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Synthesis of 6,7-dihydro-5*H*-dibenzo[*c*,*e*]azepines and biaryls by palladium-catalyzed Ullmann reaction

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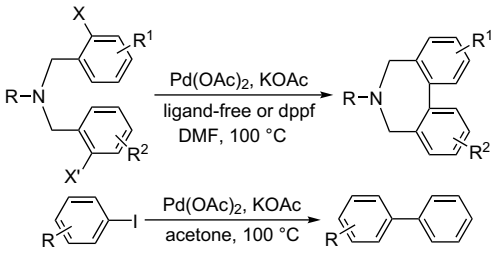
ABSTRACT

A novel palladium-catalyzed Ullmann protocol is described for the synthesis of 6,7-dihydro-5*H*-dibenzo[*c*,*e*]azepines and biaryls. In the presence of $Pd(OAc)_2$ and KOAc, intramolecular or intermolecular Ullmann coupling of aryl halides proceeds efficiently under ligand-free and aerobic conditions to afford the corresponding 6,7-dihydro-5*H*-dibenzo[*c*,*e*]azepines and biaryls in moderate to excellent yields.

1. Introduction

The Ullmann-type coupling of aryl halides has emerged as one of the most popular methods for the synthesis of biaryls.[1–5] Traditionally, copper and its complexes were used as the catalysts for the reaction.[1,2] However, these copper-mediated transformations are usually conducted under harsh conditions (neat, >200 °C) besides the requirement of a stoichiometric amount of Cu catalyst. A room temperature Ullmann coupling has been developed by Liebeskind and co-workers, however, both 2.5–3.0 equiv of copper(I) thiophene-2-carboxylate catalyst and substrates (aryl halides) bearing *ortho*-activated substitutes are necessary.[2e] To overcome these drawbacks, an array of transition metal catalysts were evaluated and found as an available and efficient alternative to copper.[1,3–6] Impressive progress has been made for the palladium-catalyzed Ullmann coupling reaction during the last several years.[4–6] However, additives, such as reducing agents (H_2, zinc, indium or hydroquinone, etc.), ligand, LiCl or *n*-Bu_4NBr, were required to improve the Ullmann coupling reaction.[4] Moreover, only few papers on the palladium-catalyzed intramolecular Ullmann coupling to construct carbocycles and heterocycles have been reported.[4f,4g,6] Rawal and co-workers have described an intramolecular reductive Ullmann coupling method using $Pd(OAc)_2$/As(*o*-tol)$_3$/hydroquinone system.[4g] However, the scope of this intramolecular Ullmann reaction has not yet been extensively explored (only three examples). Domínguez and co-workers have also reported an efficient palladium-catalyzed stannylation/biaryl coupling protocol for the synthesis of phenanthro[9,10-*d*]pyrazoles, but both PPh_3 and excess stoichiometric amount of Me_6Sn_2 were added.[6] An efficient Pd–C/In/LiCl catalytic system was found for the intramolecular Ullmann coupling recently, and only three examples were tested.[4f] Therefore, the development of some novel and additive-free routes for palladium-catalyzed Ullmann reactions, in particular for intramolecular Ullmann coupling, is still challenging in view of both economy and environment. Here, we wish to report an additive-free and aerobic palladium-catalyzed Ullmann coupling method for constructing 6,7-dihydro-5*H*-dibenzo[*c*,*e*]azepines, nitrogen-containing seven-member-ring compounds, and biaryls in moderate to excellent yields (Scheme 1).



Scheme 1.

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2. Results and discussion

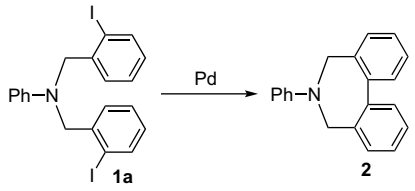
The intramolecular Ullmann coupling of *N*,*N*-bis(2-iodobenzyl)benzenamine was conducted to screen the optimal reaction conditions, and the results are summarized in Table 1. Initially, the temperature effect was tested, and heat was found to favor the reaction (entries 1–4). While at room temperature trace amount of the target product **2** was observed in the reaction of substrate **1a** with $Pd(OAc)_2$ and KOAc (entry 1), the yield of **2** was enhanced sharply to 93% at 100 °C (entry 4). Subsequently, effect of solvents was examined. We found that both DMA (*N*,*N*-dimethylacetamide) and acetone were inferior to DMF (entries 4–6). The screening results demonstrated that the amount of KOAc affected the reaction to some extent (entries 7–11). Two equivalents of KOAc, for instance, reduced the yield of **2** to 45%, and no reaction was observed without bases. Other two bases, K_2CO_3 and Cs_2CO_3, were less efficient for the reaction (entries 12 and 13). It is worth noting that a moderate yield is still achieved even at 5 mol% loading of $Pd(OAc)_2$, but no reaction takes place in the absence of Pd (entries 14 and 15). Finally, a set of other Pd catalytic systems, such as $PdCl_2$, $PdCl_2(PPh_3)_2$, Pd–C, $Pd(OAc)_2$/dppf (1,1′-bis(diphenylphosphino) ferrocene), $Pd(OAc)_2$/S-Phos (2-(dicyclohexylphosphino)-2′,6′-dimethoxy-1,1′-biphenyl) or $Pd(OAc)_2$/X-Phos (2-(dicyclohexylphosphino)-2′,4′,6′-tri-*i*-propyl-1,1′-biphenyl), were evaluated (entries 16–22). The results turned out that $PdCl_2$, $PdCl_2(PPh_3)_2$, and Pd–C were less efficient than $Pd(OAc)_2$ (entries 16–18), and these ligands have no effect on the reaction (entries 19–22).

