An efficient synthesis of carbazoles from $PtCl_2$-catalyzed cyclization of 1-(indol-2-yl)-2,3-allenols†

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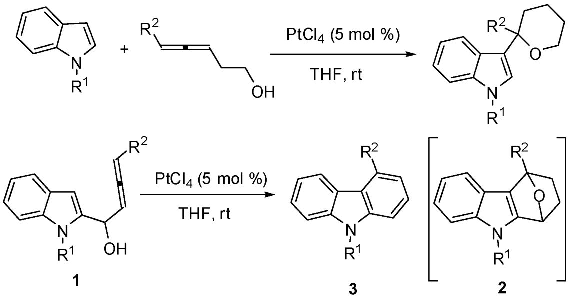
The $PtCl_2$-catalyzed reaction of 1-(indol-2-yl)-2,3-allenols occurred smoothly to form carbazoles by connecting the 3-carbon atom of indole with the 4-carbon atom of the allenol moiety, referring to the carbon atom connected to the hydroxyl group.

The tricyclic carbazole ring system is the core structure for a wide range of alkaloids displaying a variety of biological activities,[1] and are important building blocks for the construction of polymers with special thermal,[2] electrical[3] and photoelectrical properties,[4] and polymer-blend additives for the fabrication of photorefractive materials.[5] Thus, the development of simple, mild, efficient and general methods[6] to synthesize the carbazole ring system from easily available starting materials are of current interest. On the other hand, we recently observed a $PtCl_4$-catalyzed intermolecular cyclization reaction of β-allenols in the presence of indoles affording indole derivatives with a saturated 6-membered cyclic ether group at the 3-position (Scheme 1).[7] Based on these results, we envisioned that the reaction of 1-(indol-2-yl)-2,3-allenols **1** would afford polycyclic products **2**. However, carbazoles **3** were formed conveniently at room temperature in toluene (Scheme 1). In this communication, we wish to report these unique observations.

The starting materials, **1a–r**, are easily available from the related 1*H*-indole-2-carbaldehydes based on known methods (see the ESI for details†).[8–10] Our initial investigation was focused on the reaction of 1-(1-ethyl-1*H*-indol-2-yl)nona-2,3-dien-1-ol (**1a**) in toluene under the catalysis of $PtCl_4$ (5 mol%).[7] Instead of forming the **2**-type of product, 9-ethyl-4-pentyl-9*H*-carbazole (**3a**) was unexpectedly formed in 65% NMR yield (entry 1, Table 1). When $PtCl_4$ was replaced with $AgBF_4$ (20 mol%), the reaction was complicated with **3a** being formed in only 13% yield (entry 2, Table 1), and $AuCl(PPh_3)$ was totally inactive (entry 3, Table 1). With the addition of 10 mol% AgOTf, **1a** decomposed quickly, probably due to the presence of the free hydroxyl group in **1a**, and the yield of **3a** was $<7\%$, if any, based on NMR analysis of the crude reaction mixture (entry 4, Table 1).[11] Further study led to the observation that $PtCl_2$ is a much better catalyst for this reaction, affording **3a** in 83% isolated yield (entry 5, Table 1).[12] Several solvents were tested for the $PtCl_2$-catalyzed reaction of **1a** at room temperature: CH_2Cl_2 was also effective affording **3a** in 80% NMR yield (entry 6, Table 1); other solvents, such as CH_3CN, xylenes, DCE (1,2-dichloroethane) and THF provided **3a** in 20%, 67%, 82% and 38% yields, respectively (entries 7–10, Table 1). When 2 mol% $PtCl_2$ was used, the yield of **3a** was lower (compare entry 11 with entry 5, Table 1). Thus, we defined the standard conditions as follows: the reaction of **1** was conducted with 5 mol% $PtCl_2$ in toluene at room temperature (entry 5, Table 1).

This new transformation is quite general. Some typical results are listed in Table 2. The 1-position of indoles may be substituted with an alkyl (entries 1–12 and entries 14–19, Table 2) or phenyl group (entry 13, Table 2). R^3 could be H (entries 1–6 and 19, Table 2), an alkyl (entries 8 and 10, Table 2) or an aryl group (entries 7, 9, 12 and 13, Table 2). The reaction of **1k** (entry 11, Table 2) is especially noteworthy, since this reaction shows an interesting exclusive cyclization of the allene instead of the alkene functionality; in addition, this reaction tolerates many functional groups such as COOMe, $CONMe_2$ and CH_2OH (entries 14–18, Table 2). In entries 16–18, it should also be noted that the secondary hydroxyl group was exclusively eliminated. R^4 could be H (entries 7–19, Table 2), an alkyl (entries 1–5, Table 2) or a benzyl group (entry 6, Table 2). Moreover, differently substituted indoles can also successfully give the corresponding carbazole derivatives (entries 4, 5, 12, 17 and 18, Table 2). The structures of **3** were further confirmed by the X-ray crystal diffraction study of **3g** (Fig. 1).[13]

A plausible mechanism involving a metal carbene intermediate **7** is depicted in Scheme 2. The reaction of $PtCl_2$ with **1** would form intermediate **5** from the coordination of the allene moiety to the platinum atom followed by nucleophilic attack of indolyl C3 to the metal-activated electrophilic C=C double bond. Subsequent protonation of the hydroxyl group followed by elimination of H_2O in intermediate **6** affords cyclic vinylic platinum carbene intermediate **7**.[14] A 1,2-H shift[15] of intermediate **7** would afford the final product **3**, with regeneration of the catalytically active species $PtCl_2$.



