Tetrahedron 67 (2011) 4455–4466

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

[3+2] Cycloaddition of metal-containing azomethine ylides for highly efficient synthesis of mitosene skeleton

Jun Takaya, Yuichi Miyashita, Hiroyuki Kusama, Nobuharu Iwasawa *

Department of Chemistry, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152-8551, Japan

ARTICLE INFO

Article history:
Received 17 January 2011
Received in revised form 29 March 2011
Accepted 5 April 2011
Available online 13 April 2011

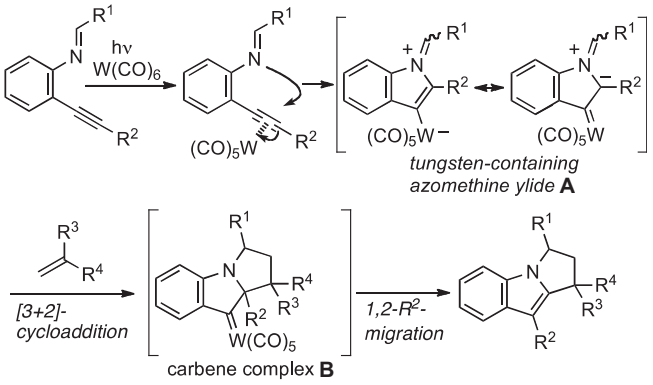
Keywords:
Indole synthesis
Azomethine ylide
Carbene complex
Electrophilic activation of alkyne
$PtCl_2$

ABSTRACT

Efficient synthesis of tricyclic indole derivatives bearing a substituent at the 3-position of the indole nucleus was achieved by the [3+2] cycloaddition reaction of transition metal-containing azomethine ylides derived from *N*-(*o*-alkynylphenyl)imines with vinyl ethers. Third-row transition metal complexes, especially $PtCl_2$, turned out to be highly efficient for the reaction of *internal* alkynes and *imidate* substrates with wide generality. Moreover, as strong support for the reaction mechanism, the intermediate Pt–carbene complex was found to undergo intramolecular C–H bond insertion reaction to give tetracyclic indoline derivatives when benzyl vinyl ether was employed as a dipolarophile. This protocol provided a facile synthesis of highly functionalized tricyclic indole derivatives found as the basic skeleton of the mitosene family, such as mitomycin C.

1. Introduction

The indole skeleton is an important core framework for pharmaceuticals, insecticides etc., and the development of concise methods for the synthesis of polycyclic indoles is highly desirable.[1] We have previously reported a novel method for the construction of polycyclic indole skeletons through $W(CO)_6$-promoted generation and reaction of metal-containing azomethine ylides.[2] These novel azomethine ylide species **A** are generated by the reaction of *N*-(*o*-ethynylphenyl)imine derivatives (R^1=Ph, OR) with a catalytic amount of $W(CO)_6$ under photoirradiation conditions, and they undergo [3+2] cycloaddition with electron-rich alkenes to give tungsten carbene complexes **B**.[3] 1,2-Migration of the substituent R^2 (R^2=H, alkyl, aryl) affords polycyclic indole derivatives with regeneration of the tungsten catalyst (Scheme 1). Importantly, this method is applicable to *internal* alkyne derivatives to give tricyclic indoles bearing a substituent R^2 at the 3-position of the indole nucleus, which is the basic structure often found in natural products, such as mitomycins (Fig. 1).[4,5] However, when internal alkyne substrates were employed, the efficiency of the tungsten catalyst was moderate and a stoichiometric amount of $W(CO)_6$ was necessary to bring the reaction to completion. Moreover, the reaction was limited to aldimine type substrates and inapplicable to imidate substrates, which would afford synthetically more useful products



Scheme 1.

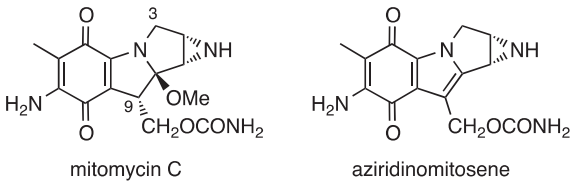


Fig. 1. Mitomycin C and its related compounds.

* Corresponding author. Tel.: +81 3 5734 2746; fax: +81 3 5734 2931; e-mail address: niwasawa@chem.titech.ac.jp (N. Iwasawa).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.04.017

possessing an *N*,*O*-acetal moiety (Fig. 2). Thus, it is highly desirable to develop efficient catalytic reactions generally applicable to *internal* alkynes and *imidate* substrates. In this paper, we describe excellent catalytic activity of third-row transition metal complexes, especially $PtCl_2$, for generation and reaction of metal-containing azomethine ylides with wide generality including *internal* alkynes and *imidate* substrates.[6,7] Reaction of highly functionalized metal-containing azomethine ylide and its synthetic application toward mitomycin C are also described. Moreover, intramolecular C–H insertion reaction of Pt–carbene intermediate to give tetracyclic indoline derivative is also demonstrated as a strong support of the reaction mechanism.

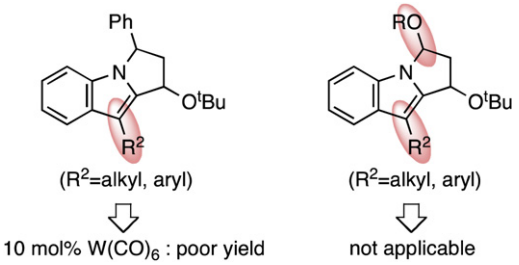


Fig. 2. Limitation of tungsten-promoted reaction.

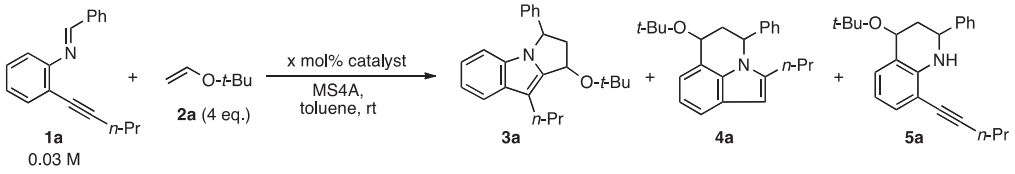
2. Results and discussion

2.1. Effect of various metal catalyst

We first investigated the reaction of a benzaldimine derivative **1a** bearing an *n*-propyl group on the alkyne terminus with *tert*-butyl vinyl ether **2a** in toluene by using various transition metal complexes, and the results are summarized in Table 1. Various metal complexes, such as Re(I), Ir(I), Pd(II), Pt(II), and Au(III) were found to catalyze this reaction efficiently, giving the [3+2] cyloaddition/1,2-Pr-migration product **3a** in good to excellent yields (entries 5,6,10,13,14,18,19).These metal complexes exhibited much higher catalytic activity than the tungsten carbonyl complex. The same mechanism is proposed for these reactions as that for $W(CO)_5(L)$-catalyzed reaction as depicted in Scheme 2. Electrophilic activation of the *internal* alkyne moiety by these metals induces nucleophilic, 5-*endo* cyclization of the imino nitrogen onto the alkyne moiety to generate the corresponding metal-containing azomethine ylides **A**. Successive [3+2] cycloaddition and 1,2-alkyl migration give tricyclic indole **3a** with regeneration of the catalyst, along with a small amount of formal [4+2] cycloadduct **4a**. Interestingly, the efficiency seemed to be roughly dependent on the 'row' and 'valence' of the metal complexes. Thus, molybdenum carbonyl gave the desired product **3a** in much lower yield than tungsten (entries 1 and 3), and except for Pd(II), the reactions with first- or second-row transition metal complexes, such as $MnBr(CO)_5$, $Ru_3(CO)_{12}$/hv, $[RhCl(cod)]_2$, and $NiCl_2$ resulted in no formation of the desired [3+2] cycloaddduct **3a** (entries 4,8,9, and 12).

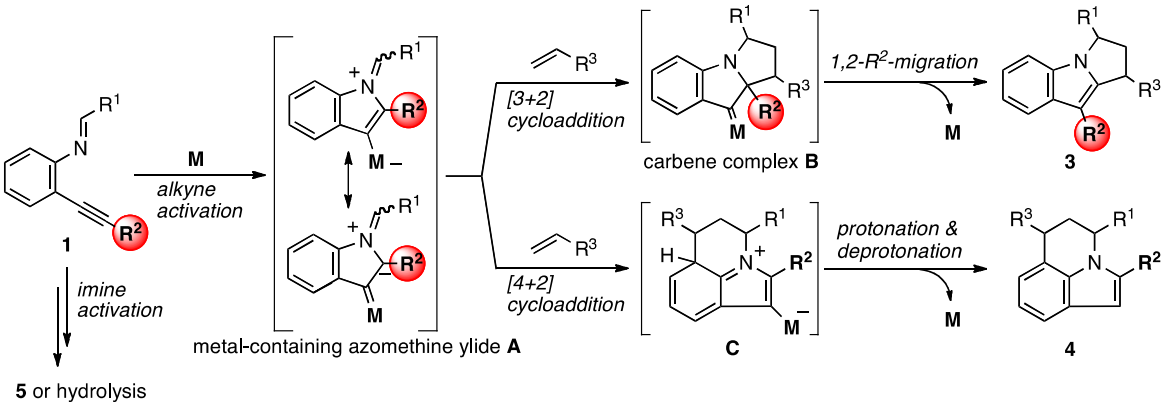
Even with third-row metals, high valent metal complexes, such as $ReCl_5$ and $IrCl_3$ tend to give hetero Diels–Alder cycloadduct **5a** through electrophilic activation of aldimine moiety (entries 7 and 11).[8] In addition, $PtCl_4$ showed lower catalytic activity and product selectivity ([3+2] vs [4+2]) than those of $PtCl_2$ (entries 14 and 15).[9] These results indicate that soft metal complexes, that is, low valent and third-row transition metal complexes, with moderate Lewis acidity activate the alkyne moiety efficiently and selectively and are the catalyst of choice for the present reaction.

Table 1
Screening of metal complexes



Entry	Catalyst	Loading of catalyst (mol %)	Time (h)	Yield of **3a** (%)	*cis*:*trans* (**3a**)	Yield of **4a** (%)	Yield of **5a** (%)
1[a]	$W(CO)_6/h\nu$	100	13	76	22:78	21[d]	0
2[a]		10	22	33	17:83	—	—
3	$Mo(CO)_6/h\nu$	100	16	15	21:79	4	0
4[b]	$Mn(CO)_5Br/h\nu$	10	12.5	0	—	0	0
5	$Re(CO)_5Cl/h\nu$	10	5.5	70	64:36	Trace	0
6	$Re(CO)_5Br/h\nu$	10	2.0	69	52:48	Trace	0
7	$ReCl_5$	10	2.0	0	—	0	94
8[b]	$Ru_3(CO)_{12}/h\nu$	3.5	11.5	0	—	0	0
9[b,c]	$[RhCl(cod)]_2$	5.0	26	0	—	0	0
10	$[IrCl(cod)]_2$	5.0	26	73	19:81	5[e]	0
11[b,c]	$IrCl_3$	10	29.5	0	—	0	13
12[b,c]	$NiCl_2$	9.0	29	0	—	0	0
13	$PdCl_2(CH_3CN)_2$	10	2.0	71	54:46	3[e]	0
14	$PtCl_2$	10	9.5	90	58:42	0	0
15	$PtCl_4$	10	24.5	57	49:51	29[e]	0
16	AuCl	10	29	49	55:45	3[e]	0
17[b]	$[Au(PPh_3)]SbF_6$[f]	10	30	42	58:42	2[e]	0
18	$AuCl_3$	10	1.2	82	57:43	3[e]	0
19	$AuBr_3$	10	0.5	70	53:47	6[e]	0

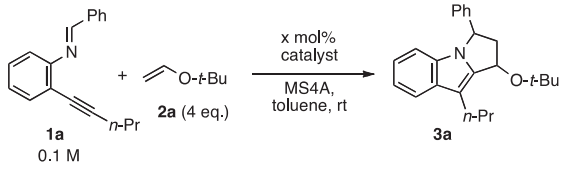
[a] Compound **2a** (10 equiv) was employed.
[b] Compound **1a** was recovered.
[c] Hydrolysis of **1a** proceeded to some extent.
[d] dr=94:6.
[e] Single isomer.
[f] Prepared from $AuCl(PPh_3)$ and $AgSbF_6$ in situ.



