FULL PAPERS

Organocatalyst-Mediated Dehydrogenation of Aldehydes to α,β-Unsaturated Aldehydes, and Oxidative and Enantioselective Reaction of Aldehydes and Nitromethane Catalyzed by Diphenylprolinol Silyl Ether

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Abstract: A one-pot transformation of aldehydes into α,β-unsaturated aldehydes was developed using both *N*-benzyl-*N*-methylamine and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) as catalysts and MnO$_2$ as a terminal oxidant. An oxidative and enantioselective reaction of aldehydes and nitromethane was established using both diphenylprolinol silyl ether and DDQ as a catalyst with MnO$_2$ as a terminal oxidant, in which synthetically important β-substituted γ-nitro aldehydes were obtained with excellent enantioselectivity.

Keywords: asymmetric reaction; one-pot reaction; organocatalysis; oxidative reaction

Introduction

α,β-Unsaturated aldehydes are synthetically important functional compounds, and there exist many methods for their synthesis. Dehydrogenation of aldehydes into the corresponding α,β-unsaturated aldehydes is one of the methods for their preparation, but other useful synthetic methods are limited. For instance, silyl enol ethers, generated from aldehydes, are converted into α,β-unsaturated aldehydes by reaction with allyl carbonates *via* palladium catalysis as reported by Tsuji,[1] in which aldehydes have to be converted into silyl enol ethers in advance. As for the direct method, aldehydes are converted into α-seleno aldehydes, which afford α,β-unsaturated aldehydes *via* oxidation and elimination.[2] Ito–Saegusa oxidation using Pd(II) is also known for the direct conversion.[3] The direct dehydrogenation of aldehydes is catalyzed by Pd(OAc)$_2$ in the presence of allyl diethyl phosphate.[4] IBX[5] and IBS[6] oxidations are further methods for the direct conversion of aldehydes into α,β-unsaturated aldehydes.

We have previously reported the oxidative and enantioselective carbon-carbon bond forming reaction at the β-position of aldehydes by the use of diphenylprolinol silyl ether[7] as a catalyst and DDQ as an oxi-
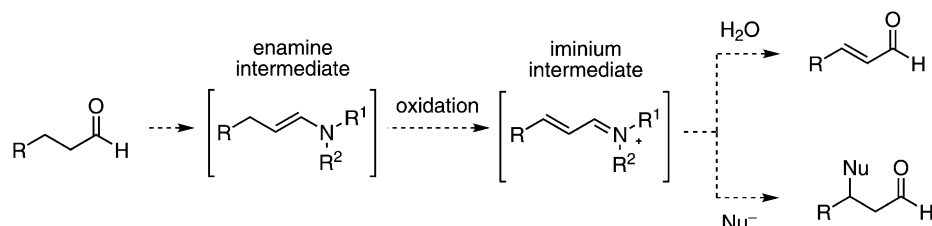
Scheme 1. Transformation of aldehydes into α,β-unsaturated aldehydes and β-substituted aldehydes.

dant (Scheme 1).[8] In this reaction, the chiral amine catalyst reacts with an aldehyde to afford an enamine. Subsequent reaction with DDQ, acting as a hydride abstracting reagent,[9] provides the iminium ion. The iminium ion further reacts with nitromethane as a nucleophile to afford the addition product with excellent enantioselectivity. If the intermediate iminium ion were trapped with water, an α,β-unsaturated aldehyde would be generated. In this way, aldehydes could be converted into α,β-unsaturated aldehydes in a "one-pot" operation. It would be desirable that an inexpensive achiral amine could be employed in this transformation instead of the chiral diphenylprolinol silyl ether as catalyst. Moreover, if DDQ can be used in a catalytic amount with an inexpensive terminal oxidant, this would be a practical synthetic transformation. In this paper, we describe the successful realization of this scenario: a practical oxidation of aldehydes into α,β-unsaturated aldehydes using a catalytic amount of achiral amine and DDQ in a one-pot operation. We also reveal the full details of the oxidative and enantioselective carbon-carbon bond forming reaction using diphenylprolinol silyl ether and DDQ, which is used both in an equimolar and a catalytic amount. When we reported our oxidative and enantioselective carbon-carbon bond forming reaction using an equimolar amount of DDQ in 2011,[8] Wang and co-workers reported the similar oxidative and enantioselective reaction using diphenylprolinol silyl ether as a catalyst and IBX as an oxidant.[10] They also reported the transformation of aldehydes into α,β-unsaturated aldehydes, using chiral diphenylprolinol siyl ether or MacMillan's catalyst with IBX, ceric ammonium nitrate (CAN), or a combination of Pd(OAc)₂ and O₂ as an oxidant.[11] However, given the achiral nature of the reaction, the use of a chiral catalyst is superfluous. Recently MacMillan and co-workers reported the direct β-arylation of carbonyl compounds *via* photoredox catalyst in combination of organocatalyst.[12]

