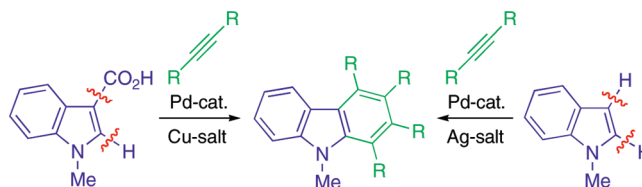


Fused Ring Construction around Pyrrole, Indole, and Related Compounds via Palladium-Catalyzed Oxidative Coupling with Alkynes

Mana Yamashita, Hakaru Horiguchi, Koji Hirano, Tetsuya Satoh,* and Masahiro Miura*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

satoh@chem.eng.osaka-u.ac.jp; miura@chem.eng.osaka-u.ac.jp

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The selective synthesis of 1,2,3,4-tetrasubstituted carbazoles can be performed effectively through the palladium-catalyzed oxidative coupling reactions of *N*-substituted indoles or their carboxylic acid derivatives with alkynes. Unsymmetrically octasubstituted carbazoles can also be obtained by the stepwise couplings of 1-methylpyrrole-2-carboxylic acid with two different alkynes. In addition, the present coupling procedure is applicable to the synthesis of other various heteroarenes possessing di-, tri-, and tetracyclic cores. Some of the products exhibit intense fluorescence in the solid state.

Introduction

The intermolecular coupling of aromatic substrates with internal alkynes by transition-metal catalysis is now recognized to be a powerful tool to construct π -conjugated molecules.¹ In particular, the catalytic oxidative coupling of these substrates via regioselective C–H bond cleavage with the aid of a directing group is a versatile and attractive way from atom- and step-economic points of view² to

selectively produce fused aromatic and heteroaromatic compounds, which are widely seen in organic functional materials.³ As such an example, we have demonstrated that the oxidative coupling of benzoic acids with alkynes takes place effectively,⁴ in which the carboxylic function acts as the directing group^{4,5} to enable the regioselective annulation. Thus, their 1:1 and 1:2 coupling products, isocoumarin and naphthalene derivatives, can be selectively obtained under rhodium and iridium catalyzes, respectively (Scheme 1). The latter involves double alkyne incorporation with decarboxylation. These reactions seem to be of considerable synthetic

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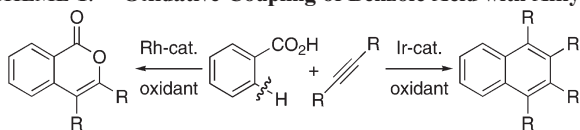
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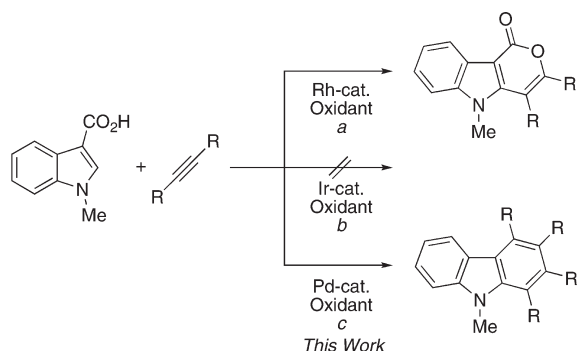
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SCHEME 1. Oxidative Coupling of Benzoic Acid with Alkynes



SCHEME 2. Oxidative Coupling of 1-Methylindole-3-carboxylic Acid with Alkynes



utility because of wide availability of the acids as aryl sources.

During our further study of the scope of the reactions, it has been found that heteroarene carboxylic acids such as 1-methylindole-3-carboxylic acid hardly undergo the decarboxylative 1:2 coupling with the Ir catalyst (Scheme 2, path *b*), while the corresponding lactones can be obtained as 1:1 coupling products under rhodium catalysis (path *a*).^{4b} To our delight, the 1:2 coupling has been observed to proceed efficiently by the use of a palladium catalyst to produce the corresponding 1,2,3,4-tetrasubstituted carbazole derivatives selectively (path *c*).⁶ Highly substituted carbazoles have been attractive synthetic targets in medicinal chemistry and materials fields because of their interesting biological activities as well as photophysical and optoelectronic properties.⁷ Expectedly, some of the carbazoles obtained by this protocol have been found to show solid-state fluorescence.

Meanwhile, the palladium-catalyzed direct arylation⁸ and vinylation⁹ of various heteroaromatics including indoles are

known to be capable of occurring regioselectively even without the aid of any directing groups. We have also succeeded in conducting the oxidative coupling of 1-methylindole itself with alkynes to furnish the 1,2,3,4-tetrasubstituted carbazoles.¹⁰ The detailed results of these new coupling reactions on not only indole but also pyrrole, benzofuran, furan, and benzothiophene rings are described herein.