Scheme 2.

Further optimization of reaction conditions with reduced loading of the catalyst disclosed that $ReBr(CO)_5$, $PtCl_2$, and $AuBr_3$ have excellent catalytic activity in terms of product yield and reaction time.[10–12] The reaction was complete within 2.5 h at room temperature using only 3 mol % of $ReBr(CO)_5/h\nu$ or $AuBr_3$ to give the desired product **3a** in 77 or 80% yield (Table 2, entry 1 and 3).The loading of the catalyst was further reduced to 1 mol % without decreasing the yield of **3a** albeit a much longer reaction time (42 h) was required for completion with $AuBr_3$ catalyst (entry 2 and 4). $PtCl_2$-catalyzed reaction proceeded very slowly at room temperature with reduced loading of the catalyst (entry 5), and therefore the reaction was carried out at 50 °C with 3 mol % or 1 mol % of the catalyst to afford the product **3a** in high yield within an acceptable reaction time (entries 6 and 7). Importantly, product selectivity was also excellent and only a small amount of [4+2] cycloadduct **4a** was obtained in these reactions (less than 4%).

Table 2
Optimized conditions using $ReBr(CO)_5$, $AuBr_3$ or $PtCl_2$



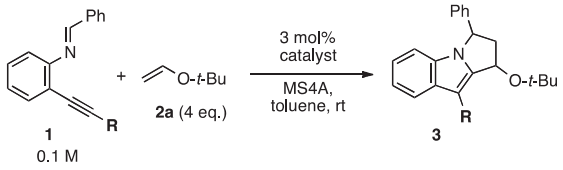
Entry	Catalyst	x	Temp (°C)	Time (h)	Yield of **3a** (%)	*cis*:*trans* (**3a**)
1	$ReBr(CO)_5/h\nu$	3.0	rt	2.5	77	56:44
2[a]	$ReBr(CO)_5/h\nu$	1.0	rt	2.5	69	57:43
3	$AuBr_3$	3.0	rt	2.5	80	58:42
4[b]	$AuBr_3$	1.0	rt	42	81	56:44
5	$PtCl_2$	3.0	rt	72	81	54:46
6	$PtCl_2$	3.0	50	6	89	51:46
7[a]	$PtCl_2$	1.0	50	16.5	74	38:62

[a] 0.3 M.
[b] 0.03 M.

2.2. Generality of the substituent on the alkyne terminus

With the efficient catalysts and reaction conditions in hand, generality of the substituent on the alkyne terminus of the aldimine was investigated. $AuBr_3$ and $PtCl_2$ catalyst showed wide generality of substrates under the same reaction conditions described above, and the results are summarized in Table 3. The reactions of methyl-substituted derivative **1b** (entry 1) and bulky cyclohexyl derivative **1c** (entry 3) proceeded smoothly to give tricyclic indoles possessing the corresponding alkyl group at the 3-position of the indole nucleus in high yield. In addition to alkyl, phenyl was also

Table 3
Reaction of various internal alkyne derivatives[a]



Entry	R		$ReBr(CO)_5/h\nu$		$AuBr_3$ at rt		$PtCl_2$ at 50 °C	
			Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)
1	Me	**1b**	3.0	89	22	81	3.5	88
2	*n*-Pr	**1a**	2.5	77	2.5	80	6.0	89
3	*c*-Hex	**1c**	3.0	0	2.0	89	35	84[b]
4	Ph	**1d**	—	—	0.5	62	7.0	84

[a] The dr of **3** varied in the range of *cis*:*trans*=23:77 to 73:27.
[b] Vinyl ether (10 equiv) was employed.

employable as a migrating group (entry 4). It should be noted that the rate of $AuBr_3$-catalyzed reaction increased as the substituent became bulkier, whereas the inverse tendency was observed in the $PtCl_2$-catalyzed reaction. This behavior may be suggestive of a change in rate-limiting step between these two catalysts since a bulkier substituent is expected to retard the formation of metal-containing azomethine ylide (Me<*n*-Pr<*c*-Hex), whereas 1,2-alkyl (or aryl) migration to the electron deficient carbene center would be accelerated by a more electron-rich substituent, such as secondary alkyl or especially aryl group (Me<*n*-Pr<*c*-Hex<Ph) (Fig. 3). On the other hand, $ReBr(CO)_5$-catalyzed reaction of cyclohexyl-substituted derivative **1c** resulted in no formation of the desired

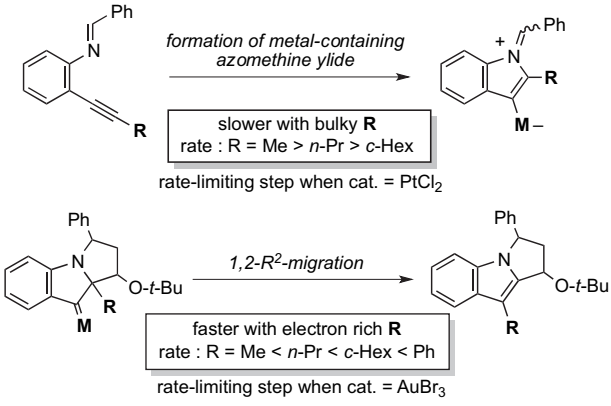
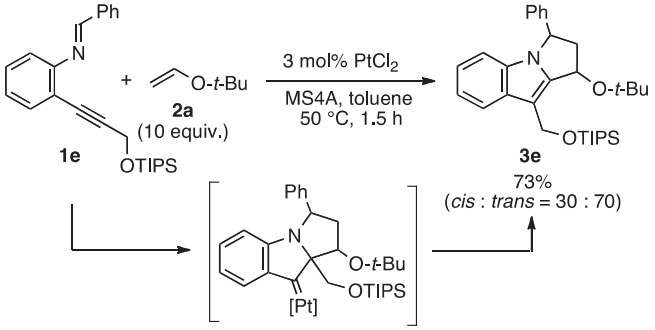


Fig. 3. Possible explanation of the effect of substituent at the alkyne terminus on the reaction rate.

[3+2] cycloadduct at all although the reaction of Me-derivative **1b** proceeded without problem. It is likely that bulky tetracarbonyl ligands on rhenium would be unfavorable for coordination of the alkyne moiety bearing a sterically demanding *c*-Hex group, and would inhibit the generation of a Re-containing azomethine ylide.

Since primary and secondary alkyl groups as well as phenyl group were successful as a migrating group with $AuBr_3$ and $PtCl_2$ catalysts, we further investigated 1,2-migration of a functionalized substituent to expand the scope of this reaction, and a siloxymethyl group was chosen considering application to mitomycin synthesis. Gratifyingly, the desired [3+2] cycloaddition and 1,2-migration of the siloxymethyl group was found to proceed smoothly by the use of $PtCl_2$ as a catalyst at 50 °C, affording the corresponding tricyclic indole **3e** in good yield (Scheme 3). Use of $AuBr_3$ caused complication of the reaction including desilylation of the TIPSO-moiety of the product probably due to its stronger Lewis acidity and harder character than $PtCl_2$. Thus, it was demonstrated that $PtCl_2$ catalyst greatly expanded generality and improved efficiency of the reaction of internal alkynes compared to $W(CO)_6$ system to realize facile synthesis of tricyclic indoles bearing various substituents at the 3-position.



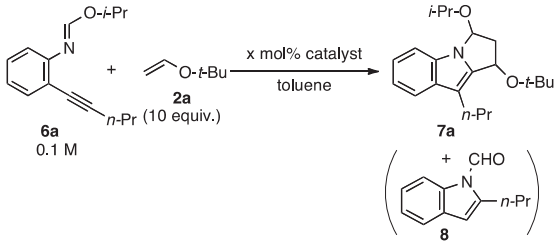
Scheme 3.

2.3. Reaction of metal-containing azomethine ylide derived from imidate derivatives

Application of this methodology not only to aldimine derivatives but also to imidates would be useful since the resulting indole derivatives possess an *N*,*O*-acetal moiety, which facilitates further functionalization of the products.[13] After screening several substrates and reaction conditions, imidate **6a** derived from *o*-(pent-1-ynyl)aniline and tri(*iso*-propyl) orthoformate was found to be employable as a precursor of the metal-containing azomethine ylide, which underwent [3+2] cycloaddition with vinyl ether **2a** (Table 4). In this case, the $PtCl_2$-catalyzed reaction gave superior results as compared with the $ReBr(CO)_5$- or $AuBr_3$-catalyzed one, leading to a tricyclic indole derivative **7a** with *N*,*O*-acetal moiety in good yield (entries 1–3) although *N*-formylindole derivative **8**, possibly generated by base-promoted β-deprotonation of metal-containing azomethine ylide was also produced as a byproduct (Fig. 4). Further optimization of reaction conditions disclosed that use of slightly acidic MS5A instead of MS4A completely suppressed the formation of **8**, and dramatically improved the yield of **7a** by the use of 3.0 mol % of $PtCl_2$ at 50 °C (entry 6).

The reaction of **6a** also proceeded with *p*-methoxybenzyl vinyl ether **2b** as a dipolarophile to give indole **9a**, which possessed an easily removable benzyl group, in high yield (Scheme 4). Furthermore, high synthetic utility of this methodology was demonstrated by the reaction of imidate **6b** bearing a siloxymethyl group on the alkyne terminus with PMB-vinyl ether **2b**, affording tricyclic indole derivative **9b** bearing three oxygen functionalities in a single operation (Scheme 5). This product contains a hydroxymethyl equivalent at the desired-position of the indole nucleus with an easily functionalizable *N*,*O*-acetal moiety, and thus, would be a highly useful synthetic precursor to mitomycins and their analogues.

Table 4
Reaction of imidate **6a**



Entry	Catalyst	x	Additive	Temp (°C)	Time (h)	Yield of **7a**[a] (%)	Yield of **8** (%)
1[b]	$ReBr(CO)_5/h\nu$	10	MS4A	rt	19.5	Trace	Trace
2	$AuBr_3$	10	MS4A	rt	1.0	60	12
3	$PtCl_2$	10	MS4A	rt	22	71	27
4	$PtCl_2$	3.0	MS4A	50	4	62	18
5	$PtCl_2$	3.0	MS4A K_2CO_3[c]	50	11	32	23
6	$PtCl_2$	3.0	MS5A	50	2	95	0

[a] The dr of **7a** varied in the range of *cis*:*trans*=58:42 to 68:32.
[b] Compound **2a** (4 equiv) was employed.
[c] 10 mol %.

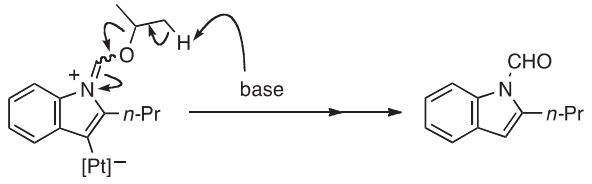
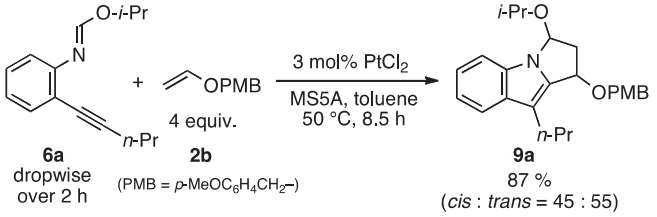


Fig. 4. Possible mechanism for the formation of *N*-formylindole derivative **8**.

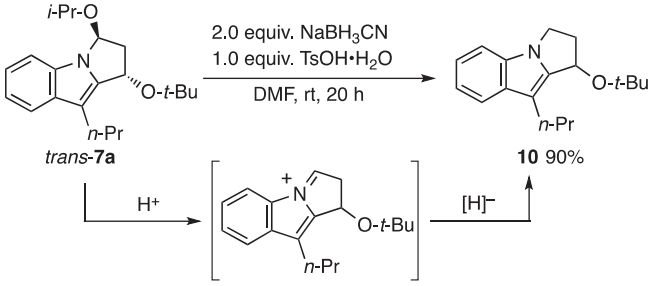


Scheme 4.

