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Quinonediimines as redox-active organocatalysts for oxidative coupling of aryl- and alkenylmagnesium compounds under molecular oxygen†

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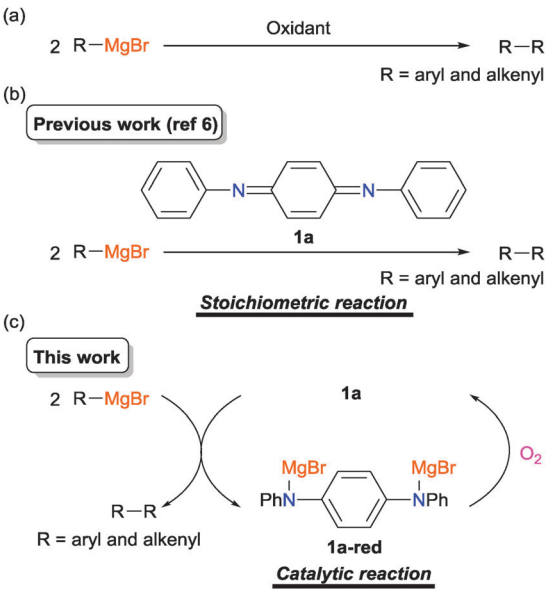
It is revealed that *N*,*N*′-diphenyl-*p*-benzoquinonediimine works as a redox-active organocatalyst for the oxidative homo-coupling of aryl- and alkenylmagnesium compounds under molecular oxygen. The catalytic cycle was formally monitored by ^{1}H NMR experiments.

Organocatalysis is now one of the most thriving areas in organic synthesis.[1] The reaction focused on here is organocatalytic oxidative homo-coupling of aryl- and alkenylmagnesium compounds under molecular oxygen (Scheme 1). However, such a catalyst has been rarely developed before (only a few examples have been reported as described later) despite the upsurge of interest in organocatalysis.

The oxidative homo-coupling of aryl- and alkenylmagnesium compounds (Scheme 1a) is one of the efficient methods for the synthesis of symmetrical biaryls and bialkenyls. Stoichiometric use of high-valent transition metal oxidants generally works well for this reaction, which has been studied since about a century ago.[2] In the last decade, some catalytic systems using transition metals have been constructed.[3] Examples for the combination of the catalyst and the terminal oxidant are shown below: $FeCl_3$ or $MnCl_2$-1,2-dihaloethane,[3a–c] Li_2CuCl_4–CuBr·SMe_2-di-*tert*-butyldiaziridinone,[3d] $FeCl_3$ or $MnCl_2$ or Li_2CuCl_4 or $RuCl(C_3S_5)H_2O(PPh_3)_2$–$O_2$,[3e–h] and $FeCl_3$ or $MnCl_2$–N_2O.[3i] On the other hand, the methodology employing organic oxidants is far more behind in this area, and the research studies have been quite limited.[4] One of the reasons is the difficulty in making the electron-transfer type reaction take place in preference to the nucleophilic addition in a competitive situation, for example employing stoichiometric 1,4-benzoquinone as an oxidant in this case.[4d] In 2006, Mayr, Knochel and co-workers proved the utility of 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone with bulky *tert*-butyl groups in both sides of carbonyls as a stoichiometric oxidant for the coupling reaction.[4c] This finding should be a milestone in this area from the viewpoint of metal-free coupling. The next challenge should be the construction of the organocatalytic system under molecular oxygen, which is one of the desirable terminal oxidants in the catalytic oxidation reactions from the viewpoint of sustainable chemistry. However, a possible side reaction, that is reaction of the arylmagnesium compounds with molecular oxygen, makes this reaction more complicated. Only two examples have been reported for the organocatalytic oxidative coupling of aryl- and alkenylmagnesium compounds. One is a 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) radical catalyzed reaction reported by Studer and co-workers.[4e] The other is a recently reported 3,4,5-trifluoro-1,2-bis(perfluorophenyl)cyclopentadienyl anion-catalyzed reaction by Korenaga and co-workers.[4f] In our



Scheme 1 (a) Oxidative homo-coupling of aryl- and alkenylmagnesium compounds. (b) Our previous study on the stoichiometric reaction. (c) This work: organocatalytic oxidative homo-coupling using quinonediimine **1a** as a redox-active catalyst under molecular oxygen.

