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Palladium-Catalyzed Cycloisomerizations of (*Z*)-1-Iodo-1,6-dienes: Iodine Atom Transfer and Mechanistic Insight to Alkyl Iodide Reductive Elimination

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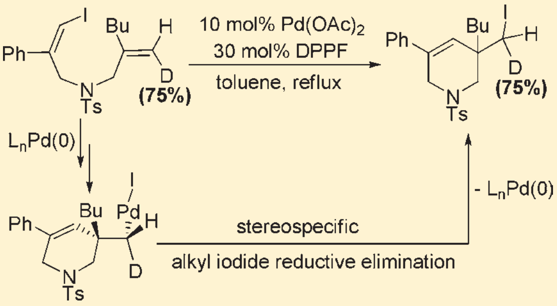
S *Supporting Information*

ABSTRACT: A palladium-catalyzed iodine atom transfer cycloisomerization of (Z)-1-iodo-1,6-diene has been developed, which provides a facile method to construct six-memebered heterocycles bearing an alkyl iodide group. The ligand screening shows that both the type and the quantity of ligand impose significant influences on this transformation, and the combination of 30 mol % 1,1′-bis(diphenylphosphino)ferrocene (DPPF) and 10 mol % $Pd(OAc)_2$ is the optimal choice. The catalytic cycle, consisting of oxidative addition of Pd(0) to vinyl iodide, intramolecular alkene insertion, and alkyl iodide reductive elimination, has been proposed and eventually supported by convincing evidence from a series of control experiments. More importantly, these control experiments disclose some features of the event of alkyl iodide reductive elimination: (1) this reductive elimination is proved to be a stereospecific process; and (2) both alkyl iodide oxidative addition and reductive elimination are not effected by a TEMPO additive. Besides its ability to undergo oxidative addition, the catalyst (palladium + DPPF) could also promote a radical transfer process. The findings described in this paper will be helpful for further development of the metal-catalyzed formation of a carbon−halide bond.



1. INTRODUCTION

Oxidative addition and reductive eliminations are fundamental transformations in numerous catalytic and stoichiometric processes.[1] In this context, oxidative addition of organic halides has received incredibly large amount of attention, as the initial step for most transition-metal-catalyzed formations of carbon−carbon[2] or carbon−X (X = N, O)[3] bonds. In contrast to the well established oxidative addition of organic halides, the reverse reaction, carbon halide reductive elimination from a transition-metal center, is substantially less documented.[4] In 1969, Ruddick et al. reported the thermolysis of the isomeric $[(PR_3)_2Pt(Me)_2(I)_2]$ complexes to yield mixtures of C−C and C−I reductive elimination products, representing an early example of $C(sp^3)$-halide reductive elimination.[5] Since then, continuous efforts have been dedicated to the Pt(IV) center related carbon halide reductive elimination, and great developments have been achieved, especially for mechanism elucidation[6] and its extension to $C(sp^2)$-halide analogues.[7] With respective to Pd(II) center, Hartwig et al. observed stoichiometric reductive elimination of arylpalladium halide induced by an excess of $P(t\text{-}Bu)_3$.[8] Interestingly, the reactivity of halide ligands followed the trend I > Br > Cl, suggesting the importance of kinetic factors in aryl halide reductive elimination. A few years later, Vigalok et al. also reported an elegant example of reductive elimination of iodoarene from the reaction of chelating arylpalladium iodide complexes with XeF_2.[9] In 2006, Milstein et al. showed that the CH_3−I reductive elimination could take place in a sterically encumbered Rh(III) pincer-type complex, representing the first direct observation of the $C(sp^3)$-X reductive elimination in a Croup 9 metal center.[10]