Results and Discussion

Transformation of Aldehydes into α,β-Unsaturated Aldehydes

Upon investigating the transformation of aldehydes into the corresponding α,β-unsaturated aldehydes, 3-phenylpropanal was selected as a model aldehyde. As we already reported that diphenylprolinol silyl ether is an effective chiral organocatalyst for the transformation of aldehydes into enamines,[13] achiral secondary amine catalysts were examined. The reaction was carried out in the presence of 20 mol% of several amine catalysts with an equimolar amount of DDQ in THF, and the results are summarized in Table 1. Al-

Table 1. Effect of amine and solvent in the conversion of 3-phenylpropanal into cinnamaldehyde.[a]

$$ \text{3-phenylpropanal} \xrightarrow[\text{THF, r.t.}]{\substack{20\ \text{mol\% amine} \\ 100\ \text{mol\% DDQ}}} \text{cinnamaldehyde} \quad (1) $$

Entry	Amine	Solvent	Time [h]	Yield [%][b]
1	diisopropylamine	THF	3	<5
2	diphenylamine	THF	2	<5
3	diisobutylamine	THF	3	55
4	dibutylamine	THF	2	47
5[c]	pyrrolidine	THF	3	25
6[c]	dibenzylamine	THF	2	59
7	*N*-cyclohexyl-*N*-methylamine	THF	2	71
8	*N*-methylaniline	THF	2	74
9	*N*-benzyl-*N*-methylamine	THF	2	96
10	*N*-benzyl-*N*-methylamine	CH₂Cl₂	2	76
11	*N*-benzyl-*N*-methylamine	toluene	2	26
12[d]	*N*-benzyl-*N*-methylamine	THF	0.5	94
13[e]	*N*-benzyl-*N*-methylamine	THF	5	75

[a] Unless otherwise shown, the reaction was performed using 3-phenylpropanal (0.4 mmol), DDQ (0.4 mmol), amine (0.08 mmol) and solvent (1.6 mL) at room temperature.
[b] Yield of the isolated cinnamaldehyde.
[c] A substantial amount of the self-aldol product of 3-phenylpropanal was obtained.
[d] THF (0.4 mL) was employed.
[e] *N*-Benzyl-*N*-methylamine (0.04 mmol) was employed.

though diisopropylamine and diphenylamine did not promote the reaction (entries 1 and 2), diisobutylamine and dibutylamine afforded the product in moderate yield (entries 3 and 4). Pyrrolidine and dibenzylamine afforded the product in moderate yield, due in part to a self-aldol reaction of 3-phenylpropanal (entries 5 and 6). These results indicate that a bulky amine is not suitable because of the slow generation of the enamine, while the self-aldol reaction becomes problematic in the case of a sterically less hindered amine. After further screening of the amine catalysts, *N*-cyclohexyl-*N*-methylamine, *N*-methylaniline, and *N*-benzyl-*N*-methylamine were found to promote the desired oxidative reaction with good yield (entries 7–9). As *N*-benzyl-*N*-methylamine gave the best yield (entry 9), we selected this amine for the further optimization.