Next, scope of the intramolecular Ullmann coupling was explored under the standard conditions (Table 2). Substitutes on the *N*-aryl moiety were firstly examined, and we were pleased to find that functional groups, including methyl, chloro, and methoxy groups were perfectly tolerated (entries 1–7). Treatment of *N*,*N*-bis(2-iodobenzyl)-4-methylbenzenamine (**1b**) with $Pd(OAc)_2$ and KOAc afforded the corresponding product **3** in 95% yield (entry 1), and substrates **1d**–**1g** bearing a chloro group also provided good yields under the same conditions (entries 3–7). However, the presence of dppf reduced the yield of **3** to 63% (entry 2). It was found that analogous amide with the *N*-aryl group replaced by a benzyl group still provided a good yield (entry 8), but by an *n*-butyl group was not a suitable substrate (entry 9). Subsequently, substrates **1j**–**1m** bearing alkoxy groups on the *N*-benzyl moieties were tested, and moderate yields were still achieved from the reactions of these substrates in the presence of $Pd(OAc)_2$ and KOAc (entries 10–13). *N*-(2-Iodo-4-methoxybenzyl)-*N*-(2-iodobenzyl)benzenamine (**1j**), for instance, underwent the intramolecular Ullmann coupling with $Pd(OAc)_2$ and KOAc smoothly to give the target product **11** in 61% yield (entry 10). The Ullmann couplings between two different groups on the same substrates were also investigated (entries 14–21). We found that the reaction between iodide and bromide was conducted successfully to afford the corresponding seven-member-ring compound **2** in 63% yield without ligands (entry 14), and 74% in the presence of dppf (entry 15). Identical results to dppf were obtained using S-Phos and X-phos (entries 16 and 17). However, the reaction of *N*-(2-chlorobenzyl)-*N*-(2-iodobenzyl)benzenamine (**1o**) was unsuccessful even in the presence of ligand, such as dppf, S-Phos and X-phos (entries 18–21). We found that no reaction occurred using *N*,*N*-bis(2-bromobenzyl)-3-methoxybenzenamine substrate (**1p**) under ligand-free conditions. Gratifyingly, dibromides **1p** and **1q** could undergo the reaction smoothly in the presence of dppf (entries 22–24). Treatment of *N*,*N*-bis(2-bromobenzyl)-3-methoxybenzenamine (**1p**), for example, with $Pd(OAc)_2$, KOAc, and dppf provided the corresponding target product **15** in 60% yield (entry 23). Finally, synthesis of nitrogen-containing six-member-ring compound was attempted, and the effect of solvents was found to affect the reaction to some extent (entries 25–28). No desired product was observed in DMF (entry 25), whereas phenanthridine **16** was isolated in 21% yield after 24 h using acetone as the solvent (entry 26). We found that the ligands displayed low activities for the reaction, and affected the reaction of substrate **1s** slightly (entries 27 and 28).

As shown in Table 3, homocoupling of aryl halides was explored under additive-free and aerobic conditions. Surprisingly, only a low yield of the desired product **17** was isolated from the reaction of 1-iodo-4-nitrobenzene (**1t**) with $Pd(OAc)_2$ and KOAc in DMF (entry 1). After a series of trials, we were happy to disclose that effect of solvents play a crucial role in the homocoupling reaction. In acetone, the yield of **17** was enhanced sharply to 92% (entry 2). Identical results were also obtained for another electron-deficient aryl iodide (**1s**), 4-iodobenzonitrile (entry 3). It was found that the prolonging reaction time was necessary to give good yields from the electron-rich aryl iodides **1v** and **1w** (entries 4 and 5). 1-Iodo-4-methylbenzene (**1v**), for instance, reacted with $Pd(OAc)_2$ and KOAc in acetone could afford 78% yield after 48 h (entry 4). Note that 2-iodothiophene (**1x**) is also a suitable substrate providing 96% yield (entry 6). However, the homocoupling reactions of aryl bromides, either electron-deficient or electron-rich, were conducted with low yields (entries 7 and 8).

Compared with the earlier reported palladium-catalyzed Ullmann coupling methods, the present reaction did not require the reported reducing agents such as H_2, Zn, In, *i*-hydroquinone, PrOH, or formate salts. Although Lemaire has reported ligand-free

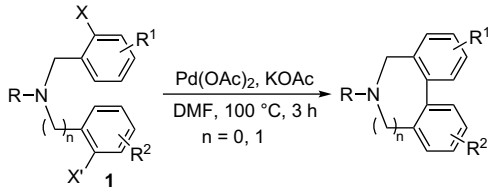
Table 1
Palladium-catalyzed intramolecular Ullmann reaction of *N*,*N*′-bis(2-iodobenzyl)-aniline (**1a**)[a]