Results and Discussion

We recently reported that 1-methylindole-3-carboxylic acid (**1a**) smoothly underwent the oxidative coupling with alkenes in the presence of Pd(OAc)₂, Cu(OAc)₂·H₂O, and LiOAc as catalyst, oxidant, and additive, respectively.¹¹ In an initial attempt, **1a** (0.8 mmol) was treated with diphenylacetylene (**2a**) (0.8 mmol) under similar conditions, using Pd(OAc)₂ (0.02 mmol), Cu(OAc)₂·H₂O (0.8 mmol), LiCl (1.2 mmol), and molecular sieves (MS4A, 400 mg) in DMAc (2.5 mL) at 140 °C under N₂ for 2 h. As a result, the corresponding 1:2 coupling product **3a** was formed in 64% yield (entry 1 in Table 1). At 120 °C, **3a** was found to be obtained almost quantitatively (entry 2), while the yield was significantly reduced at 100 °C (entry 3). Decreasing the amount of **1a** to 0.6 mmol did not affect the reaction efficiency (entry 4, conditions A). Under similar conditions, 1-methylindole-2-carboxylic acid (**1c**) also reacted with **2a**, but the yield of **3a** was considerably lower (71%, entry 5). Meanwhile, **3a** could not be obtained at all from the reaction using 1-methylindole (**1b**) in place of **1a** and **1c** with **2a** (entry 6). With the addition of benzoic acid (0.2 mmol) as promoter,¹² however, a small amount of **3a** was formed using **1b** (entry 7). The reaction with **1b** and **2a** in a ratio of 0.4:1.2 in mesitylene (4 mL) gave **3a** in 33% yield (entry 9). Under the conditions using Ag₂CO₃/PhCO₂H as oxidant and additive, respectively, in place of Cu(OAc)₂·H₂O/LiOAc/PhCO₂H, **3a** was obtained in 59% yield (entry 10). In this case, a small amount (ca. 5%) of 1,2,3,4-tetraphenylnaphthalene, which may be formed by the oxidative 1:2 coupling of PhCO₂H with **2a**,¹³ was also detected by GC–MS analysis. Eliminating PhCO₂H suppressed the reaction completely (entry 11). Expectedly, the use of 2,6-dimethylbenzoic acid in place of PhCO₂H avoided the naphthalene formation, and the yield of **3a** was improved up to 74% (entry 12, conditions B). However, these conditions were not suitable for the reactions of **1a** and **1c** with **2a**. Thus, the yields of **3a** were lower than those under conditions A (entries 13 and 14 versus entries 4 and 5, respectively).

Next, the reactions of **1a** and **1b** with various internal alkynes were examined under conditions A and B, respectively. Methyl- (**2b**), methoxy- (**2c**), and chloro-substituted (**2d**) diphenylacetylenes smoothly underwent coupling with **1a** and **1b** to afford the corresponding 1,2,3,4-tetraaryl-9-methylcarbazoles **3b–d** (entries 1–6 in Table 2). The product yields were slightly higher in the cases with **1a** under conditions

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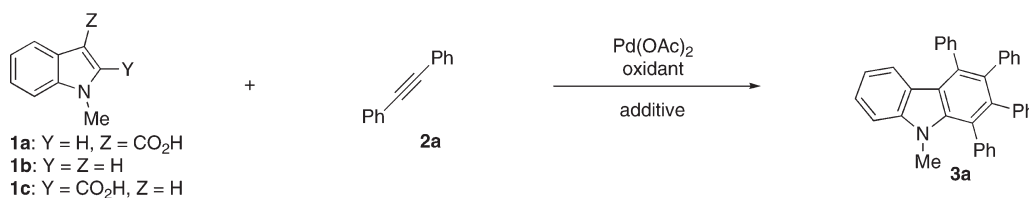
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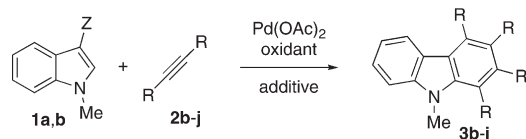
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(13) For an Ir-catalyzed version, see ref 4c.