Next the solvent and concentration were examined. Although the reaction was slow in toluene (entry 11), the reaction proceeded in CH₂Cl₂ and THF. An excellent yield was obtained in THF (entry 9) using a concentration between 0.5 M and 1.0 M. When the reaction was performed under concentrated conditions (1.0 M), the reaction was completed within 30 min (entry 12). When catalyst loading was reduced to 10 mol%, the product was obtained in 75% yield with

Table 2. Effect of amounts of amine catalyst, DDQ, and MnO$_2$ in the conversion of 3-phenylpropanal into cinnamaldehyde.[a]

Entry	X [mol%][b]	Y [mol%][c]	Z [mol%][d]	Yield [%][e]
1	30	20	600	87
2	30	20	500	87
3	30	20	300	64[f]
4	30	20	150	51[f]
5	30	20	100	41[f]
6	30	10	500	82
7	30	5	500	< 30
8	10	10	500	78

[a] Unless otherwise shown, the reaction was performed using 3-phenylpropanal (0.4 mmol), THF (0.4 mL) at room temperature for 6 h. Amounts of DDQ, MnO$_2$ and MeBnNH are listed in the Table.
[b] Amount of BnMeNH.
[c] Amount of DDQ.
[d] Amount of MnO$_2$.
[e] Yield of the isolated cinnamaldehyde.
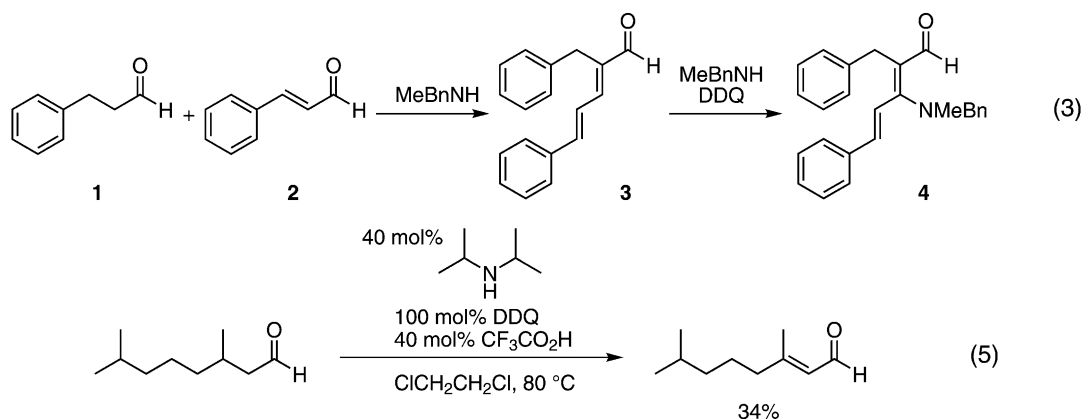[f] Substantial amounts (17–27%) of a by-product **4** were obtained.

recovery of the starting material (entry 13). Thus, the best reaction conditions comprise the use of *N*-benzyl-*N*-methylamine as a catalyst in THF with 1.0 M concentration (entry 12).

In this oxidation reaction, DDQ is reduced to its hydroquinone derivative. If hydroquinone is oxidized *in situ* back to DDQ by an inexpensive oxidant, DDQ could be used in catalytic quantities. As Floreancig reported that several oxidative reactions can be promoted by a catalytic use of DDQ with MnO$_2$ as a terminal oxidant,[14] we investigated this transformation of aldehyde into α,β-unsaturated aldehyde *via* a catalytic use of DDQ with MnO$_2$ as a terminal oxidant (Table 2). First, the amount of MnO$_2$ was screened in the presence of 20 mol% of both *N*-benzyl-*N*-methyl-

amine and DDQ (entries 1–5), which indicated that 5 equivalents of MnO$_2$ were necessary to afford cinnamaldehyde in good yield. When the amount of MnO$_2$ was decreased, a by-product **4** was generated in a substantial amount, which would be formed *via* a Michael reaction of amine to **3** and DDQ oxidation, subsequently derived from the aldol condensation of 3-phenylpropanal (**1**) and cinnamaldehyde (**2**) [Eq. (3)]. Next, the amount of DDQ was investigated with 5 equivalents of MnO$_2$ (entries 6 and 7), which indicated that 10 mol% of DDQ was efficient and the amount of *N*-benzyl-*N*-methylamine could also be reduced to 10 mol% (entry 8). Thus, the optimized reaction conditions are the use of 10 mol% of both amine catalyst and DDQ.