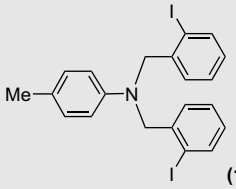
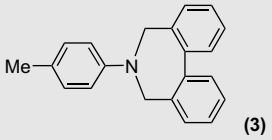
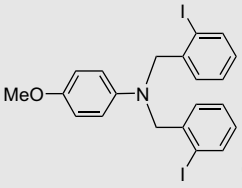
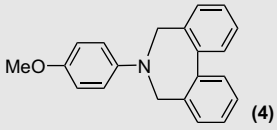
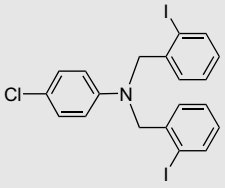
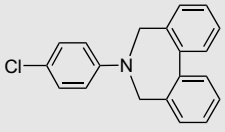
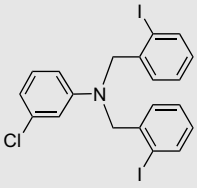
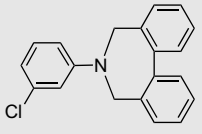
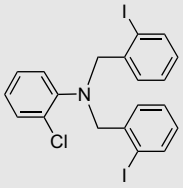
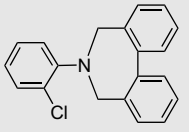
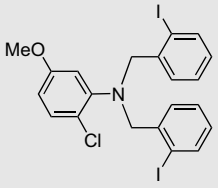
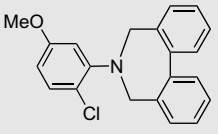
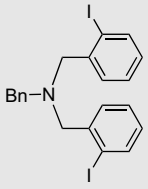
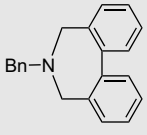


Entry	Pd (mol%)	Base (equiv)	*T* (°C)	Isolated yield (%)
1[b]	$Pd(OAc)_2$ (10)	KOAc (5)	rt	Trace
2	$Pd(OAc)_2$ (10)	KOAc (5)	60	32
3	$Pd(OAc)_2$ (10)	KOAc (5)	80	62
4	$Pd(OAc)_2$ (10)	KOAc (5)	100	93
5[c]	$Pd(OAc)_2$ (10)	KOAc (5)	100	75
6[d]	$Pd(OAc)_2$ (10)	KOAc (5)	100	54
7	$Pd(OAc)_2$ (10)	KOAc (4)	100	86
8	$Pd(OAc)_2$ (10)	KOAc (3)	100	82
9[e]	$Pd(OAc)_2$ (10)	KOAc (2)	100	45
10[e]	$Pd(OAc)_2$ (10)	KOAc (1)	100	43
11	$Pd(OAc)_2$ (10)	—	100	0
12	$Pd(OAc)_2$ (10)	K_2CO_3 (5)	100	85
13	$Pd(OAc)_2$ (10)	Cs_2CO_3 (5)	100	Trace
14	$Pd(OAc)_2$ (5)	KOAc (5)	100	60
15	—	KOAc (5)	100	0
16	$PdCl_2$ (10)	KOAc (5)	100	68
17	$PdCl_2(PPh_3)_2$ (10)	KOAc (5)	100	71
18	Pd/C (10)	86	86	86
19[f]	$Pd(OAc)_2$ (10)	KOAc (5)	100	65
20[g]	$Pd(OAc)_2$ (10)	KOAc (5)	100	91
21[h]	$Pd(OAc)_2$ (10)	KOAc (5)	100	89
22[i]	$Pd(OAc)_2$ (10)	KOAc (5)	100	92

[a] Reaction conditions: **1** (0.2 mmol), Pd and base in DMF (1 mL) under argon atmosphere for 3 h.
[b] >95% of **1a** was recovered.
[c] DMA (1 mL) instead of DMF for 24 h.
[d] Acetone (1 mL) instead of DMF. 13% of **1a** was recovered.
[e] About 25% of **1a** was recovered.
[f] Dppf (5 mol%) was added.
[g] Dppf (10 mol%) was added.
[h] S-Phos (10 mol%) was added.
[i] X-Phos (10 mol%) was added.

Table 2
Palladium-catalyzed intramolecular Ullmann reactions of **1**[a]



Entry	Substrate **1**	Product	Yield (%)[b]
1	 **(1b)**	 **(3)**	95
2[c]	(**1b**)	(**3**)	63
3	 **(1c)**	 **(4)**	81
4	 **(1d)**	 **(5)**	85
5	 **(1e)**	 **(6)**	91
6	 **(1f)**	 **(7)**	89
7[d]	 **(1g)**	 **(8)**	70
8	 **(1h)**	 **(9)**	88

(*continued on next page*)

Table 2 (*continued*)