Despite all the advances in stoichiometric carbon halide reductive elimination, the catalytic variants are still remarkably rare and remain to be formidable challenges probably because the free energy favors oxidative addition, while reductive elimination is thermodynamically uphill. In light of their importance in both theoretical consideration and synthetic practice, metal-catalyzed reactions for carbon−halide bond formation are highly desirable.[11] A famous example of rhodium-catalyzed acyl-I reductive elimination comes from the Monsanto methanol carbonylation process, where the rapid hydrolysis of acyl iodide toward a carboxylic acid renders this reductive elimination irreversible, thus promoting the catalytic effects.[12] Very recently, Buchwald and co-workers have reported the Pd(0)-catalyzed conversion of aryl triflates to aryl halides, which highlighted the contribution of sterically demanding, electron-rich biaryl monophosphine ligand to aryl-X (X = F, Cl, Br) reductive elimination.[13] While preparing for this manuscript, Lautens et al. reported an interesting palladium-catalyzed cross-coupling of polyhalogenated

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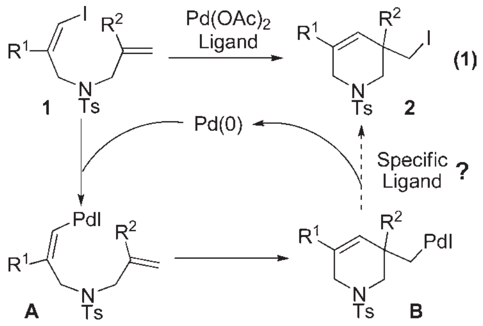
Scheme 1. Design Plan ($R^2 \neq H$)



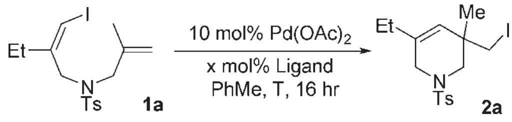
substrates to synthesize brominated indoles, which, for the first time, demonstrated that P(t-Bu)$_3$ induced reductive elimination of arylpalladium bromides could have catalytic features.[14] Although catalytic carbon halide reductive elimination in a low-valent Pd(II) metal center has not been widely reported so far, in contrast to the case of a Pd(IV) center,[15] it still provides a novel conceptual alternative. However, to the best of our knowledge, there has been no report on catalytic reactions involving the step of alkyl iodide reductive elimination from a Pd(II) center.

As part of our research on metal-catalyzed cyclizations of 1,6-enynes,[16] we have recently become interested in the substrate of (Z)-1-iodo-1,6-diene **1** (Scheme 1). It has been reported that substrate **1** offers an unique opportunity to form alkyl-Pd(II) intermediate **B** without a β-hydrogen ($R^2 \neq H$) via oxidative addition of Pd(0) species to vinyl iodide followed by alkene insertion (scheme 1).[17] Inspired by a recent report where bulky phosphine P(t-Bu)$_3$ can readily promote aryl-X (X = F, Cl, Br) reductive elimination from aryl−Pd(II) halides,[8,14] we envision that the alkyl−Pd(II) intermediate **B** would potentially undergo a similar alkyl iodide reductive elimination imposed by the same ligand effect. Herein, we report a palladium-catalyzed iodine atom transfer cycloisomerization of **1** to yield alkyl iodide **2** (first reaction, Scheme 1), where the alkyl iodide reductive elimination from intermediate **B** is proposed as the product-forming step in the catalytic cycle (Scheme 1).

