JOC Article

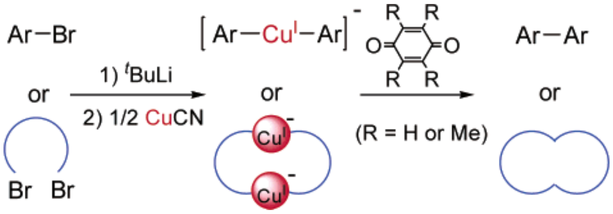
Efficient Construction of Biaryls and Macrocyclic Cyclophanes via Electron-Transfer Oxidation of Lipshutz Cuprates

Yoshihiro Miyake, Mo Wu, M. Jalilur Rahman, Yoshiyuki Kuwatani, and Masahiko Iyoda*

Department of Chemistry, Graduate School of Science, Tokyo Metropolitan University, Hachioji,
Tokyo 192-0397, Japan

iyoda-masahiko@c.metro-u.ac.jp

Received April 17, 2006



An efficient method for the homocoupling of aryl halides by electron-transfer oxidation of Lipshutz cuprates ($Ar_2Cu(CN)Li_2$) with organic electron acceptors is disclosed. Thus, various types of Lipshutz cuprates are prepared by successive treatment of aryl or heteroaryl bromides with *tert*-butyllithium and CuCN. The electron-transfer oxidation of Lipshutz cuprates with *p*-benzoquinones proceeds smoothly to afford the corresponding homocoupling products in moderate to good yields. Furthermore, it can be applied to the construction of either thiophene- or benzene-fused 10-membered ring cyclophanes. For the synthesis of 10-membered cyclophanes, the linear C−Cu−C structure of Lipshutz cuprates should be maintained in the dimetallacyclic intermediates, producing the large ring cyclophanes efficiently. The X-ray analysis of the cyclophanes reveals that the difference in the bridging atoms results in the different conformations of the macrocyclic rings. Thus, the silicon-bridged cyclophane **5a** adopts a D_2-symmetric structure with a twisted rhombic arrangement of four thiophene rings, whereas the methylene- and oxygen-bridged cyclophanes **5b** and **5c** possess C_{2h}- and C_2-symmetric structures with chair- and boatlike conformations, respectively. The ^{1}H NMR spectrum of C_2-symmetric **5c** is temperature-dependent, and the activation energy ($\Delta G^{\ddagger}$) for the conformational change is 10.1 kcal/mol.

Introduction

Aryl−aryl bond-forming reaction is one of the most important and powerful tools in modern organic synthesis.[1,2] These biaryls and their heteroaromatic analogues are some of the most attractive structural units in natural products, bioactive compounds, functional polymers, ligands in catalysts, and theoretically interesting molecules. For aryl−aryl bond formations, transition-metal-mediated coupling has been employed in most cases. Thus, the methodologies for the homocouplings and cross-couplings using transition metals such as copper, nickel, palladium, and iron have so far been developed and widely used.[3,4] Among them, homocoupling of substituted benzenes and aromatic heterocycles using copper as the reducing and

---

(1) (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359−1470. (b) Bringmann, G.; Walter, R.; Weirich, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 977−991. (c) *Metal-Catalysed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinhein, Germany, 1998. (d) Sainsbury, M. *Tetrahedron* **1980**, *36*, 3327−3359.

(2) (a) Bringmann, G.; Mortimer, A. J. P.; Keller, P. A.; Gresser, M. J.; Garner, J.; Breuning, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 5384−5427. (b) Lessene, G.; Feldman, K. S. *In Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: Weinhein, Germany, 2002; pp 479−538.

(3) For the copper-mediated reactions, see: (a) Woodward, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 5560−5562. (b) *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinhein, Germany, 2002. (c) Meyers, A. I.; Nelson, T. D.; Moorlag, H.; Rawson, D. J.; Meier, A. *Tetrahedron* **2004**, *60*, 4459−4473. (d) Erdik, D. *Tetrahedron* **1984**, *40*, 641−657.

(4) For the transition-metal-mediated reactions, see: (a) Zapf, A.; Beller, M. *Chem. Commun.* **2005**, 431−440. (b) Fürstner, A.; Martin, R. *Chem. Lett.* **2005**, *34*, 624−629. (c) Cepanec, I. *Synthesis of Biaryls*; Elsevier: Oxford, 2004. (d) *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinhein, Germany, 1998. (e) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (f) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340−348. (g) Iyoda, M.; Otsuka, H.; Sato, K.; Nisato, N.; Oda, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 80−87. (h) Hong, R.; Hoen, R.; Zhang, J. Lin, G. *Synlett* **2001**, 1527−1530.

10.1021/jo0608063 CCC: $33.50

coupling reagent is known as the Ullmann reaction.[5] Since the original Ullmann reaction[6] was reported in 1901 using metallic copper as the coupling reagent, a number of Ullmann-type couplings using activated metallic copper,[7] copper(I) salts,[8] and copper(II) salts[9] have been utilized for aryl−aryl bond formations. Diarylcopper(II) species prepared from arylmetals with copper(II) salts are known to decompose at low temperature to afford biaryls.[9,10] The reaction requires a transmetalation of arylmetals such as aryllithiums, arylmagnesium halides, and aryltin(IV) species with copper(II) salt,[11] followed by reductive elimination of the organic copper(II) intermediate. In contrast, an oxidative "decomposition" of organic cuprates (R_2CuLi) with oxidants is a promising method for the homocoupling of the ligands (R) on the copper atom. Casey and co-workers[10a] reported this type of biaryl synthesis using the reaction of diarylcopper lithium with molecular oxygen.

In 1981, Lipshutz and co-workers reported a novel cuprate prepared from 2 equiv of lithium reagent with 1 equiv of CuCN, the so-called "Lipshutz cuprate" ($R_2Cu(CN)Li_2$).[12] This cuprate has been reported to be an effective reagent for substitution reactions of alkyl halides and conjugate additions to α,β-unsaturated ketones.[13,14] Furthermore, oxidation of Lipshutz cuprates with molecular oxygen forms coupling products via ligand coupling on the copper atom.[15,16] Quite recently, 1,3-dinitrobenzene has been used for the oxidation of Lipshutz cuprates to afford medium-size ring compounds including the biaryl skeleton.[17]

Lipshutz cuprates ($R_2Cu(CN)Li_2$) show higher reactivity in chemical reactions than the traditional Gilman cuprates ($R_2CuLi\cdot LiX$).[18] The unusual reactivity was believed to be due to the structrure of Lipshutz cuprates in which the cyano group was bound to copper by means of a Cu−CN bond, resulting in a dianion species, $R_2Cu(CN)^{2-}2Li^+$.[19] After much investigation and controversial discussion on the structure of Lipshutz cuprates,[20] X-ray structural determinations have revealed that the cyano group in Lipshutz cuprats locates between two lithium atoms as a bridge and Lipshutz cuprates possess a linear carbon−copper−carbon arrangement.[21] We expected that the carbon−copper(I)−carbon linkage in Lipshutz cuprates would be easily oxidized by electron acceptors to give the corresponding carbon−copper(II)−carbon structure, and that the oxidation of Lipshutz cuprates would finally produce homocoupling products under mild conditions. In this study, we established a novel electron-transfer oxidation of Lipshutz cuprates with *p*-benzoquinones to produce biaryls as the homocoupling products (Scheme 1). Since a variety of aryl bromides **1** can be converted into Lipshutz cuprates **2**, our new methodology can produce a number of biaryls **3** in moderate to good yields. In addition, this methodology can be successfully applied for the construction of macrocycles **5a**−**5c** (Scheme 1).[22] Although the macrocyclization such as intramolecular ring closure and intermolecular cyclooligomerization usually affords cyclic products in low yields due to preferable formation of linear oligomers and five- and six-membered rings in some cases, our novel electron-transfer oxidation of metallacyclic intermediates including Lipshutz cuprates results in the formation of macrocyclic dimers owing to preferable formation of a dimetallacyclic intermediate with the linear Ar−Cu−Ar arrangement.

