ARTICLE IN PRESS

Tetrahedron Letters xxx (2017) xxx-xxx

Contents lists available at ScienceDirect



Tetrahedron Letters

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



From propargylic biscarbonate to diaryl[n]dendralenes

Shotaro Hayashi, Masakatsu Kasuya, Junsuke Machida, Toshio Koizumi*

Department of Applied Chemistry, National Defense Academy, 1-10-20, Hashirimizu, Yokosuka, Kanagawa 239-8686, Japan

ARTICLE INFO

Article history: Received 13 March 2017 Revised 29 April 2017 Accepted 8 May 2017 Available online xxxx

Keywords: Pd/C Heterogeneous catalyst Cross-coupling reaction Cross-conjugated compound [n]Dendralene

ABSTRACT

An efficient cross-coupling reaction using a low cost carbon-supported palladium (Pd/C) catalyst for the synthesis of cross-conjugated compounds, diaryl[n]dendralenes, has been developed. The reaction of a propargylic biscarbonate with phenylboronic acid using Pd/C and phosphine ligand (S-Phos) gave 2,3-diphenyl[2]dendralene in high yield. We found that Pd/C was an effective catalyst for the synthesis of dialyl[n]dendralenes. The synthesis of various dendralenes was successfully achieved under the optimized conditions, giving dialyl [2] and [4] dendralenes in good yields.

© 2017 Elsevier Ltd. All rights reserved.

 π -Conjugated compounds such as polyarylenes, polyenes and acenes have wide applications in biology and electronics.^{1,2} These compounds are recognized as model parts of graphene being a zero-band gap semimetal. Common conjugated compounds, namely *through-conjugated compounds*,³ which have alternating single and multiple bonds, are composed of unbranched π -electron frameworks. Many of such compounds show semiconducting properties.

On the other hand, *cross-conjugated compounds* are constructed by branched π -electron frameworks and the typical examples are dendralenes and radialenes.^{4a} In contrast to huge examples of through-conjugated compounds, the studies on cross-conjugated compounds have been quite limited so far. In recent years, however, the cross-conjugated compounds have received increasing attention as unique properties such as π -electron communication and charge separation.^{4b,4c} [n]Dendralenes are one of cross-conjugated compounds. The simplest dendralene is [3]dendralene (Scheme 1). 2,3-Diaryl-1,3-butadienes, which are formally [4]dendralenes, have attracted their molecular structures and electronic features.⁴

In general, 1,3-butadiene prefers an *s*-*trans* conformation, but Walree and co-workers reported that 2,3-diphenyl[2]dendralene (2,3-diphenyl-1,3-butadiene) has an *s*-gauche conformation mainly in the crystal state.⁵ This [2]dendralene would exist in equilibrium between two conformational states at room temperature since the energies of the *s*-gauche and *s*-trans conformations are very similar.^{5d}

* Corresponding author. *E-mail address:* tkoizumi@nda.ac.jp (T. Koizumi).

http://dx.doi.org/10.1016/j.tetlet.2017.05.016 0040-4039/© 2017 Elsevier Ltd. All rights reserved.

The synthesis of oligomeric dendralenes is a challenging topic because multi-step reactions are usually requiered.⁶ The Pd (0)-catalyzed Suzuki-Miyaura reaction with 1.3-butadiene-2.3-bis (pinacolatoborane) and the Stille reaction with 1.3-butadiene-2.3bis(tri-*n*-butyltin) are key processes to access [2–8]dendralene derivatives. Various 2,3-diaryl[2]dendralenes were also synthesized by Cu, Pd or Ni-catalyzed cross-coupling reaction.⁴ Ishino et al. reported that the reaction of 1,4-dimethoxy-2-butyne with aryl Grignard reagents in the presence of CuBr gave 2,3-diaryl[2]dendralenes.^{4h} The Pd(0)-catalyzed synthesis of diaryl[2]dendralenes from propargyl carbonates and aryl boronic acids was reported by Grigg.^{4g} We have recently succeeded in the synthesis of crossconjugated polymers based on [2]dendralenyl (1,3-butadiene-2,3diyl) skeleton via a palladium(0)-catalyzed cross-coupling polycondensation between propargylic biscarbonate 1 and aryl diboronic acids.⁷ The efficient polymerization was achieved by a catalytic system composed of Pd₂(dba)₃·CHCl₃ as the palladium source and dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine (S-Phos) as the electron-donating ligand. The [2]dendralenyl skeleton is generated efficiently and selectively from 1. Propargylic biscarbonates are thus powerful precursors for the synthesis of [2]dendralene derivatives.