2. RESULTS AND DISCUSSION

2.1. Reaction Optimization and Scope. To test our postulations outlined in Scheme 1, an initial attempt using substrate **1a** was conducted in toluene at 80 °C with the combination of 10 mol % Pd(OAc)$_2$ and 100 mol % P(t-Bu)$_3$ as catalyst, which really delivered the anticipated product **2a**, albeit only in 34% isolated yield (Table 1, entry 1). The structural assignment was initially supported by NMR and high-resolution mass spectrometry (HRMS) and later corroborated by X-ray crystallography of product **2b** (vide infra).[18] The yield of **2a** could increase to 41% when the reaction temperature was elevated to 120 °C (Table 1, entry 2). Moreover, the quantity of P(t-Bu)$_3$ had great impact on the reaction yield (Table 1, entries 3−5). It was found that the combination of Pd(OAc)$_2$ and phosphine ligand was essential for this transformation; no desired product was obtained in the absence of either Pd(OAc)$_2$ or ligand or both (Table 1, entries 6 and 8). Encouraged by these findings, different ligands were further evaluated. Other two monophosphine ligands, PPh$_3$ and P(n-Bu)$_3$, gave inferior results with yields of 23 and 15%, respectively (Table 1, entries 9 and 10). We therefore examined a variety of biphosphine ligands, such as 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP), 1,2-bis(diphenylphosphino)ethane (DPPE), and 1,3-bis(diphenylphosphino)propane (DPPP) as well as 1,2-bis(diphenylphosphino)benzene (DPPB), which, however, did not exhibit any superior performance than P(t-Bu)$_3$ (Table 1, entries 11−14). Fortunately, the use of 50 mol % 1,1′-bis(diphenylphosphino)ferrocene (DPPF) as ligand enabled a promising result with a 74% isolated yield (Table 1, entry 15). Once again, the quantity of DPPF was found to be an important factor, but its influence on the product yields is not monotonous (Table 1, entries 16−21). Nevertheless, the combination of 30 mol % DPPF and 10 mol % Pd(OAc)$_2$ was identified as the best choice, delivering **2a** in 84% yield (Table 1, entry 20). It should be noted that some classical radical initiators, such as (Bu$_3$Sn)$_2$, 2,2′-azobisisobutyronitrile (AIBN), or Et$_3$B/O$_2$, did not promote this cycloisomeration, and the starting material **1a** was recovered almost quantitatively in these cases.

Table 1. Initial Screening[a]

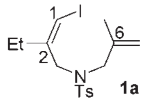
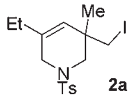
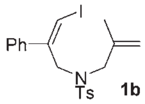
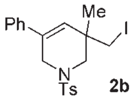
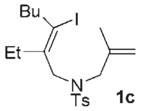
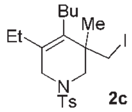
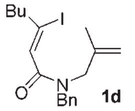
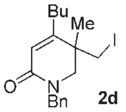
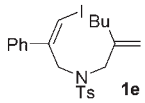
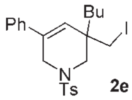
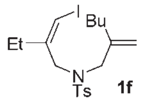
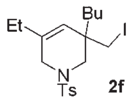
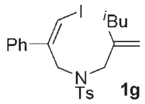
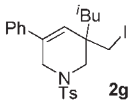
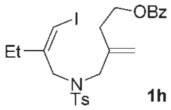
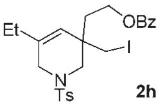
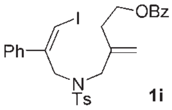
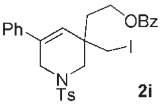
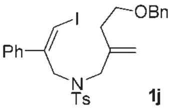
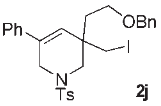
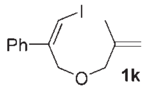
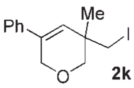
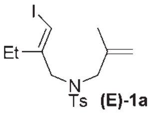


entry	ligand	x	T (°C)	yield (%)[b]
1	P(t-Bu)$_3$[c]	100	80	34
2	P(t-Bu)$_3$	100	reflux	41
3	P(t-Bu)$_3$	120	reflux	39
4	P(t-Bu)$_3$	60	reflux	27
5	P(t-Bu)$_3$	30	reflux	trace
6[d]	P(t-Bu)$_3$	100	reflux	ND[g]
7[e]	–	–	reflux	ND[g]
8[f]	–	–	reflux	ND[g]
9	PPh$_3$	100	reflux	23
10	P(n-Bu)$_3$	100	reflux	15
11	DPPE	50	reflux	trace
12	BINAP	50	reflux	10
13	DPPP	50	reflux	25
14	DPPB	50	reflux	36
15	DPPF	50	reflux	74
16	DPPF	70	reflux	75
17	DPPF	100	reflux	73
18	DPPF	20	reflux	trace
19	DPPF	25	reflux	43
20	**DPPF**	**30**	**reflux**	**84**
21	DPPF	40	reflux	71

[a] Reaction Conditions: **1a** (0.2 mmol, 83.8 mg), Pd(OAc)$_2$ (0.02 mmol, 4.5 mg), 4 mL toluene, 16 h. [b] Isolated yield. [c] [(t-Bu)$_3$PH]BF$_4$/K$_2$CO$_3$ (1:2) was used. [d] Without Pd(OAc)$_2$. [e] Without ligand. [f] Without Pd(OAc)$_2$ and ligand. [g] ND = not detected. Compound **1a** was recovered.

