The reaction mixture was stirred overnight under argon at room temperature and poured into a separatory funnel containing diethyl ether and 0.1 N HCl. The organic layer was separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic phases were dried (Na_2SO_4) and evaporated under vacuum. The residue was dissolved in methanol (50 mL), and K_2CO_3 (0.178 g, 1.37 mmol) was added. The reaction mixture was stirred for 1 h at room temperature, methanol was partially evaporated to around 1/4 of its original volume, and the resultant mixture was extracted with diethyl ether and water. The organic phase was dried (Na_2SO_4), evaporated, and chromatographed on silica gel. Eluting with a *n*-hexane/EtOAc 95/5 (v/v) mixture afforded 1.31 g (82% yield) of *o*-ethynylaniline. Spectral data were in good agreement with those reported in the literature.[20]

Typical Procedure for the Synthesis of *o*-Alkynyl-*N*-allyltrifluoroacetanilides (4). *o*-(Phenylethynyl)-N−(2-hexen-1-yl)trifluoroacetanilide (4b). A mixture of $Pd_2(dba)_3$ (0.016 g, 0.017 mmol) and (diphenylphosphino)butane (0.030 g, 0.069 mmol) in anhydrous THF (3 mL) was stirred under argon at 60 °C for 10 min. After cooling at room temperature, *o*-(phenylethynyl)trifluoroacetanilide **1a** (0.200 g, 0.69 mmol) and 2-hexen-1-yl ethyl carbonate **2b** (0.143 g, 0.83 mmol) were added, and the solution was stirred at 60 °C for 1.5 h. Then, the THF was evaporated under vacuum, and the oily residue was subjected directly to chromatography on silica gel. Elution with a *n*-hexane/EtOAc 96/4 (v/v) mixture gave 0.223 g (87% yield) of **4b**, (∼88:12:: *E*:*Z*): IR (liquid film) 2221, 1696, 761 cm^{-1}; ^1H NMR δ 7.65−7.58 (m, 1 H), 7.52−7.47 (m, 2 H), 7.37−7.30 (m, 5 H), 7.20−7.16 (m, 1 H), 5.60−5.41 (m, 2 H), 4.80 (dd, J = 13.5 Hz, J = 2.8 Hz, 1 H), 4.02−3.91 (m, 1 H), 1.96−1.79 (m, 2 H), 1.37−1.11 (m, 2 H), 0.82 (t, J = 7.2 Hz, 3 H); ^{13}C NMR δ 157.0 (q, J = 35 Hz, *C*O−CF_3), 140.0, 137.5, 132.8, 131.8, 130.0, 129.0, 128.9, 128.8, 128.6, 123.7, 122.5, 116.5 (q, J = 288 Hz, *C*F_3), 95.5, 85.0, 53.1 (N*C*H_2CH=CH, **4b** *E* isomer) and 47.2 (N*C*H_2CH=CH, **4b** *Z* isomer), 34.2, 22.2, 13.7; MS *m*/*e* (relative intensity) 371 (M^+, 20), 342 (23), 328 (65), 302 (100), 220 (73), 165 (69).