Solid-supported transition-metal catalysts have significant advantages such as stability, reusability, and reduction of residual metal catalysts in the products.⁸ For these reasons, such catalysts enable the production of organic materials to become efficient and cost-effective processes in chemical industry. Recently, heterogeneous Pd(0)-catalytic systems have accomplished many important carbon–carbon cross-coupling reactions such as Mizoroki-Heck, Suzuki-Miyaura, Sonogashira, Stille, and



Scheme 1. Dendralenes.

Tsuji-Trost reactions.⁹ Especially, palladium on carbon (Pd/C) supplied from commercial sources is one of the most frequently used catalyst for the cross-coupling reactions with good efficiency.^{9b-d} In general, Pd/C is more stable and cheaper than other homogeneous Pd catalysts. The handling is also easier. Moreover, some cases using Pd/C have successfully demonstrated its reusability.^{9a} In contrast to the previous works, to the best of our knowledge, there is no report on the coupling reaction of propargylic carbonates by the use of Pd/C. It would be a useful Pd/C-catalyzed synthesis of cross-conjugated ([2]dendralenyl) compounds via a cross-coupling reaction between propargylic biscarbonates and aryl boronic acids. In this letter, we report the synthesis of diaryl[2]dendralenes by a Pd/C-catalyzed reaction of propargylic biscarbonate **1** with boronic acids.

The cross-coupling reaction of propargylic biscarbonate **1** with arylboronic acids **2** was carried out with Pd/C, 10% Palladium on carbon (wetted with 55% water) supplied by Tokyo Chemical Industry (TCI) Corporation, and 2 M K₂CO₃ aq. at 100 °C. The Pd/C used was easily removed by filtration after the reaction. The yields

Table 1

Cross-coupling of ${\bf 1}$ with Phenylboronic Acid ${\bf 2a}$ using Palladium on Carbon as Catalyst.ª

WeO200	1 2	CON		3a
		u		ou
Entry	Phosphine Ligand	Pd/L	Solvent	Yield ^b (%)
1	-	1:2	Toluene	2
2	PPh ₃	1:2	Toluene	0
3	P(o-Tolyl) ₃	1:2	Toluene	20
4	P(o-Anisoyl) ₃	1:2	Toluene	33
5	PCy ₃ ·HBF ₄	1:2	Toluene	33
6	P ^t Bu ₃ ·HBF ₄	1:2	Toluene	20
7	X-Phos	1:2	Toluene	15
8	John-Phos	1:2	Toluene	8
9	P ^t Bu ₂ Me·HBF ₄	1:2	Toluene	57
10	S-Phos	1:2	Toluene	57
11	P ^t Bu ₂ Me·HBF ₄	1:3	Toluene	58
12	S-Phos	1:3	Toluene	73
13	S-Phos	1:4	Toluene	45
14 ^c	S-Phos	1:3	Toluene	74 (70) ^d
16	S-Phos	1:3	THF	0
17	S-Phos	1:3	DMF	0
18 ^e	S-Phos	1:3	Toluene	12
19 ^f	S-Phos	1:3	Toluene	67
20 ^g	S-Phos	1:3	Toluene	9
21 ^h	S-Phos	1:3 ^g	Toluene	3

^a Conditions: 1 (1.0 mmol), 2a (2.0 mmol), Pd/C (2.5 mol%), ligand (5.0–10.0 mol%), 2 M K₂CO₃ aq. (1.0 mL), solvent (2.0 mL), 100°C, under argon.

^b NMR yield of **3a**.

^c Pd₂(dba)₃·CHCl₃ (1.25 mol%).

^d Isolated yield.

e Pd/C (1.25 mol%), Ligand (3.75 mol%).

^f Pd/C (5.0 mol%), Ligand (15.0 mol%).

^g An equimolar amount of 3-mercaptopropyl silica gel (ca. 0.5 mmol/g, TCI) to Pd/C was added to the reaction media.

 $^{\rm h}\,$ The Pd/C collected from the reaction mixture (Entry 12) was used.

of the products **3** were estimated by ¹H NMR spectroscopy in $CDCl_3$ using nitromethane as a standard. The products **3** were separated by silica-gel column chromatography (hexane as an eluent).

