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Catalyst-Dependent Stereodivergent and Regioselective Synthesis of Indole-Fused Heterocycles through Formal Cycloadditions of Indolyl-Allenes

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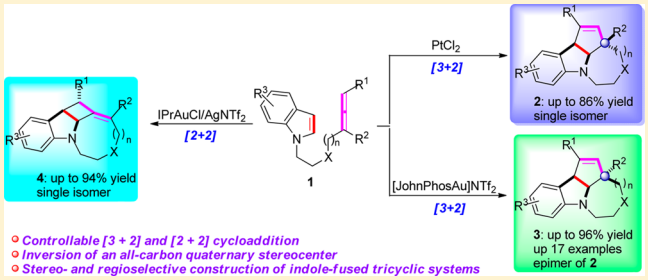
Supporting Information

ABSTRACT: Stereo- and regioselective construction of poly-heterocycles, especially those with several contiguous stereo-centers, is still a challenge. In this paper, catalyst-dependent stereodivergent and regioselective synthesis of indole-fused heterocycles through formal cycloadditions of indolyl-allenes has been developed. The reaction features total reversion of an all-carbon quaternary stereocenter when a gold or platinum complex was employed as the catalyst through [3 + 2] cycloaddition of allene with indole, affording different diazabenzo[*a*]cyclopenta[*cd*]azulenes as epimers, respectively. In addition, in the presence of IPrAuCl and $AgNTf_2$, highly regioselective *exo*-type [2 + 2] cycloaddition was observed, in which allene served as a 2C synthon. This methodology provides a simple and straightforward approach for the construction of indole-fused tricyclic systems under mild conditions in an atom-economical way.

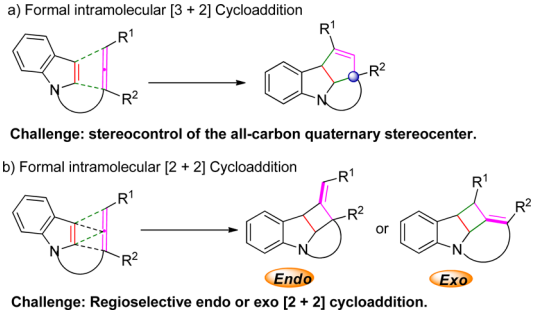


INTRODUCTION

Indole fused poly-heterocycles, as constituents of diverse natural alkaloids and pharmaceutical agents, have drawn much attention of organic and bioorganic chemists during the past several decades.[1] In the realm on the development of synthetic methodology toward such compounds, intramolecular cycloaddition of allene as a 3C or 2C synthon with indole is a viable strategy to achieve this goal. Indeed, several elegant works have been done using allenes as three-carbon components in transition-metal-catalyzed [3 + *n*] cyclo-addition.[2] For instance, Gagosz and co-workers started the pioneering work by reporting a formal Au-catalyzed [3 + 2] intramolecular cyclization of enynyl acetates, which went through allenyl ester intermediates.[3] Zhang et al. showed a Pt-catalyzed [3 + 2] annulation of allenyl esters generated in situ via a 3,3-rearrangement of propargyl precursors.[4] Addi-tionally, under varied reaction conditions, the alternative [2 + 2] and [4 + 2] cycloadditions could be selectively induced, in which the employed allenes reacted with other substances through one of the two double bonds.[5] On the basis of these elegant studies as well as our ongoing efforts in exploring novel synthetic routes for indole-fused scaffolds,[6] we envisaged that indolyl-allene substrates **1** could undergo a certain cyclo-addition under Au or Pt catalysis.[7,8]

However, due to the multiple reactive sites of allenes, there are several significant challenges to realize the desired reaction with respect to chemo- and stereoselectivity. As for the intramolecular [3 + 2] cycloaddition, to stereocontrol the all-carbon quaternary stereocenter is very difficult (Scheme 1a). Moreover, it is also troublesome to regioselectively control the *endo*- or *exo*-type in [2 + 2] cycloaddition (Scheme 1b). In addition, the competition of [3 + 2] and [2 + 2] cycloadditions remains the third one. Thus far, none of the reactions through a particular starting material aimed to tackle all of these challenges has been reported. Herein, we present novel

Scheme 1. Formal Intramolecular Cycloaddition Modes of Allenes with Indoles

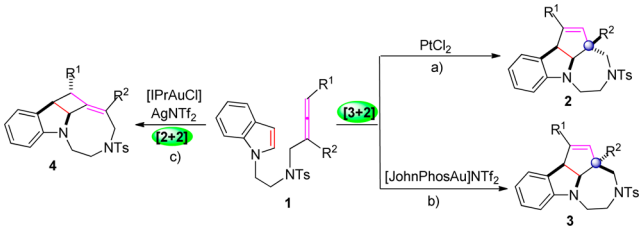


Received: February 25, 2015
Published: June 5, 2015

DOI: 10.1021/jacs.5b02080
J. Am. Chem. Soc. 2015, 137, 8131−8137

examples on the controllable [3 + 2] and [2 + 2] cycloaddition of indolyl-allenes **1**, affording divergent synthesis of indole-fused heterocycles **2**, **3**, and **4**: the all-carbon quaternary stereocenter in products **2** and **3** could be controlled by employing different Au or Pt catalysts, respectively (Scheme 2a and b), while the *exo*-type [2 + 2] cycloaddition was realized in the presence of the [IPrAuCl]/$AgNTf_2$ catalytic system (Scheme 2c).