Scheme 5.

Transformation of this *N*,*O*-acetal moiety was briefly demonstrated in Scheme 6. Thus, reductive cleavage of the *N*,*O*-acetal proceeded smoothly by treatment of *trans*-**7a** with 2 equiv of $NaBH_3CN$ and 1 equiv of *p*-toluenesulfonic acid in DMF at room temperature to give tricyclic indole derivative **10** in high yield.[14] The reaction proceeds through in situ generation of an iminium ion followed by $NaBH_3CN$-mediated reduction. It should be noted that this method is a good alternative to the [3+2] cycloaddition of

metal-containing azomethine ylide derived from methyleneamine as a precursor, which is difficult to isolate and handle due to its instability (Fig. 5).



Scheme 6.

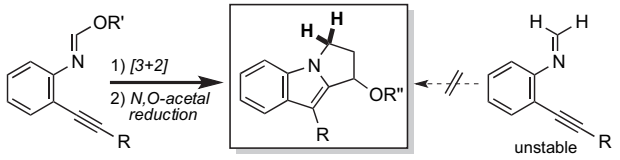


Fig. 5. Imidate substrate as a synthetic equivalent to methyleneamine precursor.

2.4. Synthetic study toward mitomycin C. Generation and reaction of metal-containing azomethine ylide from highly oxygenated imidate derivative

Since the reaction of imidate derivative **6b**, in which siloxymethyl group underwent 1,2-migration, enabled construction of the mitosene skeleton efficiently, we started a preliminary investigation toward mitomycin C (Fig. 1) utilizing the [3+2] cycloaddition of metal-containing azomethine ylide. We proposed tricyclic indole derivative **11** as a potential key intermediate, possessing two methoxy groups on the benzene ring for the construction of the quinone moiety (Fig. 6). The *N*,*O*-acetal was reduced as in Scheme 6 to form methylene moiety at 3-position and the aziridine moiety of the target compound could be constructed by utilizing the *t*-BuO-function. Our purpose in this preliminary study is to establish methodology to access this intermediate **11** by the [3+2] cycloaddition of metal-containing azomethine ylide derived from highly oxygenated imidate derivative **12**, and demonstrate the high synthetic utility of this protocol.

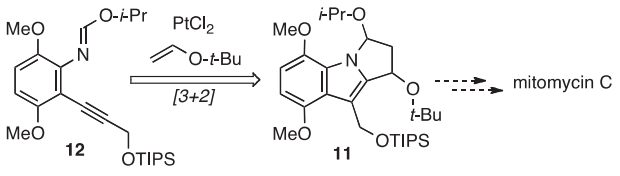
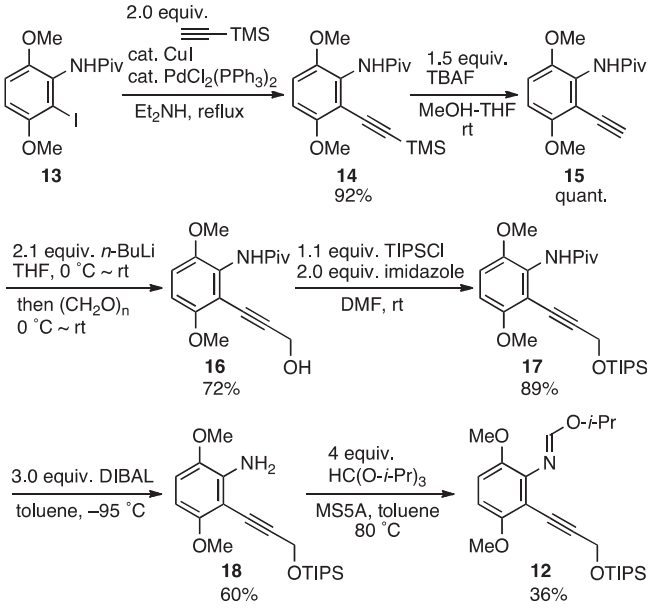


Fig. 6. Synthetic application of this protocol toward mitomycin C.

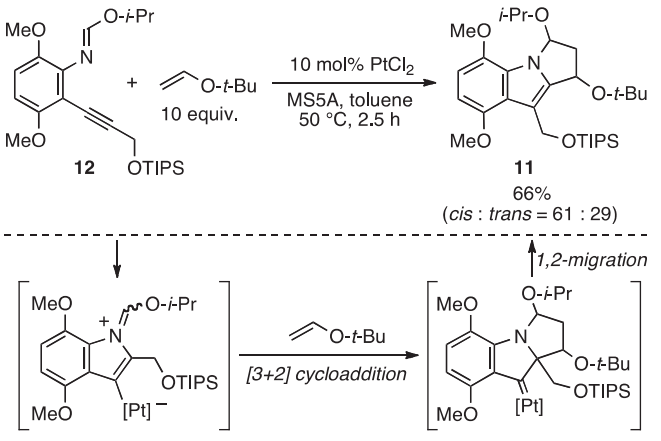
The precursor **12** was synthesized in six steps starting from *N*-pivaloyl-2-iodo-3,6-dimethoxyaniline **13** as shown in Scheme 7. Sonogashira coupling reaction of **13** with trimethylsilylacetylene followed by removal of the TMS group afforded *o*-ethynylaniline derivative **15** in high yield. The siloxymethyl moiety on the alkyne terminus was introduced by the reaction of the alkynyllithium



Scheme 7.

generated from **15** with paraformaldehyde and TIPS-protection of the resulting hydroxy group. Removal of the pivaloyl group on the nitrogen was carried out by treating **17** with DIBAL at −95 °C to give aniline **18** in good yield. Finally, the reaction of **18** with tri(*iso*-propyl) orthoformate at 80 °C in the presence of MS4A afforded the desired imidate **12** in moderate yield, which was purified by bulb-to-bulb distillation.

With the desired substrate in hand, we tried generation and [3+2] cycloaddition of metal-containing azomethine ylide from **12** using $PtCl_2$ as a catalyst. After several trials, we were pleased to find that treatment of **12** and 10 equiv of *tert*-butyl vinyl ether with 10 mol % of $PtCl_2$ afforded the desired tricyclic indole derivative **11** bearing the *N*,*O*-acetal, siloxymethyl moiety, and two methoxy groups on the benzene ring in good yield (Scheme 8). This compound possesses the basic carbon skeleton of mitomycin C with five oxygen functionalities, which would be suitable for further transformations toward mitomycin C. This result also demonstrates that the present reaction is applicable to highly oxygenated substrates, indicating the wide generality and high synthetic utility of this method.



Scheme 8.

2.5. Mechanistic considerations. Evidence for intermediacy of the Pt–carbene complex

We disclosed that $PtCl_2$ was the best catalyst for the reaction of internal alkynes and imidate substrates in terms of efficiency and generality of the reaction. Concerning the mechanism of this process, it is postulated that a Pt-containing azomethine ylide undergoes [3+2]-cycloaddition reaction with vinyl ethers to give a metal carbene complex intermediate, which undergoes 1,2-migration of the substituent R^2 to the electrophilic Pt–carbene center (Fig. 7). In our previous investigation on the reaction of internal alkyne derivatives using a stoichiometric amount of $W(CO)_6$, one of the stereoisomers of the intermediate tungsten carbene complex was successfully isolated due in part to moderate stability of group 6 metal carbene complexes having carbonyl ligands.[3] Even though the corresponding Pt–carbene complex seems to be highly unstable, it is desirable to confirm the intermediacy of the Pt–carbene complex to support the mechanism of the reaction.

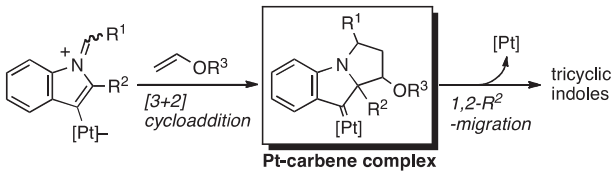
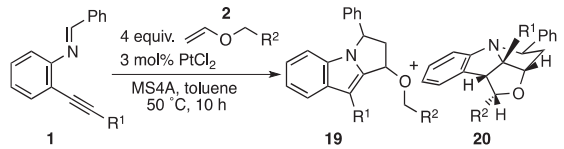


Fig. 7. Proposed key intermediate, Pt–carbene complex.

During investigation of the reaction of aldimine derivatives with various vinyl ethers, we fortunately found that the intermediate Pt–carbene complexes can be captured by an intramolecular C–H bond insertion reaction with the appropriate choice of substrates. Thus, treatment of aldimine **1a** and 4 equiv of benzyl vinyl ether **2c** with 3 mol % of $PtCl_2$ under standard reaction conditions afforded tetracyclic indoline derivative **20a** in 14% yield as a single stereoisomer along with 42% of 1,2-migration product **19a** (entry 1, Table 5). Furthermore, the yield of the tetracyclic indoline was increased by the combination of aldimine **1b** bearing Me-substituent on the alkyne terminus and *p*-methoxybenzyl vinyl ether **2b** as substrates, affording 41% of indoline **20b** and 43% of indole **19b** (entry 2). The structures of these tetracycles were assigned by ^1H, ^{13}C and various 2D NMR techniques, and confirmed by X-ray analysis in the case of **20b** (Fig. 8). The formation of tetracyclic indoline derivative was reasonably explained by considering intramolecular insertion of Pt–carbene complex **21** into the benzylic C–H bond before 1,2-*n*-Pr-migration (Fig. 9).[15] The lower electron donating ability of Me-substituent compared to *n*-Pr is expected to retard the 1,2-migration and the bond dissociation energy of the benzylic C–H bond becomes smaller due to the electron-rich aromatic ring, and therefore the relative rate of C–H insertion to 1,2-migration increased to give the indoline derivative more efficiently in entry 2.

Table 5
Formation of tetracyclic indoline derivative **20**



Entry	R^1	R^2	Yield of **19** (%)	*cis*:*trans* of **19**	Yield of **20** (%)
1	*n*-Pr (**1a**)	Ph (**2c**)	42 (**19a**)	53:47	14 (**20a**)
2	Me (**1b**)	*p*-$MeOC_6H_4$ (**2b**)	43 (**19b**)	70:30	41 (**20b**)

These results strongly support the existence of Pt–carbene complex as an intermediate in the reaction sequence, and indicate possibility of utilizing the intermediate for further C–C bond forming transformations.

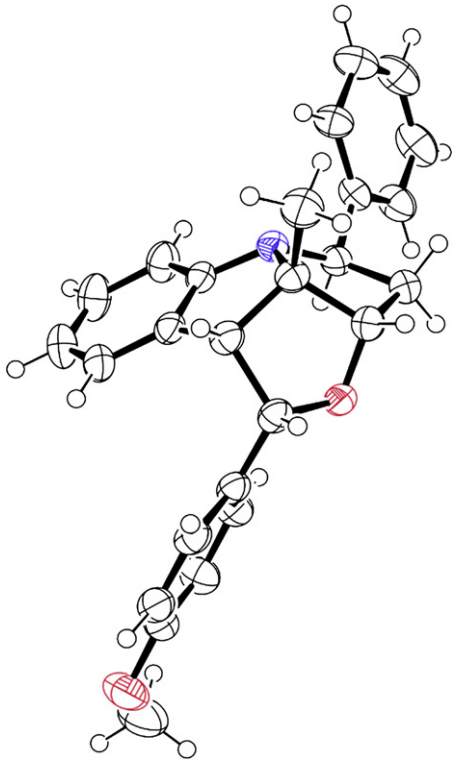


Fig. 8. ORTEP drawing of **20b** at 50% probability level.

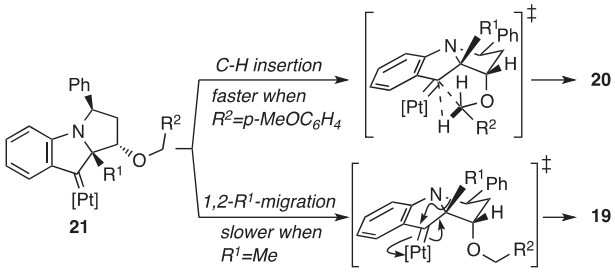


Fig. 9. C–H insertion versus 1,2-migration.