***o*-(Phenylethynyl)-N−[(3-(*p*-methoxyphenyl)-2(*E*)-propen-1-yl]trifluoroacetanilide (4p)** was obtained by allowing **4a** (0.150 g, 0.45 mmol) to react with *p*-methoxyphenyl iodide (0.160 g, 0.68 mmol), in the presence of K_2CO_3 (0.078 g, 0.57 mmol), KOAc (0.045 g, 0.45 mmol), and $Pd(OAc)_2$ (0.005 g, 0.023 mmol) in DMF (2 mL), at 80 °C, under argon for 2 h. The usual workup and purification by chromatography on silica gel, and elution with a *n*-hexane/EtOAc 90/10 (v/v) mixture, gave **4p** in 46% yield as a colorless oil: IR (liquid film) 2221, 1696, 752 cm^{-1}; ^1H NMR δ 7.63−7.31 (m, 9 H), 7.20 (d, J = 8.7 Hz, 2 H), 6.78 (d, J = 8.7 Hz, 2 H), 6.36 (d, J = 15.8 Hz, 1 H), 6.19−6.05 (m, 1 H), 4.90 (dd, J = 14.3 Hz, J = 6.1 Hz, 1 H), 4.18 (dd, J = 14.3 Hz, J = 7.7 Hz, 1 H), 3.75 (s, 3 H); ^{13}C NMR δ 159.6, 157.2 (q, J = 37 Hz), 140.1, 134.9, 132.9, 131.8, 129.8, 129.3, 129.1, 129.0, 128.6, 127.9, 123.6, 122.4, 119.6, 116.4 (q, J = 289 Hz), 113.6, 95.6, 85.0, 53.3, 53.6; MS *m*/*e* (relative intensity) 435 (M^+, 81), 147 (100). Anal. Calcd for $C_{26}H_{20}F_3NO_2$: C, 71.72; H, 4.63; N, 3.22. Found C, 71.53; H, 4.62; N, 3.20.

***o*-(Phenylethynyl)-N−[3-(*p*-acetylphenyl)-2(*E*)-propen-1-yl]trifluoroacetanilide (4q)** was prepared as described for **4p** from **4a** and *p*-acetylphenyl iodide, in 66% yield: mp 64−6 °C; IR (KBr) 2221, 1704, 1696, 752 cm^{-1}; ^1H NMR δ 7.77 (d, J = 8.4 Hz, 2 H), 7.55−7.21 (m, 11 H), 6.45 (d, J = 15.4 Hz, 1 H), 6.39−6.32 (m, 1 H), 4.81 (dd, J = 13.4 Hz, J = 5.3 Hz, 1 H), 4.28 (dd, J = 13.4 Hz, J = 6.2 Hz, 1 H), 2.51 (s, 3 H); ^{13}C NMR δ 197.6, 157.3 (q, J = 38 Hz), 140.8, 140.0, 136.4, 134.1, 133.0, 131.8, 129.6, 129.1, 129.1, 128.8, 128.6, 127.5, 126.7, 125.0, 123.6, 122.2, 116.3 (q, J = 289 Hz), 95.8, 84.9, 53.6, 26.7; MS *m*/*e* (relative intensity) 447 (M^+, 31), 404 (49), 350 (100). Anal. Calcd for $C_{27}H_{20}F_3NO_2$: C, 72.46; H, 4.51; N, 3.13. Found C, 72.28; H, 4.49; N, 3.15.

Cyclization of *o*-Alkynyl-*N*-allyltrifluoroacetanilides (Procedure a). Conditions A. 2-Phenyl-3-(2-Methyl-2-propen-1-yl)indole (3f). To a solution of *o*-(phenylethynyl)-N-(2-methyl-2-propen-1-yl)trifluoroacetanilide **4f** (0.120 g, 0.35 mmol) in acetonitrile (3 mL) were added K_2CO_3 (0.241 g, 1.75 mmol) and $Pd(PPh_3)_4$ (0.020 g, 0.017 mmol). The resultant mixture was refluxed under argon, at 90 °C, for 3 h. Then it was cooled at room temperature, diluted with ethyl acetate, and washed with water. The organic layer was dried (Na_2SO_4) and evaporated under vacuum, and the residue was chromatographed on silica gel. Eluting with a *n*-hexane/EtOAc 97/3 (v/v) mixture afforded 0.082 g (95% yield) of **3f** as a white solid: mp 62−3 °C; IR (KBr) 3344, 769, 744 cm^{-1}; ^1H NMR δ 8.05 (bs, 1 H), 7.60−7.31 (m, 7 H), 7.23−7.07 (m, 2H), 4.83 (bs, 1 H), 4.66 (bs, 1 H), 3.53 (s, 2 H), 1.83 (s, 3 H); ^{13}C NMR δ 145.0, 122.4, 119.8, 111.2, 110.9, 33.1, 23.2; MS *m*/*e* (relative intensity) 247 (M^+, 79), 232 (19), 206 (100). Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found C, 87.58; H, 6.91; N, 5.68.