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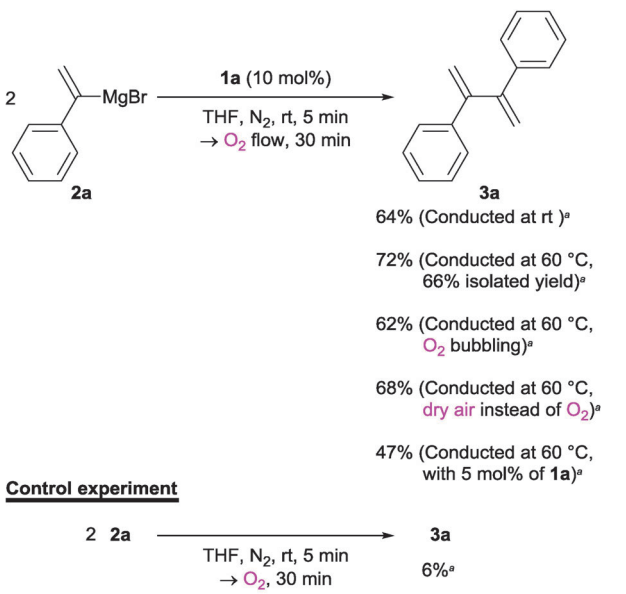
previous study, oxidation catalysts consisting of redox-active poly- and oligoaniline derivatives were developed,[5] including catalysts for oxidative coupling of phenol derivatives using molecular oxygen as a terminal oxidant.[5c] Recently, it was also revealed that *N*,*N*′-diphenyl-*p*-benzoquinonediimine (**1a**) induces the stoichiometric oxidative coupling of aryl- and alkenylmagnesium compounds (Scheme 1b).[6] Here, we report the catalytic version of the reaction under molecular oxygen as a terminal oxidant (Scheme 1c).

The investigation began with the oxidative homo-coupling of (1-phenylvinyl)magnesium bromide (**2a**) in the presence of a catalytic amount of quinonediimine **1a** under molecular oxygen. The employed **1a** was prepared by the oxidation of *N*,*N*′-diphenyl-*p*-phenylenediamine with iodosylbenzene under metal free conditions. The ICP-AES experiment of **1a** certified that the contamination of transition metals such as Cu, Fe, Mn and Pd is negligibly small for this reaction (Cu, Fe and Mn: limit of quantification, Pd: 6×10^{-5} mol% to **2**). A THF solution of **2a** was added to quinonediimine **1a** in THF under molecular nitrogen at room temperature. After 5 min, molecular oxygen was flowed through the flask for 30 min. The desired coupling product **3a** was formed in 64% yield, where the turnover number of **1a** is 3.2 because **1a** is a two-electron oxidant (Scheme 2). Acetophenone was also formed in 8% as a side product. As a control experiment, the same reaction was carried out in the absence of **1a**. The yield of **3a** was 6%.

The reaction was monitored with time by sampling (Fig. 1). First, the reaction took place under molecular nitrogen, where the red colour of **1a** changed to pale yellow. Flowing molecular oxygen (5–12 min) made the colour of the reaction mixture change to green and then red. In this period, an increase in the yield was observed. The red colour suggests the regeneration of **1a**. After the colour of the reaction mixture turned red, an increase of the yield was almost stopped. This suggests that (1-phenylvinyl)-magnesium bromide (**2a**) was almost consumed.



[a]Yield was calculated by the integral ratio of the peaks for **3a** and 1,3,5-trimethoxybenzene as an internal standard in the ^{1}H NMR spectrum of the crude mixture.