3. Conclusion

In conclusion, we have successfully established the generality and efficiency of the [3+2] cycloaddition reaction of transition metal-containing azomethine ylides. Third-row transition metal complexes, especially $PtCl_2$, proved to be the most efficient catalyst for the reaction of *internal* alkynes and *imidate* substrates. Highly functionalized tricyclic indole derivatives with oxygen functionalities, the basic skeleton of the mitosene family (e.g., mitomycin C), were easily accessible by this method. Furthermore, the key intermediate Pt–carbene complex was found to undergo intramolecular C–H bond insertion to give a tetracyclic indoline derivative. The present results demonstrate novel aspects of transition metal-containing dipoles and their high utility for the construction of various synthetically valuable indole derivatives.

4. Experimental section

4.1. General

All operations were performed under an argon atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C), a JEOL AL-400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) or a JEOL Lambda-400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) spectrometer in $CDCl_3$ (99.8% atom enriched, Acros Co., Ltd.). Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane and are referenced to residual $CHCl_3$ (δ_H 7.26) for ^{1}H and $CDCl_3$ (δ_C 77.0) for ^{13}C spectra. IR spectra were recorded on an IR-810 or an FT/IR-460 plus (JASCO Co., Ltd.). Photoirradiation was performed with a 250 W super high-pressure mercury lamp (USHIO INC.). Silica gel 60 (Kanto Chemical Co., Inc.) or aluminum oxide 90 active neutral (activity I, 0.063–0.200 mm, Merck) was used for flash column chromatography. Merck Kieselgel 60 F_{254} (0.25 mm thickness, coated on 20×20 cm^2 glass plate) was used for thin layer chromatography (TLC), and Wakogel B-5F coated on glass in a thickness of 0.7 mm was used for preparative TLC. All solvents were distilled according to the usual procedures and stored over molecular sieves. MS4A and MS5A were heated by heat-gun under reduced pressure before use. High-resolution mass analyses (FAB) were performed on a JEOL JMS-700 mass spectrometer using 2-nitrophenyl octyl ether as a matrix. Elemental analyses were performed on a Perkin–Elmer 2400 instrument. Aldimines **1a**, **1b**, **1d** were prepared according to our previously reported procedure.[2a] ^{1}H NMR spectral data of cycloadducts **3a**, **3b**, **3d**, and **4a** were identical to those in our previous report.[2a]

4.2. Preparation of aldimines derived from 2-(1-alkynyl) anilines and benzaldehyde

*4.2.1. (E)-N-Benzylidene-2-(2-cyclohexylethynyl)aniline (**1c**).* To a stirred mixture of 2-(2-cyclohexylethynyl)aniline[16] (578 mg, 2.90 mmol) and MS5A (1.5 g) in toluene (2.0 mL) was added benzaldehyde (0.35 mL, 3.4 mmol) at room temperature. After 5 days, the reaction mixture was filtered through a short pad of Celite® and the filtrate was concentrated under reduced pressure. The resulting residue was purified by bulb-to-bulb distillation to give **1c** (170 °C/0.03 mmHg, 786 mg, 2.71 mmol, 94%) as a single isomer. The geometry was confirmed to be *E* by the observation of an NOE between the aldimine proton and the C-6 aromatic proton. IR (neat) 3061, 2929, 2223, 1633 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.20–1.35 (m, 3H), 1.37–1.55 (m, 3H), 1.61–1.84 (m, 4H), 2.54–2.65 (m, 1H), 7.02 (br d, *J*=6.0 Hz, 1H), 7.11 (ddd, *J*=7.6, 7.6, 1.2 Hz, 1H), 7.27 (ddd, *J*=7.6, 7.6, 1.2 Hz, 1H), 7.42–7.60 (m, 4H), 7.89–7.97 (m, 2H), 8.47 (s, 1H); ^{13}C NMR (100 MHz) δ=24.6, 26.0, 29.7, 32.6, 78.3, 98.7, 116.6, 119.6, 124.8, 128.2, 128.6, 128.8, 131.3, 132.7, 136.1, 153.7, 161.7; Anal. Calcd for $C_{21}H_{21}N$: C, 87.76; H, 7.36; N, 4.87. Found: C, 87.71, H, 7.38, N, 4.65.

*4.2.2. (E)-N-Benzylidene-2-(3-triisopropylsiloxyprop-1-ynyl)-aniline (**1e**).* 2-(3-Triisopropylsiloxyprop-1-ynyl)aniline, the precursor of aldimine **1e**, was prepared as follows. To a stirred mixture of 2-(3-hydroxyprop-1-ynyl)aniline[17] (2.07 g, 14.1 mmol) and imidazole (2.39 g, 35.2 mmol) in DMF (5 mL) was added chlorotriisopropylsilane (3.1 mL, 14.5 mmol) at room temperature and the mixture was stirred for 1 h. The reaction was quenched with 1 N HCl, and then the aqueous layer was extracted with ether three times and the combined extracts were washed with brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=5:1) to give 2-(3-triisopropylsiloxyprop-1-ynyl)aniline (4.00 g, 13.2 mmol, 94%); IR (neat) 3478, 3384, 2943, 2866, 2225, 1615, 1493, 1090 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.08–1.23 (m, 21H), 4.13–4.27 (br s, 2H), 4.66 (s, 2H), 6.64–7.01 (m, 2H), 7.11 (ddd, *J*=7.6, 7.6, 1.6 Hz, 1H), 7.26 (dd, *J*=7.6, 1.6 Hz, 1H); ^{13}C NMR (100 MHz) δ=12.1, 18.0, 52.6, 81.1, 93.3, 107.6, 114.2, 117.7, 129.5, 132.2, 147.8; Anal. Calcd for $C_{18}H_{29}NOSi$: C, 71.23; H, 9.63; N, 4.61. Found: C, 71.01, H, 9.42, N, 4.50.

The aldimine **1e** was prepared according the procedure described for the preparation of **1c** using 2-(3-triisopropylsiloxyprop-1-ynyl)aniline (185 °C/0.05 mmHg). The geometry was confirmed to be *E* by the observation of an NOE between the aldimine proton and the C-6 aromatic proton. IR (neat) 3063, 2941, 2230, 1633, 1190, 1106 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.01–1.16 (m, 21H), 4,57 (s, 2H), 7.01 (dd, *J*=7.6, 1.2 Hz, 1H), 7.13 (ddd, *J*=7.6, 7.6, 1.2 Hz, 1H), 7.32 (ddd, *J*=7.6, 7.6, 1.2 Hz, 1H), 7.36–7.56 (m, 4H), 7.93 (dd, *J*=7.6, 1.6 Hz, 2H), 8.44 (s, 1H); ^{13}C NMR (100 MHz) δ=12.1, 18.0, 52.6, 82.1, 92.1, 115.9, 119.4, 124.9, 128.6, 128.9, 129.0, 131.4, 133.1, 136.0, 153.9, 161.8; Anal. Calcd for $C_{25}H_{33}NOSi$: C, 76.67; H, 8.49; N, 3.58. Found: C, 76.38, H, 8.75, N, 3.42.

4.3. Preparation of imidate

*4.3.1. (E)-Isopropyl N-(2-(1-pentynyl)phenyl)formimidate (**6a**).* A mixture of 2-(pent-1-ynyl)aniline (437 mg, 2.74 mmol), triisopropyl orthoformate (2.5 mL, 11 mmol) and MS5A (4.2 g) in toluene (8.5 mL) was heated at 80 °C. After 15 h, the mixture was filtered through a short pad of Celite® and the filtrate was concentrated under reduced pressure. The resulting residue was purified by bulb-to-bulb distillation to give the imidate **6a** (105 °C/0.01 mmHg, 547 mg, 2.38 mmol, 87%). The geometry was confirmed to be *E* by the observation of an NOE between the formimidic proton and the C-6 aromatic proton. IR (neat) 2966, 2229, 1644 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.03 (t, *J*=7.6 Hz, 3H), 1.39 (d, *J*=6.0 Hz, 6H), 1.55–1.66 (m, 2H), 2.38 (t, *J*=7.2 Hz, 2H), 5.19–5.33 (m, 1H), 6.84 (br d, *J*=7.6 Hz, 1H), 7.01 (ddd, *J*=7.6, 7.6, 1.6 Hz, 1H), 7.19 (ddd, *J*=7.6, 7.6, 1.6 Hz, 1H), 7.39 (dd, *J*=7.6, 1.6 Hz, 1H), 7.65 (s, 1H); ^{13}C NMR (100 MHz) δ=13.6, 21.7, 21.8, 22.3, 69.4, 78.5, 93.7, 117.1, 120.9, 123.5, 128.2, 132.6, 149.6, 155.0; Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.28, H, 8.48, N, 5.82.

*4.3.2. (E)-Isopropyl N-((3-triisopropylsiloxyprop-1-ynyl)-phenyl)-formimidate (**6b**).* The imidate **6b** was prepared according to the procedure described for the preparation of **6a** using 2-(3-triisopropylsiloxyprop-1-ynyl)aniline in 85% yield (155 °C/0.05 mmHg). The geometry was confirmed to be *E* by the observation of an NOE between the formimidic proton and the C-6 aromatic proton. IR (neat) 3065, 2943, 2232, 1645, 1189, 1108 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.06–1.17 (m, 21H), 1.38 (d, *J*=6.0 Hz, 6H), 4.60 (s, 2H), 5.17–5.28 (m, 1H), 6.85 (br d, *J*=7.6 Hz, 1H), 7.03 (br dd, *J*=7.6, 7.6 Hz, 1H), 7.23 (br dd, *J*=7.6, 7.6 Hz, 1H), 7.42 (br d, *J*=7.6 Hz, 1H), 7.63 (s, 1H); ^{13}C NMR (100 MHz) δ=12.1, 18.0, 21.7, 52.6, 69.6, 82.4, 91.4, 116.3, 120.9, 123.6, 129.0, 132.9, 149.9, 155.0; Anal. Calcd for $C_{22}H_{35}NOSi$: C, 70.73; H, 9.44; N, 3.75. Found: C, 70.48, H, 9.32, N, 3.52.

4.4. Preparation of functionalized imidate 12 (Scheme 5)

*4.4.1. N-(3,6-Dimethoxy-2-(2-(trimethylsilyl)ethynyl)phenyl)-pivalamide (**14**).* To a mixture of *N*-(2-iodo-3,6-dimethoxyphenyl) pival-amide[18] **13** (1.31 g, 3.6 mmol), dichlorobis(-triphenylphosphine)-palladium(II) (251 mg, 0.36 mmol) and copper(I) iodide (141 mg, 0.74 mmol) in diethylamine (10 mL) was added ethynyltrimethylsilane (1.0 mL, 7.1 mmol) at room temperature and the mixture was heated at 80 °C. After 3.5 h, the reaction was quenched with saturated aq NH_4Cl. The aqueous layer was extracted with ether (3×) and the combined extracts were washed with brine, and dried ($MgSO_4$). The solvent was removed under

reduced pressure and the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=2:1) to give anilide **14** (1.10 g, 92%). IR (KBr) 2959, 2835, 2147, 1691, 1270 cm^{-1}; ^1H NMR (400 MHz) δ=0.25 (s, 9H), 1.35 (s, 9H), 3.79 (s, 3H), 3.83 (s, 3H), 6.71 (d, J=8.8 Hz, 1H), 6.86 (d, J=8.8 Hz, 1H), 7.09–7.20 (br s, 1H); ^{13}C NMR (100 MHz) δ=0.2, 27.8, 39.6, 56.6, 56.7, 79.8, 97.4, 104.1, 110.7, 113.3, 129.1, 148.6, 154.8, 176.0; Anal. Calcd for $C_{18}H_{27}NO_3Si$: C, 64.83; H, 8.16; N, 4.20. Found: C, 65.03, H, 8.33, N, 4.30.

