Coupling Reactions of 1,4-Dicuprio-1,3-dienes: Formation of Carbocycles

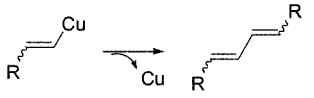
Chao Chen,[a] Chanjuan Xi,*[a] Chunbo Lai,[a] Ruji Wang,[a] and Xiaoyin Hong[a]

Keywords: Copper / Cyclization / Homocoupling / Quinones

The coupling reaction of 1,4-dicuprio-1,3-dienes in the presence of benzoquinone forms cyclobutadienes, which are easily transformed into cyclooctatetraene derivatives.

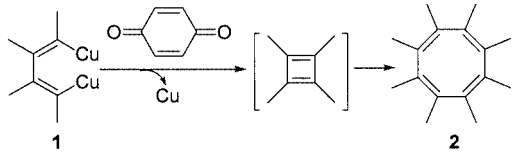
Introduction

Alkenylcopper reagents have been utilized for various reactions.[1−3] Among them, the homocoupling reaction of alkenylcopper compounds has been widely used for stereoselective C−C bond formation. The most generally accepted mechanism for this reaction involves thermal or oxidative coupling of alkenylcopper reagents with the formation of 1,3-dienes which retain the configuration at the



Scheme 1

double bond (Scheme 1).[2,3] As part of a general study of the formation of cyclic compounds, we envisioned that the coupling reaction of dialkenylcopper substrates could give cyclic compounds. In this paper, we report the coupling reaction of 1,4-dicuprio-1,3-dienes **1** in the presence of benzoquinone to give cyclobutadienes, which are easily transformed into cyclooctatetraene (COT) derivatives **2** (Scheme 2).



Scheme 2

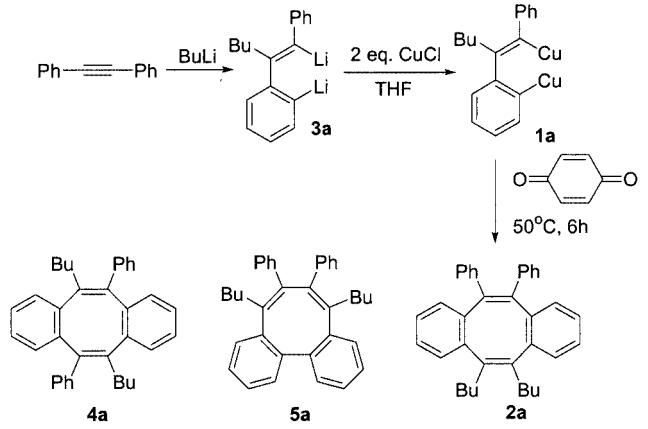
Results and Discussion

It has long been known that organocopper compounds (such as alkyl- and alkenylcopper) are very unstable and difficult to isolate. Therefore, most reactions are carried out in situ. In this work, 1,4-dicuprio-1,3-dienes **1** were prepared in situ by transmetallation of the corresponding dilithiodienes[4] or zirconacyclopentadienes according to published procedures.[5] At the outset, we tried the coupling of the dialkenylcopper reagent **1a** for the formation of carbocycles. Compound **3a**, which was prepared from diphenylacetylene and *n*BuLi,[4a] was treated with 2 equiv. of CuCl and 1 equiv. of benzoquinone at 50 °C for 6 h to give 5,6-dibutyl-11,12-diphenyldibenzo[*a*,*e*]cyclooctene (**2a**) along with a brick-red mirror of copper on the surface of the reactor. Normal workup, followed by chromatographic separation, afforded **2a** in 38% isolated yield with high regioselectivity (Scheme 3). No formation of compounds **4a** or **5a** was observed. The structure of **2a** was confirmed by X-ray analysis (Figure 1). It is noteworthy that the presence of benzoquinone is necessary for the formation of the COT derivative, although its role is not clear. Without benzoquinone, the reaction gave a mixture of products. It is possible that benzoquinone coordinates to the active alkenylcopper center, forming an alkenylcopper complex.[6] The activity of the alkenylcopper reagent is therefore reduced and thus it is suitable for the homocoupling reaction to give the final product.