---

[5] Fanta, P. E. *Synthesis* **1974**, 9−21.

[6] Ullmann, F.; Bielecki, J. *Chem. Ber.* **1901**, *34*, 2174−2185.

[7] (a) Groenendaal, L.; Peerlings, H. W. I.; van Dongen, J. L. J.; Havinga, E. E.; Vekemans, J. A. J.; Meijer, E. W. *Macromolecules* **1995**, *28*, 116−123. (b) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1984**, *49*, 5280−5282. (c) Rieke, R. D.; Rhyne, L. D. *J. Org. Chem.* **1979**, *44*, 3445−3446.

[8] (a) Nishihara, Y.; Ikegashira, K.; Toriyama, F.; Mori, A.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 985−990. (b) Pier, E.; Yee, J. G. K.; Gladstone, P. L. *Org. Lett.* **2000**, *2*, 481−484. (c) van Koten, G.; Jastrzebski, J. T. B. H.; Noltes, J. G. *J. Chem. Soc., Chem. Commun.* **1977**, 203−204. (d) van Koten, G.; Jastrzebski, J. T. B. H.; Noltes, J. G. *J. Org. Chem.* **1977**, *42*, 2047−2053.

[9] (a) Demir, A. S.; Reis, Ö.; Emrullahoglu, M. *J. Org. Chem.* **2003**, *68*, 10130−10134. (b) Iyoda, M.; Nakao, K.; Kondo, T.; Kuwatani, Y.; Yoshida, M.; Matsuyama, H.; Fukami, K.; Nagase, S. *Tetrahedron Lett.* **2001**, *42*, 6869−6872. (c) Iyoda, M.; Kondo, T.; Nakao, K.; Hara, K.; Kuwatani, Y.; Yoshida, M.; Matsuyama, H. *Org. Lett.* **2000**, *2*, 2081−2083. (d) Harada, G.; Yoshida, M.; Iyoda, M. *Chem. Lett.* **2000**, 160. (e) Kang, S.-K.; Baik, T.-G.; Jiao, X. H.; Lee, Y. T. *Tetrahedron Lett.* **1999**, *40*, 2383−2384.

[10] (a) Whitesides, G. M.; San Filippo, J.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302−5303. (b) Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 291−356. (c) Kauffmann, *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 1−19. (d) Bertz, S. H.; Gibson, C. P. *J. Am. Chem. Soc.* **1986**, *108*, 8286−8288.

[11] (a) Knochel, P.; Betzemier, B. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinhein, Germany, 2002; pp 45−78. (b) Ila, H.; Baron, O.; Wagner, A. J.; Knochel, P. *Chem. Lett.* **2006**, *35*, 2−7. (b) Kabir, S. M. H.; Hasegawa, M.; Kuwatani, Y.; Yoshida, M.; Matsuyama, H.; Iyoda, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 159−165.

[12] Lipshutz, B. H.; Wilhelm, R. S.; Floyd, D. M. *J. Am. Chem. Soc.* **1981**, *103*, 7672−7674.

[13] (a) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005−5038. (b) Lipshutz, B. H. *Synthesis* **1987**, 325−341. (c) Lipshutz, B. H. *Synlett* **1990**, 119−128. (d) Lipshutz, B. H.; Sengupta, S. *Org. React. (N. Y.)* **1992**, *41*, 135−631. (d) Lipshutz, B. H. In *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: Chichester, U.K., 1994; pp 283−382. (e) Lipshutz, B. H. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1995; Vol. 4, pp 1−64.

[14] (a) Krause, N.; Gerold, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 186−204. (b) Canisius, J.; Gerold, A.; Krause, N. *Angew. Chem., Int. Ed.* **1999**, *38*, 1644−1646. (c) Bertz, S. H.; Chopra, A.; Eriksson, M.; Ogle, C. A.; Seagle, P. *Chem.*−*Eur. J.* **1999**, *5*, 2680−2691. (d) Woodward, S. *Chem. Soc. Rev.* **2000**, *29*, 393−401. (e) Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2005**, *127*, 4697−4706.

[15] (a) Lipshutz, B. H.; Siegmann, K.; Garcia, E. *J. Am. Chem. Soc.* **1991**, *113*, 8161−8162. (b) Lipshutz, B. H.; Siegmann, K.; Garcia, E.; Kayser, F. *J. Am. Chem. Soc.* **1993**, *115*, 9276−9282. (c) Lipshutz, B. H.; Kayser, F.; Liu, Z.-P. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1842−1844.

[16] Dieter, R. K.; Li, S.; Chen, N. *J. Org. Chem.* **2004**, *69*, 2867−2870.

[17] (a) Spring, D. R.; Krishnan, S.; Schreiber, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 5656−5657. (b) Spring, D. R.; Krishnan, S.; Blackwell, H. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1354−1363. (c) Surry, D. S.; Su, X.; Fox, D. J.; Franckevicius, V.; Macdonald, S. J. F.; Spring, D. R. *Angew. Chem., Int. Ed.* **2005**, *44*, 1870−1873.

[18] Lipshutz, B. H.; Crow, R.; Dimock, S. H.; Ellsworth, E. L.; Smith, R. A. J.; Behling, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 4063−4064.

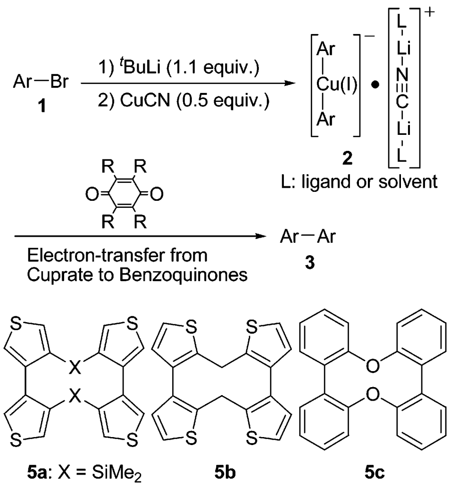
[19] (a) Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *J. Am. Chem. Soc.* **1985**, *107*, 3197−3204. (b) Lipshutz, B. H.; Ellsworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1988**, *110*, 4834−4835.