TABLE 1. Synthesis of 9-Methyl-1,2,3,4-tetraphenylcarbazole (**2a**)^a

entry	1	Y	Z	1/2a (mmol)	oxidant	additive	solvent	T (°C)	time (h)	% yield of 3a ^b
1 ^c	1a	H	CO ₂ H	0.8/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc	DMAc	140	2	64 (60)
2 ^c	1a	H	CO ₂ H	0.8/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc	DMAc	120	6	99 (80)
3 ^c	1a	H	CO ₂ H	0.8/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc	DMAc	100	8	61
4 ^c	1a	H	CO ₂ H	0.6/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc	DMAc	120	9	99
5 ^c	1c	CO ₂ H	H	0.6/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc	DMAc	120	8	71
6	1b	H	H	0.6/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc	DMAc	120	8	0
7	1b	H	H	0.6/0.8	Cu(OAc) ₂ ·H ₂ O	LiOAc/PhCO ₂ H	DMAc	120	8	10
8	1b	H	H	0.4/1.2	Cu(OAc) ₂ ·H ₂ O	LiOAc/PhCO ₂ H	DMAc	120	8	13
9	1b	H	H	0.4/1.2	Cu(OAc) ₂ ·H ₂ O	LiOAc/PhCO ₂ H	mesitylene	120	8	33
10	1b	H	H	0.4/1.2	Ag ₂ CO ₃	PhCO ₂ H	mesitylene	120	8	59
11	1b	H	H	0.4/1.2	Ag ₂ CO ₃		mesitylene	120	8	0
12	1b	H	H	0.4/1.2	Ag ₂ CO ₃	2,6-Me ₂ C ₆ H ₃ CO ₂ H	mesitylene	120	8	74 (70)
13	1a	H	CO ₂ H	0.4/1.2	Ag ₂ CO ₃	2,6-Me ₂ C ₆ H ₃ CO ₂ H	mesitylene	120	8	69
14	1c	CO ₂ H	H	0.4/1.2	Ag ₂ CO ₃	2,6-Me ₂ C ₆ H ₃ CO ₂ H	mesitylene	120	8	2

^aReaction conditions: Pd(OAc)₂ (0.02 mmol), oxidant (0.8 mmol), (LiOAc (1.2 mmol)), (ArCO₂H (0.2 mmol)), MS4A (400 mg), DMAc (2.5 mL), or mesitylene (4 mL) under N₂. ^bGC yield. Value in parentheses indicates yield after purification. ^cMS4A (400 mg) was added.

TABLE 2. Synthesis of 1,2,3,4-Tetrasubstituted 9-Methylcarbazoles **3**^a

entry	1	Z	2	R	conditions	time (h)	3, % yield
1	1a	CO ₂ H	2b	4-MeC ₆ H ₄	A	8	3b , 82
2	1b	H	2b	4-MeC ₆ H ₄	B	10	3b , 70
3	1a	CO ₂ H	2c	4-MeOC ₆ H ₄	A	8	3c , 75
4	1b	H	2c	4-MeOC ₆ H ₄	B	10	3c , 67
5	1a	CO ₂ H	2d	4-ClC ₆ H ₄	A	12	3d , 62
6	1b	H	2d	4-ClC ₆ H ₄	B	10	3d , 57
7	1a	CO ₂ H	2e	4-Bu ^c C ₆ H ₄	A	9	3e , 85
8	1a	CO ₂ H	2f	4-FC ₆ H ₄	A	9	3f , 72
9	1a	CO ₂ H	2g	Pr	A'	10	3g , 58
10	1b	H	2g	Pr	B	10	3g , 10 ^b
11	1a	CO ₂ H	2h	heptyl	A'	10	3h , 55
12	1a	CO ₂ H	2i	4-CF ₃ C ₆ H ₄	A	9	3i , 12 ^{b,c}
13	1b	H	2i	4-CF ₃ C ₆ H ₄	B	10	3i , 66
14	1b	H	2j	CO ₂ Et	B	10	3j , 45

^aReaction conditions A: **1** (0.6 mmol), **2** (0.8 mmol), Pd(OAc)₂ (0.02 mmol), Cu(OAc)₂·H₂O (0.8 mmol), LiOAc (1.2 mmol), MS4A (400 mg), DMAc (2.5 mL) at 120 °C under N₂. Reaction conditions B: **1** (0.3 mmol), **2** (0.9 mmol), Pd(OAc)₂ (0.015 mmol), Ag₂CO₃ (0.6 mmol), 2,6-Me₂C₆H₃CO₂H (0.15 mmol), mesitylene (3 mL) at 120 °C under N₂. Reaction conditions A': **1a** (0.4 mmol), **2** (1.6 mmol), Pd(OAc)₂ (0.02 mmol), Cu(OAc)₂·H₂O (0.8 mmol), LiOAc (2.4 mmol), LiOH·H₂O (1.2 mmol), MS4A (400 mg), DMAc (2.5 mL) at 100 °C under air. ^bGC yield. ^c(Z)-1-(1-Methylindole-3-carboxy)-1,2-bis[4-(trifluoromethyl)phenyl]ethene (**4**) was also formed in 46% yield.