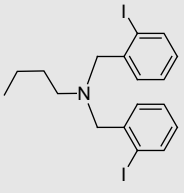
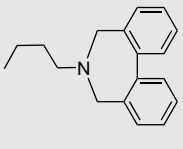
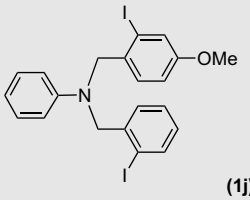
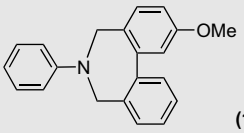
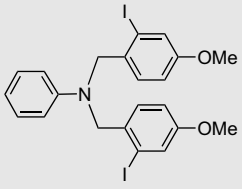
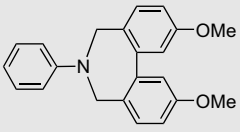
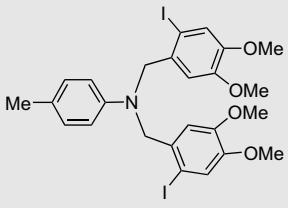
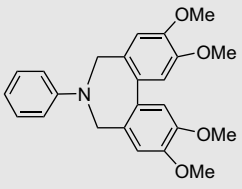
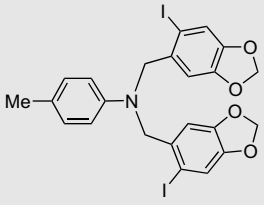
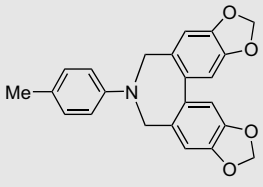
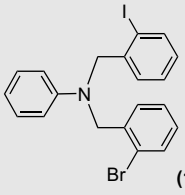
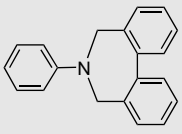
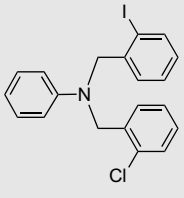
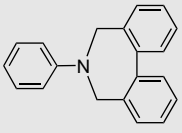
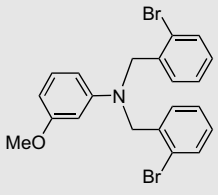
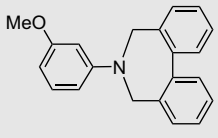
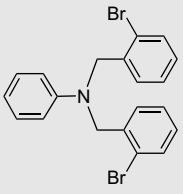
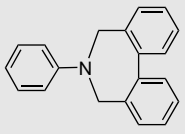
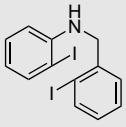
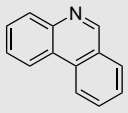
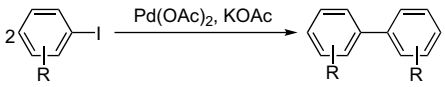
Entry	Substrate **1**	Product	Yield (%)[b]
9[e]	 **(1i)**	 **(10)**	Trace
10	 **(1j)**	 **(11)**	61
11	 **(1k)**	 **(12)**	57
12	 **(1l)**	 **(13)**	44
13	 **(1m)**	 **(14)**	56
14	 **(1n)**	 **(2)**	63
15[c]	(**1n**)	(**2**)	74
16[f]	(**1n**)	(**2**)	73
17[g]	(**1n**)	(**2**)	80
18	 **(1o)**	 **(2)**	0
19[c]	(**1o**)	(**2**)	0
20[f]	(**1o**)	(**2**)	0
21[g]	(**1o**)	(**2**)	0

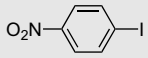
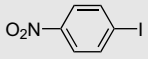
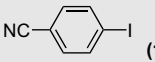
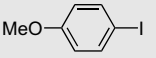
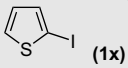
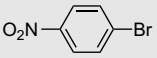
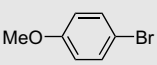
Table 2 (*continued*)

Entry	Substrate **1**	Product	Yield (%)[b]
22	 **(1p)**	 **(15)**	Trace
23[c]	(**1q**)	(**15**)	60
24[c]	 **(1r)**	 **(2)**	65
25[d]	 **(1s)**	 **(16)**	Trace
26[h]	(**1s**)	(**16**)	21
27[f,h]	(**1s**)	(**16**)	3
28[g,h]	(**1s**)	(**16**)	24

[a] Reaction conditions: **1** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), and KOAc (5 equiv) in DMF (1 mL) at 100 °C for 3 h under air atmosphere.
[b] Isolated yield.
[c] Dppf (10 mol %) was added for 24 h.
[d] For 24 h.
[e] >95% of substrate **1** was recovered.
[f] S-Phos (10 mol %) was added.
[g] X-Phos (10 mol %) was added.
[h] In acetone (1 mL) for 24 h.

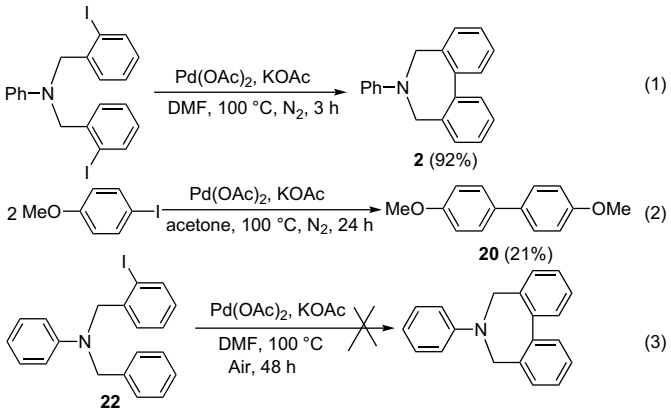
Table 3
Palladium-catalyzed homocoupling of aryl halides[a]



Entry	Substrate **1**	Time (h)	Isolated yield (%)
1[b]	 **(1t)**	12	15 (**17**)
2	 **(1t)**	12	92 (**17**)
3	 **(1u)**	12	94 (**18**)
4	 **(1v)**	48	78 (**19**)
5	 **(1w)**	48	47 (**20**)
6	 **(1x)**	12	96 (**21**)
7	 **(1y)**	48	38 (**17**)
8	 **(1z)**	48	19 (**20**)

[a] Reaction conditions: **1** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), and KOAc (5 equiv) in acetone (1 mL) at 100 °C under nitrogen atmosphere.
[b] In DMF (1 mL).