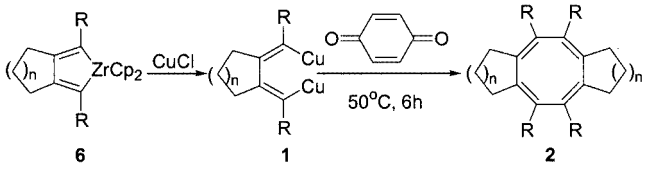
We also examined the coupling reaction of copper reagent **1b**, prepared in situ from the corresponding zirconacyclopentadienes **6**[7] and CuCl at room temperature. Interestingly, compound **2b** could also be prepared in 43% isolated yield (Scheme 4). Similarly, compound **2c** was isolated in 40% yield from **1c**.

In the above-mentioned examples, cyclic 1,4-dicuprio-1,3-diene complexes are involved and, consequently, tricyclic products formed in good yields. To extend the coupling reaction of 1,4-dicuprio-1,3-diene derivatives **1**, acyclic 1,4-dicuprio-1,3-diene derivatives were also examined. For example, 1,4-dicuprio-1,2,3,4-tetraethyl-1,3-diene (**1d**) was treated with benzoquinone at 50 °C for 6 h. Interestingly, two products (**2d** and **7d**) were obtained in a fixed ratio even with prolonged reaction times and different reaction temperatures (Scheme 5). Compound **7d** can be converted

[a] Key Laboratory for Bioorganic Phosphorus Chemistry of Ministry of Education, Department of Chemistry, Tsinghua University,
Beijing 100084, China
Fax: (internat.) + 86-10/6261-8239
E-mail: cjxi@tsinghua.edu.cn



Scheme 3



Scheme 4

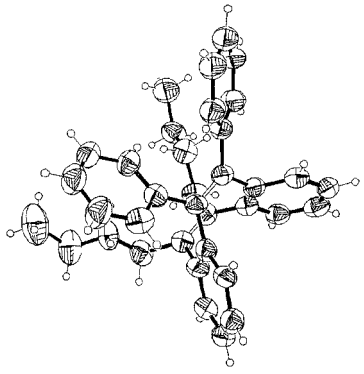
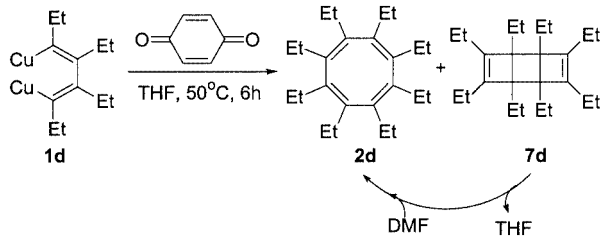


Figure 1. Structure of **2a**

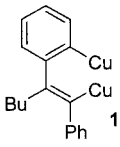
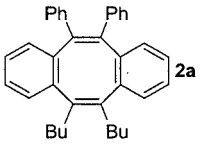
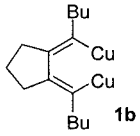
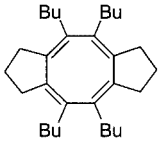
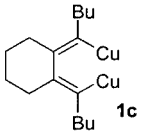
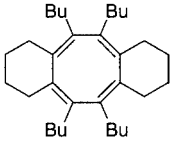
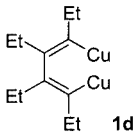
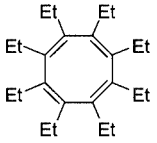
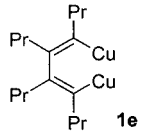
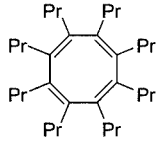
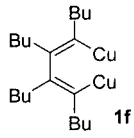
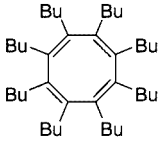
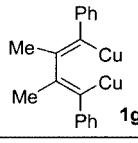
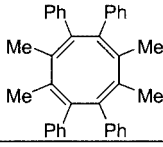
exclusively into **2d** by treating the reaction mixture with DMF.[8] The formation of **2d** and **7d** has recently been reported by Takahashi from a cross-coupling reaction of 1-cuprio-4-halobuta-1,3-dienes.[9] In the case of 1,4-dicuprio-2,3-dimethyl-1,4-diphenyl-1,3-diene (**1g**), the product **2g** only formed in 33% isolated yield. Some representative examples are collected in Table 1.