Scheme 1

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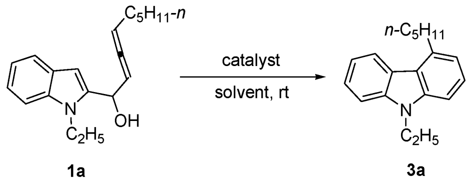
† Electronic supplementary information (ESI) available: The experimental procedures, characterization data, and copies of ^1H and ^{13}C NMR spectra for all products. CCDC 713481. For ESI and crystallographic data in CIF or other electronic format, see: 10.1039/b909649c

Table 1 Optimization of the reaction conditions for the cyclization reaction of 1-(1-ethyl-1*H*-indol-2-yl)nona-2,3-dien-1-ol **1a**



Entry	Catalyst (mol%)	Solvent	Time/h	Yield of **3a** (%)[a]
1	$PtCl_4$ (5)	Toluene	1	65
2	$AgBF_4$ (20)	Toluene	3	13
3	$AuCl(PPh_3)$ (10)	Toluene	10	—[b]
4	$AuCl(PPh_3)$(10)[c]	Toluene	4	<7
5	$PtCl_2$ (5)	Toluene	2	90 (83[d])
6	$PtCl_2$ (5)	CH_2Cl_2	3	80
7	$PtCl_2$ (5)	CH_3CN	3	20
8	$PtCl_2$ (5)	Xylenes	3	67
9	$PtCl_2$ (5)	DCE	3	82
10	$PtCl_2$ (5)	THF	3	38
11	$PtCl_2$ (2)	Toluene	5	79 (74[d])

[a] ^1H NMR yield was determined by using CH_2Br_2 as the internal standard. [b] The recovery of **1a** was 92%. [c] AgOTf (10 mol%) was added. [d] Isolated yield.

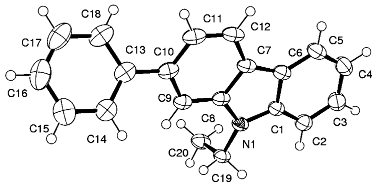
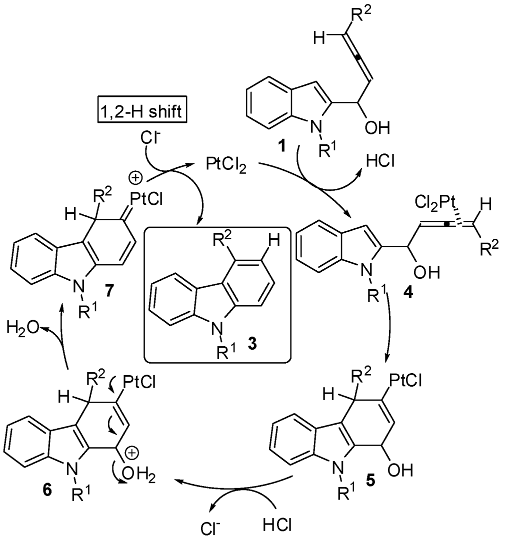


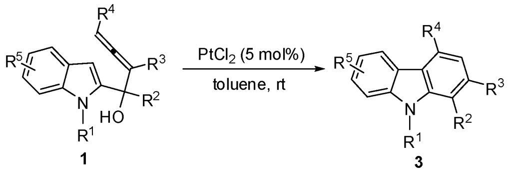
Fig. 1 ORTEP representation of product **3g**.



Scheme 2 Proposed mechanism.

In conclusion, we have developed a simple and mild $PtCl_2$-catalyzed reaction of 1-(indol-2-yl)-2,3-allenols, providing an efficient route to differently substituted carbazoles in good isolated yields under very mild conditions. Due to the easy availability of the starting materials (see the ESI for details†)[8,9] and the potential of the products,[1–5] this method may be useful in organic synthesis and medicinal chemistry. Further studies

Table 2 $PtCl_2$-catalyzed cyclization reaction of 1-(indol-2-yl)-2,3-allenols



	1						
Entry	R^1	R^2	R^3	R^4	R^5	Time/h	Yield of **3** (%)
1	Et	H	H	n-C_5H_{11}	H (**1a**)	2	83 (**3a**)
2	Et	H	H	Me	H (**1b**)	2	86 (**3b**)
3	Et	Me	H	n-C_6H_{13}	H (**1c**)	2	81 (**3c**)
4	Et	H	H	n-C_6H_{13}	5-Me (**1d**)	2	75 (**3d**)
5	Et	H	H	n-C_6H_{13}	5-OMe (**1e**)	3	75 (**3e**)
6	Et	H	H	Bn	H (**1f**)	5	50 (**3f**)
7	Et	H	Ph	H	H (**1g**)	4	70 (**3g**)
8	Et	H	n-C_4H_9	H	H (**1h**)	3	74 (**3h**)
9	Me	H	Ph	H	H (**1i**)	4	81 (**3i**)
10	Me	H	n-C_4H_9	H	H (**1j**)	4	71 (**3j**)
11	Et	H	allyl	H	H (**1k**)	3	74 (**3k**)
12	Et	H	Ph	H	5-Me (**1l**)	17	70 (**3l**)
13	Ph	H	Ph	H	H (**1m**)	19	78 (**3m**)
14	Et	H	COOMe	H	H (**1n**)	36	67 (**3n**)
15	Et	H	$CONMe_2$	H	H (**1o**)	24	83 (**3o**)
16	Et	H	CH_2OH	H	H (**1p**)	23	64 (**3p**)
17	Et	H	CH_2OH	H	4-Me (**1q**)	20	81 (**3q**)
18	Et	H	CH_2OH	H	7-Me (**1r**)	21	68 (**3r**)
19	Et	H	H	H	H (**1s**)	4	70 (**3s**)

on the mechanism and synthetic applications of this reaction are being carried out in our laboratory.

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