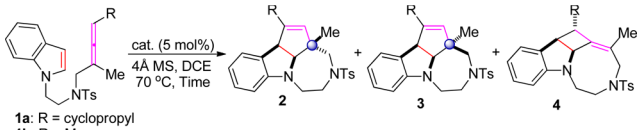
Scheme 2. Controllable Au- and Pt-Catalyzed Cycloaddition of Indolyl-Allenes



RESULTS AND DISCUSSION

We first investigated the reaction of *N*-(2-(1*H*-indol-1-yl)-ethyl)-*N*-(4-cyclopropyl-2-methylbuta-2,3-dien-1-yl)-4-methylbenzenesulfonamide **1a** in the presence of various catalysts, and the results are summarized in Table 1. Initially, the use of $PtCl_2$ afforded the [3 + 2] cycloadduct **2a** in 86% isolated yield as a single isomer (Table 1, entry 1). Unexpectedly, when [IPrAuCl]/$AgNTf_2$ was employed as the catalyst, the diazabenzo[*a*]cyclopenta[*cd*]azulene **3a** was obtained in 62% yield along with the [2 + 2] cycloadduct **4a** in 25% yield (Table 1, entry 2). Notably, **3a** was the epimer of **2a**, which aroused our interest in exploring these diverse reaction patterns. The control experiment indicated that $AgNTf_2$ had no catalytic activity in this reaction (Table 1, entry 3). Then, in the presence of [Ph_3PAuCl]/$AgNTf_2$, the [2 + 2] cycloadduct **4a** was obtained in 26% yield along with 72% of starting material **1a** (Table 1, entry 4). Replacing [Ph_3PAuCl]/$AgNTf_2$ with [Me_3PAuCl]/$AgNTf_2$ gave similar reaction outcomes (Table 1, entry 5). Subsequent gold catalyst screening revealed that [JohnPhosAuCl]/$AgNTf_2$ exhibited the best catalytic performance, furnishing the desired adduct **3a** in 95% yield (Table 1, entries 6–8). Further examination of silver salts disclosed that $AgNTf_2$ was the best choice for the formation of **3a** (Table 1, entries 8–10). As expected, the use of [JohnPhosAu]NTf_2 produced the corresponding product **3a** in 93% isolated yield (Table 1, entry 11). To our delight, the reaction of **1b** afforded the desired [2 + 2] cycloadduct **4b** in 85% isolated yield when [IPrAuCl]/$AgNTf_2$ was employed as a catalyst (Table 1, entry 12). Thus, the different reaction conditions for selective synthesis of **2**, **3**, and **4** have been smoothly optimized, respectively (Table 1, entries 1, 11, and 12). The structures of **2a**, **3a**, and **4a** have been unequivocally confirmed by X-ray diffractions.[9]

Table 1. Optimization of Conditions for Transition-Metal-Catalyzed Cycloaddition Reactions



1a: R = cyclopropyl
1b: R = Me

entry[a]	1	catalyst	time [h]	yield [%][b] 2	3	4
1	*1a*	*$PtCl_2$*	*12*	*2a, 86[c]*	*3a, 0*	*4a, 0*
2	1a	[IPrAuCl]/$AgNTf_2$	12	2a, 0	3a, 62	4a, 25
3	1a	$AgNTf_2$	12	2a, 0	3a, 0	4a, 0
4[d]	1a	[Ph_3PAuCl]/$AgNTf_2$	12	2a, 0	3a, trace	4a, 26
5[e]	1a	[Me_3PAuCl]/$AgNTf_2$	12	2a, 0	3a, trace	4a, 20
6	1a	[CySPhosAuCl]/$AgNTf_2$	6	2a, 0	3a, 67	4a, 26
7	1a	[CyJohnPhosAuCl]/$AgNTf_2$	6	2a, 0	3a, 73	4a, 20
8	1a	[JohnPhosAuCl]/$AgNTf_2$	6	2a, 0	3a, 95	4a, 5
9	1a	[JohnPhosAuCl]/AgOTf	6	2a, 0	3a, 94	4a, 4
10	1a	[JohnPhosAuCl]/$AgSbF_6$	6	2a, 0	3a, 86	4a, 7
11	*1a*	*[JohnPhosAu]NTf_2*	*6*	2a, 0	*3a, 95 (93)[c]*	*4a, 4*
12	*1b*	*[IPrAuCl]/$AgNTf_2$*	*12*	2b, 0	*3b, trace*	*4b, 85[c]*

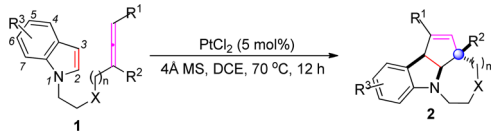
[a]The reaction was conducted with **1** (0.1 mmol) and 50 mg of 4 Å MS in DCE (1.0 mL). [b]NMR yield using 1,3,5-trimethoxybenzene as the internal standard. [c]Isolated yield. [d]72% of starting material **1a** was observed. [e]78% of starting material **1a** was observed.