Table 2 summarizes the scope of this reaction under the optimized conditions as discussed above. In general, the palladium-catalyzed iodine atom transfer cycloisomerizations can be efficiently achieved with a considerably wide range of (Z)-1-iodo-1,6-dienes irrespective of nitrogen or oxygen linkage, delivering alkyl iodide derivatives **2** in moderate to high yields. Both alkyl and aryl substituents at C2 position are well tolerated. But the C1-position functionalized substrate **1c** was completely inert under the optimized conditions (Table 2, entry 3). This problematic issue can be partially resolved by using activated vinyl iodide as the substrate.

Table 2. Substrate Scope[a]

Entry	Substrate 1	Product 2	Yield (%)[b]
1	 1a	 2a	84
2	 1b	 2b	75
3	 1c	 2c	NR[c]
4	 1d	 2d	43
5	 1e	 2e	87
6	 1f	 2f	67
7	 1g	 2g	79
8	 1h	 2h	52
9	 1i	 2i	76
10	 1j	 2j	75
11	 1k	 2k	86
12	 (E)-1a	--	--

[a] Reaction Conditions: 1 (0.2 mmol), Pd(OAc)$_2$ (0.02 mmol, 4.6 mg), DPPF (0.06 mmol, 34 mg), 4 mL toluene, 120 °C, 16 h. [b] Isolated yield. [c] NR = no reaction.

Indeed, compound **1d** with electron-deficient vinyl iodide was found to be a suitable substrate although the corresponding product **2d** was isolated in a lower yield (Table 2, entry 4). On the contrary, substitution at the C6-position showed a much wider tolerance; even the bulky isobutyl group was compatible in terms of reaction rate and yield (Table 2, entry 7). Furthermore, oxygen-functionalized tether could also be introduced into C6-position (Table 2, entries 8−10). It was worth noting that the reaction of (*E*)-**1a** did not give **2a** on the base of thin-layer chromatography (TLC) monitor and ^{1}H NMR analysis of the crud reaction mixture, although it was completely consumed within 16 h (Table 2, entry 12).

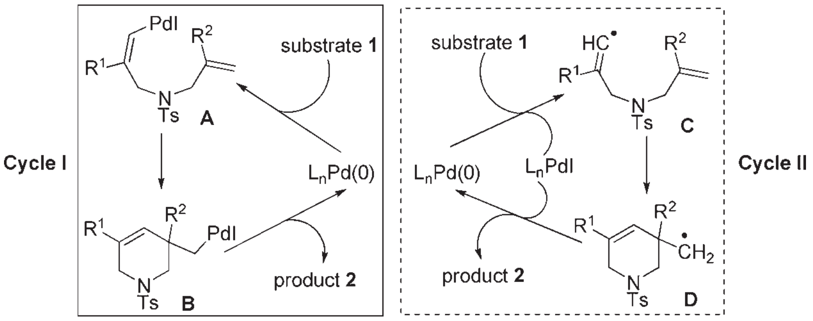
2.2. Mechanistic Consideration. Although elegant mechanistic analysis has uncovered several fundamental principles related to aryl-halide reductive elimination so far,[8−14] the alkyl−halide analogue still remains untouched. We believe that the reactions described above, especially the alkyl-I bond formation, would be a simple platform for mechanistic investigation, leading to a basic understanding for the further development of the transition-metal-catalyzed formation of carbon−halogen bond.