Scheme 2 **1a**-catalyzed oxidative coupling of **2a** and its control experiment.

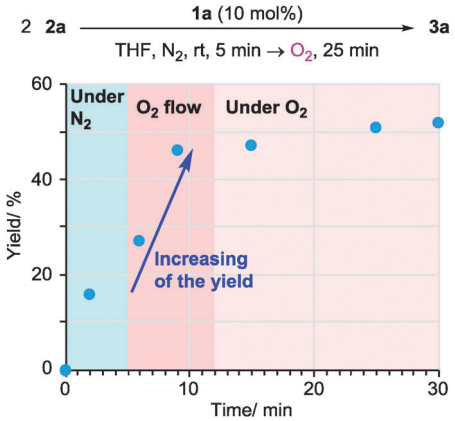
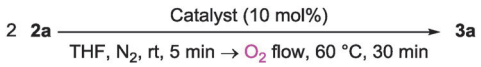


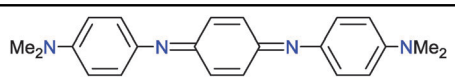
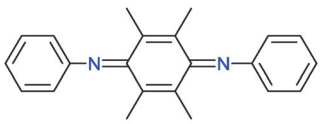
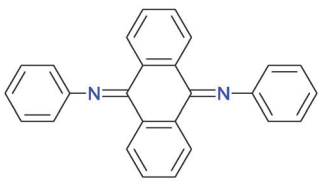
Fig. 1 Profile of the yield for **3a** with time.

Increasing the reaction temperature to 60 °C gave the product **3a** in 72% yield (Scheme 2). Bubbling of molecular oxygen instead of flowing did not induce an increase in the yield. The reaction under dry air instead of molecular oxygen gave **3a** in 68% yield. Decreasing the amount of **1a** to 5 mol% lowered the yield to 47%, whereas the turnover number of **1a** increased to 4.7.

Some quinonediimine derivatives **1b–d**[7] were also tested as catalysts instead of **1a** for this reaction. However, better results were not obtained as compared to that with **1a** (Table 1, entries 1–3). In the case of **1b**, the reaction proceeded catalytically although the efficiency was low (Table 1, entry 1). On the other hand, there seems to be a problem in the regeneration step in the case of **1c** (Table 1, entry 2). Catalyst **1d** did not give rise to the oxidative coupling of **2a** even in the stoichiometric reaction (Table 1, entry 3).

Table 1 Screening of catalysts for the oxidative coupling of **2a** under molecular oxygen

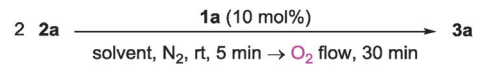


Entry	Catalyst	Yield[a]/%
1	 **1b**	38
2	 **1c**	12
3	 **1d**	1

[a] Yield was calculated by the integral ratio of the peaks for **3a** and 1,3,5-trimethoxybenzene as an internal standard in the ^{1}H NMR spectrum of the crude mixture.

Table 2 shows the screening of the solvents for this reaction. The reaction was performed at room temperature. Use of Et_2O, CH_2Cl_2 and cyclopentyl methyl ether instead of THF was not effective for this reaction (Table 2, entries 2–4). The mixed solution of THF/CH_2Cl_2 and THF/cyclopentyl methyl ether also did not give the better results than THF (Table 2, entries 5 and 6).

Table 2 Screening of solvents for the **1a**-catalyzed oxidative coupling of **2a** under molecular oxygen



Entry	Solvent	Yield[a]/%
1[b]	THF	64
2	Et_2O	42
3	CH_2Cl_2	20
4	Cyclopentyl methyl ether	36
5	CH_2Cl_2/THF	64
6	Cyclopentyl methyl ether/THF	54

[a] Yield was calculated by the integral ratio of the peaks for **3a** and 1,3,5-trimethoxybenzene as an internal standard in the ^{1}H NMR spectrum of the crude mixture. [b] This entry is the same as a result in Scheme 2.