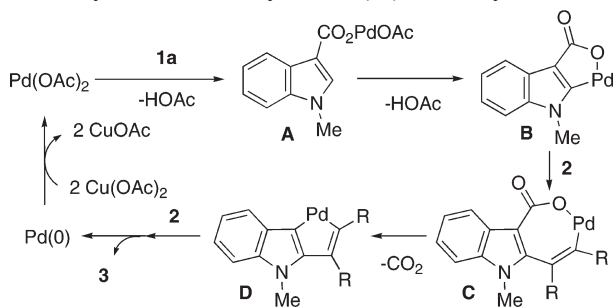
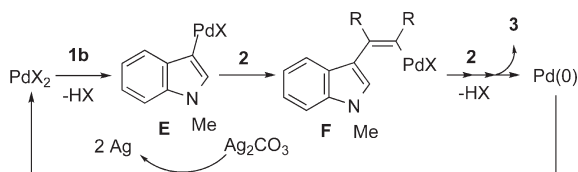
A than those in the cases with **1b** under conditions B. The reactions of *tert*-butyl- (**2e**) and fluoro-substituted (**2f**) alkynes with **1a** also proceeded efficiently to produce carbazoles **3e** and **3f** in good yields (entries 7 and 8). Compared to these diaryl-acetylenes, 4-octyne (**2g**) was found to be less reactive. Some screening experiments with respect to reaction conditions led to

the establishment of conditions A', which are suitable for the reaction with dialkylacetylenes. Thus, when an excess amount of **2g** (**1a/2g** = 1:4) in the presence of LiOH·H₂O (1.2 mmol) was used as well as LiOAc (2.4 mmol) as additive at 100 °C under air, **3g** was obtained in 58% yield (entry 9). The reaction of **1b** with **2g** under conditions B gave **3g** in only 10% yield (entry 10). The reaction of **1a** with 8-hexadecyne (**2h**) under conditions A' proceeded effectively to give 1,2,3,4-tetraheptyl-9-methylcarbazole (**3h**) in 55% yield (entry 11). On the other hand, treatment of an electron-deficient alkyne, bis[4-(trifluoromethyl)phenyl]acetylene (**2i**), with **1a** predominantly gave not the desired carbazole **3i** but an O–H adduct, (Z)-1-(1-methylindole-3-carboxy)-1,2-bis[4-(trifluoromethyl)phenyl]ethene (**4**), in 46% yield (entry 12). For producing **3i**, the reaction with **1b** under conditions B gave a better result. Thus, in the latter case, **3i** was obtained in 66% yield (entry 13). Even with a more electron-deficient alkyne, diethyl acetylenedicarboxylate (**2j**), the reaction of **1b** took place similarly to form **3j** in 45% yield (entry 14).

The reaction of **1a** with **2** seems to be initiated via fundamentally similar steps to those proposed for the oxidative coupling of **1a** with alkenes using the Pd(OAc)₂/Cu(OAc)₂·H₂O/LiOAc system.¹¹ Thus, as depicted in Scheme 3, coordination of the carboxyl oxygen to Pd(OAc)₂ with liberation of AcOH gives a palladium(II) carboxylate **A**, and directed palladation at the C2-position forms a palladacycle intermediate **B**. Subsequent alkyne insertion¹⁴ and decarboxylation occur to produce a five-membered palladacycle intermediate **D**.¹⁵ Then, the second alkyne insertion and reductive elimination steps take place to

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(15) However, the participation of other sequences involving decarboxylation on **A** (Scheme 3) or a copper carboxylate cannot be excluded (see refs 5i and 7k, respectively).

SCHEME 3. Plausible Mechanism for the Oxidative Coupling of 1-Methylindole-3-carboxylic Acid (1a) with Alkynes 2

SCHEME 4. Plausible Mechanism for the Oxidative Coupling of 1-Methylindole (1b) with Alkynes 2


produce carbazole **3**. The resulting Pd(0) species may be oxidized in the presence of the copper(II) salt to regenerate Pd(OAc)₂. During palladium-catalyzed oxidative reactions, in general, the regeneration of Pd(II) from Pd(0) is considered to be the crucial step to determine catalyst efficiency.¹⁶ One of the possible roles of added LiOAc is to provide acetate anions as ligand to prevent the deactivation of Pd(0) to metallic species.¹⁷

In the cases using dialkylacetylenes, the addition of LiOH·H₂O in combination with LiOAc improved the reaction efficiency. Without this base, the formation of 1:1 oxidative coupling products together with **3** was detected by GC–MS. One of its possible roles appears to be the trap of acids formed during the reaction, which may induce the ring-opening of palladacycle intermediates such as **C** and **D** to form the corresponding acyclic vinylpalladium species. Such aliphatic vinylpalladium intermediates are known to undergo β-hydrogen elimination to produce allene derivatives.¹⁸

The reaction of **1b** with **2** seems to proceed via a route similar to those proposed for the palladium-catalyzed direct arylation and vinylation reactions.^{2,8,9} As in the initial step of these reactions, regioselective direct palladation on the indole ring occurs at the 3-position to form an indol-3-ylpalladium species **E** (Scheme 4). It was confirmed that the oxidative coupling of **1b** with butyl acrylate using a Pd(OAc)₂/Cu(OAc)₂·H₂O/LiOAc system gave 3-vinylated product selectively.¹¹ In the present coupling with **2**, the alkyne insertion into the Pd–C bond of **E** occurs to form a vinylpalladium intermediate **F**. Subsequently, the second alkyne insertion, cyclopalladation at the 2-position of the indole ring, and final reductive elimination may take place to produce **3**. The use of 2,6-dimethylbenzoic acid as cocatalyst in less polar mesitylene appears to promote the first regio-

selective palladation-deprotonation step, as suggested in the ruthenium-catalyzed direct arylation of aromatic C–H bonds using this cocatalyst.^{12a} The parallel use of Ag₂CO₃ as oxidant rather than Cu(OAc)₂·H₂O may facilitate the coordination of the benzoate on the Pd center, although the details of the operation mechanism are not clear at the present time.