With the optimal reaction conditions in hand, we next sought to expand the substrate scope of this platinum-catalyzed cyclization. As can be seen from Table 2, the substrate scope of this synthetic protocol was broad. For substrates **1b**–**1h** bearing various R^1 and R^2 substituents, the reactions proceeded smoothly to deliver the functionalized diazabenzo[*a*]-cyclopenta[*cd*]azulenes **2b**–**2h** in 54–85% yields (Table 2, entries 1–7), while a messy reaction result was observed when substrate **1i** was examined, presumably due to the steric hindrance of the 2,4,6-trimethylphenyl group (R^2) (Table 2, entry 8). Substrate **1j** with a longer carbon tether (n = 2) was also suitable for this cycloaddition, giving the desired eight-membered heterocyclic adduct **2j** in 79% yield (Table 2, entry 9). At the same time, the corresponding heterocyclic product **2k** was also obtained in 79% yield when **1k** bearing a NBs group (Bs = 4-bromobenzenesulfonyl) was utilized as the substrate (Table 2, entry 10). Substrate **1l** with an oxygen linker provided the desired adduct **2l** in 30% yield (Table 2, entry 11), while **1m** with a carbon linker gave a messy reaction result (Table 2, entry 12). In the cases of substrates **1n**–**1q**, the electronic properties of R^3 had no significant impact on the reaction outcomes and the desired cycloadducts **2n**–**2q** were furnished in 60–72% yields (Table 2, entries 13–15).

Furthermore, the formation of epimeric product **3a** in the presence of [JohnPhosAu]NTf_2 inspired us to explore the substrate generality, and the results are exhibited in Table 3. Among a diverse array of tosylamide-linked substrates **1b**–**1h** (X = NTs), different R^1 and R^2 groups were tested, giving the desired [3 + 2] annulation products **3b**–**3h** in 23–74% yields along with the [2 + 2] cycloadducts **4b**–**4h** in 13–54% yields (Table 3, entries 1–7), while for substrate **1i** bearing a large 2,4,6-trimethylphenyl group (R^2), the [3 + 2] cycloadduct **3i** was obtained in 21% yield along with 71% of starting material **1i** (Table 3, entry 8). As for substrate **1j**, the corresponding eight-membered heterocyclic product **3j** was delivered in 88% yield (Table 3, entry 9). Moreover, for substrate **1k** with X as the NBs anchor, the corresponding product **3k** was obtained in 91% yield (Table 3, entry 10), while substrates **1l** and **1m** with oxygen and carbon linkers provided the desired adducts **3l** and **3m** successfully as well, albeit in relatively low yields (Table 3, entries 11–12). In addition, substrates **1n** and **1r**–**1u** with a series of substituents on the indole ring (R^3) were also well-tolerated, furnishing the corresponding diazabenzo[*a*]-cyclopenta[*cd*]azulenes **3n**–**3r** in 88–96% yields (Table 3, entries 13–17).

DOI: 10.1021/jacs.5b02080
J. Am. Chem. Soc. 2015, 137, 8131–8137

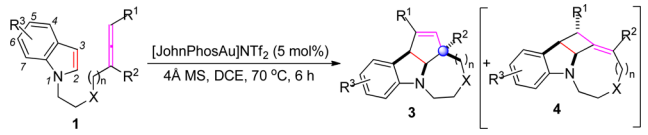
Table 2. Substrate Scope for Pt-Catalyzed [3 + 2] Cyclization



entry[a]	1	X	n	R^1	R^2	R^3	2, yield[b] (%)
1	**1b**	NTs	1	Me	Me	H	**2b**, 71
2	**1c**	NTs	1	Et	Me	H	**2c**, 81
3	**1d**	NTs	1	^{n}Pr	Me	H	**2d**, 62
4	**1e**	NTs	1	cyclobutyl	Me	H	**2e**, 85
5	**1f**	NTs	1	CH_2CH_2Ph	Me	H	**2f**, 54
6	**1g**	NTs	1	cyclopropyl	Et	H	**2g**, 69
7	**1h**	NTs	1	cyclopropyl	^{n}Bu	H	**2h**, 56
8	**1i**	NTs	1	cyclopropyl	2,4,6-TriMePh	H	**2i**, complex
9	**1j**	NTs	2	cyclopropyl	Me	H	**2j**, 79
10	**1k**	NBs	1	cyclopropyl	Me	H	**2k**, 79
11[c]	**11**	O	1	cyclopropyl	Me	H	**21**, 30
12	**1m**	C	1	cyclopropyl	Me	H	**2m**, complex
13	**1n**	NTs	1	cyclopropyl	Me	5-OMe	**2n**, 71
14	**1o**	NTs	1	Et	Me	5-CI	**2o**, 66
15	**1p**	NTs	1	Et	Me	6-F	**2p**, 72
16	**1q**	NTs	1	Et	Me	7-Me	**2q**, 60

[a]The reaction was conducted with **1** (0.1 mmol), $PtCI_2$ (5 mol %), and 50 mg of 4 Å MS in DCE (1.0 mL). [b]Isolated yield. [c]10 mol % Tris(pentafluorophenyl)phosphine was added.