Conditions B. 2-Phenyl-3-(2-hexen-1-yl)indole (3′b) and 2-Phenyl-3-(hex-1-en-3-yl)indole (3″b). A mixture of $Pd_2(dba)_3$ (0.009 g, 0.010 mmol) and tris(2,4,6-$(MeO)_3C_6H_4)_3P$ (0.065 g, 0.12 mmol) in DME (3 mL) was stirred under argon at 60 °C for 10 min. The solution was cooled at room temperature, and 0.150 g (0.40 mmol) of *o*-(phenylethynyl)-N-(2-hexen-1-yl)trifluoroacetanilide **4b** and 0.278 g (2.02 mmol) of K_2CO_3 were added. The reaction mixture was stirred at 100 °C for 15 h and workup as before to afford a residue which was purified by chromatography eluting with a *n*-hexane/EtOAc 94/6 (v/v) mixture to provide 0.093 g (84% yield) of **3′b** and **3″b** as a 97:3 mixture. The presence of **3″b** was indicated by a multiplet (ddd) at 6.28−6.18 (H_2C=C*H*CH) and a multiplet at 5.09−4.99 ppm (H_2C=CHCH); **3′b** was obtained as an approximately 83:17 *E*:*Z* mixture: IR (liquid film) 3329, 1688, 740, 695 cm^{-1}; ^1H NMR δ 8.42 (bs, 1 H), 7.96−7.08 (m, 9 H), 5.69 (dt, J = 15.2 Hz, J = 5.6 Hz, 1 H), 5.50 (dt, J = 15.2 Hz, J = 6.4 Hz, 1 H), 3.61 (d, J = 6.5 Hz, 0.28 H, CCH_2CH=, **3′b** *Z* isomer), 3.57 (dd, J = 5.6 Hz, J = 1.6 Hz, 1.72 H, CCH_2CH=, **3′b** *E* isomer), 2.24−2.14 (m, 0.34 H, =CHCH_2CH$_2$, **3′b** *Z* isomer), 2.02−1.92 (m, 1.72 H, =CHCH_2CH$_2$, **3′b** *E* isomer),1.50−1.12 (m, 2H), 0.95 (t, J = 7.3 Hz, 0.42 H, CH_3−CH$_2$, **3′b** *Z* isomer), 0.85 (t, J = 7.3 Hz, 2.58 H, CH_3CH$_2$, **3′b** *E* isomer); ^{13}C NMR δ 136.0, 134.5, 122.2, 119.5, 111.5, 110.8, 34.6 (C*C*H_2CH=, **3′b** *E* isomer) and 29,7 (C*C*H_2CH=, **3′b** *Z* isomer), 22.7, 13.7; MS *m*/*e* (relative intensity) 275 (M^+, 22), 242 (36), 208 (100), 193 (54).

