# Carbazole Synthesis by Platinum-catalyzed C–H Functionalizing Reaction Using Water as Reoxidizing Reagent

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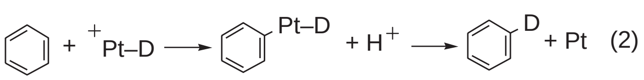
Treatment of 1-aminobiphenyl and diphenylamine with catalytic amount of Pt/C in hydrothermal water (250 °C, 4 MPa) affords 9*H*-carbazole in good yield. In this catalytic cycle, water works as reoxidizing reagent for platinum catalyst.

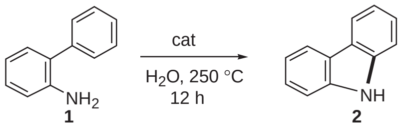
Transition metal-catalyzed cross-coupling reactions are among the most popular processes in modern organic synthesis.[1] As the research has been focused not only on C–C bond-forming reactions but also on C–N bond-forming reactions,[2] the preparation of carbazoles by the cross-coupling reaction has been developed using the ring-closure with C–N or C–C bond-forming reactions.[3] Recently, these synthetic routes have gained additional diversity because of the development of C–H bond functionalization.[4] By this method, carbazole derivatives can be prepared without using an organic halide as substrate. For example, C–H functionalization in *N*-acyl-1-aminobiphenyl by palladium catalyst followed by C–N bond coupling reaction afforded *N*-acylcarbazole.[5] This Pd-catalyzed reaction was driven by copper salt and oxygen gas as reoxidant of the catalyst. In the same manner, the Pd-catalyzed C–H bond functionalization in *N*-phenylaniline followed by C–C bond-forming reaction also gave the carbazole under $O_2$ atmosphere as reoxidizing reagent of the catalyst.[6] These oxidizing reagents are indispensable in order to maintain a catalytic cycle, because the key species for C–H functionalization in both transformations was $Pd^{II}$ species, which will be converted into $Pd^0$ species at the terminal reductive elimination. Although oxygen gas is a relatively mild reagent, it may still cause a limitation of the substrate and the process. We tried to use hydrothermal water as an oxidizing reagent. Recently, we had reported that treatment of hydrocarbons with hot deuterium oxide (250 °C/4 MPa) in the presence of Pd or Pt catalyst resulted in a complete H/D exchange reaction.[7] This process includes C–H functionalization with $Pd^{II}$ or $Pt^{II}$ which is formed by an oxidation with deuterium oxide as shown in eqs 1 and 2.[8] These results implied that the carbazole synthesis based on C–H fuctionalization with a transition-metal catalyst may be driven by water as the reoxidizing reagent.

$$\mathrm{Pt} + \mathrm{D_2O} \rightleftharpoons \mathrm{D{-}Pt{-}OD} \rightleftharpoons [\mathrm{D{-}Pt}]^+ + [\mathrm{OD}]^- \quad (1)$$



(2)

We examined two types of carbazole syntheses: One was metal-catalyzed C–N bond-forming cross-coupling reaction in a 2-biphenylamine derivative and the other was metal-catalyzed C–C bond-forming cross-coupling reaction in a diarylamine derivative. As shown in eq 3, 2-aminobiphenyl (**1**, 2.0 mmol) was treated with metal catalyst (3–5 mol %) and water (15 g) in a 30-mL Teflon©-lined autoclave at 250 °C.[8] The water was degassed by bubbling $N_2$ gas for 30 min in advance. The internal pressure reached 4 MPa. The combination was heated at the same temperature for 12–48 h. After cooling, the mixture was extracted with ethyl acetate. Platinum was shown to be effective for the cyclization. Carbazole **2** was obtained in 76% yield after 12 h heating in the presence of 5 mol % Pt/C (10 wt % on active carbon).

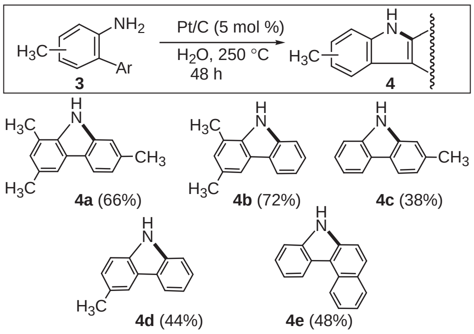


(3)

| Catalyst (/mol %) | Yield of **2**/% | recovery/% |
|---|---|---|
| Pd/C (5) | 7 | 90 |
| $Pd(OAc)_2$ (5) | 5 | 93 |
| Pt/C (5) | 76 | < 3 |
| Pt/C (3) | 16 | 77 |

The yields of carbazole derivatives **4** from 2-aminobiphenyl derivatives **3** by treatment with hot water and platinum catalyst are summarized in Scheme 1. The low yield of carbazole **4c** from 2-amino-4′-methylbiphenyl (**3c**) compared to the moderate yield of **2** from **1** was notable.