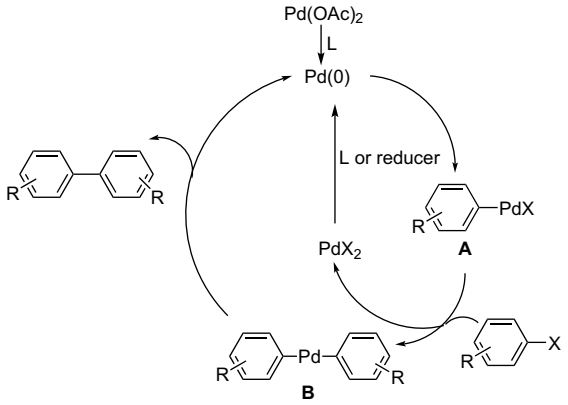
palladium-catalyzed Ullmann coupling for the synthesis of bithiophenes using $Pd(OAc)_2/(i\text{-}Pr)_2NEt$ system, the mechanism was not discussed because the reducing agent was not confirmed.[5] This identical problem is now presented in the present reaction. To elucidate the mechanism, three controlled reactions were conducted as listed in Scheme 2 to evaluate the role of oxygen. The former reaction was carried out under nitrogen atmosphere, and a high yield was still obtained (Eq. 1). The second reaction was carried out under nitrogen atmosphere with a reduced yield (Eq. 2). The oxidative Ullmann coupling reaction was not observed using *N*-(2-iodobenzyl)-*N*-benzylbenzenamine as the substrates (Eq. 3). The controlled results suggested that oxygen has no effect on the



Scheme 2. Three controlled reactions.

intramolecular Ullmann coupling reaction, but affected the intermolecular Ullmann homocoupling reaction. On the other hand, the results in Table 1 showed that the amount of both Pd and KOAc was found to affect the reaction (entries 7 and 11 in Table 1). Particularly, 5 equiv of KOAc was required to provide the best results. Thus, we deduced that KOAc might play the same role of the precursor of reductant as formic salts.[4i,4j]

Thus, a working Pd(II) mechanism for the present reaction is proposed as outlined in Scheme 3 on the basis of the earlier reported mechanism.[4,6,7] Initially, aryl-Pd(II)-X complexes **A** are generated from the reaction of Pd(0) with aryl halides, followed by the second reaction with aryl halides to afford intermediate Ar–Pd–Ar (**B**) and PdX_2. Intermediate **B** undergoes reductive elimination to give the product and regenerate the active Pd(0) species. PdX_2 can be reduced readily by ligand or reducer (H_2) to afford the active Pd(0) species. H_2 may be obtained in situ from the reaction of $CHCO_2^-$ and water.[4i,4j,7] Further study of the true mechanism is in progress.



Scheme 3. A possible mechanism.

3. Conclusion

In summary, we have developed a simple and additive-free palladium-catalyzed Ullmann coupling protocol. This method allows not only for efficient cyclization of a variety of dihalides into the corresponding 6,7-dihydro-5*H*-dibenzo[*c*,*e*]azepines, but also for homocoupling of aryl halides into the desired biaryls. It is noteworthy that these products are important compounds that widely occur in nature pharmacological products and materials as well as are often utilized as intermediates in organic synthesis.

4. Experimental section

4.1. General

NMR spectroscopy was performed on both a Bruck-300 spectrometer operating at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR) and a Bruck-400 spectrometer operating at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). TMS (tetramethylsilane) was used an internal standard and $CDCl_3$ was used as the solvent. Mass spectrometric analysis was performed on GC–MS analysis (SHIMADZU GCMS-QP 2010 plus).

4.2. Typical experimental procedure for the palladium-catalyzed intramolecular Ullmann reaction (Tables 1 and 2)

A mixture of dihalides **1** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), dppf (the indicated loading), and KOAc (5 equiv) was stirred in DMF (1 mL) at 100 °C for the indicated reaction time until complete consumption of starting material as monitored by TLC and GC–MS analysis. Then the mixture was washed with saturated NaCl and extracted with diethyl ether. The organic layers were dried with anhydrous Na_2SO_3 and evaporated under vacuum, the residue was purified by flash column chromatography (hexane/ethyl acetate) to afford the pure product.

4.3. Typical experimental procedure for the palladium-catalyzed homocoupling of aryl halides (Table 3)

A mixture of aryl halide **1** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), and KOAc (5 equiv) was stirred in acetone (1 mL) at 100 °C for the indicated reaction time until complete consumption of starting material as monitored by TLC and GC–MS analysis. Then the mixture was filtered with a crude column chromatography and washed with diethyl ether. The organic layers were evaporated under vacuum, the residue was purified by flash column chromatography (hexane, or hexane/ethyl acetate) to afford the pure product.