[20] (a) Bertz, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 4031−4032. (b) Lipshutz, B. H.; Sharma, S.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 4032−4034. (c) Bertz, S. H. *J. Am. Chem. Soc.* **1991**, *113*, 5470−5471. (d) Singer, R. D.; Oehlschlager, A. C. *J. Org. Chem.* **1992**, *57*, 2192−2195. (e) Snyder, B. J. P.; Spangler, D. P.; Behling, J. R. *J. Org. Chem.* **1994**, *59*, 2665−2667. (f) Lipshutz, B. H.; James *J. Org. Chem.* **1994**, *59*, 7585−7587. (g) Stemmler, T. L.; Barnhart, T. M.; Penner-Hahn, J. E.; Tucker, C. E.; Knochel, P.; Böhme, M.; Frenking, G. *J. Am. Chem. Soc.* **1995**, *117*, 12489−12497. (h) Huang, H.; Alvarez, K.; Lui, Q.; Barnhart, T. M.; Snyder, J. P.; Penner-Hahn, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 8808−8816. (i) Cabezas, J. A.; Oehlschlager, A. C. *J. Am. Chem. Soc.* **1997**, *119*, 3878−3886. (j) Bertz, S. H.; Nilsson, K.; Davidsson, Ö.; Snyder, J. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 314−317. (k) Mobley, T. A.; Müller, F.; Berger, S. *J. Am. Chem. Soc.* **1998**, *120*, 1333−1334. (l) Gschwind, R. M.; Rajamohanan, P. R.; John, M.; Boche, G. *Organometallics* **2000**, *19*, 2868−2873.

[21] (a) Boche, G.; Bosold, F.; Marsch, M.; Harms, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 1684−1686. (b) Kronenburg, C. M. P.; Jastrzebski, J. T. B. H.; Spek, A. L.; van Koten, G. *J. Am. Chem. Soc.* **1998**, *120*, 9688−9689. (c) Krause, N. *Angew. Chem., Int. Ed.* **1999**, *38*, 79−81. (d) Hwang, C.-S.; Power, P. P. *J. Am. Chem. Soc.* **1998**, *120*, 6409−6410.

[22] Miyake, Y.; Wu, M.; Rahman, M. J.; Iyoda, M. *Chem. Commun.* **2005**, 411−413.

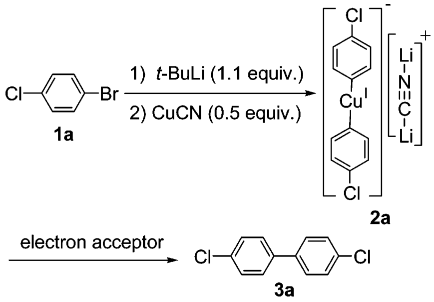
SCHEME 1. Electron-Transfer Oxidation of Lipshutz Cuprates



Results and Discussion

Coupling of Aryl Bromides using Electron-Transfer Oxidation of Lipshutz Cuprates. As has been reported previously, Lipshutz cuprates can be oxidized with molecular oxygen or dinitrobenzene to afford the corresponding homocoupling products.[15−17] We first investigated the oxidation of Lipshutz cuprate **2a** prepared from the reaction of *p*-bromochlorobenzene (**1a**) with 1.1 equiv of *tert*-butyllithium, followed by treatment with 0.5 equiv of CuCN (Table 1). Our preliminary experiments showed that the reactions of **2a** with molecular oxygen and 1,3-dinitrobenzene gave 4,4′-dichlorobiphenyl (**3a**) in 35% and 54% yields, respectively (Table 1, entries 1 and 4). To increase the yield of **3a**, a variety of electron acceptors were examined. After several attempts, 1,4-benzoquinones were found to be effective for the oxidation of **2a** (Table 1, entries 5−11).

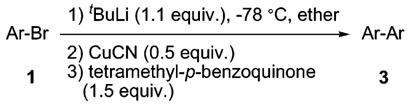
TABLE 1. Homocoupling of 1a via Electron-Transfer Oxidation of 2a with Electron Acceptors[a]



entry	electron acceptor (amt, equiv)	yield[b] (%)
1	oxygen (excess)	35
2	tetracyanoethylene (1.5)	29
3	tetracyanoquinodimethane (1.5)	76
4	1,3-dinitrobenzene (3.0)	54
5	*p*-benzoquinone (1.5)	76
6	2,6-dimethyl-*p*-benzoquinone (1.5)	81
7	2,5-dimethyl-*p*-benzoquinone (1.5)	82
8	tetramethyl-*p*-benzoquinone (1.0)	74
9	tetramethyl-*p*-benzoquinone (1.5)	96
10	tetramethyl-*p*-benzoquinone (2.0)	93
11	tetramethyl-*p*-benzoquinone (3.0)	92

[a] *t*BuLi (1.1 equiv) was added to a solution of **1a** (1.0 mmol) in Et_2O (60 mL) at −78 °C before CuCN (0.5 equiv) was added. After an electron acceptor was added, the mixture was stirred for 3 h at room temperature. [b] Isolated yield.

TABLE 2. Homocoupling of Aryl Halides 1 via Electron-Transfer Oxidation of Lipshutz Cuprates[a]



entry	Ar (**1**)	yield[b] (%)	entry	Ar (**1**)	yield[b] (%)
1	4-ClC_6H_4 (**1a**)	96	14	4-BrC_6H_4 (**1j**)	88
2[c]	4-ClC_6H_4 (**1a**)	0	15	3-BrC_6H_4 (**1k**)	95
3[d]	4-ClC_6H_5 (**1a**)	75	16	2-BrC_6H_4 (**1l**)	91
4	C_6H_4 (**1b**)	84	17	2,4,6-$Me_3C_6H_2$ (**1m**)	0
5	4-FC_6H_4 (**1c**)	73	18[g]	2,4,6-$Me_3C_6H_2$ (**1m**)	64
6	4-$(MeO)C_6H_4$ (**1d**)	91	19[g]	1-naphthyl (**1n**)	99
7[e]	4-$(MeO)C_6H_4$ (**1d**)	55	20[g]	2-naphthyl (**1o**)	99
8[f]	4-$(MeO)C_6H_4$ (**1d**)	75	21	2-thienyl (**1p**)	62
9	3-$(MeO)C_6H_4$ (**1e**)	96	22	3-thienyl (**1q**)	82
10	2-$(MeO)C_6H_4$ (**1f**)	87	23	4-Br-3-thienyl (**1r**)	87
11	4-MeC_6H_4 (**1g**)	90	24	2-pyridyl (**1s**)	0
12	3-MeC_6H_4 (**1h**)	91	25	4-$(CN)C_6H_5$ (**1t**)	0
13	2-MeC_6H_4 (**1i**)	80	26	4-$(Me_2N)C_6H_5$ (**1u**)	0

[a] The reaction was carried out using a procedure similar to that noted in Table 1. [b] Isolated yield. [c] Without CuCN. [d] *n*-BuLi (1.1 equiv) was used instead of *t*-BuLi. [e] CuI was used instead of CuCN. [f] CuSCN was used instead of CuCN. [g] *t*-BuLi (2.5 equiv) was used.