Generality of the Catalytic DDQ Oxidation

Once the best reaction conditions for the conversion of 3-phenylpropanal into cinnamaldehyde *via* the catalytic use of *N*-benzyl-*N*-methylamine and DDQ had been established, the generality of the reaction was investigated (Table 3). As for the β-substituent of the α,β-unsaturated aldehydes, not only phenyl (entry 1), but also electron-rich *p*-methoxyphenyl (entry 2) and electron-deficient *p*-bromophenyl, *p*-nitrophenyl, *p*-trifluoromethylphenyl groups were suitable (entries 3–5). In addition to the aromatic substituents, heteroaromatic groups such as furyl and indole were successfully employed as β-substituent (entries 6 and 7). Pent-4-enal derivatives were also suitable substrates (entries 8–12). As for the substituents at the 5-position of pent-4-enal, aromatic groups with both electron-rich and electron-deficient substituents were used to afford the products with good yield. Unfortunately, aldehydes such as 7-phenylhept-4-enal and 3-benzyloxypropanal were not suitable substrates and did not afford the oxidized product. A linear unsubstituted aliphatic aldehyde such as nonanal was also not a suitable substrate with the recovery of the starting material. In the case of 3,7-dimethyloctanal, 3,7-dime-

Table 3. The generality of the conversion of aldehyde into α,β-unsaturated aldehyde.[a]

$$\text{(4)}$$

Entry	Starting material	Product	Yield [%][b]
1			78
2			86
3			80
4			77
5			75
6			71
7			84
8			86
9			89
10			88
11			85
12			75

[a] Unless otherwise shown, the reaction was performed using aldehyde (0.4 mmol), DDQ (0.04 mmol), MeBnNH (0.04 mmol), MnO$_2$ (2.0 mmol), and THF (0.4 mL) at room temperature for 6 h.
[b] Yield of the isolated α,β-unsaturated aldehyde.

thyloct-2-enal was obtained in 34% yield catalyzed by 40 mol% of diisopropylamine in dichloroethane at 80 °C for 4 h [Eq. (5)].

Conversion of Aldehydes into α,β-Unsaturated Aldehydes Catalyzed by Diphenylprolinol Silyl Ether

We have described the oxidation of aldehydes into α,β-unsaturated aldehydes *via* an achiral amine as a catalyst. When a chiral amine catalyst can be employed in this reaction instead of *N*-benzyl-*N*-methylamine, a chiral iminium ion would be formed *in situ*. When the nucleophile reacts with this chiral iminium ion, a chiral stereogenetic center at the β-position of the formyl moiety could be constructed (Scheme 1). As we have already reported this type of oxidative and enantioselective reaction, utilizing stoichiometric quantities of DDQ, it was envisioned that DDQ could be employed in catalytic quantities by use of MnO$_2$ as a terminal oxidant. Before investigation of the oxidative and enantioselective carbon-carbon bond forming reaction in the catalytic use of both diphenylprolinol silyl ether and DDQ, we investigated the first oxidation reaction using a chiral amine catalyst instead of achiral *N*-benzyl-*N*-methylamine (Table 4). When 3-phenylpropanal was treated with 10 mol% of both diphenylprolinol silyl ether and DDQ and 500 mol% of MnO$_2$, which are the best reaction conditions for the reaction using *N*-benzyl-*N*-methylamine, a good yield was obtained (80%, entry 1). The concentration of the reaction was found to be important, and dilute reaction condition (0.25 M) gave an excellent result (entry 4). Further-

Table 4. Effects of the amount of MnO$_2$ and concentration in the transformation of 3-phenylpropanal to cinnamaldehyde catalyzed by diphenylprolinol silyl ether.[a]

$$\text{(6)}$$

Entry	Conc. [M][b]	X [mol%][c]	Time [h]	Yield [%][d]
1	1.00	500	6	80
2	0.75	500	6	87
3	0.50	500	6	86
4	0.25	500	6	97
5	0.25	400	6	94
6	0.25	300	6	87
7	0.25	200	6	91
8	0.25	150	9	57
9	0.25	100	9	37

[a] Unless otherwise shown, the reaction was performed using 3-phenylpropanal (0.4 mmol), diphenylprolinol silyl ether (0.04 mmol) and DDQ (0.04 mmol) at room temperature for 6 h.
[b] Concentration of the reaction mixture.
[c] Amount of MnO$_2$.
[d] Yield of the isolated cinnamaldehyde.