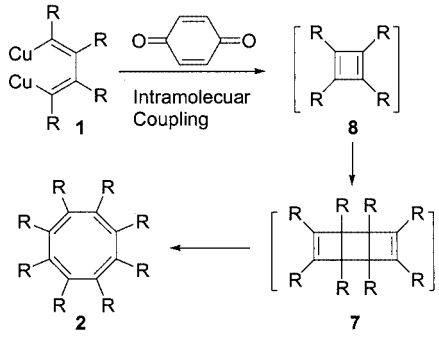
Scheme 5

In the light of these results we proposed a mechanism for this reaction (Scheme 6), although the mechanistic details of the coupling process of the alkenylcopper reagent in the presence of benzoquinone remain unclear. The cyclobutadiene derivative **8** is formed in situ by an intramolecular coupling reaction, and it then dimerizes to form the tricy-

Table 1. Formation of COT derivatives from dicupriodienes

Entry	1,4-Dicuprio-1,3-diene	Product	Yield (%)[a]
1	 **1a**	 **2a**	– (38)
2	 **1b**	 **2b**	– (43)
3	 **1c**	 **2c**	– (40)
4	 **1d**	 **2d**	73 (51)
5	 **1e**	 **2e**	68 (56)
6	 **1f**	 **2f**	40 (23)
7	 **1g**	 **2g**	– (33)

[a] GC yields. Isolated yields are given in parentheses.



Scheme 6

clo[4.2.0.0^{2,5}]octa-3,7-octadiene derivative **7** regioselectively. This result was indirectly confirmed by X-ray analysis of **2a**. The dimer **7** is thermally unstable at high temperatures, due to steric hindrance and ring strain, and transforms into the cyclooctatetraene derivative **2**.[10] This mechanism is consistent with the experimental results (Entries 1, 2, 3, and 6 in Table 1).

Conclusion

A convenient method for the preparation of fully substituted COTs has been developed based on the intramolecular coupling reaction of 1,4-dicuprio-1,3-dienes to form cyclobutadiene, which is subsequently transformed into the COT in the presence of benzoquinone.

Experimental Section

General: All reactions involving organometallic compounds were carried out using standard Schlenk techniques under nitrogen. THF was distilled from sodium/benzophenone. Zirconocene dichloride was purchased from Aldrich Chemical Co., Ltd. The other starting materials were purchased from commercial sources and used as received. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL AL-300MHz NMR spectrometer. GC analysis was performed with a Shimadzu GC-14B, equipped with a fused-silica capillary column. Appropriate alkanes were used as internal standards.

Procedure for the Preparation of 5,6-Dibutyl-11,12-diphenyldibenzo[*a*,*e*]cyclooctene (2a) from the Corresponding Dilithio Compound 3a: CuCl (2.0 mmol, 198 mg) and benzoquinone (1.0 mmol, 108 mg) were added at 0 °C to a solution of compound **3a** in THF (5.0 mL), prepared from diphenylacetylene (2.0 mmol, 356 mg) and *n*BuLi. The mixture was heated at 50 °C for 6 h. It was then quenched with 3 N HCl and the aqueous layers were extracted four times with 20 mL of diethyl ether. The combined organic layers were dried with Na_2SO_4. The diethyl ether extract was concentrated and the crude product was purified by column chromatography on silica gel (diethyl ether/petroleum ether, 1:90) to afford compound **2a** as a white solid (178 mg, 36%). ^{1}H NMR ($CDCl_3$, $SiMe_4$): δ = 0.80 (m, *J* = 7 Hz, 6 H), 1.23−1.37 (m, 4 H), 2.36−2.47 (m, 4 H), 2.74 (t, *J* = 7.6 Hz, 4 H), 7.02−7.19 (m, 10 H), 7.23−7.30 (m, 8 H) ppm. ^{13}C NMR ($CDCl_3$, $SiMe_4$): δ = 13.8, 23.2, 31.4, 34.3, 125.6, 126.3, 126.5, 127.0, 127.6, 128.4, 131.0, 138.4, 140.7, 141.4, 143.3, 143.4 ppm. M.p. 109−111 °C. IR (Et_2O solution): $\tilde{\nu}$ = 2966, 2932, 2882, 1464, 1377, 745, 695 cm^{-1}. HRMS: calcd. for $C_{36}H_{36}$ 468.2817; found 468.2815.