As shown in Table 1, the reaction of **2a** with electron acceptors proceeded smoothly, giving **3a** in good to excellent yields (Table 1, entries 3−11). Initially, 1.5 equiv of electron acceptors was applied to the reactions, except 1,3-dinitrobenzene. Since 1,3-dinitrobenzene is a comparatively mild oxidant, 3.0 equiv of the reagent was used to afford a satisfactory yield of **3a** (entry 4). Among all of the oxidants, tetramethyl-*p*-benzoquinone led to the best yield of **3a** (96%, entry 9). In all cases, the biaryl **3a** was the sole product. A byproduct that may arise from the ligand coupling of the cyano group and the aryl moieties was not detected, in contrast to the reactions of lithium cyanocuprates (ArCuCNLi),[23,24] nor was the conjugate adduct of the aryl group to the *p*-benzoquinones detected, and 1,4-benzoquinones were recovered in 80−90% yields. Further reactions that were carried out with different amounts of tetramethyl-*p*-benzoquinone revealed that 1.5 equiv was the best amount under the present conditions (entries 8−11). Therefore, 1.5 equiv of tetramethyl-*p*-benzoquinone was used as the electron acceptor in the following work.

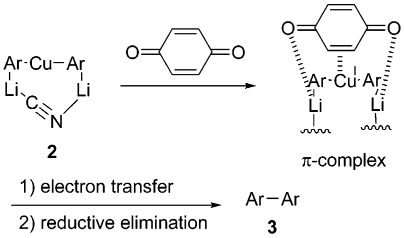
Next, various aryl bromides **1a**−**u** were subjected to the optimized homocoupling conditions (Table 2). As expected, no coupling reaction of **1a** occurred without CuCN (Table 2, entry 2). In this reaction system, *t*-BuLi was found to work more effectively than *n*-BuLi (entries 1 and 3), and the reactions with *n*-BuLi sometimes formed a trace amount of homocoupling products. However, similarly to the reaction of **1a** (entry 1), bromobenzene (**1b**), *p*-bromofluorobenzene (**1c**), and *p*-bromoanisole (**1d**) readily afforded the corresponding **3b**, **3c**, and **3d** in 84%, 73%, and 91% yields, respectively (entries 4−6). Besides the reaction with CuCN, similar reactions with two other copper(I) salts, CuI and CuSCN, were also carried out (entries 7 and 8). The homocoupling of *p*-bromoanisole (**1d**) with CuI led to 55% **3d**, while the reaction with CuSCN produced 75% **3d**. These results revealed that the cyano group plays an important role in the high reactivity of Lipshutz cuprates. A

---

(23) Kronenburg, C. M. P.; Amijs, C. H. M.; Wijkens, P.; Jastrzebski, J. T. B. H.; van Koten, G. *Tetrahedron Lett.* **2002**, *43*, 1113−1115.

(24) Gronowitz, S. *Acta Chem. Scand.* **1961**, *15*, 1393.

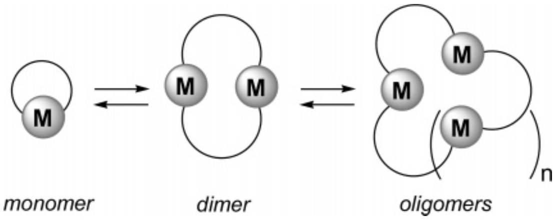
SCHEME 2. Plausible Reaction Pathway



variety of substrates with electron-deficient substituents, such as *p*-bromoflurobenzene (**1c**) and *p*-dibromobenzene (**1j**), and those with electron-rich substituents, such as *p*-bromoanisole (**1d**) and *p*-bromotoluene (**1g**), furnished high yields of the biaryl products (entries 3, 5, 11, and 14). Although steric hindrance was considered to be one of the factors which greatly affect the formation of biaryls via cuprate intermediates,[9a] *para*-, *meta*-, and *ortho*-subsituted substrates all gave good yields of the products under these conditions. The *p*-, *m*-, and *o*-methoxyl-substituted substrates gave the corresponding biaryls in 91%, 96%, and 87% yields, respectively (entries 5, 9, and 10). Similarly, the methyl-substituted substrates furnished the biaryl products in 90%, 91%, and 80% yields, and the bromo-substituted substrates in 88%, 95%, and 91% yields, respectively (entries 11−16). When a very hindered substrate, 2-bromo-1,3,5-trimethylbenzene (**1m**), was subjected to the optimized conditions, no formation of **3m** was observed. However, the reaction of **1m** with the addition of 2.5 equiv of *t*-BuLi proceeded to give the corresponding product **3m** in 64% yield (entries 17 and 18). In the coupling of 1- and 2-bromonaphthalenes (**1n** and **1o**), 2.5 equiv of *t*-BuLi was also necessary to afford the products in excellent yields (entries 19 and 20). Thiophene derivatives were also successfully coupled under the present conditions (entries 21−23). For example, 4,4′-dibromo-3,3′-bithienyl (**3r**) was obtained in 87% yield by the coupling of **1r**, whereas the reported methods for the preparation of **3r** using reactions of 4-bromo-2-thienyllithium or 4-bromo-2-thienylzinc chloride with $CuCl_2$ gave 65% or 52% yield.[24,25] It is worth noting that the present conditions allow employment of an aryl dihalide (**1j**, **1k**, **1l**, or **1r**), selectively affording the desired product without loss of bromo substituents (entries 13−15 and 23). Unfortunately, our reaction system cannot be applied for the reaction of nitrogen-containing substrates such as **1s**, **1t**, and **1u** (entries 24−26).

A plausible reaction pathway is shown in Scheme 2. Treatment of aryl bromide **1** with *t*-BuLi, followed by the reaction with CuCN, affords Lipshutz cuprate **2**. The complexation of **2** with 1,4-benzoquinones results in the formation of the π-complex using lithium···carbonyl and copper···olefin coordinations.[26] Finally, electron transfer from cuprate to the π-acceptor, followed by reductive elimination, produces the corresponding biaryl.[27] Although the details of the electron-transfer step are not yet clear, 1,4-benzoquinone was found to be recovered in high yields after the reactions. No formation of 1,4-hydroquinone was observed during or after the reaction. In addition, we tried the transformation of 1,4-hydroquinone to 1,4-benzoquinone under the present workup conditions. However, within 15−30 min, only ca. 5−10% 1,4-benzoquinone was formed. The reaction under neutral and acidic (pH 3) conditions also led to similar results. Thus, the formation of 1,4-hydroquinone is not necessary, and 1,4-benzoquinone might be reproduced directly from semiquinone radical anion under the workup conditions. Atmospheric oxygen or other oxidants in the reaction media may take part in the reproduction of 1,4-benzoquione.

SCHEME 3. Equilibrium among Metallacycle Intermediates



Construction of Macrocyclic Systems. After the investigation of aryl−aryl bond formation with this novel methodology, it was applied to the construction of macrocyclic compounds in the following work. Metallacycles are one of the most important and available reaction intermediates in organometallic chemistry. The existence of equilibrium among monomeric, dimeric, and oligomeric metallacycles has been known, and the reaction conditions, such as metals, solvents, temperatures, and so on, are expected to have an effect on the structures and the distribution of the oligomeric intermediates (Scheme 3).[28,29] Generally, modifications are necessary to induce the equilibrium to favor the formation of the desired product. Since Lipshutz cuprate has a linear carbon−copper−carbon (C−Cu−C) structure, favorable formation of oligomeric metallacycles is expected. The preparation of thiophene-fused cyclophanes has always attracted our interest, and the synthesis of methylene-bridged 10-membered ring **5b** has already been carried out by the reaction of Lipshutz cuprate with oxygen.[30] However, it exhibited low reproducibility and was not able to be applied to the construction of its analogues. The present method that involves an electron-transfer procedure found its application in the formation of the cyclophanes **5a**−**c**.