*4.3.1. 6-Phenyl-6,7-dihydro-5H-dibenzo[c,e]azepine (**2**)*

Yellow liquid; ^{1}H NMR (300 MHz) δ: 7.58 (d, J=7.6 Hz, 2H), 7.510–7.36 (m, 6H), 7.24 (t, J=8.0 Hz, 2H), 7.06 (d, J=8.2 Hz, 2H), 6.74 (t, J=8.0 Hz, 1H), 4.14 (s, 4H); ^{13}C NMR (75 MHz) δ: 149.5, 140.9, 134.9, 129.6, 129.2, 128.9, 127.7, 127.5, 118.2, 115.0, 52.2; LRMS (EI, 70 eV) m/z (%): 271 (M^+, 88), 270 (M^+-1, 100); HRMS (EI) for $C_{20}H_{17}N$ (M^+): calcd 271.1361, found 271.1361.

*4.3.2. 6-p-Tolyl-6,7-dihydro-5H-dibenzo[c,e]azepine (**3**)*

Yellow liquid; ^{1}H NMR (300 MHz) δ: 7.89 (d, J=8.0 Hz, 2H), 7.35–7.21 (m, 4H), 7.00 (t, J=7.9 Hz, 4H), 6.46 (d, J=8.2 Hz, 2H), 4.54 (s, 4H), 2.24 (s, 3H); ^{13}C NMR (75 MHz) δ: 141.1, 136.3, 135.7, 134.5, 129.7, 129.1, 129.0, 127.8, 127.5, 59.1, 54.8, 21.0; LRMS (EI, 70 eV) m/z (%): 285 (M^+, 86), 284 (M^+-1, 100); HRMS (EI) for $C_{21}H_{19}N$ (M^+): calcd 285.1518, found 285.1517.

*4.3.3. 6-(4-Methoxyphenyl)-6,7-dihydro-5H-dibenzo[c,e]-azepine (**4**)*

Yellow solid, mp 107–109 °C (uncorrected); ^{1}H NMR (300 MHz) δ: 7.54 (d, J=7.7 Hz, 2H), 7.47–7.43 (m, 2H), 7.34–7.32 (m, 4H), 6.98 (d, J=7.7 Hz, 2H), 6.86 (d, J=8.0 Hz, 2H), 4.04 (s, 4H), 3.75 (s, 3H); ^{13}C NMR (75 MHz) δ: 160.8, 153.1, 140.7, 134.8, 129.5, 128.2, 128.0, 127.6, 117.4, 114.5, 55.6, 53.4; LRMS (EI, 70 eV) m/z (%): 302 (21), 301 (M^+, 100), 300 (78), 286 (54); HRMS (EI) for $C_{21}H_{19}NO$ (M^+): calcd 301.1467, found 301.1466.

*4.3.4. 6-(4-Chlorophenyl)-6,7-dihydro-5H-dibenzo[c,e]azepine (**5**)*

Yellow solid, mp 141–143 °C (uncorrected); ^{1}H NMR (300 MHz) δ: 7.54 (d, J=8.2 Hz, 2H), 7.48–7.46 (m, 2H), 7.35–7.33 (m, 4H), 7.22 (dd, J=6.8 Hz, J=2.2 Hz, 2H), 6.91 (d, J=8.2 Hz, 2H), 4.09 (s, 4H); ^{13}C NMR (75 MHz) δ: 148.0, 140.6, 134.5, 129.5, 128.9, 128.4, 128.1, 127.7, 123.6, 116.1, 52.3; LRMS (EI, 70 eV) m/z (%): 307 (M^++2, 32), 306 (47), 305 (M^+, 88), 304 (M^+-1, 100), 270 (–Cl, 2), 269 (4), 268 (5); HRMS (EI) for $C_{20}H_{16}^{35}ClN$ (M^+): calcd 305.0971, found 305.0971.

*4.3.5. 6-(3-Chlorophenyl)-6,7-dihydro-5H-dibenzo[c,e]azepine (**6**)*

Yellow liquid; ^{1}H NMR (300 MHz) δ: 7.57 (d, J=7.4 Hz, 2H), 7.50–7.45 (m, 2H), 7.37–7.35 (m, 4H), 7.19 (t, J=8.0 Hz, 1H), 6.96–6.80 (m, 3H), 4.13 (s, 4H); ^{13}C NMR (75 MHz) δ: 150.4, 140.6, 135.0, 134.4, 130.0, 129.5, 128.4, 128.2, 127.8, 117.8, 114.5, 112.8, 51.9; LRMS (EI, 70 eV) m/z (%): 307 (M^++2, 31), 306 (48), 305 (M^+, 90), 304 (M^+-1, 100), 268 (M^+–Cl, 5); HRMS (EI) for $C_{20}H_{16}^{35}ClN$ (M^+): calcd 305.0971, found 305.0970.