Table 3 summarizes the results for the coupling reactions of various heteroarenes and their carboxylic acid derivatives with **2a**. Under conditions A, 1-(methoxymethyl)indole-3-carboxylic acid (**1d**) underwent the coupling with **2a** to produce the corresponding carbazole **3k** selectively in 72% yield (entry 1). The carbazole **3k** was also obtained in 38% yield by the reaction of the parent 1-(methoxymethyl)indole (**1e**) with **2a** under conditions B (entry 2). One of reasons for the lower efficiency in the latter case is due to the deprotection of once produced **3k** to form *N*-unsubstituted 1,2,3,4-tetraphenyl-9*H*-carbazole (**3l**) under conditions B. The reaction of 1-phenylindole-3-carboxylic acid (**1f**) with **2a** gave a mixture of 1:2 and 1:1 coupling products. Thus, when these substrates were treated using Pd(OAc)₂ (0.04 mmol) for 12 h, not only the expected product, 1,2,3,4,9-pentaphenyl-9*H*-carbazole (**3m**) (14%), but also a tetracyclic compound, 5,6-diphenylindolo[1,2-*a*]quinoline (**5a**) (32%), was formed by a vinyl bridging (entry 3). In contrast, only **3m** was obtained in the reaction of 1-phenylindole (**1g**) under conditions B albeit with a low yield (entries 4 and 5). Imidazo[1,2-*a*]pyridine (**1h**) (0.8 mmol) also reacted with **2a** (0.4 mmol) in a ratio of 1:1 under modified conditions A using a mixture of pivalic acid (2 mL) and DMAc (1 mL) as a solvent system to afford a tricyclic product **6** (entry 6).¹⁹ The yield of **6** decreased to less than 10% under conditions B or similar ones using silver oxidants. From the reaction of 1-methylpyrrole-2-carboxylic acid (**7a**), a highly substituted indole derivative **8a** was obtained in 61% yield (entry 7). In this case, increasing in the amounts of the substrate **7a** (0.8 mmol) and LiOAc (2.4 mmol) resulted in a better product yield. Expectedly, product **8a** could undergo further oxidative coupling under conditions B (vide infra).

Meanwhile, the reactions of benzofuran- (**7b**) and furan-2-carboxylic acids (**7d**) with **2a** were found to proceed effectively under air with the addition of an appropriate acid. The reaction of **7b** using LiOH·H₂O (1.2 mmol) and 2,2-dimethylsuccinic acid (2.4 mmol) as additives in place of LiOAc afforded 1,2,3,4-tetraphenyldibenzofuran (**9a**) in 72% yield (entry 8). In the reaction of **7d**, once produced 1,2,3,4-tetraphenylbenzofuran (**9b**) was decomposed under conditions A. Therefore, the amount of Cu(OAc)₂·H₂O was decreased to 0.05 mmol under air, and pivalic acid (2.4 mmol) was added in place of LiOAc. Under such modified conditions, **9b** was obtained with a substantial yield (entry 10). The reaction of benzofuran (**7c**) itself under conditions B hardly proceeded to give only a trace amount of **9a** (entry 9). The couplings of benzothiophene-2-carboxylic acid (**7e**) as well as benzothiophene (**7f**) were sluggish under the conditions examined (entries 11 and 12).

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(17) Amatore, C.; Jutand, A. *J. Organomet. Chem.* **1999**, *576*, 254 and references therein.

(18) For example, see: Pivsa-Art, S.; Satoh, T.; Miura, M.; Nomura, M. *Chem. Lett.* **1997**, 823.

(19) For recent examples of the direct arylation and vinylation of **1h**, see: (a) Koubachi, J.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. *Synthesis* **2009**, 271. (b) Koubachi, J.; Kazzouli, S. E.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. *J. Org. Chem.* **2007**, *72*, 7650. (c) Koubachi, J.; Kazzouli, S. E.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. *Synlett* **2006**, 3237.