The cyclization of **4a** via aryl−aryl bond formations using CuX (X = CN, SCN, and I) was examined as a model reaction, and typical results are shown in Table 3. Although the cyano (CN) and thiocyano (SCN) ligands promoted the formation of the 10-membered ring cyclophane **5a**, CuI was not effective for the cyclodimerization (Table 3, entries 1, 3, and 5).[31] When triethylamine (2.0 equiv) was added after the formation of Liphsutz cuprate, using CuCN as the copper salt, remarkable improvement in the selectivity was observed, leading to a 48% yield of **5a** and 25% yield of **6a** (entry 2). However, the reaction of **3a** with CuSCN in the presence of Et_3N afforded a result similar to that without Et_3N (entry 4). Similarly, 1,4-benzo-

---

(25) Kabir, S. M. H.; Miura, M.; Sasaki, S.; Harada, G.; Kuwatani, Y.; Yoshida, M.; Iyoda, M. *Heterocycles* **2000**, *52*, 761−774.

(26) (a) Berlan, J.; Battioni, J.-P.; Koosha, K. *Bull. Soc. Chim. Fr.* **1979**, *II*, 183−190. (b) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015−6018. (c) Vellekoop, A. S.; Smith, R. A. J. *J. Am. Chem. Soc.* **1994**, *116*, 2902−2913.

(27) For electron-transfer oxidation of organometallics, see: (a) Cheng, J.-W.; Luo, F.-T. *Tetrahedron Lett.* **1988**, *29*, 1293−1294. (b) Chen, C.; Xi, C.; Lai, C.; Wang, R.; Hong, X. *Eur. J. Org. Chem.* **2004**, 647−650.

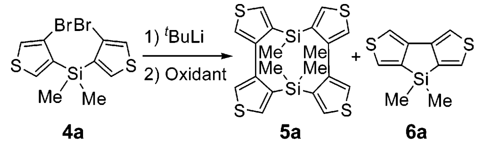
(28) Freijee, F. J. M.; Seetz, J. W. F. L.; Akkerman, O. S.; Bickelhaupt, F. *J. Organomet. Chem.* **1982**, *224*, 217−221.

(29) Iyoda, M.; Kabir, S. M. H.; Vorasingha, A.; Kuwatani, Y.; Yoshida, M. *Tetrahedron Lett.* **1998**, *39*, 5393−5396.

(30) Kabir, S. M. H.; Iyoda, M. *Chem. Commun.* **2000**, 2329−2330.

(31) Recently, a similar 10-membered ring cyclophane was obtained as a byproduct in 2% yield from the reaction of 2,2-dilithio-3,3-bithienyl: Rajca, A.; Miyasaka, M.; Pink, M.; Wang, H.; Rajca, S. *J. Am. Chem. Soc.* **2004**, *126*, 15211−15222.

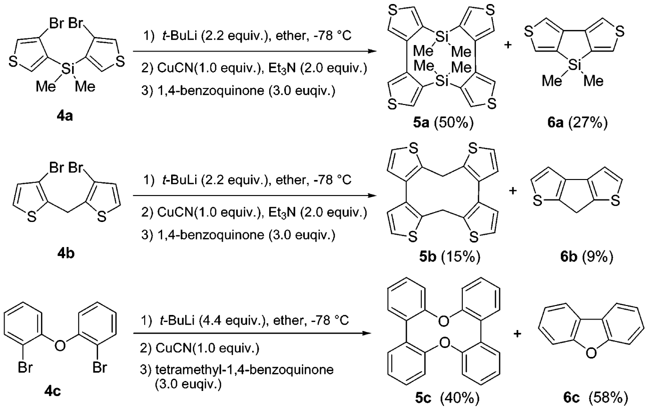
TABLE 3. Cyclization of 4a via Aryl−Aryl Bond Formations[a]



entry	copper(I) salt	yield[b] (%) 5a	yield[b] (%) 6a
1	CuCN	18	57
2[c]	CuCN	48	25
3[d]	CuSCN	12	61
4[c,d]	CuSCN	16	46
5	CuI	2	52
6[c,e]	CuCN	50	27
7[c,f]	CuCN	0[g]	0[g]
8[c,f,h]	CuCN	17	56

[a] *t*BuLi (2.2 equiv) was added to a solution of **4a** (1.0 mmol) in Et$_2$O (60 mL) at −78 °C before CuCN (1.0 equiv) was added. After tetramethyl-1,4-benzoquinone was added, the mixture was stirred for 3 h at room temperature. [b] Isolated yields. [c] With Et$_3$N (2 equiv). [d] t-BuLi (4.4 equiv) was added. [e] 1,4-Benzoquinone was used as an acceptor. [f] CuCl$_2$ was used instead of 1,4-benzoquinones. [g] The reduction product of **4a** was obtained in high yield. [h] THF was used as the solvent.

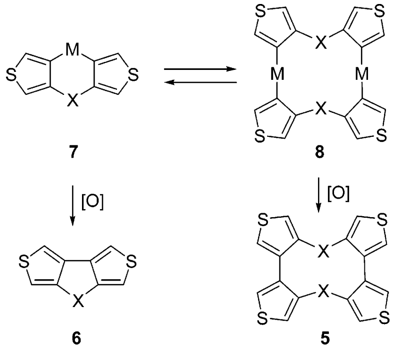
SCHEME 4. Cyclodimerization of 4a−c to 10-Membered Cyclophanes 5a−c



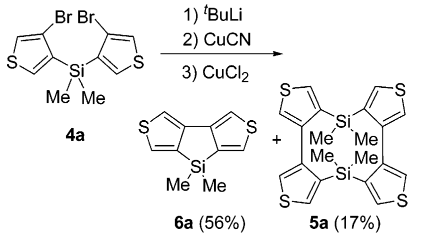
quinone worked effectively as an electron acceptor (entry 6). When CuCl$_2$ was used as the oxidant, no coupling products **5a** and **6a** formed with the reduced product of **4a** (Table 3, entry 7). The coupling reaction of **4a** with CuCl$_2$ in THF proceeded to mainly afford **6a** (entry 8).

On the basis of the results shown in Table 3, this procedure was applied to the cyclodimerization of **4b** and **4c** (Scheme 4). For the cyclodimerization of **4a** and **4b**, 1,4-benzoquinone works a little better than tetramethyl-1,4-benzoquinone to lead to the cyclophenes **5a** and **5b** in 50% and 17% yields, respectively; the similar reactions with tetramethyl-1,4-benzoquinone gave **5a** and **5b** in 48% and 15% yields, respectively. In contrast, the cyclodimerization of **4c** proceeded smoothly with tetramethyl-1,4-benzoquinone as the oxidant to produce **5c** in 40% yield. Unfortunately, the reaction of the sulfur-bridged substrates afforded the five-membered ring compounds as the main products, and ten-membered ring cyclophanes were isolated only in low yields. This is supposed to be the reason the coordination of the bridging sulfur atom to the copper atom decreased the reactivity of the Lipshutz cuprate intermediate.[32] In contrast, the cyclodimerization of 2,3-disubstituted substrate **4b** proceeded to give the methylene-bridged 10-membered ring cyclophane **5b** in 15% yield. Furthermore, dibromodiphenyl ether **4c** also furnished a moderate yield of the corresponding cyclophane **5c**.