The Pd/C-catalyzed cross-coupling reaction of **1** with phenylboronic acid (**2a**) was conducted under ligand-free conditions to afford a very low yield of 2,3-diphenyl-1,3-butadiene (diphenyl [2]dendralene) **3a** (Table 1, Entry 1). Although the reaction with PPh₃ as a ligand did not give **3a** (Entry 2), a 20% yield of **3a** was obtained when P(o-tolyl)₃ was used as a ligand (Entry 3). P(o-anisoyl)₃, PCy₃·HBF₄, P^tBu₃·HBF₄, dicyclohexyl(2',4',6'-triiso-propyl-1,1'-biphenyl-2-yl)phosphine (X-Phos), and di-*tert*-butyl [2-(diphenylphosphino)phenyl]phosphine (John-Phos) also gave **3a**, but the yields were not good (entries 4–8). Among the ligands tested, P^tBu₂Me·HBF₄ and dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine (S-Phos) raised the yield of **3a** up to 57% (Entries 9 and 10).

We next examined the ratio of phosphine ligand to Pd. Although changing the ratio of Pd to P^tBu₂Me HBF₄ from 1:2 to 1:3 did not increase the yield of **3a** (Table 1, Entries 9 and 11), the Pd/S-Phos ratio of 1:3 raised the yield to 73% (Entry 12). We reported that Pd₂(dba)₃·CHCl₃ is an effective palladium source for the cross-coupling reaction with 1.7 To compare with the results with Pd/C, the reaction of 1 with 2a was carried out using Pd₂(dba)₃·CHCl₃ instead of Pd/C. The yield (74%) of **3a** was similar to the case with Pd/C (Entry 14). The results show that Pd/C as well as $Pd_2(dba)_3 \cdot CHCl_3$ is highly effective for the reaction. The kind of solvent affected the reaction largely. THF and DMF were not suitable (Entries 16 and 17). The higher Pd/C catalyst loading (5.0 mol%) did not increase the yield of 3a (Entries 18 and 19). Thus, the optimized reaction conditions were found to be as follows: 1 (1.0 mmol), 2 (2.0 mmol), Pd/C (2.5 mol%), S-Phos (7.5 mol%), 2 M K₂CO₃ aq. (1.0 mL), toluene (2.0 mL) at 100 °C.

It is known that a solid-supported metal catalyst acts as a soluble metal source by leaching of the metal into solution. ^{9a,10} In order to learn whether the Pd/C used plays a role as a heterogeneous catalyst, the reaction of 1 with 2a was carried out under the optimized conditions in the presence of an equimolar amount of 3-mercaptopropyl-functionalized silica gel (2.5 mol% of SH). which is known to be a good palladium scavenger,¹⁰ to Pd/C. A dramatic decrease of yield (9%) of **3a** was observed (Table 1, Entry 20). The leached Pd species would be captured by the scavenger. This result suggests that the Pd/C used would play a homogeneous catalyst under our optimized conditions because the phosphine ligand leads to leaching of Pd atoms on carbon to form the phosphineligated palladium species in the bulk solution.^{9a} The reusability was tested by the use of the used Pd/C. The yield of **3a** dropped to 3%, probably due to the decrease of amount of the palladium atoms supported on the carbon surface (Entries 12 and 21).

With the optimized conditions in hand, the coupling reaction of 1 with a variety of aryl boronic acids 2 was investigated by using Pd/C or Pd₂(dba)₃·CHCl₃ (Table 2).^{12,13} 4-Methylphenylboronic acid (2b) and 3,5-dimethylphenylboronic acid (2c) gave dendralenes 3b and 3c in good yields (Entries 1 and 2). In the reaction using Pd₂(dba)₃·CHCl₃ as a catalyst, 4-methoxyphenylboronic acid (2d) and 3-acetylphenylboronic acid (2e) afforded 3d and 3e in good yields, but the use of Pd/C catalyst results in lower yields of 3d and 3e (Entries 3 and 4). Although 4-chlorophenyl-substituted dendralene **3f**¹¹ was obtained from 4-chlorophenylboronic acid (**2f**), the yields were not good in the cases using the both palladium sources (Entry 5). The reaction of 1 with 2-thienylboronic acid (2g) gave 3g in 41% (Entry 6). 3-Thienylboronic acid (2h) was a much better reaction partner than 2g, and gave 3h in 89% (Entry 7). The yield of **3h** was higher in the reaction with Pd/C. Potassium(4-pyridinyl) trifluoroborate was also used, but the product was not formed at all.

We next tried to synthesize [4]dendralenes from 1 and vinylboronic acids under the optimized conditions. The reaction of 1

Please cite this article in press as: Hayashi S., et al. Tetrahedron Lett. (2017), http://dx.doi.org/10.1016/j.tetlet.2017.05.016

ARTICLE IN PRESS

Table 2





^a Conditions: **1** (1.0 mmol), **2** (2.0 mmol), Pd/C (2.5 mol%), S-Phos (7.5 mol%), 2 M K₂CO₃ aq. (1.0 mL), solvent (2.0 mL), 100 °C, under argon.