Table 3. Substrate Scope for Au-Catalyzed [3 + 2] Cycloaddition



							yield[b] (%)	
entry[a]	1	X	n	R^1	R^2	R^3	3	4
1[c]	**1b**	NTs	1	Me	Me	H	**3b**, 74	**4b**, 18
2[c]	**1c**	NTs	1	Et	Me	H	**3c**, 61	**4c**, 27
3[c]	**1d**	NTs	1	^{n}Pr	Me	H	**3d**, 40	**4d**, 21
4	**1e**	NTs	1	cyclobutyl	Me	H	**3e**, 70	**4e**, 21
5	**1f**	NTs	1	CH_2CH_2Ph	Me	H	**3f**, 23	**4f**, 54
6	**19**	NTs	1	cyclopropyl	Et	H	**3g**, 71	**4g**, 13
7	**1h**	NTs	1	cyclopropyl	^{n}Bu	H	**3h**, 52	**4h**, 26
8[d]	**1i**	NTs	1	cyclopropyl	2,4,6-TriMePh	H	**3i**, 21	n. d.[e]
9	**1j**	NTs	2	cyclopropyl	Me	H	**3j**, 88	n. d.
10	**1k**	NBs	1	cyclopropyl	Me	H	**3k**, 91	n. d.
11	**11**	O	1	cyclopropyl	Me	H	**31**, 60	n. d.
12	**1m**	C	1	cyclopropyl	Me	H	**3m**, 38	n. d.
13	**1n**	NTs	1	cyclopropyl	Me	5-OMe	**3n**, 96	n. d.
14	**1r**	NTs	1	cyclopropyl	Me	5-CI	**3o**, 92	n. d.
15	**1s**	NTs	1	cyclopropyl	Me	6-F	**3p**, 91	n. d.
16	**1t**	NTs	1	cyclopropyl	Me	7-Me	**3q**, 92	n. d.
17	**1u**	NTs	1	cyclopropyl	Me	7-Br	**3r**, 88	n. d.

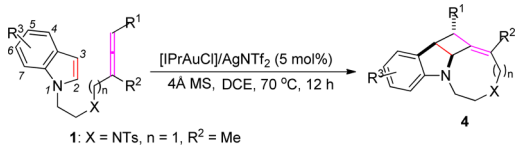
[a]The reaction was conducted with **1** (0.1 mmol), [IPrAuCI]/$AgNTf_2$ (5 mol %), and 50 mg of 4 Å MS in DCE (1.0 mL). [b]Isolated yield. [c]$[Ph_3PAu]NTf_2$ was used as the catalyst. [d]71% of starting material **1i** was observed. [e]Not determined.

Notably, in the presence of [IPrAuCl]/$AgNTf_2$, the alternative [2 + 2] cyclization could be exclusively achieved with a broad substrate scope (Table 4). Accordingly, the intriguing eight-membered diazoheterocyclic ring compounds **4b**–**4k** with a diverse array of R^1 and R^3 groups could be easily obtained in 74–94% yields.

Furthermore, under the standard conditions, different reaction pathways could occur when substrates **1v** and **1w** were utilized. As shown in Scheme 3, as for substrate **1v**, in which the indole functional group was replaced by a pyrrole group, an intramolecular Friedel–Crafts reaction[10] took place smoothly, providing the seven-membered diazoheterocyclic ring product **5** in 95% yield.[9] At the same time, when substrate

DOI: 10.1021/jacs.5b02080
J. Am. Chem. Soc. 2015, 137, 8131–8137

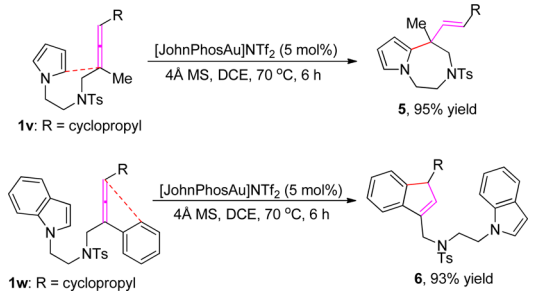
Table 4. Scope of Au-Catalyzed [2 + 2] Cycloaddition



entry[a]	1	R^1	R^3	4, yield[b] (%)
1	**1b**	Me	H	**4b**, 85
2	**1c**	Et	H	**4c**, 88
3	**1d**	^{n}Pr	H	**4d**, 83
4	**1f**	CH_2CH_2Ph	H	**4f**, 74
5	**1o**	Et	5-CI	**4i**, 91
6	**1p**	Et	6-F	**4j**, 94
7	**1q**	Et	7-Me	**4k**, 83

[a]The reaction was conducted with **1** (0.1 mmol), [IPrAuCl]/$AgNTf_2$ (5 mol %), and 50 mg of 4 Å MS in DCE (1.0 mL). [b]Isolated yield.

