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Pd(OAc)$_2$-Catalyzed Macrocyclization of 1,2-Diazonaphthoquinones with Cyclic Ethers

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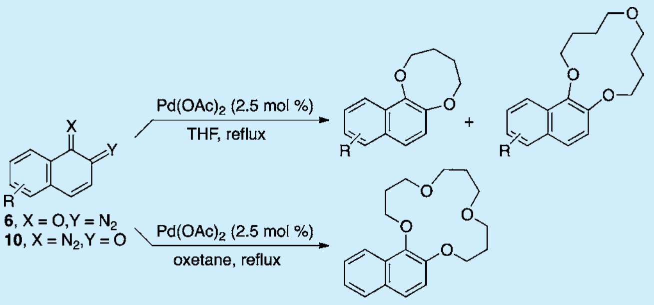
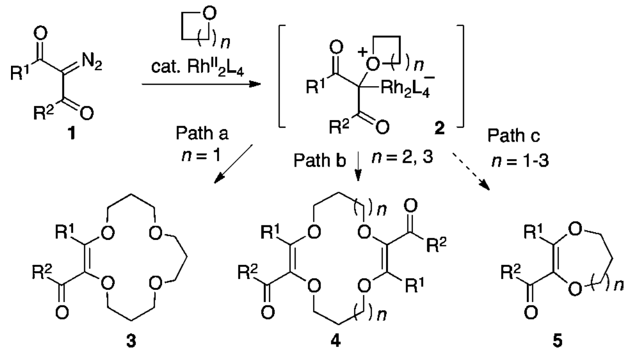
Ⓢ *Supporting Information*

ABSTRACT: Pd(OAc)$_2$ was found to be an efficient catalyst for the macrocyclization of 1,2-diazonaphthoquinones and cyclic ethers. This transformation serves as an efficient method for the synthesis of protected 1,2-naphthalenediols.



α-Diazocarbonyl compounds are easily decomposed to the corresponding α-carbonylcarbenes or metal carbenes via photoirradiation, electrophilic activation, or the treatment of metal complexes.[1] Thus formed, these carbenes are electrophilic and readily react with various nucleophilic Lewis bases to generate the corresponding ylides, which are widely used in organic synthesis.[1] For example, oxonium ylides are formed via the reaction of these carbenes and cyclic ethers, and then Stevens-type rearrangement,[2] polymerization,[3]or macrocyclization[4−6] proceeds subsequently. In the presence of a Rh-catalyst, carbenes formed from relatively stable diazo compounds, such as 2-diazo-1,3-dicarbonyl compounds **1**, react with cyclic ethers followed by preferential macrocyclization via oxonium ylide **2** to give the large cyclic ethers **3** and **4** with more than two molecules incorporated (Scheme 1, Paths a and b).[5,6] Although there are few reports on the formation of medium-sized ring products **5** via the intramolecular cyclization of ylide **2** (Path c),[5a] recently, Rh-catalyzed cyclization of 2-diazo-1,3-dicarbonyl compounds **1** and five- or six-membered ring cyclic acetals was achieved, which was designed by [N]-*endo-trig* cyclization ([N] = 8 or 9).[5b]

Scheme 1. Rh-Catalyzed Formation of Macro Cyclic Ethers via the Reaction of 2-Diazo-1,3-dicarbonyl Compounds 1 and Small Cyclic Ethers



Previously, we developed an efficient synthetic method for the preparation of 1,2-diazonaphthoquinones via diazo-transfer with 2-azido-1,3-dimethylimidazolinium salts[7] and have been investigating the metal-catalyzed synthesis of substituted-naphthol derivatives using these products.[8] Pd(OAc)$_2$ is found to be an efficient catalyst for several coupling reactions of 1,2-diazonaphthoquinones.[8a,b] During the evaluation of the stability of 2-diazonaphthoquinone **6a**[9] in the presence of a catalytic amount of Pd(OAc)$_2$ in various solvents (CH$_2$Cl$_2$, toluene, benzene, CH$_3$CN, and THF) at reflux, the unexpected formation of 8-membered cyclic ether **7a** and 13-membered cyclic ether **8a** was observed in THF. We were intrigued by this uncommon formation of medium-sized rings and anticipated that this transformation could be a new method for the synthesis of protected 1,2-naphthalenediols. Similar to catechol derivatives, 1,2-naphthalenediols are attractive candidates as aromatic functional materials (or their building blocks), such as for use in solar cells, metal ligands, and antioxidants.[10] However, to date, only a few synthetically useful processes have been reported for the synthesis of 1,2-naphthalenediols.[11] Therefore, the generality and efficiency of this Pd(OAc)$_2$-catalyzed cyclization of 1,2-diazonaphthoquinones with THF were explored. In addition, the Pd(II) catalyst was efficient for the macrocyclization of 1,2-diazonaphthoquinones and oxetane.