^b Isolated yield.

with *trans*-2-phenylvinylboronic acid was carried out. The ¹H NMR of the reaction mixture showed small signals of the expected [4]-dendralene, but isolation of the product failed. This is probably because the [4]dendralene can be regarded as 3,3-coupled bis(1-phenyl-1,3-butadine). It is known that 1-phenyl-1,3-butadiene is not chemically and thermodynamically stable. On the other hand, [4]dendralene **3i**^{4d} could be synthesized and isolated by the use of 1-phenylvinylboronic acid (**2i**; Entry 8).

The UV-vis absorption spectra of styrene, diphenyl[2]dendralene **3a** and diphenyl[4]dendralene **3i** were measured in chloroform at room temperature (Fig. 1a). Absorption maximum (λ_{max}) of **3a** was at 246 nm ascribed to the π - π^* transition, whereas styrene showed a slight red-shift peak (250 nm). The absorption of **3i** appeared in the higher energy π - π^* transition (240 nm) region than that of **3a**. The blue-shift of [4]dendralene **3i** is probably due to a twisted conformation by rotating of C-C bonds of the dendralene moiety. It seems that an increasing in the number of *exo*methylene group tends to prefer a twisted conformation.^{4d}



Fig. 1. UV-vis absorption spectra of styrene, **3a** and **3i** in chloroform (a) and **3a** (i) and **3i** (ii) in various solvents (b).

Interestingly, both **3a** and **3i** showed solvatochromic behavior. Red-shifts were observed changing from polar to non-polar solvents (Fig. 1b). The conformational change by rotating the C–C single bonds probably would take place in the solvents with different polarities. In both **3a** and **3i**, each spectrum was shifted to the highest energy region in methanol.

In conclusion, we have successfully achieved a Pd/C-catalyzed synthesis of various diaryl[n]dendralenes (n = 2 and 4) from propargylic biscarbonate and aryl boronic acids. The UV-vis absorption spectra of diphenyl[4]dendralene revealed a more blue-shifted absorption maximum than that of diphenyl[2]dendralene. Further study on the reactions and properties of the obtained dendralenes is now under investigation.

Acknowledgments

The authors thank Grant-in-Aid for Scientific Research (C) 26410141 and Grant-in Aid for Scientific Research on Innovative Areas " π -figuration" 17H05171 for financial support. This work was partly performed under the Cooperative Research Program of "Network Joint Research Center for Materials and Devices."

References

- (a) Thomas AW, Henson ZB, Du J, Vandenberg CA, Bazan GC. J Am Chem Soc. 2014;136:3736–3739;
 (b) Theorem III (W) Jobs CD, Support TM, Chem Pay, 2007;107:1071120, 1286.
 - (b) Thomas III SW, Joly GD, Swager TM. *Chem Rev.* 2007;107:1339–1386; (c) Irimia-Vladu M. *Chem Soc Rev.* 2014;43:588–610.
- 2. (a) Wu W, Liu Y, Zhu D. Chem Soc Rev. 2010;39:1489-1502;
- (b) Reiss P, Couderc E, Girolamo JD, Pron A. Nanoscale. 2011;3:446–489.
- Kertesz M, Choi CH, Yang S. Chem Rev. 2005;105:3448–3481.
 (a) Gholami M, Tykwinski RR. Chem Rev. 2006;106:4997–5027;
- (a) Gildiani M, Tykwinski KK, Chen Rev. 2006;100:4997–3027;
 (b) van Walree CA, van der Wiel BC, Williams RM. Phys Chem Chem Phys. 2013;15:15234–15242;
 (c) Van Walree CA, van der Wiel CA, Van Derberge 2005;100:4997–3027;
- (c) Leu WCW, Hartley CS. Org Lett. 2013;14:3762–3765;
- (d) Shimizu M, Kurahayashi T, Shimono K, et al. *Chem Asian J.* 2007;2:1400–1408;
- (e) Fielder S, Rowan DD, Sherburn MS. *Angew Chem Int Ed*. 2000;39:4331–4333; (f) Yamamoto T, Yasuda T, Kobayashi K, et al. *Bull Chem Soc Jpn*.
- 2006;79:498–500;
- (g) Böhmer J, Grigg R. Tetrahedron. 1999;55:13463–13470;

(h) Ishino Y, Nishiguchi I, Takihira F, Hirashima T. Tetrahedron Lett. 1980;21:1527–1528.