more, we found the amount of MnO_2 can be reduced to 2 equivalents (entry 7), which is in contrast to the reaction of *N*-benzyl-*N*-methylamine, requiring 5 equivalents of MnO_2. As the side reaction is the self-aldol reaction of the aldehyde, it is necessary to oxidize the hydroquinone derivative to DDQ before the self-aldol reaction proceeds. In the case of *N*-benzyl-*N*-methylamine, the self-aldol reaction is rather fast and we have to oxidize the hydroquinone rapidly. In this case we have to use 5 equivalents of MnO_2. On the other hand, as the self-aldol reaction is slow in the case of the bulky diphenylprolinol silyl ether, we do not have to oxidize the hydroquinone derivative readily, and two equivalents of MnO_2 are enough to promote efficient reaction.

One-Pot Oxidation and 1,4-Addition using an Equimolar Amount of DDQ

With reaction conditions for the transformation of aldehydes into α,β-unsaturated aldehydes by the catalytic use of both diphenylprolinol silyl ether and DDQ in hand, the one-pot sequential oxidation and asymmetric Michael reaction were investigated. As we have already reported the asymmetric Michael reaction of nitromethane with α,β-unsaturated aldehydes catalyzed by diphenylprolinol silyl ether [Eq. (7)],[15] we chose nitromethane as a nucleophile for the one-pot reaction. Our previous study of the asymmetric Michael reaction indicates that MeOH and benzoic acid are effective as solvent and additive. Therefore we utilized these previously defined conditions as a starting point, employing DDQ as a stoichiometric oxidant. 3-Phenylpropanal was treated with 20 mol% of diphenylprolinol silyl ether and an equimolar amount of DDQ in THF. After the oxidation was complete, we added MeOH, $MeNO_2$ and benzoic acid, but the reaction scarcely proceeded. Although the second reaction proceeds by the use of isolated cinnamaldehyde, it did not proceed in sequential reactions. The difference would be the presence of the hydroquinone derivative, which is generated in the first oxidation. Hydroquinone would suppress the second Michael reaction. To promote the second Michael reaction, we investigated the effect of additives (Table 5). Although acids such as benzoic acid and *p*-nitrophenol were not suitable (entries 1 and 2), a weak base such as Na_2HPO_4, $NaHCO_3$,

Table 5. The effects of additive on the one-pot reaction of 3-phenylpropanal and nitromethane catalyzed by diphenylprolinol silyl ether using equimolar amounts of DDQ.[a]

| Entry	Additive	Time [h][b]	Yield [%][c]	ee [%][d]
1	$C_6H_5CO_2H$	48	<5	nd
2	*p*-$NO_2C_6H_4OH$	48	<5	nd
3	KH_2PO_4	48	<5	nd
4	Na_2HPO_4	48	36	93
5	$NaHCO_3$	48	38	90
6	Et_3N	48	50	85
7	$AcONH_4$	48	36	92
8	AcOLi	24	53	94
9	AcONa	24	76	92

[a] Unless otherwise shown, the reaction was performed using 3-phenylpropanal (0.4 mmol), diphenylprolinol silyl ether (0.08 mmol), DDQ (0.4 mmol), $MeNO_2$ (4.0 mmol), additive (0.96 mmol), THF (1.6 mL) and MeOH (0.8 mL) at room temperature. The first oxidation is for 6 h.
[b] The reaction time for the second Michael reaction.
[c] Yield of the isolated Michael product.
[d] Enantiomeric excess of the Michael product, which was determined by HPLC analysis of chiral column.