2.2.1. Catalytic Cycle. As mentioned in the Introduction Section, this transformation is initiated by oxidative addition of Pd(0) to vinyl iodide to yield vinyl−palladium intermediate **A**, which is followed by alkene insertion to form alkyl−Pd(II) intermediate **B** (Scheme 2, Cycle I). The lack of *β*-hydrogen and the presence of excess DPPF ligand might enforce intermediate **B** to undergo alkyl iodide reductive elimination. Thus, the alkyl iodide product **2** is obtained, and the Pd(0) catalyst is regenerated. However, in light of the structural relationship between **1** and **2**, an alternative possibility, the classic metal-catalyzed radical cyclization, should also be considered (Scheme 2, Cycle II).[19] At the initial stage, the Pd(0) species abstracts[20] the iodine atom from the vinyl iodide to generate a vinyl radical intermediate **C** and the metallic species L$_n$PdI.[21] According to Nagashima's finding,[22] the interactions between the radical species **C** and metallic species L$_n$PdI are not so strong. Thus, intermediate **C** will undergo radical addition in 6-exotrig fashion to form intermediate **D**, which abstracts the iodine atom from L$_n$PdI to yield product **2**. However, the fact that (*Z*)-**1a** and (*E*)-**1a** (Table 2, entries 1 and 12) presented completely different behavior under the same conditions primarily indicated the pathway of Cycle II to be unlikely. Further evidence against Cycle II has been obtained from the following experiment.

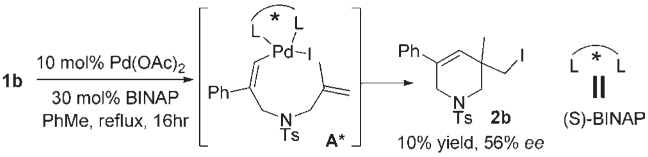
When the reaction of **1b** was performed by using a chiral ligand (*S*)-BINAP instead of DPPF, as expected, **2b** was obtained with 56% ee, albeit only in 10% yield (Scheme 3). These results strongly suggested the existence of vinyl−Pd(II) intermediate **A***, which induced asymmetric alkene insertion to realize the enantioselectivity. Obviously, the pathway of Cycle II, if possible, is unlikely to produce the enantioriched **2b** because the interaction between L$_n$PdI and intermediate **C** is too weak to promote asymmetric induction.[22]

The above results lead us to conclude that vinyl iodide **1** and Pd(0) species are prone to the formation of a regular oxidative addition adduct, such as intermediate **A**, rather than a radical pair (intermediate **C** + L$_n$PdI). One more evidence to support this argument comes from the results of HCO$_2$H·NEt$_3$ testing (Scheme 4). In fact, compound **3** could be isolated in 48% yield when the reaction of **1b** was conducted with HCO$_2$H·NEt$_3$ (5 equiv) as the additive; while under the same conditions, product **4** was obtained in the yield of 56% starting from substrate (*E*)-**1a** (Scheme 4). Therefore, the oxidative addition adduct (*E*)-**A**-**1a** was supposed to be involved, which was subsequently reduced by the reagent HCO$_2$H·NEt$_3$ to generate compound **4** (Scheme 4). The configuration of vinyl-Pd(II) intermediate (*E*)-**A**-**1a** is believed to be the reason for the failed conversion of (*E*)-**A**-**1a** into **2a** (Table 2, entry 12), thus the possibility of cycle II in scheme 2 can be further precluded.