SCHEME 5. Selective Cyclization via Metallacyclic Intermediates



SCHEME 6. Coupling of Lipshutz Cuprate Using CuCl$_2$



Metallacycles are key intermediates in this cyclization. As shown in Scheme 5, the dithiophene **6** is produced via six-membered monomeric metallacycle **7**, while **5** is produced via 12-membered dimeric metallacycle **8**. When we investigated the palladium-catalyzed coupling reaction of **4a** with Me$_3$SnSnMe$_3$, the intramolecular cyclization proceeded to afford **6a** in 64% yield with no formation of **5a**.[33] Since the palladium complex possesses a common square planar structure and the *cis*- carbon−palladium−carbon conformation, the intermediate **7** should be thermodynamically stable and the dimeric metallacycle **8** is hardly formed in situ. On the contrary, the intermediate **8**, which has a linear C−Cu−C linkage, is expected to be more favorable than **7** bearing the bent structure in the case of the present reaction because Lipshutz cuprates are known to have a linear C−Cu−C linkage.[21a,b] In addition, triethylamine coordinates to lithium atoms, and the structure of the diarylcopper segment is preserved. The cation part of the cuprate might be stabilized by the coordination of triethylamine; hence, the stability of the whole ion pair could be enhanced.

In the cyclophane synthesis, the electron-transfer step also contributes to the efficient maintenance of the linear structure of the Lipshutz cuprate intermediate upon oxidation. As mentioned in Table 3 (entry 8), CuCl$_2$ was not an effective oxidant for the cyclodimerization (Scheme 6). After the formation of the Lipshutz cuprate intermediate, CuCl$_2$ was added to furnish a transmetalation step. The copper(I) intermediate was transformed to copper(II), and **6a** was obtained as the major product and **5a** the minor product.

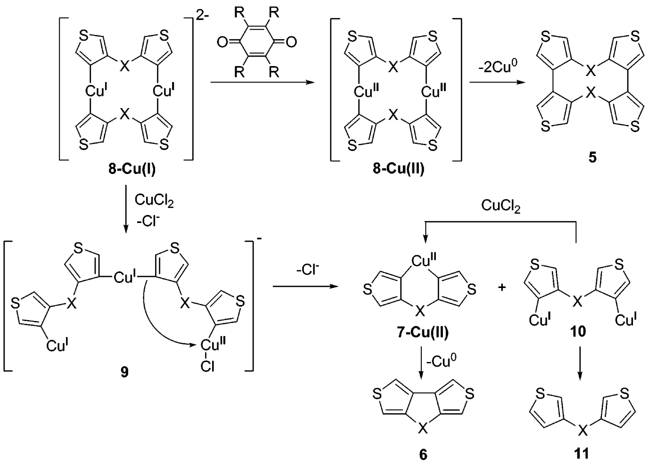
Compared to the coupling reaction via transmetalation (Scheme 6), the electron-transfer reaction obviously favors the formation of the 10-membered ring compound (Scheme 7). This

---

(32) Triphenylphosphine causes a structural change of cyanocuprate. See: Davis, R. P.; Hornauer, S. *Eur. J. Inorg. Chem.* **2005**, 51−54.

(33) Iyoda, M.; Miura, M.; Sasaki, S.; Kabir, S. M. H.; Kuwatani, Y.; Yoshida, M. *Tetrahedron Lett.* **1997**, *38*, 4581−4582.

SCHEME 7. Electron-Transfer Process from Copper to Electron Acceptors



should be the reason electron transfer is a fast reaction and the conformation (the linear structure) of the intermediate is conserved during the reaction. Thus, after electron transfer from **8**−Cu(I) to benzoquinones, the intermediate **8**−Cu(II) still possesses the linear structure and finally produces the 10-membered ring **5** upon fast reductive elimination. On the other hand, the transmetalation of **8**−Cu(I) with $CuCl_2$ breaks the carbon−copper(I) bond, and the acyclic intermediate **9** is formed. The disproportionation of **9** proceeds to afford the monomeric metallacycle **7**−Cu(II) and the lower order cyanocuprate **10**. The transmetalation of **10** with $CuCl_2$ might occur to give **7**−Cu(II). Finally, reductive elimination of **7**−Cu(II) gives the five-membered ring **6**, and the protonation of **10** gives the reduction product **11** (Scheme 7).

Structures and Properties of 10-Membered Ring Cyclophanes 5a−c. The 10-membered ring cyclophanes **5a**−**c** are novel compounds bearing unique molecular structures. As shown in Figure 1, (*all*-*Z*)-cyclodeca-1,3,6,8-tetraene **12** has three possible conformations with chairlike C_{2h} symmmetry (**12a**), boatlike C_2 symmetry (**12b**), and twisted D_2 symmetry (**12c**). The difference between **12a** and **12b** is the relative arrangement of two *cisoid*-butadiene units, whereas **12c** has two *transoid*-butadiene moieties. The dihedral angles of the butadiene units in **12a**−**c** are estimated as 54.2°, 47.5°, and 104.5° for **12a**, **12b**, and **12c**, respectively, by B3LYP/6-31G(d) level DFT calculations. The most stable conformer of the macrocycle **12** is considered to be chairlike C_{2h} structure **12a**, and other two conformers **12b** and **12c** are less stable than **12a** by 3.9 and 15.4 kcal/mol, respectively.

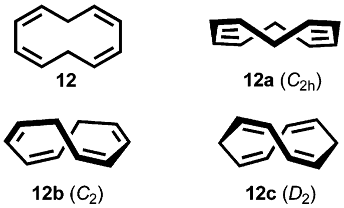


FIGURE 1. Three possible conformers for (*all*-*Z*)-cyclodeca-1,3,6,8-tetraenes **12a**−**c**. The symmetry of each structure is shown in parentheses.

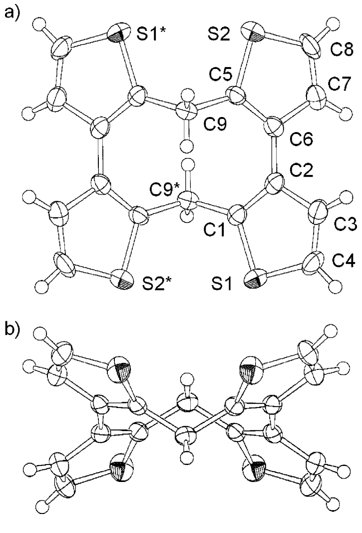


FIGURE 2. X-ray structure of **5b**: (a) top view, (b) side view.