Typical Procedure for the Preparation of 4,5,9,10-Tetrabutyl-1,2,3,6,7,8-hexahydrodicyclopenta[*a*,*e*]cyclooctene (2b) from the Corresponding Zirconacyclopentadienes: *n*BuLi (1.57 M in *n*-hexane, 2.4 mmol) was added at −78 °C to a solution of Cp_2ZrCl_2 (1.2 mmol, 0.352 g) in THF (5.0 mL) and the mixture was stirred for 1 h. After addition of pentadeca-5,10-diyne (1.0 mmol, 240 μL), the mixture was warmed to room temperature and stirred for 3 h. CuCl (2.0 mmol, 198 mg) and benzoquinone (1.0 mmol, 108 mg) were then added to give a black suspension. The suspension was heated at 50 °C for 6 h and a brick-red mirror of copper appeared. The slurry was quenched with 3 N HCl and extracted four times with 20 mL. The combined organic layers were dried with Na_2SO_4. The solvent was evaporated and the product was purified by column chromatography with petroleum ether as eluent to afford a colorless liquid; isolated yield 88 mg (43%). ^{1}H NMR ($CDCl_3$, $SiMe_4$): δ = 0.88 (t, *J* = 6.2 Hz, 12 H), 1.26−1.50 (m, 16 H), 1.90−1.99 (m, 4 H), 2.28−2.40 (m, 16 H) ppm. ^{13}C NMR ($CDCl_3$, $SiMe_4$): δ = 14.1, 23.1, 29.4, 30.1, 31.7, 36.1, 135.0, 140.6 ppm. IR (neat): $\tilde{\nu}$ = 2957, 2925, 2855, 1716, 1460, 1375, 1262, 1095 cm^{-1}. HRMS: calcd. for $C_{30}H_{48}$ 408.3756; found 408.3760.

5,6,11,12-Tetrabutyl-1,2,3,4,7,8,9,10-octahydrodibenzo[*a*,*e*]cyclooctene (2c): Isolated yield 174 mg (40%). ^{1}H NMR ($CDCl_3$, $SiMe_4$): δ = 0.94 (t, *J* = 7.2 Hz, 12 H), 1.36−1.58 (m, 16 H), 1.67−1.74 (m, 8 H), 2.00−2.18 (m, 16 H) ppm. ^{13}C NMR ($CDCl_3$, $SiMe_4$): δ = 14.1, 22.9, 23.1, 28.5, 29.2, 31.5, 31.9, 134.0, 137.4 ppm. IR (neat): $\tilde{\nu}$ = 2956, 2929, 2871, 1706, 1458, 1378, 1260, 1142 cm^{-1}. HRMS: calcd. for $C_{32}H_{52}$ 436.4069; found 436.4073.

Octaethylcyclooctatetraene (2d): The THF was pumped off, 10 mL of DMF was added and the mixture was refluxed for 12 h before normal workup. Isolated yield 51%. GC yield 73%. The analytical data are identical with the reported values.[9a]

Octapropylcyclooctatetraene (2e): Isolated yield 56%. GC yield 68%. The analytical data are identical with the reported values.[9a]

Octabutylcyclooctatetraene (2f): Isolated yield 23%. GC yield 40%. The analytical data are identical with the reported values.[9a]

1,2,5,6-Tetramethyl-3,4,7,8-tetraphenylcyclooctatetraene (2g): Isolated yield 153 mg (33%). ^{1}H NMR ($CDCl_3$, $SiMe_4$): δ = 1.71 (s, 12 H), 7.11−7.42 (m, 20 H) ppm. ^{13}C NMR ($CDCl_3$, $SiMe_4$): δ = 19.2, 126.5, 127.9, 128.0, 129.4, 134.3, 140.6 ppm. IR (neat): $\tilde{\nu}$ = 3057, 3025.24, 2977, 2936, 2869, 1719, 1491, 1446, 1379, 1260, 1142, 1073, 1027, 700 cm^{-1}. HRMS: calcd. for $C_{36}H_{32}$ 464.2504; found 464.2509.

Crystallographic Data for 2a: Colorless prism, trigonal, space group $R\bar{3}$ (no. 14), *a* = 41.160(9), *b* = 41.160(9), *c* = 9.079(3) Å, *Z* = 18, R_1 = 0.0854, wR_2 = 0.1632 (all data), GOF = 1.006. CCDC-225888 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

This work was supported by the National Natural Science Foundation of China (20172032) and Tsinghua University.