*4.3.6. 6-(2-Chlorophenyl)-6,7-dihydro-5H-dibenzo[c,e]azepine (**7**)*

Yellow solid, mp 62.0 °C (uncorrected); ^{1}H NMR (300 MHz) δ: 7.56 (d, J=7.4 Hz, 2H), 7.47–7.33 (m, 7H), 7.16–7.12 (m, 2H), 6.98

(m, 1H), 4.00 (s, 4H); ^{13}C NMR (75 MHz) δ: 148.7, 140.9, 139.7, 134.7, 130.8, 129.7, 128.1, 128.0, 127.5, 127.1, 123.2, 121.4, 54.3; LRMS (EI, 70 eV) *m*/*z* (%): 307 (M^++2, 27), 306 (48), 305 (M^+, 73), 304 (M^+−1, 100), 268 (M^+−Cl, 5); HRMS (EI) for $C_{20}H_{16}^{35}ClN$ (M^+): calcd 305.0971, found 305.0971.

*4.3.7. 6-(2-Chloro-5-methoxyphenyl)-6,7-dihydro-5H-dibenzo-[c,e]azepine (**8**)*

Pale yellow liquid; ^{1}H NMR (300 MHz) δ: 7.55 (d, *J*=6.8 Hz, 2H), 7.49–7.46 (m, 2H), 7.37–7.30 (m, 5H), 6.66 (s, 1H), 6.53 (d, *J*=8.7 Hz, 1H), 4.00 (s, 4H), 3.74 (s, 3H); ^{13}C NMR (75 MHz) δ: 158.8, 149.5, 140.9, 134.7, 131.0, 129.8, 128.2, 128.1, 127.6, 119.5, 108.1, 107.6, 55.4, 54.3; LRMS (EI, 70 eV) *m*/*z* (%): 335 (M^+, 79), 334 (M^+−1, 100), 300 (M^+−Cl, 6); HRMS (EI) for $C_{18}H_{14}ClNO_3$ (M^+): calcd 327.0662, found 327.0662.

*4.3.8. 6-(4-Methylbenzyl)-6,7-dihydro-5H-dibenzo[c,e]azepine (**9**)*

Yellow liquid; ^{1}H NMR (300 MHz) δ: 7.52 (d, *J*=7.7 Hz, 2H), 7.51–7.35 (m, 8H), 7.20 (d, *J*=7.7 Hz, 2H), 3.68 (s, 2H), 3.40 (s, 4H), 2.39 (s, 3H); ^{13}C NMR (75 MHz) δ: 141.1, 136.4, 135.7, 129.7, 129.1, 128.9, 127.8, 127.5, 59.1, 54.8, 21.0; LRMS (EI, 70 eV) *m*/*z* (%): 300 (32), 299 (M^+, 100), 298 (95); HRMS (EI) for $C_{22}H_{21}N$ (M^+): calcd 299.1674, found 299.1674.

*4.3.9. 2-Methoxy-6-phenyl-6,7-dihydro-5H-dibenzo[c,e]-azepine (**11**)*

Yellow liquid; ^{1}H NMR (300 MHz) δ: 7.51–7.44 (m, 3H), 7.35–7.28 (m, 4H), 7.03–7.00 (m, 3H), 6.92 (s, 1H), 6.83 (t, *J*=8.0 Hz, 1H), 4.15 (s, 4H), 3.83 (s, 3H); ^{13}C NMR (75 MHz) δ: 159.4, 149.5, 140.5, 136.2, 134.6, 133.2, 129.6, 129.2, 128.8, 128.2, 127.4, 118.2, 115.0, 114.9, 113.6, 55.3, 52.4; LRMS (EI, 70 eV) *m*/*z* (%): 301 (M^+, 99), 300 (M^+−1, 100), 286 (M^+−CH_3, 5); HRMS (EI) for $C_{21}H_{19}NO$ (M^+): calcd 301.1467, found 301.1466.

*4.3.10. 2,10-Dimethoxy-6-phenyl-6,7-dihydro-5H-dibenzo[c,e]-azepine (**12**)*

Yellow solid, mp 107–109 °C (uncorrected); ^{1}H NMR (300 MHz) δ: 7.40 (d, *J*=8.4 Hz, 2H), 7.30–7.27 (m, 2H), 7.00–6.94 (m, 4H), 6.88 (s, 2H), 6.81 (t, *J*=8.0 Hz, 1H), 4.11 (s, 4H), 3.82 (s, 6H); ^{13}C NMR (75 MHz) δ: 159.0, 135.8, 133.0, 129.1, 128.5, 118.1, 115.0, 114.9, 113.6, 55.3, 52.5; LRMS (EI, 70 eV) *m*/*z* (%): 332 (24), 331 (M^+, 100), 330 (78); HRMS (EI) for $C_{22}H_{21}NO_2$ (M^+): calcd 331.1572, found 331.1572.

*4.3.11. 2,3,9,10-Tetramethoxy-6-phenyl-6,7-dihydro-5H-dibenzo-[c,e]azepine (**13**)*

Yellow solid, mp 72 °C (uncorrected); ^{1}H NMR (300 MHz) δ: 7.32–7.30 (m, 3H), 7.03–6.98 (m, 4H), 6.86 (s, 2H), 4.09 (s, 4H), 3.98 (s, 6H), 3.90 (s, 6H); ^{13}C NMR (75 MHz) δ: 149.6, 148.8, 148.4, 133.1, 129.1, 127.5, 118.0, 114.8, 112.9, 110.6, 56.2, 56.0, 52.0; LRMS (EI, 70 eV) *m*/*z* (%): 392 (25), 391 (M^+, 100), 390 (73), 376 (M^+−CH_3, 30), 286 (49); HRMS (EI) for $C_{24}H_{25}NO_4$ (M^+): calcd 391.1784, found 391.1783.