*4.4.2. N-(3,6-Dimethoxy-2-ethynylphenyl)pivalamide (**15**).* To a solution of anilide **14** (670 mg, 2.0 mmol) in THF/MeOH (1:1, 6.0 mL) was added tetra-*n*-butylammonium fluoride (1.0 M in THF, 3.0 mL, 3.0 mmol) at 0 °C. After the mixture was stirred for 2 h at room temperature, the reaction was quenched with pH 7 phosphate buffer and the product was extracted with ethyl acetate (3×). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate=2:1) to give the title compound **15** (531 mg, 100%). IR (KBr) 3092, 2971, 2842, 2100, 1762 cm^{-1}; ^1H NMR (400 MHz) δ=1.34 (s, 9H), 3.50 (s, 1H), 3.79 (s, 3H), 3.85 (s, 3H), 6.73 (d, J=9.2 Hz, 1H), 6.88 (d, J=9.2 Hz, 1H), 7.10–7.21 (br s, 1H); ^{13}C NMR (100 MHz) δ=27.7, 39.4, 56.5, 56.6, 76.8, 86.1, 108.8, 110.0, 113.0, 129.3, 148.3, 155.0, 176.3; Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.70, H, 7.39, N, 5.47.

*4.4.3. N-(3,6-Dimethoxy-2-(3-hydroxyprop-1-ynyl)phenyl)pival-amide (**16**).* To a stirred solution of **15** (230 mg, 0.880 mmol) in THF (1.0 mL) was added *n*-butyllithium (1.53 M in THF, 1.20 mL, 1.83 mmol, 2.1 equiv) at 0 °C and the reaction mixture was stirred at room temperature for 0.5 h. The reaction mixture was cooled to 0 °C, paraformaldehyde (139 mg, 4.63 mmol) was added, and the reaction mixture was stirred for 8 h at room temperature. The reaction mixture was quenched with pH 7 phosphate buffer and the product was extracted with ethyl acetate (3×), and the combined extracts were dried ($MgSO_4$). After removal of solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=1:1 then ethyl acetate) to give the title compound **16** (186 mg, 72%) along with starting material **15** (23 mg, 10%). IR (KBr) 3651, 2957, 2836, 1656, 1038 cm^{-1}; ^1H NMR (400 MHz) δ=1.35 (s, 9H), 1.92 (t, J=5.6 Hz, 1H), 3.79 (s, 3H), 3.84 (s, 3H), 4.50 (d, J=5.6 Hz, 2H), 6.71 (d, J=9.2 Hz, 1H), 6.85 (d, J=9.2 Hz, 1H), 7.19–7.24 (br s, 1H); ^{13}C NMR (100 MHz) δ=27.7, 39.5, 51.7, 56.4, 56.5, 79.0, 96.9, 108.6, 110.5, 112.2, 128.9, 148.0, 154.3, 176.5; Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 66.02, H, 7.23, N, 4.64.

*4.4.4. N-(3,6-Dimethoxy-2-(3-triisopropylsiloxyprop-1-ynyl)-phenyl)pivalamide (**17**).* To a stirred mixture of **16** (182.3 mg, 0.626 mmol) and imidazole (106.3 mg, 1.56 mmol) in DMF (1 mL) was added chlorotriisopropylsilane (0.15 mL, 0.70 mmol) at room temperature and the mixture was stirred overnight. The reaction was quenched with 1 N HCl, and then the aqueous layer was extracted with ether (3×) and combined extracts were washed with brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=2:1) to give the title compound **17** (250.7 mg, 89%). IR (KBr) 2944, 2865, 2238, 1664, 1084 cm^{-1}; ^1H NMR (400 MHz) δ=1.03–1.20 (m, 21H), 1.34 (s, 9H), 3.78 (s, 3H), 3.79 (s. 3H), 4.65 (s, 2H), 6.69 (d, J=9.2 Hz, 1H), 6.84 (d, J=9.2 Hz, 1H), 7.07–7.18 (br s, 1H); ^{13}C NMR (100 MHz) δ=12.0, 18.0, 27.7, 39.4, 52.7, 56.4, 56.6, 77.2, 97.2, 109.0, 110.7, 112.7, 128.8, 148.5, 154.6, 176.2; Anal. Calcd for $C_{25}H_{41}NO_4Si$: C, 67.07; H, 9.23; N, 3.13. Found: C, 67.08, H, 9.35, N, 2.92.

*4.4.5. 3,6-Dimethoxy-2-(3-triisopropylsiloxyprop-1-ynyl)aniline (**18**).* To a stirred solution of anilide **17** (65.2 mg, 0.146 mmol) in toluene (1.0 mL) was added diisobutylaluminum hydride (1.0 M in toluene, 0.44 mL, 0.44 mmol) at −95 °C and the mixture was stirred at this temperature for 3 h. The reaction was quenched with saturated aqueous solution of potassium sodium (+)-tartrate at −95 °C and the mixture was stirred at room temperature until the biphasic solution became clear. The aqueous layer was extracted with ethyl acetate (3×) and the combined extracts were washed with brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by PTLC (hexane/ethyl acetate=5:1) to give aniline **18** (31.6 mg, 60%) along with *N*-neopentyl-3,6-dimethoxy-2-(3-triisopropylsiloxyprop-1-ynyl)-aniline (10.0 mg, 16%) as a byproduct and the staring material **17** (16.7 mg, 26%). IR (KBr) 3482, 3373, 2940, 2863, 2218, 1615, 1493, 1057 cm^{-1}; ^1H NMR (400 MHz) δ=1.16–1.23 (m, 21H), 3.78 (s, 3H), 3.80 (s, 3H), 4.35–4.48 (br s, 2H), 4.71 (s, 2H), 6.12 (d, J=8.8 Hz, 1H), 6.65 (d, J=8.8 Hz, 1H); ^{13}C NMR (100 MHz) δ=12.1, 18.0, 52.8, 55.9, 56.0, 77.6, 97.4, 97.9, 100.5, 110.5, 139.9, 141.0, 154.7; Anal. Calcd for $C_{20}H_{33}NO_3Si$: C, 66.07; H, 9.15; N, 3.85. Found: C, 65.85, H, 9.19, N, 3.70.

*4.4.6. (E)-Isopropyl N-(3,6-dimethoxy-2-(3-triisopropylsiloxy-prop-1-ynyl)phenyl)formimidate (**12**).* This compound was prepared according to the procedure described for the preparation of **6a** using aniline **18** in 36% yield (170 °C/0.05 mmHg). The product was contaminated with a small amount of aniline **18** (less than 5%), and analytically pure sample was not obtained. The geometry was deduced to be *E* since the chemical shift of formimidic proton is similar to those of imidate **6a** and **6b**; ^1H NMR (400 MHz) δ=1.00–1.62 (m, 21H), 1.39 (d, J=6.4 Hz, 6H), 3.73 (s, 3H), 3.80 (s, 3H), 4.62 (s, 2H), 5.24–5.32 (m, 1H), 6.49 (d, J=8.8 Hz, 1H), 6.77 (d, J=8.8 Hz, 1H), 7.64 (s, 1H); ^{13}C NMR (100 MHz) δ=12.1, 18.0, 21.7, 52.7, 56.1, 56.6, 69.3, 78.4, 95.5, 105.2, 106.7, 112.3, 141.1, 145.7, 155.1, 156.6.

4.5. Procedure for $PtCl_2$-, $AuBr_3$-, or $ReBr(CO)_5$-catalyzed reaction of imine and imidate derivatives with vinyl ether

Procedure for the 3.0 mol % $PtCl_2$-catalyzed reaction of **1a** with **2a** was described (entry 6, Table 2) as a representative example. To a stirred suspension of a mixture of an imine **1a** (31.2 mg, 0.126 mmol), vinyl ether **2a** (67 μl, 0.51 mmol) and MS4A (251 mg) in toluene (1.2 mL) was added $PtCl_2$ (1.0 mg, 0.0038 mmol) at room temperature. The mixture was heated at 50 °C for 6 h. After disappearance of **1a** was confirmed by TLC, the reaction was quenched with saturated aq $NaHCO_3$ and the reaction mixture was filtered through a short pad of Celite®. The filtrate was extracted with ethyl acetate (3×) and the combined organic layers were washed with brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by preparative TLC (toluene/hexane=2:1, R_f=0.4) to afford a tricyclic indole derivative **3a** (39.9 mg, 89%).

*4.5.1. 1-tert-Butoxy-9-cyclohexyl-2,3-dihydro-3-phenyl-1H-pyrr-olo[1,2-a]indole (**3c**).* The stereochemistry of *trans*-**3c** was determined by X-ray structure analysis as shown below (Fig. 10).

cis-**3c**; IR (neat) 3046, 2972, 2924, 2850, 1456, 1363 cm^{-1}; ^1H NMR (500 MHz) δ=1.39–1.48 (m, 3H), 1.34 (s, 9H), 1.75–1.81 (m, 1H), 1.86–2.05 (m, 6H), 2.47 (ddd, J=13.2, 7.3, 5.2 Hz, 1H), 2.97–3.06 (m, 1H), 3.25 (ddd, J=13.2, 7.3, 7.3 Hz, 1H), 5.16 (dd, J=7.3, 7.3 Hz, 1H), 5.31 (dd, J=7.3, 5.2 Hz, 1H), 6.66 (br d, J=8.1 Hz, 1H), 6.89 (ddd, J=8.1, 8.1, 1.0 Hz, 1H), 6.96 (ddd, J=8.1, 8.1, 1.0 Hz, 1H), 7.27–7.37 (m, 3H), 7.37–7.41 (m, 2H), 7.70 (br d, J=8.1 Hz, 1H); ^{13}C NMR (125 MHz) δ=26.4, 27.37, 27.39, 28.9, 33.2, 33.9, 36.1, 49.7, 59.7, 68.0, 74.4, 110.5, 114.2, 118.4, 120.2, 120.6, 127.0, 127.7, 128.7, 131.8, 132.2, 140.3, 141.2; Anal. Calcd for $C_{27}H_{33}NO$: C, 83.68; H, 8.58; N, 3.61. Found: C, 83.43; H, 8.56; N, 3.33.

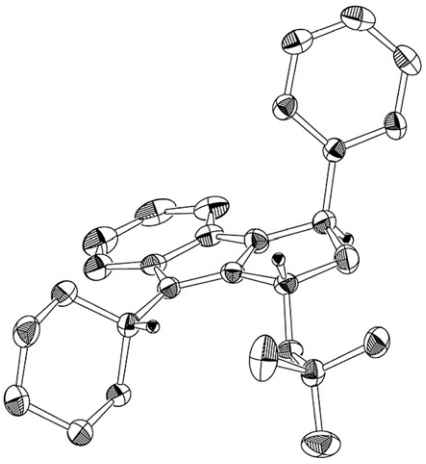
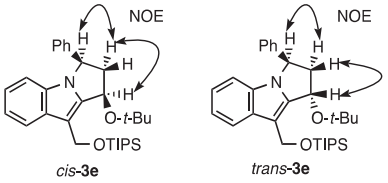


Fig. 10. ORTEP plot of *trans*-**3c** at 50% probability level (hydrogen atoms are omitted for clarity).

trans-**3c**; IR (neat) 3047, 2973, 2926, 2850, 1455, 1364 cm^{-1}; ^1H NMR (500 MHz) δ=1.32–1.50 (m, 3H), 1.33 (s, 9H), 1.77–1.82 (m, 1H), 1.87–2.03 (m, 6H), 2.70 (ddd, *J*=12.6, 6.5, 6.4 Hz, 1H), 2.92–3.10 (m, 2H), 5.36 (dd, *J*=6.4, 3.0 Hz, 1H), 5.54 (dd, *J*=7.0, 6.5 Hz, 1H), 6.65 (br d, *J*=8.1 Hz, 1H), 6.87–6.92 (m, 1H), 6.95–7.00 (m, 1H), 7.07–7.11 (m, 2H), 7.27–7.34 (m, 3H), 7.72 (br d, *J*=8.1 Hz, 1H); ^{13}C NMR (125 MHz) δ=26.4, 27.35, 27.37, 28.9, 33.3, 33.7, 36.4, 50.3, 59.2, 67.2, 74.5, 110.7, 114.2, 118.3, 120.4, 120.7, 126.3, 127.7, 128.8, 131.8, 132.3, 140.2, 141.6; Anal. Calcd for $C_{27}H_{33}NO$: C, 83.68; H, 8.58; N, 3.61. Found: C, 83.42; H, 8.85; N, 3.33.

*4.5.2. 1-tert-Butoxy-2,3-dihydro-9-triisopropylsiloxymethyl-3-phenyl-1H-pyrrolo[1,2-a]indole (**3e**).* The stereochemistry was determined by the observation of NOEs as shown below.