Initially, the reaction of 2-diazonaphthoquinone **6a** and THF was examined under several reaction conditions (Table 1). First, several palladium catalysts were examined (Table 1, entries 1−8). When 10 mol % Pd(OAc)$_2$ was used, **6a** was consumed within 10 min, and cyclic ethers **7a** and **8a** were

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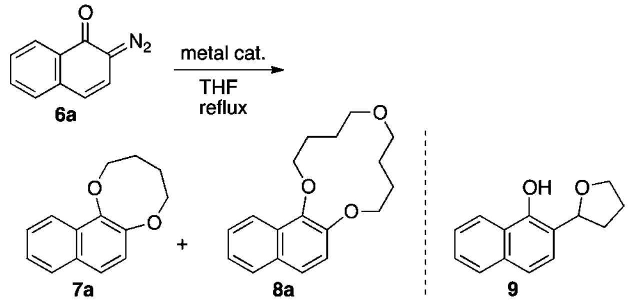
Table 1. Metal-Catalyzed Macrocyclization of 2-Diazonaphthoquinone 6a with THF[a]



entry	metal cat.	time	7a (%)	8a (%)
1	$Pd(OAc)_2$ (10 mol %)	10 min	29	26
2	$Pd(OAc)_2$ (5 mol %)	40 min	27	28
3	$Pd(OAc)_2$ (2.5 mol %)	1.5 h	33	36
4	$Pd(OAc)_2$ (1 mol %)	6.5 h	13	9
5[b]	$Pd(OAc)_2$ (2.5 mol %)	3.5 h	21	31
6[c]	$Pd(OAc)_2$ (2.5 mol %)	2.5 h	0	0
7	$PdCl_2$ (2.5 mol %)	2.5 h	20	21
8	$Pd(OCOCF_3)_2$ (2.5 mol %)	1 h	21	25
9	$Rh_2(OAc)_4$ (1 mol %)	3 h	trace[d]	trace
10	$Rh_2(OCOCF_3)_4$ (1 mol %)	2.5 h	4[e]	13
11	$Rh_2(Oct)_4$ (1 mol %)[f]	2 h	11[g]	5
12	$Cu(OAc)_2$ (2.5 mol %)	3 h	0[h]	0
13	$CuCl_2$ (2.5 mol %)	2.5 h	0[i]	0
14	$Cu(OTf)_2$ (2.5 mol %)	3 h	0[j]	0
15	$Cu(OTf)\cdot C_6H_6$ (2.5 mol %)	2.5 h	0[k]	0

[a] Reaction conditions: **6a** (0.5 mmol) in THF (2 mL) at reflux. [b] The reaction was performed at 45 °C. [c] LiCl (1.0 equiv) was added. [d] **6a** was recovered in 28% yield. [e] **6a** was recovered in 19% yield. [f] $Rh_2(OCOC_7H_{15})_4$. [g] **6a** was recovered in 39% yield. [h] **6a** was recovered in 92% yield. [i] **6a** was recovered in 80% yield. [j] **9** was obtained in 9% yield. **6a** was recovered in 32% yield. [k] **9** was obtained in 3% yield. **6a** was recovered in 25% yield.

obtained in 29% and 26% yields, respectively. As shown in Table 1, entries 1−4, the amount of $Pd(OAc)_2$ could be reduced to 2.5 mol % (Table 1, entry 3). At 45 °C, the yields of the cyclization products were decreased slightly (Table 1, entry 5). The addition of a halide anion has been reported to be effective in some Pd-catalyzed reactions.[12] Although **6a** was consumed with 2.5 mol % $Pd(OAc)_2$ in the presence of an equimolar amount of LiCl, cyclic ethers **7a** and **8a** were not obtained (Table 1, entry 6). Use of $PdCl_2$ and $Pd(OCOCF_3)_2$ resulted in low yields of both products (Table 1, entries 7 and 8).