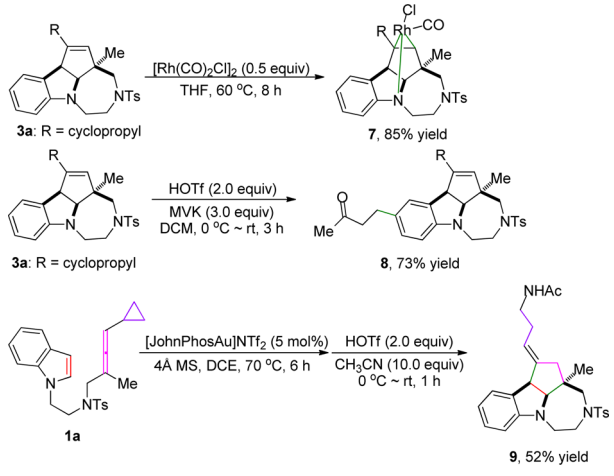
Scheme 3. Different Pathways of Other Substrate 1 under the Standard Conditions



1w with a phenyl group on the allene moiety was employed, a varied intramolecular Friedel–Crafts reaction[10] between the phenyl group and the allene moiety took place, affording the corresponding product **6** in 93% yield.[9]

To illustrate the synthetic utility, several transformations of product **3** were conducted (Scheme 4). Interestingly, a Rh-complex **7** was obtained in 85% yield upon treatment of **3a** with $[Rh(CO)_2Cl]_2$ in THF at 60 °C. **3a** could also be transformed into compound **8** in 73% yield through a conjugate addition with HOTf (trifluoromethanesulfonic acid) and MVK (methyl vinyl ketone) in DCM. Moreover, a one-pot tandem reaction to transform **1a** into compound **9**[9] could be realized in 52% yield

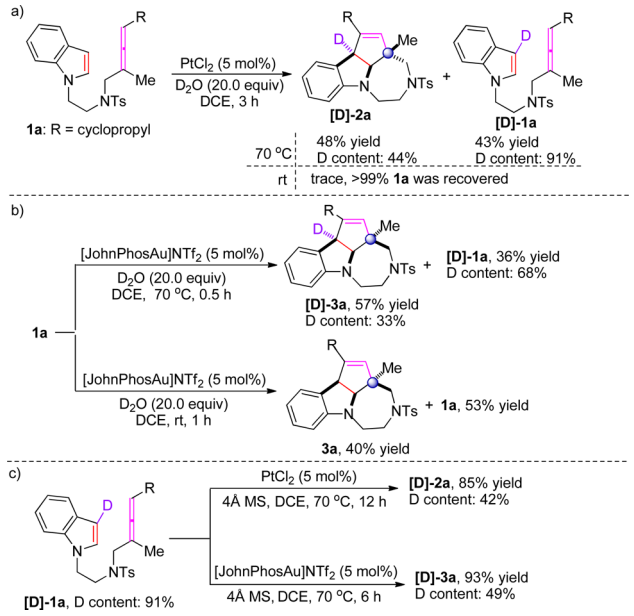
Scheme 4. Transformations of Product 3a



in the presence of [JohnPhosAu]NTf_2 and followed by treatment with HOTf and CH_3CN (for more related transformations of **3**, see Scheme SI-1 in the Supporting Information).

To verify the Au- and Pt-catalyzed [3 + 2] cycloaddition reaction pathways, deuterium labeling experiments were performed, as shown in Scheme 5. First, treating **1a** with