The C–H functionalization on aromatic ring by $Pt^{II}$ is considered to proceed via electrophilic substitution like a Friedel–Crafts reaction.[9] In order for carbazole **4c** to be formed, C–H functionalization should occur at 2′ or 6′-position in biphenylamine derivative **3c**. As shown in eq 4, treatment of **3c** in $D_2O$ with platinum catalyst for 2 h at 250 °C afforded deuterated **3c** with 11% yield of **4c**. Distribution of D-atom in recovered **3c** implies the efficiency of C–H functionalization.[10] Amino-group has strong orientation and acceleration of electrophilic substitution at *o*- and *p*-position on benzene ring, and methyl-group also has moderate those on benzene ring. In addition to these electronic effects, a steric hindrance may rationalize the low distribution of D-atom at 2′ and 6′-position in **3c**-d$_n$ in eq 4. As the result, **4c** could not be formed in good yield because of the low efficiency of C–H functionalization at 2′ and 6′-position in **3c**.



**Scheme 1.** Preparation of carbazole derivatives **4** from 2-biphenylamine derivatives **3** (Bold line is the newly formed bond).

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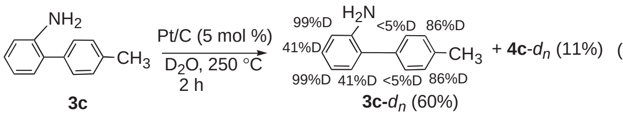
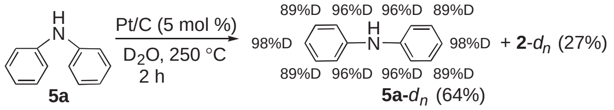


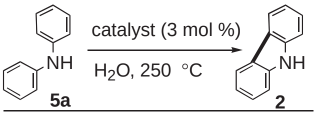
(4)

On the contrary, treatment of diphenyl amine **5a** with hydrothermal deuterium oxide in the presence of Pt/C catalyst for 2 h afforded deuterium-labeled diphenylamine in 64% yield along with deuterated carbazole in 27% yield. In this case, both aromatic rings in **5a** are electrophilic because of the nitrogen atom. Especially the ortho position was labeled with D-atoms efficiently (96%). This result implied the C–H functionalization based on carbazole ring formation from diarylamine is easier than that from 2-aminobiphenyl.



(5)

As shown in eq 6, oxidative cyclization of diphenylamine was examined. In this case, Pt/C was also effective for this transformation.[8] Without the catalyst, diphenylamine was recovered completely via heating in water at 250 °C for 48 h.

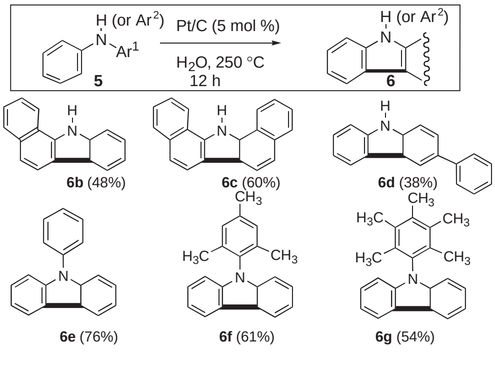


(6)

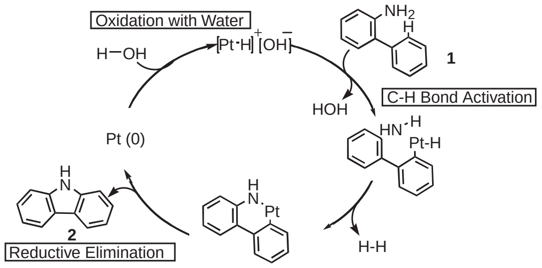
| Catalyst | Yield of **2**/% | recovery/% |
|---|---|---|
| None | <1 | >95 |
| Pt/C | 69 | 11 |
| $PtO_2$ | 48 | 30 |
| Pd/C | 12 | 70 |
| $NiCl_2$ | 8 | 84 |

Various diarylamines were examined for the cyclization. As shown in Scheme 2, carbazole derivatives **6b**–**6g** were obtained in good yields.

In the carbazole formation described above, the reaction proceeds via 1) oxidation of Pt with water; 2) C–H bond functionalization; 3) hydrogen gas generation; 4) reductive elimination, as shown in Scheme 3. One of the most important steps is platinum metal oxidation with water. The redox potential of $Pt^{2+}$/Pt is 0.98 V in both basic and acidic condition. The value of redox potential, however, refers to the redox process of the metal bulk. As a catalytic process, partial dissociation of water (e.g., $H_2O$ into Mtl–H and Mtl–OH) on the metal surface is important. Thiel and Madey reported that DH for partial dissociation on the Pt surface is only 25 kJ/mol.[11] The hydrogen gas, which is formed during the reaction may be released from vessel considering the structure of the autoclave, which is shown in Supporting Information.[7,12]



**Scheme 2.** Various carbazole derivatives **6** preparation by oxidative coupling of diaryl amine derivatives **5**.



**Scheme 3.** Plausible pathway from 2-aminobiphenyl (**1**) into carbazole (**2**).

An indirect proof of the oxidation of platinum with water is the following reaction. Treatment of triphenyl phosphine and 1-tetradecene with hydrothermal water (250 °C, 6 h) resulted in the recovery of starting material. In the presence of 5 mol % Pt/C, triphenylphosphine oxide (80% yield) and tetradecane (98% yield) were obtained after treatment with hydrothermal water (250 °C, 6 h). Thus, carbazole synthesis based on Pt-catalyzed C–H functionalization can be driven by water as oxidizing reagent. The search for more examples of C–H functionalization using water and metal catalyst is underway.

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12 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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