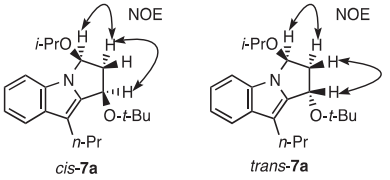


cis-**3e** (minor); IR (neat) 3049, 2965, 2942, 2865, 1456, 1364, 1192, 1060 cm^{-1}; ^1H NMR (400 MHz) δ=1.09–1.31 (m, 21H), 1.34 (s, 9H), 2.45 (ddd, *J*=12.8, 7.2, 6.0 Hz, 1H), 3.30 (ddd, *J*=12.8, 7.2, 6.0 Hz, 1H), 5.09 (d, *J*=12.0 Hz, 1H), 5.14 (d, *J*=12.0 Hz, 1H), 5.22 (dd, *J*=7.2, 7.2 Hz, 1H), 5.36 (dd, *J*=6.0, 6.0 Hz, 1H), 6.65 (d, *J*=8.0 Hz, 1H), 6.91 (dd, *J*=8.0, 8.0 Hz, 1H), 7.02 (dd, *J*=8.0, 8.0 Hz, 1H), 7.27–7.38 (m, 5H), 7.78 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz) δ=12.2, 18.3, 28.8, 49.9, 56.9, 59.9, 67.8, 74.4, 108.0, 110.3, 119.1, 120.5, 120.7, 126.9, 127.8, 128.7, 132.0, 132.6, 140.9, 141.3; Anal. Calcd for $C_{31}H_{45}NO_2Si$: C, 75.71; H, 9.22; N, 2.85. Found: C, 75.47; H, 9.45; N, 3.02.

trans-**3e** (major); IR (neat) 3050, 2964, 2942, 2865, 1456, 1365, 1191, 1059 cm^{-1}; ^1H NMR (500 MHz) δ=1.11–1.16 (m, 18H), 1.17–1.26 (m, 3H), 1.36 (s, 9H), 2.75 (ddd, *J*=13.3, 6.7, 5.5 Hz, 1H), 2.95 (ddd, *J*=13.3, 7.7, 3.7 Hz, 1H), 5.09 (d, *J*=11.8 Hz, 1H), 5.15 (d, *J*=11.8 Hz, 1H), 5.39 (dd, *J*=6.7, 3.7 Hz, 1H), 5.58 (dd, *J*=7.7, 5.5 Hz, 1H), 6.69 (d, *J*=8.0 Hz, 1H), 6.94 (dd, *J*=8.0, 8.0 Hz, 1H), 7.04 (dd, *J*=8.0, 8.0 Hz, 1H), 7.07–7.12 (m, 2H), 7.27–7.35 (m, 3H), 7.80 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ=12.2, 18.2, 28.7, 50.4, 57.1, 59.4, 67.0, 74.4, 108.2, 110.4, 119.1, 120.6, 120.9, 126.3, 127.7, 128.8, 132.2, 132.7, 141.4, 141.5.l; Anal. Calcd for $C_{31}H_{45}NO_2Si$: C, 75.71; H, 9.22; N, 2.85. Found: C, 75.44; H, 9.49; N, 2.66.

*4.5.3. 4-Methoxy-2-phenyl-8-(prop-1-ynyl)-1,2,3,4-tetrahydro-quinoline (**5a**).* NMR (400 MHz) δ=0.94 (t, *J*=7.3 Hz, 3H), 1.33 (s, 9H), 1.48–1.61 (m, 2H), 2.06 (dd, *J*=23.4, 12.1 Hz, 1H), 2.23–2.31 (m, 1H), 2.64 (t, *J*=7.1 Hz, 2H), 4.68 (dd, *J*=12.1, 3.2 Hz, 1H), 4.80 (br s, 1H), 4.87 (dd, *J*=10.7, 5.1 Hz, 1H), 6.61 (t, *J*=7.6 Hz, 1H), 7.14 (d, *J*=7.6 Hz, 1H), 7.27–7.50 (m, 6H).

*4.5.4. 1-tert-Butoxy-2,3-dihydro-3-isopropoxy-9-propyl-1H-pyrrolo[1,2-a]indole (**7a**).* The stereochemistry of the products was determined by the observation of NOEs as shown below.

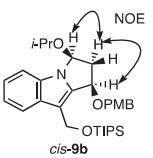


cis-**7a**; IR (neat) 3050, 2972, 2930, 2870, 1456, 1365 cm^{-1}; ^1H NMR (400 MHz) δ=0.96 (t, *J*=7.2 Hz, 3H), 1.06 (d, *J*=6.0 Hz, 3H), 1.26 (d, *J*=6.0 Hz, 3H), 1.35 (s, 9H), 1.63–1.78 (m, 2H), 2.42 (ddd, *J*=14.0, 2.4, 2.4 Hz, 1H), 2.71–2.77 (m, 2H), 3.02 (ddd, *J*=14.0, 7.0, 7.0 Hz, 1H), 4.02–4.12 (m, 1H), 5.06 (dd, *J*=7.0, 2.4 Hz, 1H), 5.76 (dd, *J*=7.0, 2.4 Hz, 1H), 7.08 (dd, *J*=8.0, 8.0 Hz, 1H), 7.14 (dd, *J*=8.0, 8.0 Hz, 1H), 7.37 (d, *J*=8.0 Hz, 1H), 7.55 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz) δ=14.3, 23.3, 23.5, 24.2, 26.1, 28.7, 46.7, 65.2, 68.1, 74.3, 83.8, 108.9, 110.4, 119.2, 119.3, 121.0, 132.0, 133.3, 140.0; Anal. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.27; H, 9.77; N, 3.97.

trans-**7a**; IR (neat) 3051, 2972, 2931, 2870, 1456, 1364 cm^{-1}; ^1H NMR (500 MHz) δ=0.98 (t, *J*=7.4 Hz, 3H), 1.17 (d, *J*=6.1 Hz, 3H), 1.24 (d, *J*=6.1 Hz, 3H), 1.33 (s, 9H), 1.64–1.78 (m, 2H), 2.62 (ddd, *J*=13.4, 6.5, 6.0 Hz, 1H), 2.75–2,80 (m, 2H), 2.82 (dd, *J*=13.4, 6.5 Hz, 1H), 3.94–4.01 (m, 1H), 5.49 (dd, *J*=6.5, 6.5 Hz, 1H), 5.88 (d, *J*=6.0 Hz, 1H), 7.08 (dd, *J*=7.9, 7.9 Hz, 1H), 7.13 (dd, *J*=7.9, 7.9 Hz, 1H), 7.30 (d, *J*=7.9 Hz, 1H), 7.54 (d, *J*=7.9 Hz, 1H); ^{13}C NMR (125 MHz) δ=14.3, 22.5, 23.1, 24.4, 25.7, 28.6, 48.9, 67.0, 69.9, 74.3, 83.2, 109.6, 109.9, 119.1, 119.3, 121.0, 132.2, 133.6, 139.9; Anal. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.32; H, 9.70; N, 4.06.

*4.5.5. N-Formyl-2-propylindole (**8**).* ^1H NMR (400 MHz) δ=1.07 (t, *J*=7.3 Hz, 3H), 1.79 (sextet, *J*=7.3 Hz, 2H), 2.36–2.95 (m, 2H), 6.39 (s, 1H), 7.25–7.31 (m, 2H), 7.46–7.50 (m, 2H), 9.30 (br s, 1H).

*4.5.6. 2,3-Dihydro-3-isopropoxy-1-(4-methoxybenzyloxy)-9-tri-isopropylsiloxymethyl-1H-pyrrolo[1,2-a]indole (**9b**).* The stereochemistry of the major product was determined to be *cis* by the observed NOEs shown below. Therefore, the minor product was assigned to be the corresponding *trans* isomer.

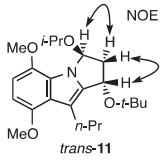


cis-**9b**; IR (neat) 2941, 2865, 1457, 1368 cm^{-1}; ^1H NMR (400 MHz) δ=0.90–1.41 (m, 21H), 1.19 (d, *J*=6.0 Hz, 3H), 1.25 (d, *J*=6.0 Hz, 3H), 2.62 (d, *J*=14.4 Hz, 1H), 2.94 (ddd, *J*=14.4, 6.8, 6.4 Hz, 1H), 3.80 (s, 3H), 4.07–4.18 (m, 1H), 4.53 (d, *J*=11.2 Hz, 1H), 4.65 (d, *J*=11.2 Hz, 1H), 4.98 (d, *J*=12.0 Hz, 1H), 5.05 (d, *J*=12.0 Hz, 1H), 5.09 (d, *J*=6.8 Hz, 1H), 5.77 (d, *J*=6.4 Hz, 1H), 6.86 (d, *J*=8.4 Hz, 2H), 7.13 (dd, *J*=7.6, 7.6 Hz, 1H), 7.20 (dd, *J*=7.6, 7.6 Hz, 1H), 7.28

(d, J=8.4 Hz, 2H), 7.38 (d, J=7.6 Hz, 1H), 7.73 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz) δ=12.2, 18.2, 22.9, 23.3, 43.8, 55.3, 57.5, 69.1, 69.7, 71.1, 83.2, 110.0, 113.6, 119.9, 120.5, 122.0, 129.4, 130.5, 132.0, 132.7, 139.0, 159.0; Anal. Calcd for $C_{32}H_{47}NO_4Si$: C, 71.46; H, 8.81; N, 2.60. Found: C, 71.25; H, 9.04; N, 2.49.

trans-**9b**; IR (neat) 2941, 2865, 1456, 1367 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.04–1.19 (m, 21H), 1.22 (d, J=5.6 Hz, 3H), 1.23 (d, J=5.6 Hz, 1H), 2.73–2.79 (m, 2H), 3.81 (s, 3H), 3.93–4.05 (m, 1H), 4.55 (s, 2H), 5.05 (s, 2H), 5.37 (dd, J=5.6, 5.6 Hz, 1H), 5.96 (dd, J=4.4, 4.4 Hz, 1H), 6.88 (d, J=8.4 Hz, 2H), 7.12 (dd, J=7.6, 7.6 Hz, 1H), 7.18 (dd, J=7.6, 7.6 Hz, 1H), 7.28 (d, J=8.4 Hz, 2H), 7.31 (d, J=7.6 Hz, 1H), 7.75 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz) δ=12.2, 18.2, 22.7, 23.0, 45.4, 55.3, 57.2, 70.3, 70.6, 84.3, 109.7, 110.2, 113.8, 119.7, 120.5, 121.6, 129.4, 130.1, 132.3, 132.5, 139.0, 159.2; Anal. Calcd for $C_{32}H_{47}NO_4Si$: C, 71.46; H, 8.81; N, 2.60. Found: C, 71.17; H, 9.11; N, 2.60.

*4.5.7. 1-tert-Butoxy-2,3-dihydro-5,8-dimethoxy-3-phenyl-9-tri-iso-propylsiloxymethyl-1H-pyrrolo[1,2-a]indole (**11**).* The stereochemistry of the minor product was determined to be *trans* by the observed NOEs shown below. Therefore, the major product was assigned to be the corresponding *cis* isomer.