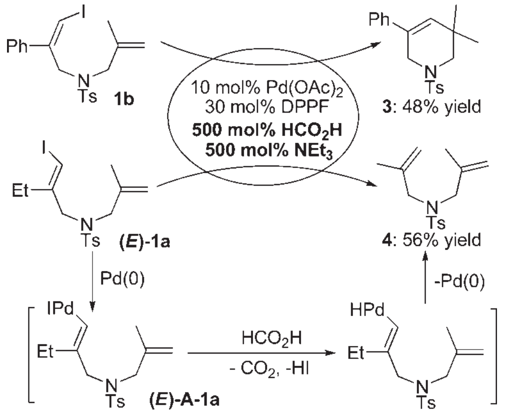
Scheme 2. Proposed Reaction Mechanisms



Scheme 3. Asymmetric Induction



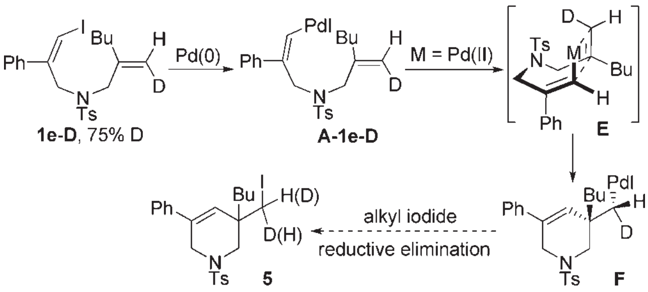
Scheme 4. $HCO_2H\cdot NEt_3$ Testing



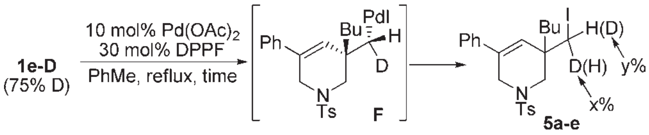
2.2.2. Mechanism of Alkyl Iodide Reductive Elimination. While the reaction mechanism depicted in Scheme 2 is a lack of direct evidence at this stage and still needs to be further verified, the pathway of Cycle I seems to be more consistent with the current experimental findings. After the establishment of the steps of oxidative addition and alkene insertion in Cycle I, we then focus on the subsequent step of alkyl iodide reductive elimination (RE).

To this purpose, we synthesized the deuterated substrate **1e-D** (75% D) with (*Z*)-configuration terminal olefin. The reaction of deuterated substrate **1e-D** would involve intermediate **F** with well-defined stereochemistry resulted from stereospecifically intramolecular insertion of olefin to vinyl—palladium bond in intermediate **A-1e-D** via a transition state **E**[17] (Scheme 5). Intermediate **F** will then undergo an alkyl iodide RE process to afford product **5**. In turn, the stereochemical information of **5** can be used to deduce the corresponding mechanism of alkyl iodide RE process.

Scheme 5. Investigation of the Mechanism of Alkyl Iodide RE



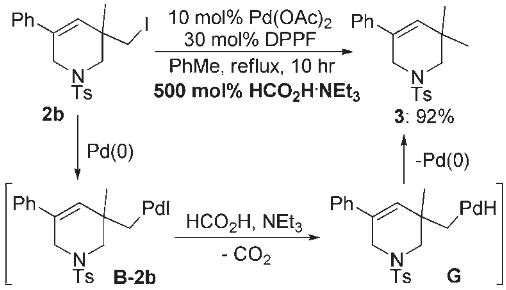
Scheme 6. Effect of Reaction Time on Deuterium Scrambling



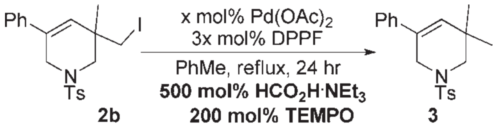
entry	time	1e-D recovery	product	isolated yield
1	2 hr	33%	**5a** (x = 75, y = 0)	60%
2	6 hr	20%	**5b** (x = 73, y = 2)	64%
3	10 hr	5%	**5c** (x = 71, y = 4)	75%
4	16 hr	0%	**5d** (x = 58, y = 17)	79%
5	24 hr	0%	**5e** (x = 40, y = 35)	72%

Initially, we subjected compound **1e-D** to the optimized conditions and ran this reaction for 16 h. To our delight, deuterated product **5d** was obtained in 79% yield without deuterium erosion but with deuterium scrambling (17% and 58%) (entry 4, Scheme 6). Apparently, the observation of deuterium scrambling seems to support a radical-involved process. However, the fact that only partial deuterium scrambling was observed in **5d** needs to be further elucidated. This finding inspired us to examine the reaction of **1e-D** more carefully. Surprisingly, compound **5e** with more even deuterium scrambling (35 and 40%) was obtained when the reaction time was prolonged to 24 h (entry 5, Scheme 6), implying a great effect of reaction time on deuterium scrambling. Thus, a series of control experiments with different reaction times was tested. When the reaction of **1e-D** was interrupted at 2 h, compound **5a** was unexpectedly isolated in