One-Pot Synthesis of 3-Allylindoles from *o*-Alkynyltrifluoroacetanilides (1) and Allyl Esters (2) (Procedure b). 2-[*o*-(2-Tetrahydropyranyloxy)phenyl]-3-cinnamylindole (3′y). To a solution of 2-[*o*-(2-tetrahydropyranyloxy)-phenyl]trifluoroacetanilide **1i** (0.200 g, 0.514 mmol) and cinnamyl ethyl carbonate **2c** (0.127 g, 0.617 mmol) in anhydrous THF (3 mL) was added, under argon, $Pd(PPh_3)_4$ (0.029 g, 0.026 mmol). The mixture was stirred at 60 °C for 3 h, till the disappearance of **1i**. Then, K_2CO_3 (0.355 g, 2.57 mmol) was added, and the reaction was stirred at 80 °C for 24 h. After the usual workup, the residue was chromatographed on silica gel. Eluting with a *n*-hexane/EtOAc (95/5 v/v) mixture gave 0.135 g (64% yield) of **3′y**: mp 40−2 °C; IR (KBr) 3427, 744 cm^{-1}; ^1H NMR δ 9.03 (bs, 1 H), 7.65 (d, J = 7.6 Hz, 1 H), 7.54 (dd, J = 7.7 Hz, J =1.2 Hz, 1 H), 7.44−6.95 (m, 11 H), 6.56 (dt, J = 15.8 Hz, J = 4.0 Hz, 1 H), 6.40 (d, J = 15.8 Hz, 1 H), 5.40−5.35 (m, 1 H), 3.90−3.82 (m, 1 H), 3.76 (d, J = 4.0 Hz, 2 H), 3.56−3.47 (m, 1 H), 1.80−1.90 (m, 6 H); ^{13}C NMR δ 154.5, 138.0, 135.8, 132.3, 131.4, 130.2, 130.0, 129.3, 128.6, 128.1, 127.0, 126.2, 123.1, 122.7, 122.1, 119.5, 119.3, 117.1, 111.1, 110.7, 98.7, 63.2, 30.8, 28.8, 25.2, 19.6; MS *m*/*e* (relative intensity) 409 (M^+, 8), 325 (100). Anal. Calcd for $C_{28}H_{27}NO_2$: C, 82.11; H, 6.65; N, 3.42. Found C, 82.30; H, 6.67; N, 3.41.

Reaction of *o*-Alkynyltrifluoroacetanilides 1 with Allyl Carbonates 2 in the Presence of the $Pd_2(dba)_3$/ttmpp Combination (Procedure c). 2-Phenyl-3-(2-octen-1-yl)-indole (3′z) and 2-Phenyl-3-(1-octen-3-yl)indole (3″z). A mixture of $Pd_2(dba)_3$ (0.012 g, 0.013 mmol) and ttmpp (0.083 g, 0.156 mmol) in anhydrous THF (3 mL) was stirred at 60 °C for 10 min, under an argon atmosphere. The solution was cooled at room temperature and *o*-(phenylethynyl)trifluoroacetanilide **1a** (0.150 g, 0.519 mmol) and 2-octenyl ethyl carbonate **2h** (0.125 g, 0.623 mmol) were added, and the mixture was stirred at 60 °C for 3 h. THF was evaporated under vacuum, and the residue was chromatographed on silica gel eluting with a *n*-hexane/EtOAc 94/6 (v/v) mixture to give 0.126 g (80% yield) of **3′z** and **3″z** as a 97:3 mixture. The presence of **3″z** was indicated by a multiplet (ddd) at 6.23−6.20 ppm (H_2C=C*H*CH) and a multiplet at 5.09−4.99 ppm (H_2C=CHCH). **3′z** was obtained as an approximately 88:12 *E*:*Z* mixture: IR (liquid film) 3329, 1687, 1622, 741, 695 cm^{-1}; ^1H NMR δ 7.92 (bs, 1 H), 7.53−7.09 (m, 9 H), 5.67 (dt, J = 15.1 Hz, J = 5.5 Hz, 1 H), 5.49 (dt, J = 15.1 Hz, J = 6.6 Hz, 1 H), 3.54 (d, J = 5.5

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Hz, 2 H), 1.99−1.82 (m, 2 H), 1.38−0.60 (m, 9 H); ^{13}C NMR δ 142.1, 113.9 (H_2C=), 41.0, 34.5, 32.7, 31.8, 31.6, 29.4, 28.0, 27.7, 22.7, 14.3, 14.2; MS *m*/*e* (relative intensity) 303 (M^+, 33), 232 (100), 208 (57).

Acknowledgment. The authors gratefully acknowledge the Consiglio Nazionale delle Ricerche (CNR) and the Ministero dell'Università e della Ricerca Scientifica (MURST) for financial support of this research. The authors are also greatly indebted to Dr. Luciana Turchetto of the Istituto Superiore di Sanità for obtaining the mass spectra of new products.

Supporting Information Available: Characterization data for **1b**−**e**,**g**, **i**,**j**, **4a**, **c**−**o**, **r**, **s**, **3a**, **3′c**, **′e**, **′g**−**j**, **′l**−**x**, **′za**−**-zc** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO971237P