TABLE 3. Synthesis of Fused Heteroaromatic Compounds^a

entry	1	conditions	time (h)	product(s), % yield
1		A	8	72 0
2		B	8	38 ^b 7
3		A ^c	12	14 32
4		B	8	tr 0
5		B ^d	8	11 0
6		A ^e	8	49
7		A ^{f,g}	10	61
8		A ^{f,h,i}	10	70
9		B	8	tr
10		C	6	44
11		A ^{f,i,j}	8	11
12		B	8	10 ^b

^aReaction conditions A: **1** or **7** (0.6 mmol), **2a** (0.8 mmol), Pd(OAc)₂ (0.02 mmol), Cu(OAc)₂·H₂O (0.8 mmol), LiOAc (1.2 mmol), MS4A (400 mg), DMAc (2.5 mL) at 120 °C under N₂. Reaction conditions B: **1** or **7** (0.3 mmol), **2a** (0.9 mmol), Pd(OAc)₂ (0.015 mmol), Ag₂CO₃ (0.6 mmol), 2,6-Me₂C₆H₃CO₂H (0.15 mmol), mesitylene (3 mL) at 120 °C under N₂. Reaction conditions C: **7d** (0.8 mmol), **2a** (0.8 mmol), Pd(OAc)₂ (0.02 mmol), Cu(OAc)₂·H₂O (0.05 mmol), pivalic acid (2.4 mmol), MS4A (400 mg), DMAc (2.5 mL) at 120 °C under air. ^bGC yield. ^cPd(OAc)₂ (0.04 mmol) was used. ^dIn DMAc. ^e**1h** (0.8 mmol) and **2a** (0.4 mmol) were used in the absence of MS4A in pivalic acid (2 mL)/DMAc (1 mL). ^f**7** (0.8 mmol) was used. ^gLiOAc (2.4 mmol) was used. ^hLiOH·H₂O (1.2 mmol) and 2,2-dimethylsuccinic acid (2.4 mmol) were used in place of LiOAc. ⁱUnder air. ^jLiOH·H₂O (1.2 mmol), 2,2-dimethylsuccinic acid (2.4 mmol), and ZnCl₂ (0.8 mmol) were used in place of LiOAc.

Next, the stepwise synthesis of unsymmetrically substituted carbazole derivatives was examined. Thus, in the first step, **7a** (2.4 mmol) was treated with **2b** (2.4 mmol) in

the presence of Pd(OAc)₂ (0.06 mmol), Cu(OAc)₂·H₂O (2.4 mmol), LiOAc (7.2 mmol), and MS4A (800 mg) in DMAc (7.5 mL) at 120 °C under N₂ for 6 h. Then, for-

TABLE 4. Synthesis of Unsymmetrically Substituted Carbazoles 10^a

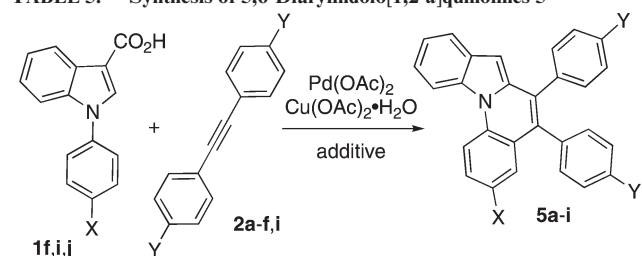
entry	2	R ¹	8, % yield	2'	R ²	10, % yield
1	2b	4-MeC ₆ H ₄	8b , 61	2a	Ph	10a : X = H, 64
2				2d	4-ClC ₆ H ₄	10b : X = Cl, 77
3 ^b	2g	Pr	8c , 35	2a	Ph	10c : X = H, 77
4 ^b				2b	4-MeC ₆ H ₄	10d : X = Me, 75
5 ^b				2d	4-ClC ₆ H ₄	10e : X = Cl, 82

^aReaction conditions: (i) **7a** (2.4 mmol), **2** (2.4 mmol), Pd(OAc)₂ (0.06 mmol), Cu(OAc)₂·H₂O (2.4 mmol), LiOAc (7.2 mmol), MS4A (800 mg), DMAc (7.5 mL) at 120 °C under N₂ for 6 h; (ii) **8** (0.4 mmol), **2'** (1.2 mmol), Pd(OAc)₂ (0.02 mmol), Ag₂CO₃ (0.8 mmol), 2,6-Me₂C₆H₃CO₂H (0.2 mmol), mesitylene (4 mL) at 120 °C under N₂ for 8 h. ^bWith **7a** (1.2 mmol) and **2** (4.8 mmol) at 100 °C for 10 h (for step i).

med 1-methyl-4,5,6,7-tetrakis(4-methylphenyl)indole (**8b**) (0.4 mmol) was treated with **2a** (1.2 mmol) as the second alkyne in the presence of Pd(OAc)₂ (0.02 mmol), Ag₂CO₃ (0.8 mmol), and 2,6-dimethylbenzoic acid (0.2 mmol) in mesitylene (4 mL) at 120 °C under N₂ for 8 h to afford 9-methyl-1,2,3,4-tetrakis(4-methylphenyl)-5,6,7,8-tetraphenylcarbazole (**10a**) in 64% yield (entry 1 in Table 4). Treatment of **8b** with **2d** in the second step gave the corresponding octaarylcarbazole **10b** in 77% yield (entry 2). The reaction using **2g** in the first step afforded 1-methyl-4,5,6,7-tetrapropylindole (**8c**) in a moderate yield. This can be converted to 1,2,3,4-tetraalkyl-5,6,7,8-tetraarylcarbazoles **10c–e** in 75–82% yields (entries 3–5).