Et_3N, NH_4OAc, AcOLi and AcONa is effective (entries 4–9). AcONa was found to be a suitable additive, affording the product in good yield with excellent enantioselectivity (entry 9). After the first oxidation was complete, AcONa was added. The sodium salt of hydroquinone was precipitated within 5 min. The effective removal of the acidic hydroquinone from the solution could be the key to the success of this additive. After the generation of the precipitate, addition of $MeNO_2$ and MeOH promoted the second Michael reaction to afford the product. Evaporation and solvent swap are not necessary. What we do is to add reagents and solvent. The absolute configuration of the reaction product was determined by comparison with the product synthesized by our previous procedure.[15]
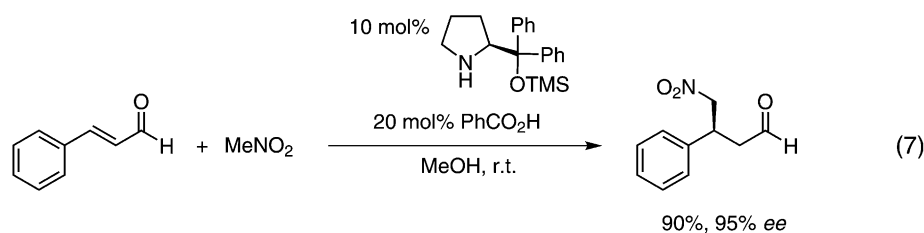
Table 6. Amount of AcONa in the one-pot oxidation and Michael reaction.[a]
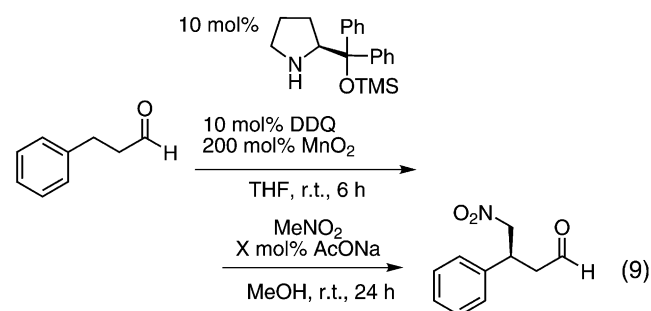
Entry	X [mol%][b]	Yield [%][c]	ee [%][d]
1	24	73	95
2	10	72	96
3	5	56	95

[a] Unless otherwise shown, the reaction was performed using 3-phenylpropanal (0.4 mmol), diphenylprolinol silyl ether (0.04 mmol), DDQ (0.04 mmol), MnO_2 (0.8 mmol), $MeNO_2$ (4.0 mmol), THF (1.6 mL) and MeOH (0.8 mL) at room temperature. Amount of AcONa is listed in Table. The first oxidation is for 6 h, and the second Michael reaction is for 24 h.

[b] Amount of AcONa.

[c] Yield of the isolated Michael product.

[d] Enantiomeric excess of the Michael product, which was determined by HPLC analysis of chiral column.

One-Pot Oxidation and 1,4-Addition using Catalytic Amounts of both Diphenylprolinol Silyl Ether and DDQ

Once we had established the one-pot sequential oxidation and Michael reaction using an equimolar amount of DDQ, the reaction using DDQ in catalytic amounts was investigated (Table 6). We have already described the reaction using DDQ in a catalytic amount with MnO_2 as a terminal oxidant. These catalytic conditions were applied to the one-pot sequential reaction, which was found to proceed in good yield with excellent enantioselectivity (entry 1). Moreover, the amount of AcONa could be reduced to 10 mol% (entry 2). When it was reduced to 5 mol%, the reaction did not proceed to completion (entry 3). Thus, as reagents such as diphenylprolinol silyl ether, DDQ and AcONa can be employed in 10 mol%, the reaction can be regarded to be efficient and green.

Generality of the One-Pot Reaction

After the best reaction conditions for the one-pot reaction had been determined, the generality of the reaction was investigated using two different stes of conditions: the use of an equimolar amount of DDQ (conditions A) and the catalytic use of DDQ with

MnO_2 as a terminal oxidant (conditions B). In conditions A, where an equimolar amount of DDQ was employed, diphenylprolinol silyl ether was employed in 20 mol% as we could not reduce the amount of this catalyst to 10 mol% because of the gradual reaction of this catalyst with DDQ. The results are summarized in Table 7. In both sets of reaction conditions, the results are similar. As for the β-substituent of the α,β-unsaturated aldehyde, not only a phenyl group (entry 1) but also electron-rich *p*-methoxyphenyl (entry 2) and electron-deficient *p*-bromophenyl and *p*-nitrophenyl groups (entries 3 and 4) were suitable, where hydride abstraction and subsequent asymmetric Michael reaction proceeded efficiently to afford the product with excellent enantioselectivity. In addition to the aromatic group, heteroaromatic groups such as furyl and indole were successfully employed as β-substituent of the α,β-unsaturated aldehydes (entries 5 and 6). Pent-4-enal derivatives were also suitable substrates. As for the substituents at the 5-position of pent-4-enal, aromatic groups with both electron-rich and electron-deficient substituents and heteroaromatic substituents were employed as suitable substrates to afford the products with excellent enantioselectivity (entries 7–10).