[1] [1a] G. H. Posner, *Org. React.* **1972**, *19*, 1. [1b] G. H. Posner, *Org. React.* **1975**, *22*, 253. [1c] A. Alexakis, J. Normant, J. Villieras, *Tetrahedron Lett.* **1976**, 3461. [1d] H. Westmijize, P. Vermeer, *Synthesis* **1977**, 784. [1e] J. B. Campbell, Jr., H. C. Brown, *J. Org. Chem.* **1980**, *45*, 550. [1f] H. C. Brown, G. A. Molander, *J. Org. Chem.* **1981**, *46*, 647.

[2] [2a] G. M. Whitesides, C. P. Casey, *J. Am. Chem. Soc.* **1966**, *88*, 4541. [2b] G. M. Whitesides, C. P. Casey, J. K. Krieger, *J. Am. Chem. Soc.* **1971**, *93*, 1379.

[3] [3a] J. F. Normant, G. Cahiez, C. Chuit, J. Villieras, *J. Organomet. Chem.* **1974**, *77*, 269. [3b] R. B. Banks, H. M. Walborsky, *J. Am. Chem. Soc.* **1976**, *98*, 3732. [3c] E. Piers, M. A. Romero, *J. Am. Chem. Soc.* **1996**, *118*, 1215. [3d] E. Piers, E. J. McEachern, M. A. Romero, P. L. Gladstone, *Can. J. Chem.* **1997**, *75*, 694. [3e] E. Piers, P. L. Gladstone, J. G. K. Yee, E. J. McEachern, *Tetrahedron.* **1998**, *54*, 10609.

[4] [4a] M. D. Rausch, L. P. Klemann, W. H. Boon, *Synth. React.*

Inorg. Met.-Org. Chem. **1985**, *15*, 923. [4b] S. L. Buchwald, R. B. Nielsen, *J. Am. Chem. Soc.* **1989**, *111*, 2870. [4c] E. Negishi, S. J. Holmes, J. M. Tour, J. A. Miller, F. E. Cederbaum, D. R. Swanson, T. Takahashi, *J. Am. Chem. Soc.* **1989**, *111*, 3336. [4d] C. Xi, S. Huo, T. H. Afifi, R. Hara, T. Takahashi, *Tetrahedron Lett.* **1997**, *38*, 4099.

[5] [5a] E. Negishi, F. E. Cederbaum, T. Takahashi, *Tetrahedron Lett.* **1986**, *27*, 2829. [5b] T. Takahashi, M. Kotora, K. Kasai, N. Suzuki, N. Nakajima, *Organometallics* **1994**, *13*, 4183. [5c] R. Hara, Y. Liu, W.-H. Sun, T. Takahashi, *Tetrahedron Lett.* **1997**, *38*, 4104. [5d] M. Kotora, C. Umeda, T. Ishida, T. Takahashi, *Tetrahedron Lett.* **1997**, *38*, 8355. [5e] T. Takahashi, R. Hara, Y. Nishihara, M. Kotora, *J. Am. Chem. Soc.* **1996**, *118*, 5154. [5f] M. Kotora, C. Xi, T. Takahashi, *Tetrahedron Lett.* **1998**, *39*, 4321.

[6] [6a] P. E. Fanta, *Synthesis* **1974**, 9. [6b] A. H. Lewin, T. Cohen, *Tetrahedron Lett.* **1965**, 4531.

[7] E. Negishi, *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming, L. A. Paquette), Pergamon Press, Oxford, U. K., **1991**, vol. 5, p. 1163.

[8] H. M. Frey, H.-D. Martin, *J. Chem. Soc., Chem. Commun.* **1975**, 204.

[9] [9a] T. Takahashi, W.-H. Sun, K. Nakajima, *Chem. Commun.* **1999**, 1595. [9b] H. Ubayama, W.-H. Sun, Z. Xi, T. Takahashi, *Chem. Commun.* **1998**, 1931.

[10] [10a] E. Hedaya, R. D. Miller, D. W. McNeil, P. F. D'Angelo, P. Schissel, *J. Am. Chem. Soc.* **1969**, *91*, 1875. [10b] T. R. Boussie, A. Streitwieser, *J. Org. Chem.* **1993**, *58*, 2377.

Received August 1, 2003