Scheme 5. Isotopic Labeling Experiments

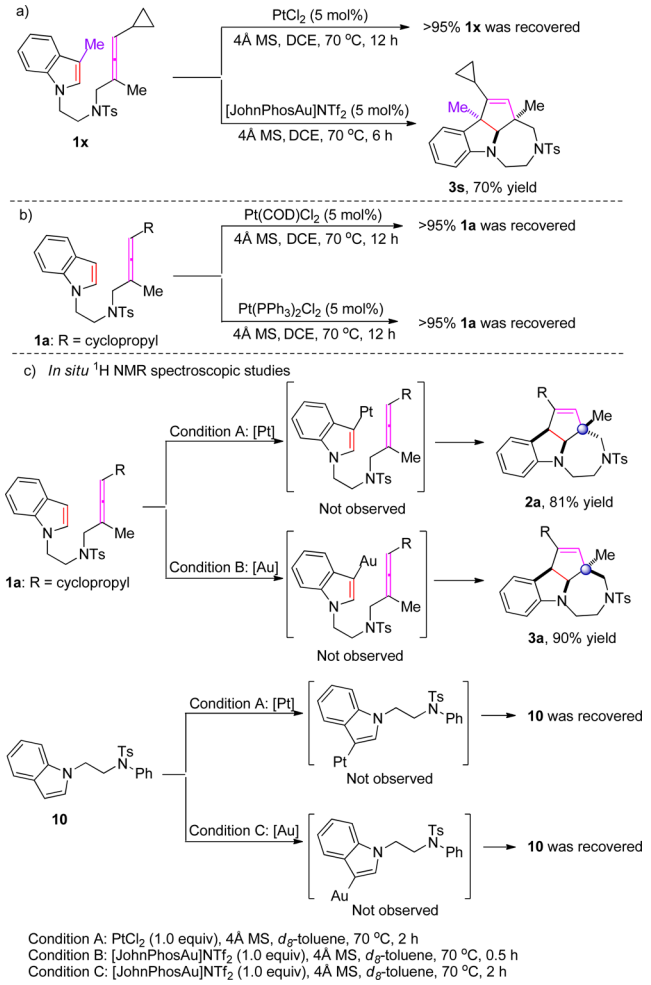


$PtCl_2$ or [JohnPhosAu]NTf_2 at 70 °C in the presence of D_2O (20.0 equiv), deuterated products [D]-**2a** and [D]-**3a** could be formed, suggesting the formation of a metallo-carbon intermediate (Scheme 5a and b).[11] While conducting the reactions at 25 °C (room temperature), $PtCl_2$ showed very low catalytic activity (Scheme 5a). In gold catalysis, **3a** was obtained in 40% yield but with no deuterium corporation at 25 °C, indicating that the gold complex prefers to coordinate with the allene moiety instead of C-3 metalation of indole (Scheme 5b). Then, by using [D]-**1a** in the presence of Pt and Au catalysts, the corresponding adducts [D]-**2a** and [D]-**3a** were obtained in 85% yield with 42% D and 93% yield with 49% D content at 70 °C, respectively (Scheme 5c). Furthermore, the different reaction results of substrate **1i** under Pt or Au catalysis also revealed that there might be two different reaction mechanisms (Table 2, entry 8 vs Table 3, entry 8).

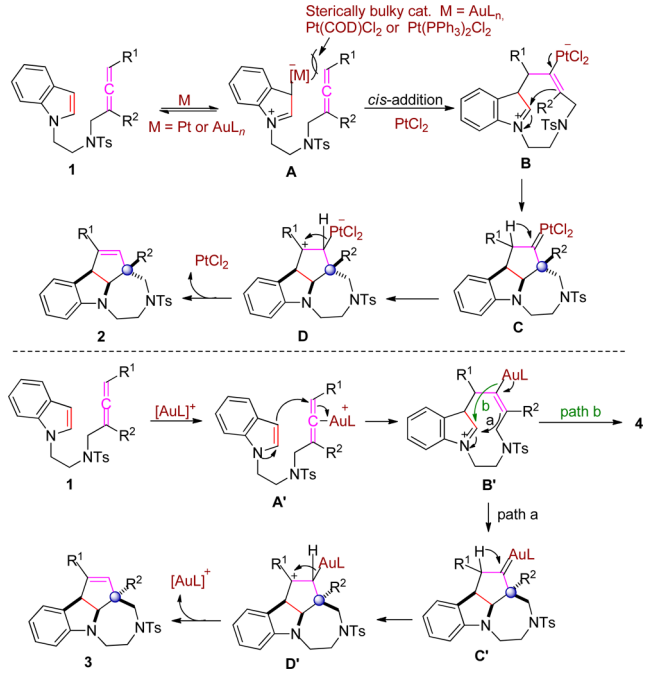
To further verify these cycloaddition reaction mechanisms, several control experiments were also performed and the results are shown in Scheme 6. First, when substrate **1x** with a methyl substituent at the C3 position of the indole ring was examined under the standard reaction conditions, no desired product was detected in the presence of $PtCl_2$, while cycloadduct **3s** was obtained in 70% yield under gold catalysis, which suggested the different catalytic behavior of Pt and Au catalysts (Scheme 6a). Then, when substrate **1a** was examined by employing $Pt(COD)Cl_2$ or $Pt(PPh_3)_2Cl_2$ as the catalyst, no desired product was obtained, probably due to the steric effect of catalysts (Scheme 6b). Furthermore, we have also treated substrate **1a** and the newly synthesized substrate **10** with stoichiometric $PtCl_2$ or [JohnPhosAu]NTf_2 in nuclear magnetic tubes respectively, so as to find direct evidence of the

DOI: 10.1021/jacs.5b02080
J. Am. Chem. Soc. 2015, 137, 8131–8137

Scheme 6. Control Experiments



Scheme 7. Proposed Mechanisms for Au- and Pt-Catalyzed Cycloadditions



corresponding metallo-carbon intermediates (Scheme 6c). However, no metallo-carbon intermediate was observed through ^{1}H NMR spectroscopic analysis in the nuclear magnetic resonance spectrometer at 70 °C, presumably due to the fact that the equilibrium largely leans to the starting materials **1a** or **10** with metal catalyst and a very small trace of the metallo-carbon intermediate was formed (see SI-151−SI-154 in the Supporting Information). At the same time, the desired adducts **2a** and **3a** were obtained in 81% yield and 90% yield, respectively, when substrate **1a** was examined (for more information, see SI-155 in the Supporting Information).