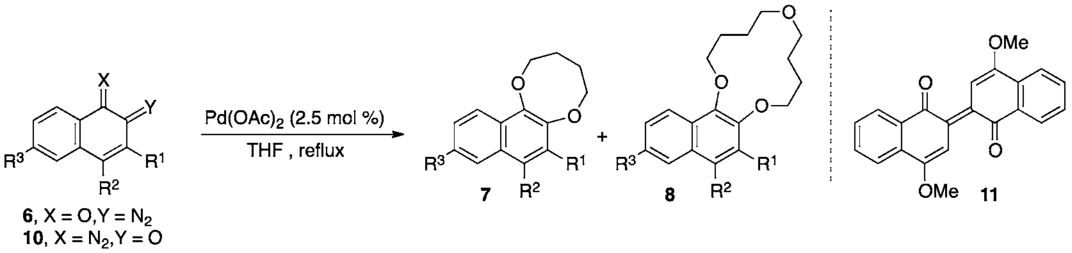
Interestingly, while only the Rh catalysts were reported to be effective for the metal-catalyzed macrocyclization reaction of cyclic ethers and α-carbonylcarbenes,[5,6] they were not efficient for the cyclization of **6a** and THF (Table 1, entries 9−11).

The series of Cu reagents examined for the reaction, including $Cu(OAc)_2$, $CuCl_2$, $Cu(OTf)_2$, and $Cu(OTf)\cdot C_6H_6$, also did not provide the cyclized products **7a** and **8a** (Table 1, entries 12−15), although a minor amount of C−H insertion product **9** was formed in the reactions with $Cu(OTf)_2$ and $Cu(OTf)\cdot C_6H_5$ (Table 1, entries 14 and 15, respectively).

On the basis of these results, the optimum cyclization conditions were determined to be $Pd(OAc)_2$ (2.5 mol %) in THF at reflux.

Next, the scope and limitations of the $Pd(OAc)_2$-catalyzed cyclization of 1,2-diazonaphthoquinones and THF were examined (Table 2). The substrate 2-diazonaphthoquinone **6b** bearing an electron-withdrawing group at the C-4 position gave cyclization products **7b** and **8b** in 16% and 21% yields, respectively (Table 2, entry 1). On the other hand, 4-methoxy-2-diazonaphthoquinone **6c** was completely consumed within 20 min, but the expected cyclization products were not generated, and dimerization product **11** was obtained in 10% yield (Table 2, entry 2). Introduction of a C-3 substituent was, however, efficient for the selective formation of 8-membered ring cyclic ethers **7**, as shown in Table 2, entries 3 and 4. The reactions of 1-diazonaphthoquinones **10**[9] also proceeded smoothly and selectively to give 8-membered cyclic ethers **7** in good to high yields (Table 2, entries 5−9). Simple 1-diazonaphthoquinone **10a** gave **7a** in 45% yield, accompanied by 2% of the 13-membered cyclic ether **8a** (Table 2, entry 5). The reaction of 6-bromo-1-diazonaphthoquinone **10b** gave 8-membered ether **7f**

Table 2. $Pd(OAc)_2$-Catalyzed Macrocyclization of 1,2-Diazonaphthoquinones 6 and 10 with THF[a]