Some carbazoles showed solid-state fluorescence in a range of 380–450 nm (see Figure S1 in the Supporting Information). Notably, **3b** and **10c** exhibited relatively strong emissions compared to a typical emitter, anthracene, by factors of 3.7 and 2.6, respectively.

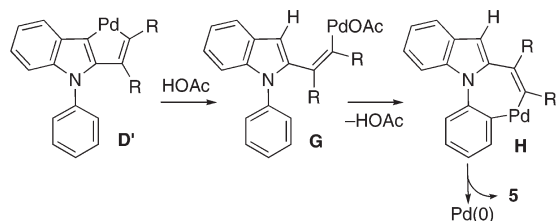
It was found that not only these carbazoles but also the tetracyclic compound 5,6-diphenylindolo[1,2-*a*]quinoline (**5a**), obtained as the major product in the reaction of **1f** with **2a** (entry 3 in Table 3), showed solid-state fluorescence. Therefore, we attempted the synthesis of variously substituted indolo[1,2-*a*]quinoline derivatives by the 1:1 coupling of 1-arylidole-3-carboxylic acids with diarylacetylenes. When **1f** (0.3 mmol) was treated with **2a** (0.45 mmol) in the presence of Pd(OAc)₂ (0.03 mmol), Cu(OAc)₂·H₂O (0.6 mmol), LiCl (1.8 mmol), and molecular sieves (MS4A, 200 mg) in DMAc (1.5 mL) at 120 °C under N₂ for 12 h, **5a** was obtained in a somewhat improved yield (entry 1 in Table 5). Under similar conditions, **1f** was also coupled with **2b–f** and **2i** to afford the corresponding 5,6-diarylindolo[1,2-*a*]quinolines **5b–g** (entries 2–7). Methoxy- (**1i**) and methyl-substituted (**1j**) 1-phenylindole-3-carboxylic acids also underwent the 1:1 coupling with **2a** and **2d** to give **5h** and **5i**, respectively (entries 8 and 9).

TABLE 5. Synthesis of 5,6-Diarylyndolo[1,2-*a*]quinolines 5^a

entry	1	X	2	Y	5, % yield
1	1f	H	2a	H	5a, 52
2	1f	H	2b	Me	5b, 55
3	1f	H	2c	OMe	5c, 40
4	1f	H	2d	Cl	5d, 36
5	1f	H	2e	Bu'	5e, 50
6	1f	H	2f	F	5f, 39
7	1f	H	2i	CF ₃	5g, 25
8	1i	OMe	2a	H	5h, 46
9	1j	Me	2d	Cl	5i, 36

^aReaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), Pd(OAc)₂ (0.03 mmol), Cu(OAc)₂·H₂O (0.6 mmol), LiOAc (1.8 mmol), MS4A (200 mg), DMAc (1.5–2 mL) at 120 °C under N₂ for 12 h.

SCHEME 5. Plausible Mechanism for the Oxidative Coupling of 1-Phenylindole-3-carboxylic Acid (1f) with Alkynes 2



As depicted in Scheme 5, the 1:1 coupling of 1-phenylindole-3-carboxylic acid (**1f**) with **2** seems to proceed via steps similar to those for the 1:2 coupling of **1a** with **2** to form an intermediate **D'**, related to **D** in Scheme 3. Then, protonolysis of the indolyl–Pd bond in **D'** may occur,²⁰ rather than the second alkyne insertion, to form a vinylpalladium intermediate **G**. Subsequently, cyclopalladation on the phenyl group to afford a seven-membered palladacycle **H** and reductive elimination may take place to afford product **5**.

Most 5,6-diarylyndolo[1,2-*a*]quinolines **5** obtained above showed solid-state fluorescence in a range of 470–560 nm (see Figure S2 in the Supporting Information). Interestingly, **5e** exhibited significantly intense luminescence (λ_{emis} 476 and 506 nm), and the intensity was at least seven times stronger than that of a typical emitter, coumarin 153, in the preliminary estimation. It is apparent that the introduction of two bulky *tert*-butyl substituents on the parent molecule **5a** significantly enhances the intensity of solid-state fluorescence. Remarkably, the quantum efficiency (Φ) of the solid-state fluorescence of **5e** was measured at an absolute value of $68 \pm 2\%$.

In summary, we have demonstrated that the palladium-catalyzed oxidative couplings of heteroarenes and

their carboxylic acid derivatives, especially indole derivatives, with alkynes proceeds efficiently via regioselective C–H bond cleavage to afford fused heteroaromatic compounds. Some products multiply substituted around the heteroaromatic cores show relatively strong solid-state fluorescence.