Mechanism of the One-Pot DDQ Oxidation/Michael Reaction

The reaction is thought to proceed *via* two reaction pathways (Scheme 2). The first path is oxidation, which is rather fast, while the second reaction is the addition to nitromethane, which is slow. Diphenylprolinol silyl ether reacts with the aldehyde to afford an enamine along with the generation of water. The enamine reacts with DDQ, which abstracts a hydride, to provide an iminium ion, and further with water to afford an α,β-unsaturated aldehyde with regeneration of the catalyst. The α,β-unsaturated aldehyde then reacts with diphenylprolinol silyl ether to generate the iminium ion, which reacts with nitromethane to afford the enamine. The enamine reacts with water to give the product with regeneration of the catalyst. The iminium ion is also generated directly from an iminium ion by reaction with AcONa. 4,5-Dichloro-3,6-dihydroxy-1,2-benzenecarbonitrile is too acidic and suppresses the second addition reaction of nitromethane. Addition of AcONa is essential for the success for the sequential reaction, which reacts with the hydroquinone derivative to generate its sodium salt. This sodium salt is efficiently removed from the reaction mixture by the precipitation.

**Table 7.** The generality of the one-pot, oxidative asymmetric Michael reaction.[a]

Conditions A: X = 20, Y = 100, Z = 0
Conditions B: X = 10, Y = 10, Z = 200
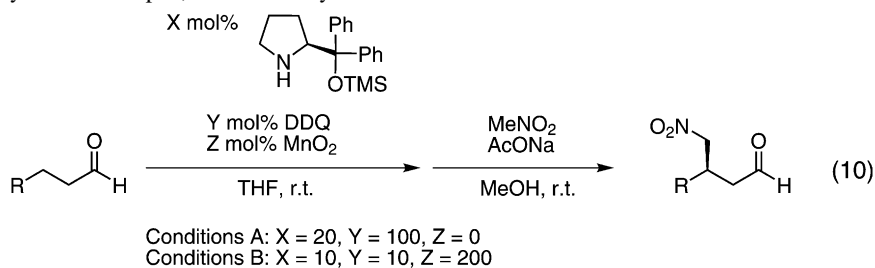
Entry	Product	Time [h][b]	Conditions A		Conditions B	
			Yield [%][c]	ee [%][d]	Yield [%][c]	ee [%][d]
1		12	75	92	72	96
2		12	77	95	76	96
3		12	66	95	63	95
4		12	65	94	62	95
5		20	62	94	60	81
6		12	70	92	62	94
7		4	78	91	71	90
8		3	80	92	74	91
9		4	71	90	73	90
10		8	64	85	62	87