*4.3.12. Product (**14**)*

Yellow solid, mp 176 °C (uncorrected); ^{1}H NMR (300 MHz) δ: 7.07 (d, *J*=8.4 Hz, 2H), 6.91 (s, 2H), 6.87 (d, *J*=8.5 Hz, 2H), 6.78 (s, 2H), 5.97 (s, 4H), 3.94 (s, 4H), 2.27 (s, 3H); ^{13}C NMR (75 MHz) δ: 147.5, 147.3, 146.9, 134.4, 129.7, 128.5, 127.8, 115.5, 109.8, 107.7, 101.2, 52.4, 20.3; LRMS (EI, 70 eV) *m*/*z* (%): 374 (25), 373 (M^+, 100), 372 (49), 255 (12), 254 (61); HRMS (EI) for $C_{23}H_{19}NO_4$ (M^+): calcd 373.1314, found 373.1314.

*4.3.13. 6-(3-Methoxyphenyl)-6,7-dihydro-5H-dibenzo[c,e]-azepine (**15**)*

Yellow oil; ^{1}H NMR (300 MHz) δ: 7.57 (d, *J*=7.8 Hz, 2H), 7.50–7.45 (m, 2H), 7.38–7.36 (m, 4H), 7.23 (d, *J*=8.4 Hz, 1H), 6.68 (d, *J*=8.0 Hz, 1H), 6.56 (t, *J*=2.4 Hz, 1H), 6.42 (d, *J*=8.0 Hz, 1H), 4.16 (s, 4H), 3.84 (s, 3H); ^{13}C NMR (75 MHz) δ: 160.7, 150.8, 140.7, 134.8, 129.8, 129.6, 128.3, 128.1, 127.7, 107.9, 102.8, 101.5, 55.2, 52.1; LRMS (EI, 70 eV) *m*/*z* (%): 302 (27), 301 (M^+, 100), 300 (98), 286 (54); HRMS (EI) for $C_{21}H_{19}NO$ (M^+): calcd 301.1467, found 301.1467.

*4.3.14. Phenanthridine (**16**)*[4]

Yellow solid; ^{1}H NMR (300 MHz) δ: 9.26 (s, 1H), 8.57 (t, *J*=9.3 Hz, 2H), 8.17 (d, *J*=8.0 Hz, 1H), 8.02 (d, *J*=8.0 Hz, 1H), 7.86–7.81 (m, 1H), 7.75–7.56 (m, 3H); ^{13}C NMR (75 MHz) δ: 153.5, 144.4, 132.6, 131.0, 130.1, 128.8, 128.7, 127.5, 127.1, 126.4, 122.2, 121.9; LRMS (EI, 70 eV) *m*/*z* (%): 179 (M^+, 100).

*4.3.15. 4,4′-Dinitrobiphenyl (**17**)*[4]

Yellow solid; ^{1}H NMR (300 MHz) δ: 8.36 (d, *J*=8.8 Hz, 4H), 7.78 (d, *J*=8.8 Hz, 4H); ^{13}C NMR (75 MHz) δ: 148.0, 145.0, 128.3, 124.4; LRMS (EI, 70 eV) *m*/*z* (%): 244 (M^+, 100).

*4.3.16. Biphenyl-4,4′-dicarbonitrile (**18**)*[4]

Pale yellow solid; ^{1}H NMR (300 MHz) δ: 7.76 (dd, *J*=6.6 Hz, 1.9 Hz, 4H), 7.67 (dd, *J*=6.6 Hz, 1.9 Hz, 4H); ^{13}C NMR (75 MHz) δ: 143.5, 132.9, 127.9, 118.4, 112.5; LRMS (EI, 70 eV) *m*/*z* (%): 204 (M^+, 100).

*4.3.17. 4,4′-Dimethylbiphenyl (**19**)*[4]

White solid; ^{1}H NMR (300 MHz) δ: 7.47 (d, *J*=8.0 Hz, 4H), 7.23 (d, *J*=8.0 Hz, 4H), 2.38 (s, 6H); ^{13}C NMR (75 MHz) δ: 138.3, 126.7, 129.4, 126.8, 21.0; LRMS (EI, 70 eV) *m*/*z* (%): 182 (M^+, 100), 167 (M^+−CH_3, 55).

*4.3.18. 4,4′-Dimethoxy-biphenyl (**20**)*[4]

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, *J*=8.8 Hz, 4H), 6.94 (d, *J*=8.8 Hz, 4H), 3.83 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.7, 133.5, 127.7, 114.1, 55.3; LRMS (EI, 70 eV) *m*/*z* (%): 214 (M^+, 100).

*4.3.19. 2,2′-Bithiophene (**21**)*[4]

Colorless liquid; ^{1}H NMR (300 MHz) δ: 7.22–7.19 (m, 4H), 7.04–7.00 (m, 2H); ^{13}C NMR (75 MHz) δ: 137.4, 127.8, 124.3, 123.8; LRMS (EI, 70 eV) *m*/*z* (%): 166 (M^+, 100).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.02.040.

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