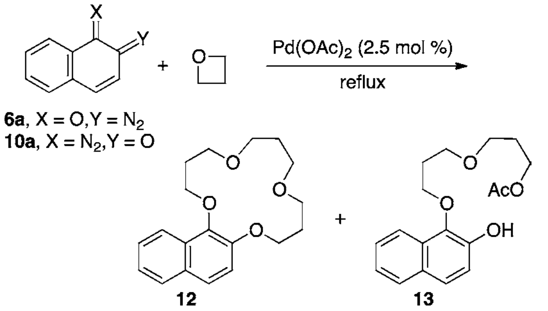
entry	R¹	R²	R³	6 or 10	time	7	(%)	8	(%)
1	H	Cl	H	**6b**	1 h	**7b**	16	**8b**	21
2	H	OMe	H	**6c**	20 min	**7c**	0[b]	**8c**	0
3	CH_2OTBS	H	H	**6d**	2 h	**7d**	60	**8d**	0
4	CO_2Me	H	H	**6e**	1 h	**7e**	55	**8e**	5
5	H	H	H	**10a**	1.5 h	**7a**	45	**8a**	2
6	H	H	Br	**10b**	1.5 h	**7f**	53	**8f**	0
7	CH_2OTBS	H	H	**10c**	2 h	**7d**	78	**8d**	0
8	CO_2Me	H	H	**10d**	20 min	**7e**	84	**8e**	0
9	CO_2Ph	H	H	**10e**	1.5 h	**7g**	35	**8g**	0

[a] Reaction conditions: **6** or **10** (0.5 mmol), $Pd(OAc)_2$ (2.5 mol %) in THF (2 mL) at reflux. [b] **11** was obtained in 10% yield.

as the sole product in 53% yield (Table 2, entry 6). With these substrates, introduction of an appropriate substituent at the C-3 position also clearly improved the yield of cyclic ether **7** (Table 2, entries 7 and 8). In the reaction of 3-siloxymethyl-1-diazonaphthoquinone **10c**, cyclic ether **7d** was formed in 78% yield (Table 2, entry 7), and the reaction of 3-methoxycarbonyl-1-diazonaphthoquinone **10d** gave 8-membered cyclic ether **7e** in 84% yield (Table 2, entry 8). However, the corresponding of phenyl ester **10e** afforded cyclic ether **7g** in a lower yield (35%) (Table 2, entry 9).

We also examined the $Pd(OAc)_2$-catalyzed reaction of 1,2-diazonaphthoquinones and oxetane (Table 3). In the reaction of 2-diazonaphthoquinone **6a**, 15-membered cyclic ether **12** was formed in 66% yield after stirring for 3 h at reflux.[13] A similar $Rh_2(OAc)_4$-catalyzed reaction has been reported for 2-diazo-1,3-dicarbonyl compounds.[6b] However, $Rh_2(OAc)_4$ was ineffective for the cyclization of diazonaphthoquinone **6a**, as shown in Table 3, entry 2. In addition, the reaction of 1-diazonaphthoquinone **10a** was slower than that of 2-diazonaphthoquinone **6a**, and 15-membered product **12** was formed in just 26% yield along with acyclic ether **13** (5%) after stirring for 20 h (Table 3, entry 3).

Table 3. $Pd(OAc)_2$-Catalyzed Macrocyclization of 1,2-Diazonaphthoquinones 6a and 10a with Oxetane[a]



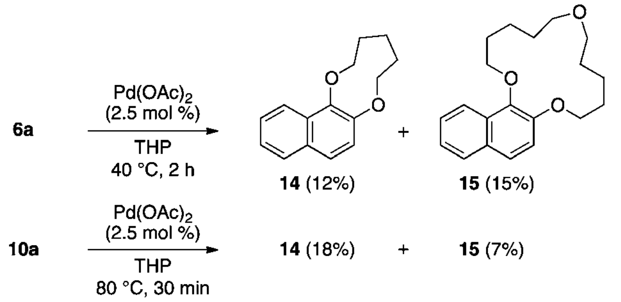
entry	**6a** or **10a**	time	**12** (%)	**13** (%)
1	**6a**	3 h	66	0
2[b]	**6a**	3.5 h	0[c]	0
3	**10a**	20 h	26[d]	5

[a] Reaction conditions: **6a** or **10a** (0.5 mmol), $Pd(OAc)_2$ (2.5 mol %) in oxetane (2 mL) at reflux. [b] $Rh_2(OAc)_4$ (1 mol %) was used instead of $Pd(OAc)_2$. [c] **6a** was recovered in 84% yield. [d] **10a** was recovered in 34% yield.