Although the full mechanistic details of these transformations remain to be elucidated, plausible mechanisms for the reactions are outlined in Scheme 7 on the basis of the above deuterium labeling and control experiments and previous reports to date.[2−4,11,12] For [3 + 2] annulation, both platinum and gold can form a metallo-carbon intermediate **A** via reversible C-3 metalation of indole. The following *cis*-addition to give heterocyclic intermediate **B** only takes place when $PtCl_2$ is used presumably due to the fact that gold complexes are sterically hindered. The lack of catalytic activity of $Pt(COD)Cl_2$ and $Pt(PPh_3)_2Cl_2$ is in accordance with this proposal as well. Then, a Pt-carbene intermediate **C** is generated, following by 1,2-hydride migration and regeneration of catalyst to yield product **2**. As for gold-catalyzed reactions, the coordination of gold complex with allene is a dominant process, though the formation of intermediate **A** is possible. The intramolecular nucleophilic attack of indole (C3) onto the Au-activated allene **A′** forms the alkenylgold(I) complex **B′**, which diverges into different products. On one hand, similar to Pt catalysis, the desired adduct **3** is formed by tandem cyclization, hydride migration, and an elimination process through Au-carbene intermediate **C′** and cationic intermediate **D′** (path a). The all-carbon quaternary stereocenters in products **2** and **3** were stereoselectively constructed presumably due to the different *E* and *Z* configurations of alkenylmetal complexes **B** and **B′**. On the other hand, cyclobutane compound **4** is formed via a nucleophilic trap of the iminum intermediate by the C−Au bond (path b). Substrates with a cyclopropyl group (R^1) tend to give [3 + 2] cycloadducts **3** probably because the three-membered ring can significantly stabilize the cationic intermediate **D′**, while substrates with a larger R^2 group disfavored the formation of a metal−carbene intermediate **C** or **C′**, which led to a lower yield of **2** and **3**. In addition, the ligands of the gold complex as well as the steric and electronic properties of the R^1 and R^2 groups make a combined influence on the selective formation of **3** and **4**.

■ CONCLUSION

We have disclosed the catalyst-dependent stereodivergent and regioselective synthesis of an indole-fused tricyclic system with several contiguous stereocenters through formal cycloadditions of indolyl-allenes in an atom-economical way. The reaction features total reversion of an all-carbon quaternary stereocenter when a gold or platinum complex was employed as the catalyst through [3 + 2] cycloaddition of allene with indole, affording different diazabenzo[*a*]cyclopenta[*cd*]azulenes as epimers, respectively. In addition, in the presence of IPrAuCl and $AgNTf_2$, highly regioselective *exo*-type [2 + 2] cycloaddition was observed, in which the allene moiety acted as a 2C synthon. Different reaction mechanisms have also been proposed on the basis of deuterium labeling and control experiments. Further investigations on expanding the scope of this reaction toward a

DOI: 10.1021/jacs.5b02080
J. Am. Chem. Soc. 2015, 137, 8131−8137

variety of novel and potentially useful polycyclic compounds as well as the applications of this protocol to natural product synthesis are in progress.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of Product 2. To a flame-dried Schlenk tube was added indolyl-allene 1 (0.1 mmol), $PtCl_2$ (0.005 mmol, 5 mol %), 50 mg of 4 Å MS, and the anhydrous solvent DCE (1.0 mL) under argon. Then, the resulting solution was allowed to stir at 70 °C for 12 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel to give the desired product **2**.

Compound ***2a***. A white solid, 86% yield (36 mg). Mp 175−178 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.45−0.51 (m, 1H, CH_2), 0.61−0.67 (m, 1H, CH_2), 0.72 (s, 3H, CH_3), 0.75−0.88 (m, 2H, CH_2), 1.50−1.58 (m, 1H, CH), 2.42 (s, 3H, CH_3), 2.46 (dd, J = 11.6 Hz, 11.6 Hz, 1H, CH_2), 3.16 (dd, J = 11.6 Hz, 15.6 Hz, 1H, CH_2), 3.50 (dd, J = 11.6 Hz, 12.4 Hz, 1H, CH_2), 3.61 (dd, J = 4.0 Hz, 12.4 Hz, 1H, CH_2), 3.85 (dd, J = 11.6 Hz, 11.6 Hz, 1H, CH_2), 4.05 (d, J = 8.8 Hz, 1H, CH), 4.18 (d, J = 8.8 Hz, 1H, CH), 4.25 (dd, J = 4.0 Hz, 15.6 Hz, 1H, CH_2), 5.10 (s, 1H, =CH), 6.28 (d, J = 7.6 Hz, 1H, ArH), 6.64 (dd, J = 7.6 Hz, 7.6 Hz, 1H, ArH), 7.08 (dd, J = 7.6 Hz, 7.6 Hz, 1H, ArH), 7.18 (d, J = 7.6 Hz, 1H, ArH), 7.31 (d, J = 8.0 Hz, 2H, ArH), 7.66 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 5.9, 7.9, 11.7, 21.5, 23.6, 46.3, 48.3, 52.6, 54.2, 57.6, 74.7, 105.0, 117.3, 123.8, 126.9, 127.5, 128.0, 129.76, 129.8, 136.4, 143.3, 147.0, 152.2. IR (CH_2Cl_2) ν 3033, 2922, 2852, 1728, 1601, 1481, 1456, 1378, 1331, 1303, 1281, 1249, 1234, 1184, 1156, 1118, 1091, 1073, 1019, 1003, 974, 924, 906, 876, 814, 765, 733, 708, 699, 660 cm^{-1}. HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_2S^{1+}$ $(M + H)^+$ Requires 421.1944, Found 421.1943.