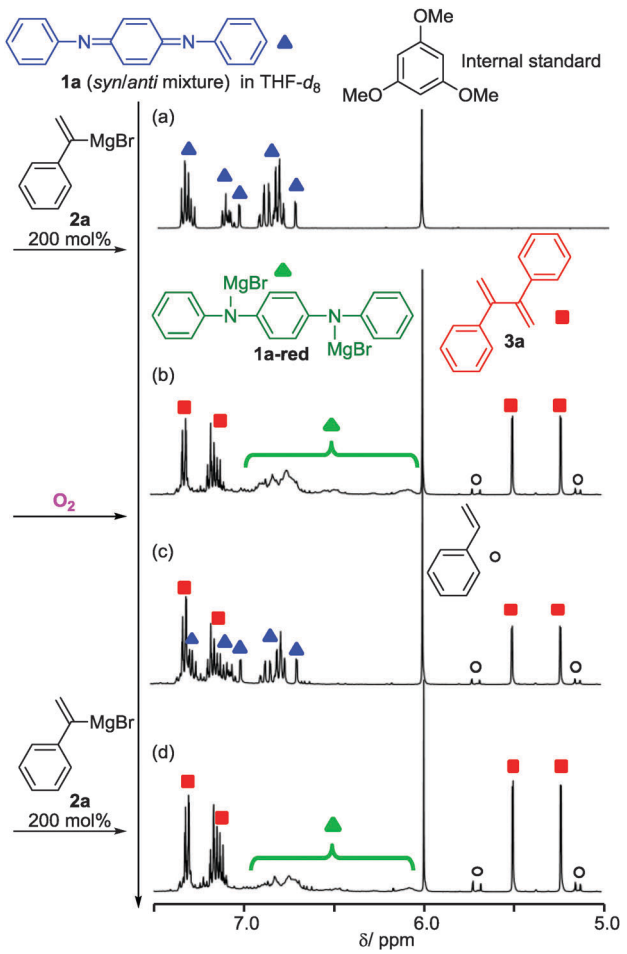
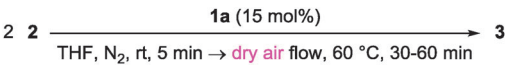
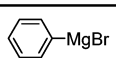
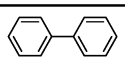
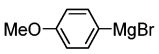
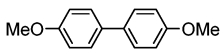
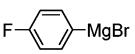
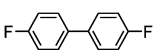
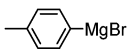
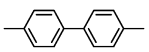
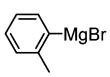
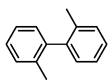
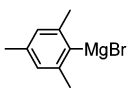
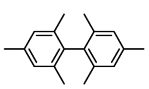
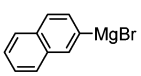
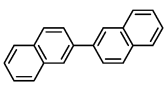
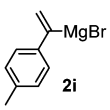
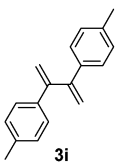
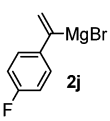
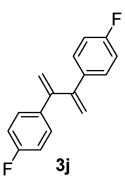


Fig. 2 ^{1}H NMR experiment to follow the redox cycle of **1a** in the oxidative coupling of **2a** and reoxidation under molecular oxygen.

To gain information on the reaction path, the reaction was followed by ^{1}H NMR spectroscopy (Fig. 2, and the enlarged figure is shown in Fig. S1, ESI†). At first, **1a** is dissolved in THF-d_8, the spectrum is shown in Fig. 2a. To the solution was added a stoichiometric amount of **2a** (200 mol%) under molecular nitrogen. The peaks for **1a** disappeared and the peaks for the homo-coupling product **3a** appeared with the reduced quinonediimine compound **1a**-red (Fig. 2b). The broad signals of **1a**-red well-accorded with those for the separately prepared one by the reaction of *N*,*N*′-diphenyl-*p*-phenylenediamine with phenylmagnesium bromide (see the supporting information of ref. 6). The broadening seems to be due to aggregation. Introduction of molecular oxygen clearly showed the regeneration of **1a** (Fig. 2c). To the mixture