- . (a) van Walree CA, van der Wiel BC, Jenneskens LW, et al. *Eur J Org Chem.* 2007;4746-4751;
- (b) van Walree CA, van Lenthe JH, van der Wiel BC. Chem Phys Lett. 2012;528:29;

(c) Lutz M, Spek AL, van der Wiel BC, Walree CA. Acta Crystallogr, Sect C. 2005;61:o300;

(d) Limacher PA, Lüthi HP. J Phys Chem A. 2008;112:2913-2919.

Please cite this article in press as: Hayashi S., et al. Tetrahedron Lett. (2017), http://dx.doi.org/10.1016/j.tetlet.2017.05.016

ARTICLE IN PRESS

S. Hayashi et al./Tetrahedron Letters xxx (2017) xxx-xxx

- (a) Mackay EG, Sherburn MS. Pure Appl Chem. 2013;85:1227-1239; 6. (b) Hops H, Sherburn MS. Angew Chem Int Ed. 2012;51:2298-2338.
- 7. Nishioka N, Hayashi S, Koizumi T. Angew Chem Int Ed. 2012;51:3682-3685. 8. (a) Pagliaro M, Pandarus V, Ciriminna R, Béland F, Carà PD. ChemCatChem.
- 2012;4:432-445; (b) Choi M, Lee D-H, Na K, Yu B-W, Ryoo R. Angew Chem Int Ed. 2009;48:3673-3676.
- (a) Yin L, Liebscher J. Chem Rev. 2007;107:133-173; 9.

4

- (c) Hayashi S, Kojima Y, Koizumi T. Polym Chem. 2015;6:881–885;
- (d) Tang D-TD, Collins KD, Glorius F. J Am Chem Soc. 2013;135:7450-7453.
- Parisien M, Valette D, Fagnou K. J Org Chem. 2005;70:7578–7584.
 Jiang H, He L, Li X, Chen H, Wu W, Fu W. Chem Commun. 2013;49:9218–9220.
- 12. Typical experimental procedure: 1 (202 mg, 1.0 mmol), 2i (296 mg, 2.0 mmol), Pd/C (53.3 mg, 0.025 mmol), S-Phos (30.6 mg, 0.075 mmol) were dissolved in 2.0 mL of toluene under argon. To the solution were added K₂CO₃ (aq) (2.0 M, 1 mL). After stirred for 2 h at 100 °C, the organic phase of reaction mixture was filtered, washed with methanol, and concentrated under reduced pressure. The

crude product was purified by column chromatography (SiO₂, hexane) to give 3i (163 mg, 63%).

13. Analytic data of new dendralene compounds: 3e: white crystal. ¹H NMR (300 MHz, CDCl₃): δ 7.90 (Ar-H, s, 1H), 7.74 (Ar-H, d, J = 7.5 Hz, 2H), 7.48 (Ar-H, d, J = 7.8 Hz, 2H), 7.29 (Ar-H, t, J = 7.8 Hz, 2H), 5.53 (exo-methylene-H, s, 2H), 5.32 (exo-methylene-H, s, 2H), 2.49 (Ar(CO)CH₃, s, 6H). Anal. Calcd. for C₂₀H₁₈O₂: C, 82.73; H, 6.25. Found: C, 82.36; H, 6.18. 3f: white crystal. ¹H NMR (300 MHz, CDCl₃): δ 7.21-7.49 (*Ar*-*H*, m, 8H), 5.54 (*exo*-methylene-H, d, *J* = 1.5 Hz, 2H), 5.34 (*exo*-methylene-H, d, *J* = 0.9 Hz, 2H). ¹³C NMR (75.45 MHz, CDCl₃): δ 148.32, 138.16, 133.47, 129.02, 128.70, 128.43, 128.21, 116.99. 3g: pail-yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.11 (*Ar-H*, d, J = 4.2 Hz, 2H), 6.89-6.83 (*Ar-H*, m, 4H), 5.57 (*exo*-methylene-H, s, 2H), 5.20 (*exo*-methylene-H, s, 2H). ¹³C NMR (75.45 MHz, CDCl₃): δ 143.53, 142.46, 127.42, 126.05, 124.89, 114.26. 3h: pailyellow oil. ¹H NMR (300 MHz, CDCl₃): *δ* 7.35-7.12 (*Ar-H*, m, 6H), 5.58 (*exo*-methylene-H, s, 2H), 5.28 (*exo*-methylene-H, s, 2H). ¹³C NMR (75.45 MHz, CDCl₃): δ 144.20, 141.30, 126.18, 125.43, 122.76, 114.14. Anal. Calcd. for C₁₂H₁₀S₂: C, 66.02; H, 4.62. Found: C, 66.27; H, 4.55.

Please cite this article in press as: Hayashi S., et al. Tetrahedron Lett. (2017), http://dx.doi.org/10.1016/j.tetlet.2017.05.016