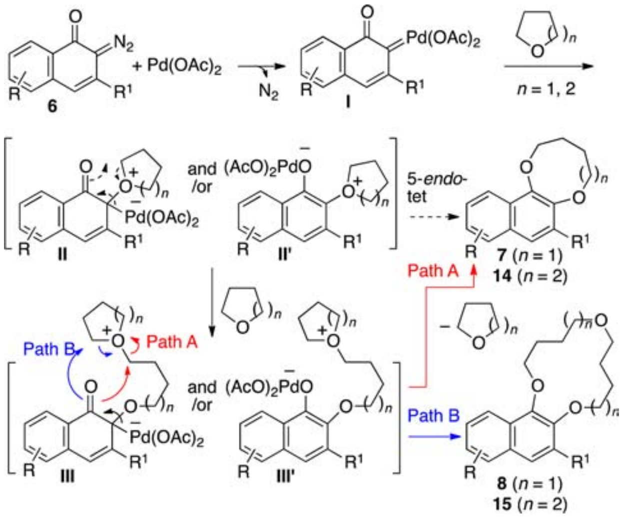
In addition, the 1,2-diazonaphthoquinones also reacted with tetrahydropyrane (THP) in the presence of a catalytic amount of $Pd(OAc)_2$ to afford a mixture of 9-membered cyclic ether **14** and 15-membered ether **15** (Scheme 2).

In Scheme 3, a possible reaction mechanism is depicted for the $Pd(OAc)_2$-catalyzed formation of medium-sized cyclic ethers (**7**, **14**) and macrocyclic ethers (**8**, **15**) from 2-diazonaphthoquinone **6** in cyclic ether (THF, THP). First, $Pd(OAc)_2$ reacts with diazonaphthoquinone **6** to form Pd(II) carbene complex **I**.[14] In the case of the reaction in THF, nucleophilic attack of THF on carbene complex **I** proceeds to form oxonium ylide **II**,[15] which may be aromatic palladium naphtholate **II′**. Successively, **II** reacts with THF giving **III**. Since 5 *endo*-tet cyclization is highly disfavered commonly,[16] 8-membered cyclic ether **7** is not formed directly from **II**, but is formed by 8-*exo*-tet cyclization of **III** (Path A). Macrocyclic ether **8** is formed from the same intermediate **III** by 10-*endo*-tet cyclization (Path B). The C-3 substituted substance R^1 can more easily attain the required conformation of **III** for 8-*exo*-cyclization as compared to the C-3 unsubstituted substance. For the reaction of 1-diazonaphthoquinone **10** and THF, the hydrogen at the C-8 position in **10** is assumed to function similarly to C-3 substituent R^1 in 2-diazonaphthoquinone **6**, resulting in the selective formation of *exo*-cyclization product **7**.

Scheme 2. $Pd(OAc)_2$-Catalyzed Cyclization of 1,2-Diazonaphthoquinones 6a and 10a with THP



Scheme 3. Possible Reaction Mechanism



Compared to the reaction with THF, the reaction with THP gave lower yields of cyclic ethers, and different selectivity in the formation of cyclic ethers (medium-sized cyclic ether/macro cyclic ether) was observed, which would be attributed to the cyclization mode, that is 8-*exo*-tet/10-*endo*-tet cyclization for THF vs 9-*exo*-tet/11-*endo*-tet cyclization for THP.

In conclusion, we developed a new method for the synthesis of medium-sized/macrocyclic ethers via the reaction of diazonaphthoquinones in the presence of a catalytic amount of $Pd(OAc)_2$. This transformation also serves as an efficient method for the preparation of protected 1,2-naphthalenediols.

Further studies on the $Pd(OAc)_2$-catalyzed cyclization reaction of diazonaphthoquinones with heterocyclic compounds are in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and characterization data, including ^1H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(9) In this manuscript, 2-diazonaphthoquinone means 2-diazo-1(2*H*)-naphthalenone derivative and 1-diazonaphthoquinone means 1-diazo-2(1*H*)-naphthalenone derivative.

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