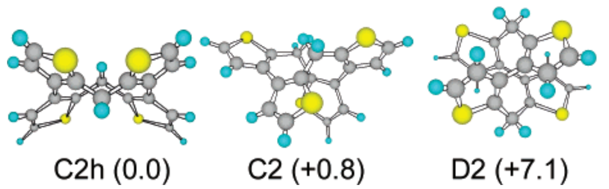


FIGURE 3. Optimized molecular structures of **5b** by B3LYP/6-31G(d) level DFT calculations. The symmetry for each conformer is shown with the relative energy (kcal/mol) in parentheses.

The X-ray analysis revealed that **5b** possesses a chairlike C_{2h} conformation with an *anti* arrangement of the two methylene bridges as shown in Figure 2.[30b] The crystal contains two crystallographically independent molecules, which locate at crystallographic symmetric centers. Both molecules show essentially the same C_{2h} structures with torsional angles at the bithiophene units of 53.7° (C1−C2−C6−C5) and 56.3° (corresponding angle for another molecule). Three possible conformations for **5b** are shown in Figure 3. The most stable conformation of **5b** is the chairlike C_{2h} structure obtained by B3LYP/6-31G(d) level DFT calculations. The other two conformers, boatlike C_2 and twisted D_2 structures, are less stable than the C_{2h} conformer by 0.8 and 7.1 kcal/mol, respectively. The ^{1}H NMR spectrum of **5b**, which is composed of two sets of AB pattern signals (δ 7.30 and 6.89 for the thiophene ring protons and δ 4.45 and 4.02 for the methylene protons), clearly shows the C_{2h} conformation for **5b** in solution.

The silicon-bridged cyclophane **5a** is considered to have a conformation different from that shown by the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of **5a** exhibited only one singlet for the methyl protons on the bridged Si atoms at δ 0.35, and the methyl signal kept a singlet at low temperatures. This indicates that **5a** possesses a symmetric conformation in which all the methyl protons are in the same chemical environment. Furthermore, considerable higher field shifts of thiophene ring protons were observed in the ^{1}H NMR spectrum of **5a**. The signals for ring protons of **5a** were observed at δ 7.00 and 6.98, which are at ca. 0.35 ppm higher field than those of **4a** (δ 7.37 and 7.32). On the other hand, the chemical shifts for the ring protons of **5b** (δ 7.28 and 6.88) showed chemical shifts similar to those of **4b** (δ 7.18 and 6.93). DFT calculations of **5a** suggest the twisted D_2 conformer as the most stable structure, where all the methyl substituents are equivalent. The corresponding C_{2h} structure of **5a** is 5.9 kcal/mol less stable, and the boatlike C_2 conformer is not an energy-minimum structure any more. The preference of the D_2 conformation in **5a** is attributable to

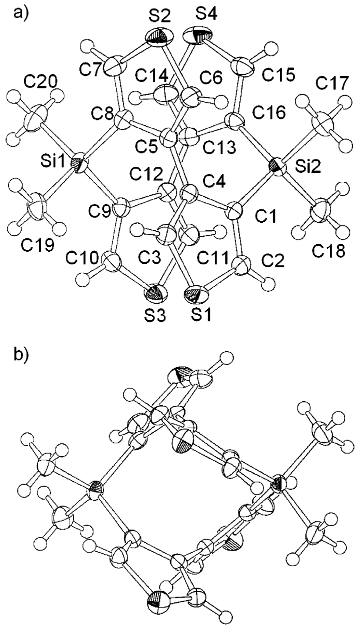


FIGURE 4. X-ray structure of **5a**: (a) side view, (b) top view.

two methyl substituents on the Si bridge, which can cause repulsive interaction in other conformers.

The molecular structure of the cyclophane **5a** elucidated by the X-ray analysis is depicted in Figure 4. The molecule **5a** adopts a twisted D_2 conformation with a rhombic arrangement of the four thiophene rings. Although the conformation of **5a** is chiral, the crystal is totally racemic on the basis of the achiral space group ($C2/c$). The torsional angles between the neighboring thiophene rings are 96.6° (C1−C4−C5−C8) and 98.0° (C9−C12−C13−C16). Two opposite thiophene rings locate at a distance of 3.4 Å at the 10-membered ring and are slightly opened at the end with dihedral angles of 19°. Therefore, the inside of the cyclophane has no more space for accommodation of any guest molecule. The stacked arrangement of the thiophene rings in **5a** is in good accordance with higher field shifts of the thiophene ring protons in the ^{1}H NMR spectrum of **5a**.

The cyclophane **5c** possesses a boatlike C_2 conformation, which was proved by the X-ray analysis, as shown in Figure 5. The torsional angles of the two phenylene groups in the biphenyl units are 47.2° (C1−C6−C7−C12) and 48.4° (C13−C18−C19−C24). Two phenylene groups in **5c** are stacked face-to-face at a distance of 3.0 Å between the 10-membered ring carbons and are opened at the end with a dihedral angle of 42°. The other two phenylene groups are projected outward in a propeller-like arrangement. The crystal of **5c** is composed of a single enantiomer and is totally chiral with an asymmetric space group ($P2_12_12_1$). This molecular structure is related to the C_2 conformer of **5b**, and the boatlike **5c** with C_2 conformation is estimated to be more stable than the corresponding twisted D_2 structure by 6.0 kcal/mol from DFT calculations. In this case, the chairlike C_{2h} conformation is considerably unstable, presumably because of the torsional strain between the phenyl groups in the diphenyl ether moieties.

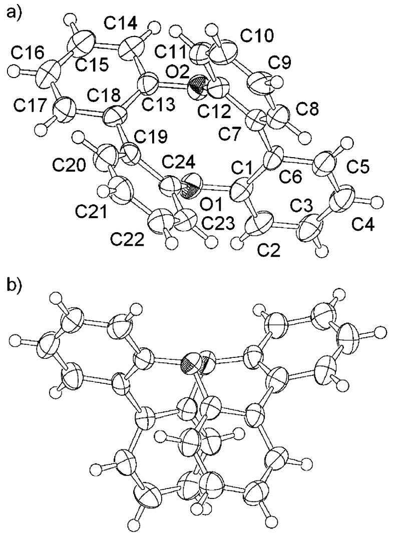


FIGURE 5. X-ray structure of **5c**: (a) side view, (b) top view.

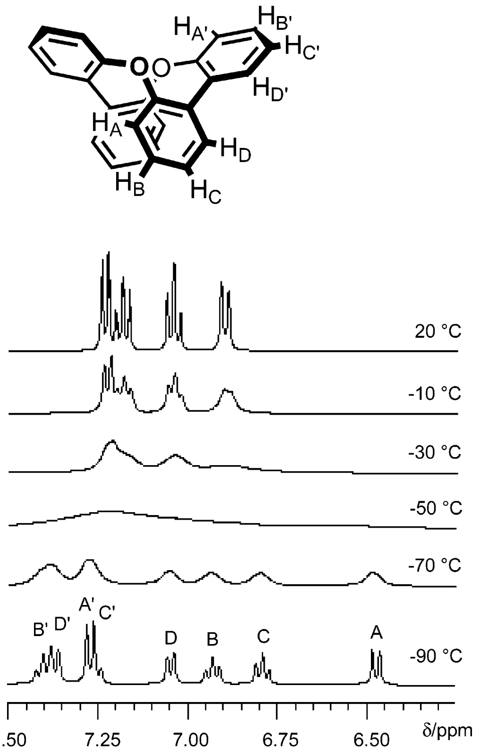


FIGURE 6. VT ^{1}H NMR spectra of **5c**. The signal assignments are shown in the spectrum.