General Procedure for the Synthesis of Products 3, 5, and 6. To a flame-dried Schlenk tube was added indolyl-allene **1** (0.1 mmol), [JohnPhosAu]NTf_2 (0.005 mmol, 5 mol %), 50 mg of 4 Å MS, and the anhydrous solvent DCE (1.0 mL) under argon. Then, the resulting solution was allowed to stir at 70 °C for 6 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel to give the desired cycloadducts **3**, **5**, or **6**.

Compound ***3a***. A white solid, 93% yield (39 mg). Mp: 130−133 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.32−0.43 (m, 2H, CH_2), 0.65−0.73 (m, 2H, CH_2), 1.28−1.36 (m, 4H, CH, CH_3), 2.41 (s, 3H, CH_3), 2.53 (d, J = 13.2 Hz, 1H, CH_2), 2.60 (ddd, J = 2.4 Hz, 12.0 Hz, 14.4 Hz, 1H, CH_2), 3.16 (ddd, J = 2.4 Hz, 12.0 Hz, 14.4 Hz, 1H, CH_2), 3.54 (d, J = 13.2 Hz, 1H, CH_2), 3.75 (dd, J = 14.4 Hz, 14.4 Hz, 1H, CH_2), 3.83 (dd, J = 12.0 Hz, 12.0 Hz, 1H, CH_2), 3.88 (d, J = 8.4 Hz, 1H, CH), 4.40 (d, J = 8.4 Hz, 1H, CH), 4.84 (s, 1H, =CH), 6.26 (d, J = 8.0 Hz, 1H, ArH), 6.60 (dd, J = 8.0 Hz, 8.0 Hz, 1H, ArH), 7.02 (dd, J = 8.0 Hz, 8.0 Hz, 1H, ArH), 7.21 (d, J = 8.0 Hz, 1H, ArH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 7.64 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 6.8, 7.4, 9.8, 21.7, 25.2, 50.1, 51.2, 55.0, 55.6, 57.5, 79.8, 105.5, 117.1, 125.0, 126.8, 127.4, 128.0, 129.3, 130.0, 135.3, 143.6, 147.0, 150.5. IR (CH_2Cl_2) ν 3022, 2919, 2842, 1730, 1601, 1484, 1452, 1369, 1336, 1288, 1272, 1189, 1160, 1129, 1089, 1013, 957, 942, 904, 870, 814, 737, 723, 661 cm^{-1}. HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_2S^{1+}$ $(M + H)^+$ Requires 421.1944, Found 421.1945.

General Procedure for the Synthesis of Product 4. A solution of [IPrAuCl] (0.005 mmol, 5 mol %) and $AgNTf_2$ (0.005 mmol, 5 mol %) in DCE (0.5 mL) was stirred at room temperature under an argon atmosphere for 15 min. To the solution was added a solution of indolyl-allenes **1** (0.1 mmol) in DCE (0.5 mL), and the reaction mixture was stirred at 70 °C for 12 h. The mixture was concentrated in vacuo to yield the crude product, which was purified by flash chromatography on silica gel to furnish the desired adduct **4** as a solid.

Compound ***4a***. A white solid, 26% yield (11 mg). Mp: 131−134 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.19−0.31 (m, 2H, CH_2), 0.50−0.65 (m, 2H, CH_2), 1.06−1.12 (m, 1H, CH), 1.48 (s, 3H, CH_3), 2.38−2.45 (m, 4H, CH, CH_3), 2.69 (ddd, J = 3.6 Hz, 7.6 Hz, 11.6 Hz, 1H, CH_2), 2.96 (d, J = 17.2 Hz, 1H, CH_2), 3.44−3.48 (m, 2H, CH_2), 3.66 (dd, J = 3.2 Hz, 8.4 Hz, 1H, CH), 3.86 (ddd, J = 2.8 Hz, 4.4 Hz, 7.6 Hz, 1H, CH_2), 4.23 (d, J = 17.2 Hz, 1H, CH_2), 5.14 (d, J = 8.4 Hz, 1H, CH), 6.29 (d, J = 8.0 Hz, 1H, ArH), 6.57 (dd, J = 8.0 Hz, 8.0 Hz, 1H, ArH), 6.99−7.04 (m, 2H, ArH), 7.34 (d, J = 8.4 Hz, 2H, ArH), 7.72 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 3.1, 6.1, 15.8, 16.6, 21.8, 45.1, 45.7, 52.0, 54.4, 56.6, 64.8, 105.9, 117.2, 124.9, 126.9, 127.4, 128.0, 130.1, 132.5, 135.7, 139.3, 143.8, 151.9. IR (CH_2Cl_2) ν 3044, 2922, 2842, 1726, 1603, 1486, 1459, 1444, 1376, 1357, 1338, 1267, 1184, 1158, 1111, 1090, 1013, 917, 876, 815, 737, 706, 655 cm^{-1}. HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_2S^{1+}$ $(M + H)^+$ Requires 421.1944, Found 421.1947.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, NMR spectra, and crystallographic data (CIF). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b02080.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful for the financial support from the National Basic Research Program of China (973)-2015CB856603, Shanghai Municipal Committee of Science and Technology (11JC1402600), and the National Natural Science Foundation of China (20472096, 21372241, 21361140350, 20672127, 21421091, 21372250, 21121062, 21302203, and 20732008).

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