Scheme 7. Reaction of **2b** and $HCO_2H \cdot NEt_3$

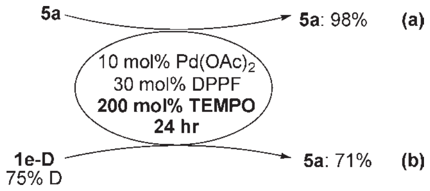


Scheme 8. Reaction of **2b** and $HCO_2H \cdot NEt_3$ in the Presence of TEMPO

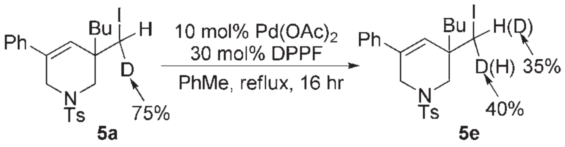


entry	x	yield (%)	
		3	**2b**
1	10	63	27
2	20	89	0

Scheme 9. TEMPO Testing



60% yield without deuterium scrambling; meanwhile **1e-D** was recovered in 33% yield (entry 1, Scheme 6). With the reaction time increased to 6 and 10 h, the corresponding products were isolated at higher yields, but the deuterium scrambling was still negligible (entries 2 and 3, Scheme 6). Furthermore, we found that **5a** could be readily converted into **5e** under the optimized conditions (eq 1).[23] These results strongly indicated that the event of deuterium scrambling should be promoted by the reaction of the newly formed product **5a** with Pd(0) catalyst, rather than the palladium-catalyzed cycloisomerization. Thus, we conclude that alkyl iodide reductive elimination in this palladium catalysis is a stereospecific process.



(2)

2.2.3. Explanation for the Observed Deuterium Scrambling. The control experiments as outlined in Scheme 6 and eq 1 have established that alkyl iodide reductive elimination in this palladium catalysis is a stereospecific step. Based on the principle of microscopic reversibility, it is reasonable to deduce that the reverse reaction, alkyl iodide oxidative addition, if possible under the same conditions, should also be a stereospecific process. Thus, it seems that the observed deuterium scrambling should be caused by a process other than the oxidative addition reaction of the newly formed product **5a** and Pd(0) catalyst.

To address the event of deuterium scrambling more clearly, we first sought to determine what actually happened to the newly formed alkyl iodides under the optimized conditions. We employed $HCO_2H \cdot NEt_3$ (500 mol %) as an additive[24] to probe the chemical behavior of **2b** (Scheme 7). To our delight, compound **3** was isolated in 92% yield, which was postulated to be formed via the route as depicted in Scheme 7. Additionally, it was found that the reagent $HCO_2H \cdot NEt_3$ could not realize this transformation without $Pd(OAc)_2$ or DPPF. These results suggest the facile oxidative addition of Pd(0) to the newly formed alkyl−I bond, resulting in alkyl−Pd(II) intermediate **B-2b** (Scheme 7). Furthermore, we found that TEMPO imposed some effects on the reaction of **2b** and $HCO_2H \cdot NEt_3$ (Scheme 8). Indeed, when the reaction of **2b** and $HCO_2H \cdot NEt_3$ was conducted in the presence of 200 mol % TEMPO, the corresponding yield of compound **3** was dropped to 63% with 27% of **2b** recovered (Scheme 8, entry 1), although it failed to isolate any adducts derived from radicals and TEMPO. However, the performance could be improved by increasing the catalyst loading to 20 mol % (Scheme 8, entry 2). Theses results strongly indicated that TEMPO might impose a negative effect on the catalyst itself rather than the process of alkyl iodide oxidative addition.

The above results inspired us to investigate the effect of TEMPO on the reaction of **5a** under the optimized conditions. In fact, compound **5a** could be recovered quantitatively with 200 mol % TEMPO as additive under the optimized conditions for 24 h (Scheme 9a), which was completely different from the case in the absence of TEMPO (eq 1). With combination of the results from both $HCO_2H \cdot NEt_3$ and TEMPO testing (Schemes 8 and 9), the following conclusions can be drawn: (1) alkyl iodide oxidative addition and the deuterium scrambling of **5a** are two separate processes, both of which can be initiated by the combination of Pd(0) and DPPF; and (2) the reaction accounting for the deuterium scrambling seems to be a standard process of radical transfer,[20,26] which can be completely inhibited by a radical scavenger (TEMPO).