The dynamic NMR measurements of **5c** clearly show flexibility of this molecule. The ^{1}H NMR spectrum of **5c** at room temperature shows only four kinds of signals, which suggests the symmetric nature of the molecule. However, in the ^{1}H NMR spectra at lower temperature, eight kinds of signals were observed corresponding to the most stable C_2 conformer. As shown in Figure 6, the assignment of the signals was unambiguously determined on the basis of the coupling connectivity and qualitative saturation transfer experiments. This type of temperature dependence of the NMR can be ascribed to the exchange of the two sets of phenylene groups in the C_2 conformer, and the corresponding activation energy was estimated as $\Delta G^\ddagger = 10.1$ kcal/mol by the coalescence method.

In conclusion, we have developed an efficient homocoupling reaction of aryl bromides via Lipshutz cuprates under electron-transfer conditions. This unique electron-transfer step from the cuprates to 1,4-benzoquinones as the electron acceptors is a key step for this coupling reaction. No conjugated addition of cuprates to quinones takes place under these conditions, and the coupling reaction offers a novel aspect of Lipshutz cuprates. We have also applied this system to the synthesis of 10-membered cyclophanes. The key intermediate for the cyclophanes is a metallacycle having a Lipshutz cuprate structure which possesses linear C−Cu−C linkages. Therefore, this intermediate more favorably produces ten-membered cyclophanes over ordinary five-membered ring structures.

Experimental Section

General Procedure for the Synthesis of Biaryl 3 Using Electron-Transfer Oxidation of Lipshutz Cuprates. To a solution of aryl bromide **1** (1.0 mmol) in anhydrous ether (60 mL) was added *t*-BuLi (0.77 mL, 1.1 mmol, 1.43 M in pentane) at −78 °C. The mixture was stirred at the same temperature for 1.5 h, and CuCN (45.0 mg, 0.5 mmol) was added. The mixture was vigorously stirred at room temperature till CuCN dissolved. To the clear solution of Lipshutz cuprate was added tetramethyl-*p*-benzoquinone (246 mg, 1.5 mmol) to form a deep-blue-green solution of durosemiquinone.[34] The mixture was stirred at room temperature for 3 h. After the reaction finished, 2 N aqueous HCl was added (the deep-blue-green color disappeared quickly to give a yellow solution). The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 with hexane/benzene as the eluent gave the corresponding coupling products.

When tetramethyl-*p*-benzoquinone was added to the solution of Lipshutz cuprate prepared from **1a** at −78 °C, the deep-blue-green color gradually appeared. However, the electron-transfer oxidation took place at −78 °C for 3 h to produce **3a** in 77% yield. To quench the oxidation of Lipshutz cuprate prepared from **1a**, water can be used instead of 2 M aqueous HCl. In this case, the deep-blue-green color of durosemiquinone gradually disappeared after the addition of water, and tetramethyl-*p*-benzoquinone gradually appeared in the mixture.

General Procedure for the Synthesis of the 10-Membered Ring Cyclophane 5. To a solution of **4** (1.0 mmol) in anhydrous ether (60 mL) was added *t*-BuLi (1.54 mL, 2.2 mmol, 1.43 M in pentane) at −78 °C. The mixture was stirred at the same temperature for 1.5 h before CuCN (89 mg, 1.0 mmol) was added. The mixture was vigorously stirred at room temperature till all CuCN dissolved. Then triethylamine (0.28 mL, 2.0 mmol) was added, and the mixture was stirred at room temperature for another 1 h. To the reaction mixture was added tetramethyl-*p*-benzoquinone (493 mg, 3.0 mmol), and the resulting mixture was stirred for 3 h at room temperature. After the reaction finished, 2 N aqueous HCl was added. The organic layer was separated, and the aqueous layer was extracted with benzene. The combined organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 with hexane/benzene as the eluent gave the corresponding cyclization products.

Data for Silicon-bridged 10-membered ring cyclophane 5a: colorless crystals (48%); mp 204.5−205 °C subl; IR (Nujol) 3043, 2950, 1644, 1563, 1453 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.00 (d, $J = 2.8$ Hz, 4H), 6.98 (d, $J = 2.8$ Hz, 4H), 0.35 (s, 12H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.5 (C), 139.9(C), 131.7(CH), 123.5 (CH), 0.1 (CH_3); UV (EtOH) 243.5 nm (log $\epsilon = 4.05$); EI-MS *m*/*z* 444 (M^+). Anal. Calcd for $C_{20}H_{20}S_4Si_2$: C, 54.00; H, 4.53. Found: C, 53.98; H, 4.55.

Data for methylene-bridged 10-membered ring cyclophane 5b: colorless crystals (15%); mp 259−259.6 °C subl; IR (Nujol) 3050, 2955, 1650, 1560, 1460, 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.28 (d, $J = 5.1$ Hz, 4H), 6.88 (d, $J = 5.1$ Hz, 4H), 4.45 (d, $J = 16.0$ Hz, 2H), 4.02 (d, $J = 16.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.9 (C), 133.3 (C), 129.0 (CH), 124.1 (CH), 27.9 (CH_2); UV (EtOH) 245.5 nm (log $\epsilon = 4.24$); EI-M *m*/*z* 356 (M^+). Anal. Calcd for $C_{18}H_{12}S_4$: C, 60.63; H, 3.39. Found: C, 60.24; H, 3.49.

Data for benzene-fused 10-membered ring 5c: colorless crystals (18%); mp 206.1−206.6 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ 7.22 (d, $J = 7.9$ Hz, 4H), 7.16 (dd, $J = 7.9$ and 7.3 Hz, 4H), 7.02 (dd, $J = 7.9$ and 7.3 Hz, 4H), 6.91 (d, $J = 7.9$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C) δ 154.4 (C), 131.2 (CH), 128.9 (CH), 128.8 (CH), 123.4 (CH), 119.8 (C); EI-MS *m*/*z* 336 (M^+). Anal. Calcd for $C_{24}H_{16}O_2$: C, 85.69; H, 4.79. Found: C, 85.79; H, 4.91.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Areas of Exploitation of Multi-element Cyclic Molecules (No. 14044086) from the Ministry of Education, Culture, Sports, Science and Technology of Japan. We are grateful to Dr. Kenji Hara, Dr. T. Nishinaga, and Dr. Masashi Hasegawa (Tokyo Metropolitan University) for their helpful discussions.

Supporting Information Available: Experimental section, including X-ray crystallographic files in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0608063

---

(34) (a) Giordani, R.; Buc, J. *Eur. J. Biochem.* **2004**, *271*, 2400−2407. (b) Pasimeni, L.; Brustolon, M.; Corvaja, C. *J. Chem. Soc., Faraday Trans. 2* **1972**, *68*, 223−233. (c) Gough, T. E.; Hindle, P. R. *Can. J. Chem.* **1969**, *47*, 1698−1700.