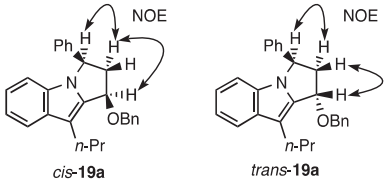


trans-**11**

cis-**11**; IR (neat) 2968, 2938, 2865, 1465, 1366, 1111 cm^{-1}; ^{1}H NMR (500 MHz) δ=0.87–1.22 (m, 27H), 1.35 (s, 9H), 2.36 (d, J=14.1 Hz, 1H), 2.84 (ddd, J=14.1, 6.5, 5.9 Hz, 1H), 3.81 (s, 3H), 3.86 (s, 3H), 3.98–4.08 (m, 1H), 4.91 (d, J=11.2 Hz, 1H), 5.13 (d, J=6.5 Hz, 1H), 5.33 (d, J=11.2 Hz, 1H), 5.95 (d, J=5.9 Hz, 1H), 6.32 (d, J=8.4 Hz, 1H), 6.42 (d, J=8.4 Hz, 1H); ^{13}C NMR (125 MHz) δ=12.2, 18.1, 23.1, 23.2, 28.7, 46.7, 55.1, 55.5, 56.7, 65.2, 68.5, 74.0, 85.4, 99.1, 101.4, 109.3, 123.4, 123.7, 141.8, 142.0, 149.2.; HRMS calcd for $C_{30}H_{52}NO_5Si$: MH+534.3615. Found: m/z 534.3607.

trans-**11**; IR (neat) 2967, 2940, 2865, 1465, 1366, 1114 cm^{-1}; ^{1}H NMR (500 MHz) δ=0.92–1.20 (m, 27H), 1.35 (s, 9H), 2.52 (ddd, J=12.9, 6.7, 5.5 Hz, 1H), 2.77 (dd, J=12.9, 6.7 Hz, 1H), 3.80 (s, 3H), 3.87 (s, 3H), 3.94–4.03 (m, 1H), 4.98 (d, J=10.9 Hz, 1H), 5.27 (d, J=10.9 Hz, 1H), 5.54 (dd, J=6.7, 6.7 Hz, 1H), 6.07 (d, J=5.5 Hz, 1H), 6.31 (d, J=8.4 Hz, 1H), 6.42 (d, J=8.4 Hz, 1H); ^{13}C NMR (125 MHz) δ=12.3, 18.1, 22.4, 23.2, 28.8, 49.2, 54.9, 55.2, 56.0, 67.5, 69.1, 74.1, 84.7, 98.9, 101.1, 110.1, 123.3, 123.8, 141.4, 141.8, 149.2.

*4.5.8. 1-Benzyloxy-2,3-dihydro-3-phenyl-9-propyl-1H-pyrrolo-[1,2-a]indole (**19a**).* The stereochemistry of the products was determined by the observation of NOEs as shown below.



cis-**19a** *trans*-**19a**

cis-**19a**; IR (neat) 3064, 2966, 1609, 1456, 1360 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.02 (t, J=7.6 Hz, 3H), 1.73–1.86 (m, 2H), 2.66 (ddd, J=14.0, 4.0, 3.2 Hz, 1H), 2.79–2.93 (m, 2H), 3.30 (ddd, J=14.0, 8.8, 6.8 Hz, 1H), 4.64 (s, 2H), 5.20 (dd, J=6.8, 3.2 Hz, 1H), 5.34 (dd, J=8.8, 4.0 Hz, 1H), 6.86 (d, J=7.6 Hz, 1H), 6.98–7.08 (m, 2H), 7.27–7.38 (m, 10H), 7.62 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz) δ=14.5, 24.0, 27.0, 45.7, 59.2, 70.6, 73.5, 109.5, 110.4, 118.8, 119.6, 121.1, 126.6, 127.50, 127.54, 127.6, 128.3, 128.6, 132.3, 132.5, 138.2, 139.9, 141.5; Anal. Calcd for $C_{27}H_{27}NO$: C, 85.00; H, 7.13; N, 3.67. Found: C, 84.80; H, 7.03; N, 3.47.

trans-**19a**; IR (neat) 2955, 1604, 1455, 1358 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.03 (t, J=7.6 Hz, 3H), 1.74–1.89 (m, 2H), 2.68 (ddd, J=13.6, 7.2, 6.0 Hz, 1H), 2.78–2.95 (m, 2H), 3.11 (ddd, J=13.6, 7.2, 1.6 Hz, 1H), 4.62 (s, 2H), 5.24 (dd, J=6.0, 1.6 Hz, 1H), 5.58 (dd, J=7.2, 7.2 Hz, 1H), 6.58 (d, J=7.6 Hz, 1H), 6.94 (dd, J=7.6, 7.6 Hz, 1H), 7.04 (dd, J=7.6, 7.6 Hz, 1H), 7.14–7.21 (m, 2H), 7.28–7.40 (m, 8H), 7.62 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz) δ=14.5, 24.1, 27.2, 47.8, 59.9, 70.4, 73.1, 109.7, 110.7, 118.6, 119.7, 121.1, 126.7, 127.6, 127.8, 127.9, 128.4, 128.8, 132.1, 132.4, 138.1, 138.7, 140.5.; HRMS calcd for $C_{27}H_{28}NO$: MH$^+$382.2172. Found: m/z 382.2151.

*4.5.9. Tetracyclic indoline (**20a**).* IR (neat) 2959, 2925, 2866, 1601, 1481, 1274, 1026 cm^{-1}; ^{1}H NMR (500 MHz) δ=1.00 (t, J=7.3 Hz, 3H), 1.35–1.47 (m, 1H), 1.63–1.47 (m, 1H), 1.77–1.86 (m, 2H), 2.10 (ddd, J=14.1, 10.3, 3.6 Hz, 1H), 2.87 (dd, J=14.1, 7.1 Hz, 1H), 3.57 (d, J=6.8 Hz, 1H), 4.33 (d, J=3.6 Hz, 1H), 4.62 (dd, J=10.3, 7.1 Hz, 1H), 5.13 (d, J=6.8 Hz, 1H), 5.87 (d, J=7.6 Hz, 1H), 6.35–6.42 (m, 2H), 6.88 (dd, J=7.6, 7.6 Hz, 1H), 6.95–6.99 (m, 2H), 7.15–7.23 (m, 3H), 7.29 (dd, J=7.4, 7.4 Hz, 1H), 7.40 (dd, J=7.4, 7.4 Hz, 2H), 7.52 (d, J=7.4 Hz, 2H); ^{13}C NMR (125 MHz) δ=14.7, 18.0, 40.3, 42.1, 57.7, 70.4, 85.4, 86.7, 87.3, 112.0, 120.2, 125.8, 126.2, 126.6, 126.8, 127.4, 127.6, 128.0, 128.6, 131.1, 137.1, 145.6, 156.1; Anal. Calcd for $C_{27}H_{27}NO$: C, 85.00; H, 7.13; N, 3.67. Found: C, 85.07; H, 7.34; N, 3.50.

*4.5.10. 2,3-Dihydro-1-(4-methoxybenzyloxy)-9-methyl-3-phenyl-1H-pyrrolo[1,2-a] indole (**19b**).* This compound was obtained as an inseparable mixture of diastereomers.

IR (neat) 2933, 2860, 1612, 1455, 1358 cm^{-1}; ^{1}H NMR (400 MHz) δ=2.39 (s, 2.25H), 2.42 (s, 0.75H), 2.53–2.67 (m, 1H), 3.03 (ddd, J=13.6, 6.4, 1.2 Hz, 0.25H), 3.23 (ddd, J=15.6, 8.8, 6.8 Hz, 0.75H), 3.75 (s, 2.25H), 3.76 (s, 0.75H), 4.46–4.60 (m, 2H), 5.11 (dd, J=6.8, 2.5 Hz, 0.75H), 5.14 (dd, J=6.0, 1.2 Hz, 0.25H), 5.28 (dd, J=8.8, 4.0 Hz, 0.75H), 5.53 (dd, J=8.4, 6.4 Hz, 0.25H), 6.51 (d, J=8.0 Hz, 0.25H), 6.79–6.87 (m, 2.75H), 6.90 (br d, J=8.0 Hz, 0.25H), 6.95–7.06 (m, 1.75H), 7.11–7.15(m, 0.5H), 7.16–7.32 (m, 6.5H), 7.51–7.56 (m, 1H); ^{13}C NMR (100 MHz) δ=9.3, 9.6, 45.8, 48.2, 55.3, 59.2, 60.0, 70.2, 72.6, 72.9, 104.1, 104.2, 110.3, 110.6, 113.7, 113.8, 118.6, 118.9, 119.2, 119.3, 121.2, 121.3, 126.6, 126.7, 127.5, 127.9, 128.6, 128.7, 129.1, 129.4, 130.26, 130.29, 132.0, 132.3, 132.88, 132.94, 140.0, 140.1, 140.3, 141.6, 159.0, 159.1 (2C missing); Anal. Calcd for $C_{26}H_{25}NO_2$ (*cis* and *trans* mixture): C, 81.43; H, 6.57; N, 3.65. Found: C, 81.64; H, 6.79; N, 3.35.

*4.5.11. Tetracyclic indoline (**20b**).* The stereochemistry of indoline **20b** was determined by X-ray analysis as shown in Fig. 8.

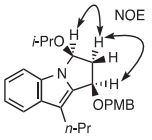
IR (neat) 3066, 2956, 2927, 2833, 1602, 1482, 1245, 1037 cm^{-1}; ^{1}H NMR (400 MHz) δ=1.62 (s, 3H), 2.12, (ddd, J=14.0, 10.4, 3.2 Hz, 1H), 2.85 (dd, J=14.0, 7.2 Hz, 1H), 3.43 (d, J=6.8 Hz, 1H), 3.78 (s, 3H), 4.27 (d, J=3.2 Hz, 1H), 4.61 (dd, J=10.4, 7.2 Hz, 1H), 5.12 (d, J=6.8 Hz, 1H), 5.96 (d, J=7.6 Hz, 1H), 6.39 (d, J=7.6 Hz, 1H), 6.47 (d, J=7.6 Hz, 1H), 6.73 (d, J=8.4 Hz, 2H), 6.87 (d, J=8.4 Hz, 2H), 6.93 (dd, J=7.6, 7.6 Hz, 1H), 7.30 (dd, J=7.6, 7.6 Hz, 1H), 7.40 (dd, J=7.6, 7.6 Hz, 2H), 7.54 (d, J=7.6 Hz, 2H); ^{13}C NMR (100 MHz) δ=24.4, 42.2, 55.2, 60.0, 70.5, 83.7, 84.9, 87.4, 112.0, 112.9, 120.3, 126.3, 126.4, 126.8, 127.9, 128.0, 128.5, 129.1, 130.7, 145.3, 155.3, 158.9; Anal. Calcd for $C_{26}H_{25}NO_2$: C, 81.43; H, 6.57; N, 3.65. Found: C, 81.67; H, 6.76; N, 3.60.

4.6. Procedure for $PtCl_2$-catalyzed reaction of imidate 6a with *p*-methoxybenzyl vinyl ether

To a mixture of *p*-methoxybenzyl vinyl ether **2b** (82 mg, 5.0 mmol), activated MS5A (200 mg), and $PtCl_2$ (1.0 mg,

0.003 mmol) in toluene (2.5 mL) was added an imidate **6a** (28.5 mg, 0.125 mmol) in toluene (1.5 mL) over 2 h at 50 °C. After heating for further 6.5 h, the reaction was quenched with saturated aq $NaHCO_3$ and the reaction mixture was filtered through a short pad of Celite®. The filtrate was extracted with ethyl acetate (3×) and the combined organic layer was washed with brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by preparative TLC (toluene/ethyl acetate=40:1) to give **9a** (42.6 mg, 87% (*cis*:*trans*=45:55)).