As expected, TEMPO additive also ensured the reaction of **1e-D** to produce compound **5a** without deuterium scrambling under the optimized conditions even for 24 h (Scheme 9b). More importantly, the isolated yield of **5a** was 71%. The negligible effect of TEMPO on the yield of the deuterated product **5a** suggests that the TEMPO additive does not disturb the process of alkyl iodide reductive elimination, which is consistent with the observation from alkyl iodide oxidative addition (Scheme 8). Thus, it is believed that alkyl iodide reductive elimination and oxidative addition in this palladium catalysis is more likely to be a nonradical process.

3. CONCLUSIONS

We have found a Pd(0)-catalyzed cycloisomerization of (*Z*)-1-iodo-1,6-diene with an iodine atom transfer. This reaction provides a facile entry to 1,2,3,6-tetrahydropyridines with a quaternary carbon center. The reaction mechanism, consisting of oxidative addition of vinyl iodide, alkene insertion, and alkyl iodide reductive elimination, has been established on the basis of the results of a series of control experiments. More importantly, these control experiments disclose some features of the event of alkyl iodide reductive elimination: (1) this reductive elimination is proved to be a stereospecific process; and (2) both alkyl iodide oxidative addition and reductive elimination are not effected by TEMPO additive. Furthermore, it was found that the combination of palladium and DPPF might promote the process of radical transfer, which could make the scrambling of stereochemistry of alkyl iodide. We believe that the findings described in this paper will be helpful for further development of metal-catalyzed formation of carbon−halide bond.

4. EXPERIMENTAL SECTION

General Procedure for Pd-Catalyzed Cycloisomerization. In a 25 mL Schlenk tube, the mixture of **1a** (0.2 mmol, 84 mg), $Pd(OAc)_2$ (0.02 mmol, 4.6 mg), and DPPF (0.06 mmol, 34 mg) were dissolved in toluene (4 mL). Then, the reaction mixture was heated to reflux under nitrogen atmosphere. The reaction was monitored by TLC. When compound **1a** disappeared, the mixture was cooled to room temperature and directly subjected to column chromatography (silica gel, petroleum ether/EtOAc 50:1 to 5:1 gradient) to give a yellow oil (70 mg, 84% yield). See also Supporting Information.

2a: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (t, J = 7.2 Hz, 3H), 1.08 (s, 3H), 1.96 (q, J = 7.2 Hz, 2H), 2.43 (s, 3H), 2.54 (d, J = 11.2 Hz, 1H), 3.16−3.22 (m, 2H), 3.28 (d, J = 10.0 Hz, 1H), 3.33 (d, J = 11.2 Hz, 1H), 3.55 (d, J = 15.6 Hz, 1H), 5.20 (s, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 12.0, 18.2, 21.5, 25.4, 27.0, 36.0, 47.5, 52.4, 124.3, 127.7, 129.7, 133.1, 136.3, 143.6; MS (m/z): 419 (M^+); HRMS calcd for $C_{16}H_{22}INO_2S$: 419.0416, found: 419.0414.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Preparative methods and spectral and analytical data for all new compounds and X-ray crystallographic data for **2b** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(23) When compound **5a** was treated with refluxing toluene for 24 h, it was recovered quantitatively, and no deuterium scrambling was observed. Deuterium scrambling was also not observed in the presence of either 10 mol% Pd(OAc)$_2$ or 30 mol% DPPF in refluxing toluene for 24 h.

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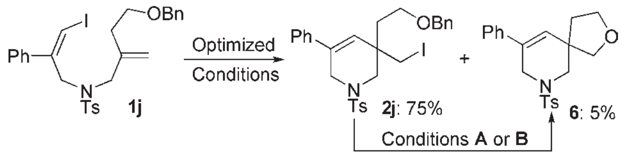
(26) Actually, 5% of byproduct **6** was isolated along with **2j** in the case of **1j**. Compound **2j** can be transformed into **6** under either the optimized conditions or the classical radical reaction conditions, indicating that the catalyst (palladium + DPPF) might also promote a radical process.



A: 200 mol% AIBN, toluene, reflux, 16 hr, 20%
B: 10 mol% Pd(OAc)$_2$, 30 mol% DPPF, toluene, reflux, 16 hr, 34%