Experimental Section

General Procedure for Oxidative Coupling of 1-Methylindole-3-carboxylic Acid (**1a**) with Diarylacetylenes **2** under Conditions A.

To a 20 mL two-necked flask were added LiOAc (1.2 mmol, 79 mg) and MS4A (400 mg), which were dried at 150 °C in vacuo for 1 h. Then, **1a** (0.6 mmol, 105 mg), alkyne **2** (0.8 mmol, 160 mg), dibenzyl (ca. 40 mg) as internal standard, and DMAc (2.5 mL) were added. The resulting mixture was stirred under N₂ at 120 °C. GC and GC–MS analyses of the mixtures confirmed formation of **3**. After cooling, the reaction mixture was poured into diluted HCl aq (50 mL) and extracted with Et₂O (50 mL). Then, the organic layer was washed with saturated NaCl aq (50 mL, twice) and dried over Na₂SO₄. Product **3** was isolated by column chromatography on silica gel using hexane–ethyl acetate.

9-Methyl-1,2,3,4-tetraphenyl-9H-carbazole (3a): mp 276–278 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.23 (s, 3H), 6.75–6.90 (m, 12H), 7.18–7.37 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 32.3, 108.4, 118.8, 121.2, 122.4, 122.7, 123.9, 125.0, 125.1, 125.5, 126.3, 126.4, 126.7, 126.7, 127.2, 128.0, 130.3, 131.6, 131.8, 131.9, 132.7, 135.4, 137.9, 138.8, 139.7, 140.3, 140.4, 140.5, 142.9; HRMS *m/z* (M⁺) calcd for C₃₇H₂₇N 485.2143, found 485.2141.

General Procedure for Oxidative Coupling of 1-Methylindole (1b) with Alkynes 2 under Conditions B. To a 20 mL two-necked flask were added **1b** (0.4 mmol, 52 mg), alkyne **2** (1.2 mmol), Pd(OAc)₂ (0.02 mmol, 4.5 mg), Ag₂CO₃ (0.8 mmol, 221 mg), *n*-docosane (ca. 40 mg) as internal standard, and mesitylene (4 mL). The resulting mixture was stirred under N₂ at 120 °C. GC and GC–MS analyses of the mixtures confirmed formation of **3**. After cooling, the reaction mixture was poured into H₂O (50 mL) and extracted with Et₂O (50 mL). Then, the organic layer was washed with saturated NaCl aq (50 mL, twice) and dried over Na₂SO₄. Product **3** was isolated by column chromatography on silica gel using hexane–ethyl acetate.

General Procedure for Oxidative Coupling of 1-Methylindole-3-carboxylic Acid (**1a**) with Dialkylacetylenes **2** under Conditions A'.

To a 20 mL two-necked flask were added LiOAc (2.4 mmol, 158 mg) and MS4A (400 mg), which were dried at 150 °C in vacuo for 1 h. Then, 1-methylindole-3-carboxylic acid (**1a**) (0.4 mmol, 70 mg), alkyne **2** (1.6 mmol), Pd(OAc)₂ (0.02 mmol, 4.5 mg), Cu(OAc)₂·H₂O (0.8 mmol, 160 mg), LiOH·H₂O (1.2 mmol, 50 mg), dibenzyl (ca. 40 mg) as internal standard, and DMAc (2.5 mL) were added. The resulting mixture was stirred under air at 100 °C for 10 h. GC and GC–MS analyses of the mixtures confirmed formation of **3**. After cooling, the reaction mixture was poured into diluted HCl aq (50 mL) and extracted with Et₂O (50 mL). Then, the organic layer was washed with saturated NaCl aq (50 mL, twice) and dried over Na₂SO₄. Product **3** was isolated by thin-layer chromatography on silica gel using hexane–toluene.

9-Methyl-1,2,3,4-tetrapropyl-9H-carbazole (3g): oil; ¹H NMR (400 MHz, CDCl₃) δ 1.08–1.13 (m, 9H), 1.19 (t, *J* = 7.3 Hz, 3H), 1.55–1.63 (m, 4H), 1.67–1.81 (m, 4H), 2.70–2.75 (m, 4H), 3.04–3.08 (m, 2H), 3.14–3.18 (m, 2H), 4.02 (s, 3H), 7.16–7.22 (m, 1H), 7.34–7.42 (m, 2H), 8.03 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 14.4, 14.8, 15.0, 15.1, 23.2, 25.4, 25.5, 25.8, 30.6, 31.6, 32.2, 32.5, 32.7, 108.4, 118.7, 120.7, 121.6,

(20) For example, see: Larock, R. C.; Tian, Q. *J. Org. Chem.* **2001**, *66*, 7372.

122.2, 123.1, 124.4, 130.5, 134.0, 138.0, 138.9, 142.7; HRMS m/z (M^+) calcd for $C_{25}H_{35}N$ 349.2770, found 349.2766.

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Supporting Information Available: Characterization data of products. This material is available free of charge via the Internet at <http://pubs.acs.org>.