*4.6.1. cis-2,3-Dihydro-3-isopropoxy-1-(4-methoxybenzyloxy)-9-propyl-1H-pyrrolo[1,2-a]indole (**9a**).* The stereochemistry of the minor product was determined to be *cis* by the observed NOEs shown below. Therefore, the major product was assigned to be the corresponding *trans* isomer.



cis-**9a**

cis-**9a** (minor); IR (neat) 3050, 2959, 2930, 2869, 1612, 1514, 1455, 1328, 1247 cm^{-1}; ^1H NMR (500 MHz) δ=0.98 (t, J=7.3 Hz, 3H), 1.21 (d, J=6.0 Hz, 3H), 1.25 (d, J=6.0 Hz, 3H), 1.68–1.80 (m, 2H), 2.62 (br d, J=14.1 Hz, 1H), 2.71–2.83 (m, 2H), 2.95 (ddd, J=14.1, 6.8, 6.8 Hz, 1H), 3.81 (s, 3H), 4.08–4.17 (m, 1H), 4.51 (d, J=11.4 Hz, 1H), 4.63 (d, J=11.4 Hz, 1H), 5.08 (br d, J=6.8 Hz, 1H), 5.76 (br d, J=6.8 Hz, 1H), 6.89 (br d, J=8.6 Hz, 2H), 7.12 (br dd, J=8.0, 8.0 Hz, 1H), 7.20 (br dd, J=8.0, 8.0 Hz, 1H), 7.31 (br d, J=8.6 Hz, 2H), 7.38 (br d J=8.0 Hz, 1H), 7.59 (br d, J=8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ=14.4, 22.8, 23.2, 23.6, 26.8, 43.7, 55.3, 69.1, 69.3, 71.0, 83.0, 110.3, 110.6, 113.7, 119.5, 119.8, 121.7, 129.3, 130.7, 132.7, 132.8, 138.9, 159.1.; HRMS calcd for. $C_{25}H_{31}NO_3$, M 393.2304. Found m/z 393.2300.

trans-**9a** (major); IR (neat) 3050, 2960, 2930, 2869, 1612, 1514, 1456, 1328, 1248 cm^{-1}; ^1H NMR (500 MHz) δ=0.99 (t, J=7.4 Hz, 3H), 1.23 (d, J=6.1 Hz, 6H), 1.68–1.79 (m, 2H), 2.72–2.87 (m, 4H), 3.80 (s, 3H), 3.95–4.04 (m, 1H), 4.52 (d, J=11.2 Hz, 1H), 4.55 (d, J=11.2 Hz, 1H), 5.35 (dd, J=6.3, 4.9 Hz, 1H), 5.95 (dd, J=5.4, 3.2 Hz, 1H), 6.91 (br d, J=8.5 Hz, 2H), 7.11 (dd, J=8.0, 8.0 Hz, 1H), 7.17 (dd, J=8.0, 8.0 Hz, 1H), 7.31 (br d, J=8.5 Hz, 2H), 7.35 (d, J=8.0 Hz, 1H), 7.58 (d, J=8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ=14.3, 22.8, 23.0, 23.9, 26.5, 45.1, 55.3, 70.3, 70.4, 72.8, 84.2, 110.1, 110.3, 113.9, 119.3, 119.7, 121.4, 129.3, 130.3, 132.2, 133.2, 138.5, 159.3.; HRMS calcd for. $C_{25}H_{31}NO_3$, M 393.2304. Found m/z 393.2309.

4.7. Reduction of *N,O*-acetal moiety of *trans*-7a

$NaBH_3CN$ (3.6 mg, 0.057 mmol) was added to a mixture of tricyclic indole *trans*-**7a** (9.5 mg, 0.029 mmol) and *p*-toluenesulfonic acid monohydrate (5.3 mg, 0.028 mmol) in DMF (0.33 mL) at room temperature. After 20 h, the reaction mixture was quenched by saturated aq $NaHCO_3$, and the aqueous layer was extracted with ethyl acetate (3×) and the combined extracts were washed with brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by PTLC (hexane/ethyl acetate=5:1) to give **10** (7.0 mg, 90%).

*4.7.1. 1-tert-Butoxy-2,3-dihydro-9-propyl-1H-pyrrolo[1,2-a]-indole (**10**).* IR (neat) 3051, 2971, 2930, 2870, 1614, 1459, 1364 cm^{-1}; ^1H NMR (400 MHz) δ=0.98 (t, J=7.6 Hz, 3H), 1.35 (s, 9H), 1.60–1.80 (m, 2H), 2.45–2.55 (m, 1H), 2.76 (t, J=7.6 Hz, 2H), 2.79–2,91 (m, 1H), 3.90–3.99 (m, 1H), 4.18–4.26 (m, 1H), 5.25 (dd, J=6.8, 3.6 Hz, 1H), 7.04 (br dd, J=7.6, 7.6 Hz, 1H), 7.11 (br dd, J=7.6, 7.6 Hz, 1H), 7.20 (br d, J=7.6 Hz, 1H), 7.55 (br d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz) δ=14.4, 24.6, 26.2, 28.7, 39.0, 41.9, 67.5, 74.3, 108.3, 109.4, 118.3, 119.3, 120.5, 132.3, 132.5, 140.3.; HRMS calcd for $C_{18}H_{26}NO$: MH^+ 272.2005. Found: m/z 272.2010.

5. Crystallographic data

Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Center, CCDC no. 819184 for compound **20b**, CCDC no. 606158 for compound *trans*-**3c**. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.Uk).

Acknowledgements

This research was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan. We thank Ms. Sachiyo Kubo for performing X-ray analysis.

Supplementary data

^1H NMR spectra of **5a**, **8**, *cis*- and *trans*-**11**, *cis*- and *trans*-**19**, *cis*- and *trans*-**9a**, and **10**. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.04.017.

References and notes

1. For reviews on the synthesis of indole derivatives, see: (a) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045–1075; (b) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873–2920; (c) Barluenga, J.; Rodríguez, F.; Fañanás, F. J. *Chem.—Asian J.* **2009**, *4*, 1036–1048.
2. (a) Kusama, H.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2002**, *124*, 11592–11593 See also: (b) Kusama, H.; Suzuki, Y.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2006**, *8*, 895–897.
3. Takaya, J.; Kusama, H.; Iwasawa, N. *Chem. Lett.* **2004**, *33*, 16–17.
4. (a) Galm, U.; Hager, M. H.; Van Lanen, S. G.; Ju, J.; Thorson, J. S.; Shen, B. *Chem. Rev.* **2005**, *105*, 739–758; (b) Rajski, S. R.; Williams, R. M. *Chem. Rev.* **1998**, *98*, 2723–2795 For recent total synthesis of mitomycins, see: (c) Wang, Z.; Jimenez, L. S. *Tetrahedron Lett.* **1996**, *37*, 6049–6052 and references cited therein. See also; (d) Andrez, J.-C. *Beilstein J. Org. Chem* **2009**, *5* No. 33.
5. For recent examples of the preparation of mitosene skeletons, see: (a) Gubler, D. A.; Williams, R. M. *Tetrahedron Lett.* **2009**, *50*, 4265–4267 and references cited therein; (b) Pérez-Serrano, L.; Domínguez, G.; Pérez-Castells, J. *J. Org. Chem.* **2004**, *69*, 5413–5418; (c) Coleman, R. S.; Felpin, F.-X.; Chen, W. *J. Org. Chem.* **2004**, *69*, 7309–7316; (d) Tsuboike, K.; Guerin, D. J.; Mennen, S. M.; Miller, S. J. *Tetrahedron* **2004**, *60*, 7367–7374; (e) Kim, M.; Vedejs, E. *J. Org. Chem.* **2004**, *69*, 7262–7265 and references cited therein.
6. Part of this work has been communicated previously. See: Kusama, H.; Miyashita, Y.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2006**, *8*, 289–292.
7. There are some reports on generation and cycloaddition of azomethine ylides through transition metal-catalyzed electrophilic activation of alkynes. See: (a) Su, S.; Porco, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 7744–7745; (b) Yeom, H.-S.; Lee, J.-E.; Shin, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 7040–7043.
8. It is likely that these high valent metals are harder than the corresponding low valent metals and preferentially activate the aldimine part, which is more basic and harder than the alkyne moiety.
9. This product selectivity could be explained by considering higher nucleophilicity at the β-position of the zwitterionic alkenylmetal intermediate A of platinum(II) than that of platinum(IV).
10. For recent reviews on Pt- and Au-catalyzed synthetic reactions through electrophilic activation of C–C multiple bonds, see: (a) Shapiro, N. D.; Toste, F. D. *Synlett* **2010**, 675–691; (b) Wang, S.; Zhang, G.; Zhang, L. *Synlett* **2010**, 692–706; (c) Fürstner, A. *Chem. Soc. Rev.* **2009**, *38*, 3208–3221; (d) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239–3265; (e) Arcadi, A. *Chem. Rev.* **2008**, *108*, 3266–3325; (f) Shen, H. C. *Tetrahedron* **2008**, *64*, 3885–3903; (g) Kirsch, S. F. *Synthesis* **2008**, 3183–3204; (h) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410–3449.
11. For examples of catalytic reactions through electrophilic activation of alkynes by Re(I) complexes, see: (a) Chatani, N.; Kataoka, K.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9104–9105; (b) Hua, R.; Tian, X. *J. Org. Chem.* **2004**, *69*, 5782–5784; (c) Ouh, L. L.; Müller, T. E.; Yan, Y. K. *J. Organomet. Chem.* **2005**, *690*, 3774–3782; (d) Kuninobu, Y.; Kawata,

A.; Takai, K. *Org. Lett.* **2005**, *7*, 4823–4825; (e) Kusama, H.; Yamabe, H.; Onizawa, Y.; Hoshino, T.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 468–470; (f) Takaya, J.; Udagawa, S.; Kusama, H.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4906–4909; (g) Saito, K.; Onizawa, Y.; Kusama, H.; Iwasawa, N. *Chem.—Eur. J.* **2010**, *16*, 4716–4720.

12. It should be noted that the reactions of a *terminal* alkyne substrate with a catalytic amount of $PtCl_2$ or $AuBr_3$ were rather sluggish, while the corresponding tungsten-catalyzed reaction gave the desired tricyclic indole in high yield as previously reported.[2a]
13. For examples of Lewis acid-promoted, nucleophilic substitution reaction onto *N,O*-acetals, see: Sugiura, M.; Hagio, H.; Hirabayashi, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 12510–12517 and references cited therein.
14. Dagousset, G.; Drouet, F.; Masson, G.; Zhu, J. *Org. Lett.* **2009**, *11*, 5546–5549.
15. It should be noted that the C–H insertion product **20** was formed stereoselectively, whereas the 1,2-migration product was obtained as a mixture of stereoisomers, and this difference could be explained as follows. First, among four possible stereoisomers of the Pt–carbene intermediate **21**, **A** and **B** in which R^1 and OR are located *cis* are not suitable for C–H insertion since they give highly strained *trans*-fused 5-5 bicycles (Fig. 11). Concerning isomer **C**, its stable conformation would be **Cb** since both substituents, Ph and OR, are located in pseudo-equatorial position, where the benzylic proton and the carbene moiety are too widely separated to undergo C–H insertion. On the other hand, isomer **D** would favor the conformation **Da**, which is suitable for C–H insertion. This would avoid a large steric repulsion of Ph at pseudo-axial position in Db, and afford the C–H insertion product stereoselectively (Fig. 12). Furthermore, the C–H insertion reaction proceeds stereoselectively via TS E due to large steric repulsion between R^2 and the [Pt] moiety in TS F (Fig. 13).

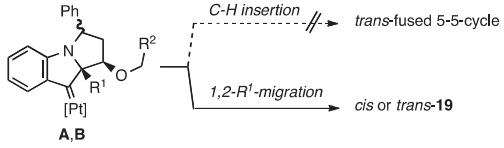


Fig. 11. Reaction of the stereoisomers **A** and **B**.

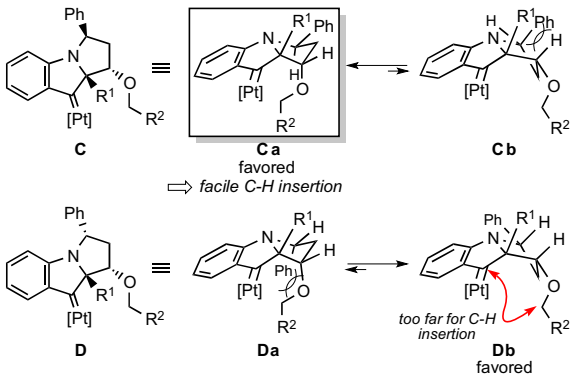


Fig. 12. Reaction of the stereoisomers **C** and **D**.

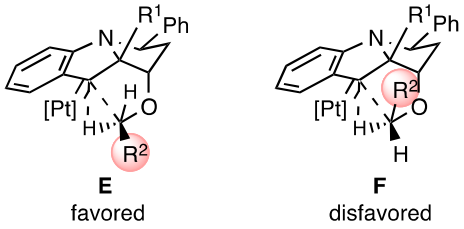


Fig. 13. Origin of diastereoselectivity in the C-H insertion.

16. Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5662–5663.
17. Villemin, D.; Goussu, D. *Heterocycles* **1989**, *29*, 1255–1261.
18. Fourquez, J. M.; Godard, A.; Marsais, F.; Quéguiner, G. *J. Heterocycl. Chem.* **1995**, *32*, 1165–1170.