Table 3 Substrate scope for the **1a**-catalyzed oxidative coupling of **2** under dry air



Entry	Substrate	Product	Yield[a]/%
1	 **2b**	 **3b**	71
2	 **2c**	 **3c**	79
3	 **2d**	 **3d**	74[b]
4	 **2e**	 **3e**	77
5	 **2f**	 **3f**	70
6	 **2g**	 **3g**	71
7	 **2h**	 **3h**	85
8[c]	 **2i**	 **3i**	70[d]
9[c]	 **2j**	 **3j**	61[d]

[a] Isolated yield. [b] Including a small amount of the impurity. [c] 10 mol% of **1a** was used and the reaction was conducted under molecular oxygen. [d] Yield was calculated by the integral ratio of the peaks for **3a** and 1,3,5-trimethoxybenzene as an internal standard in the ^{1}H NMR spectrum of the crude mixture.

was added a stoichiometric amount of **2a** (200 mol%), again resulting in the complete consumption of **1a** and the formation of **3a** and **1a**-red (Fig. 2d). These experiments formally show the catalytic cycle based on **1a** and **1a**-red with molecular oxygen as a terminal oxidant.

Table 3 shows the substrate scope for the **1a**-catalyzed oxidative homo-coupling reaction.§ For the reaction of arylmagnesium compounds **2b–h**, use of dry air instead of molecular oxygen in the presence of 15 mol% of **1a** gave the better results (Table 3, entries 1–7). Substitution of the benzene ring with *p*-MeO-, *p*-F-, *p*-Me- and *o*-Me was not a problem and gave the corresponding homo-coupling products **3c–f** in good yields (70–79%, Table 3, entries 2–5). Bulky mesitylmagnesium bromide (**2g**) also homo-coupled to give product **3g** in 71% yield (Table 3, entry 6). The coupling of 2-naphthylmagnesium bromide (**2h**) showed the best yield (85%, Table 3, entry 7). The reaction of (1-arylvinyl)magnesium bromides **2i–j** took place under molecular oxygen to provide the products **3i–j** in moderate yields (Table 3, entries 8 and 9).

In conclusion, it is revealed that quinonediimine **1a** works as a redox-active organocatalyst for the oxidative homo-coupling of aryl- and alkenylmagnesium compounds under molecular oxygen. The catalytic cycle was formally monitored by ^{1}H NMR experiments. It should be noted that this organocatalyst can catalyze the oxidative carbon–carbon bond formation using molecular oxygen as a terminal oxidant, which is one of the challenging topics in the field of organocatalysts.

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Notes and references

§ A representative procedure: To a two-neck 10 mL dried flask with a condenser was added **1a** (39.4 mg, 0.15 mmol), and the atmosphere was replaced by molecular nitrogen. Dry THF (1.0 mL) was added. A 0.50 M THF solution of 2-naphthylmagnesium bromide (**2h**) (2.0 mL, 1.0 mmol) was dropwise added at room temperature. After stirring for 5 min at room temperature, the flask was put in a pre-warmed oil bath (60 °C). Then, air dried through concentrated H_2SO_4 was flowed slowly (8.3 mL min^{-1}) for 55 min. The reaction mixture was stirred at 60 °C in this period, and then quenched with a mixed aqueous solution of $NaHCO_3$/$Na_2S_2O_3$. To the mixture was added CH_2Cl_2. The aqueous layer was filtered through filter paper and extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine and dried with Na_2SO_4. After filtration, the mixture was concentrated *in vacuo*. The residue was purified by silica-gel chromatography (0 to 10% CH_2Cl_2 in hexane) to give **3h** as a white flaky solid (108.5 mg, 0.43 mmol, 85%).

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