[a] *Conditions A:* aldehyde (0.4 mmol), DDQ (0.4 mmol), diphenylprolinol silyl ether (0.08 mmol), THF (1.6 mL), MeNO$_2$ (4.0 mmol), AcONa (0.96 mmol), MeOH (0.8 mL). *Conditions B:* aldehyde (0.4 mmol), DDQ (0.04 mmol), diphenylprolinol silyl ether (0.04 mmol), MnO$_2$ (0.8 mmol), THF (1.6 mL), MeNO$_2$ (4.0 mmol), AcONa (0.04 mmol), MeOH (0.8 mL).
[b] The reaction time of the addition reaction of nitromethane.
[c] Yield of the isolated product.
[d] For the determination of enantiomeric excess, see the Supporting Information.
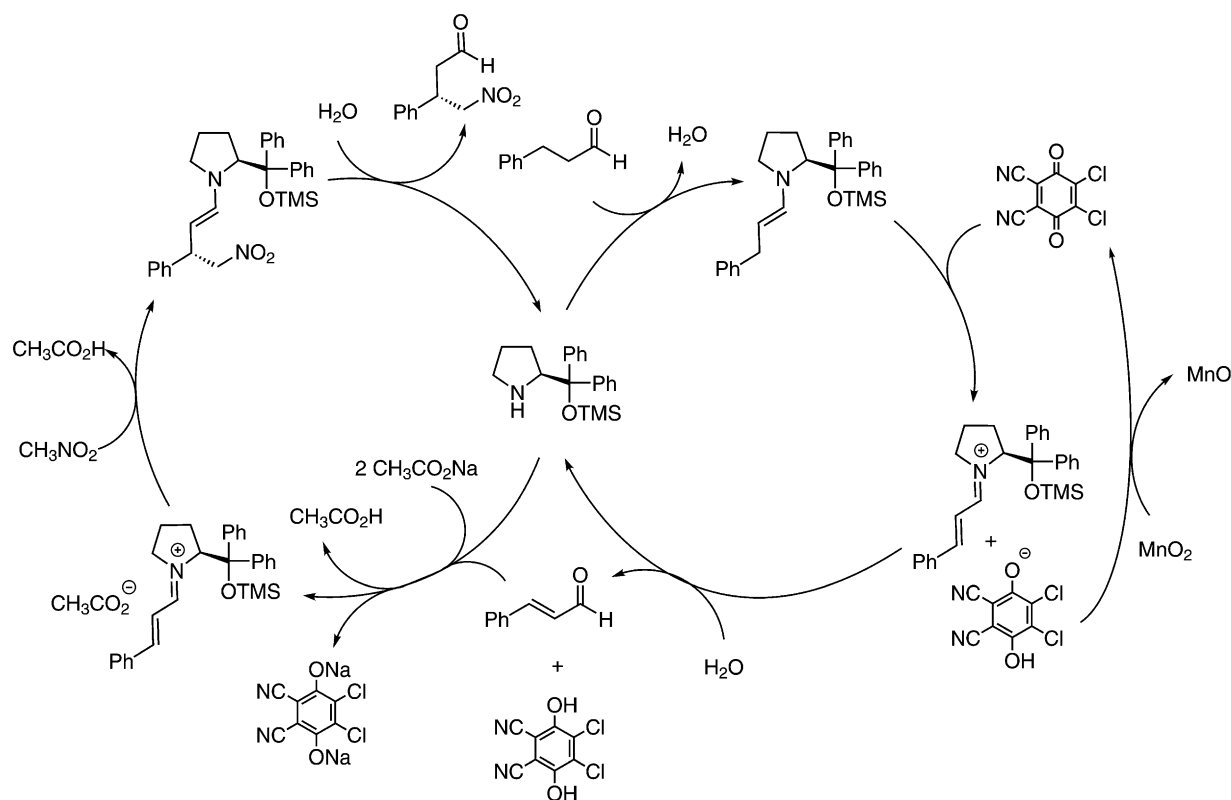
Scheme 2. Proposed reaction mechanism for the asymmetric oxidative reaction.

Conclusions

We have developed a one-pot transformation of aldehydes into α,β-unsaturated aldehydes using both *N*-benzyl-*N*-methylamine and DDQ as catalysts and MnO$_2$ as a terminal oxidant. We also disclosed the oxidative and enantioselective reaction of aldehydes and nitromethane catalyzed by both diphenylprolinol silyl ether and DDQ as a catalyst using MnO$_2$ as a terminal oxidant. There are several noteworthy features in the present reactions. As for the oxidation of aldehyde into α,β-unsaturated aldehyde: (i) an achiral amine can be used as a catalyst; and (ii) DDQ can be used in catalytic amount. As for the oxidative enantioselective addition reaction: (i) the proton at the β-carbon atom of an aldehyde was substituted with nitromethyl (CH$_2$NO$_2$) enantioselectively, (ii) this reaction is a synthetic equivalent of C−H activation at the β-carbon atom of an aldehyde; (iii) β-substituted γ-nitro aldehydes, an class of important synthetic intermediate, can be synthesized with excellent enantioselectivity; (iv) the secondary amine catalyst plays two different roles: one is the generation of an enamine and the other is the generation of an α,β-unsaturated iminium ion; and finally (v) DDQ can act as a catalyst.

Experimental Section

Representative Procedure for the One-Pot, Oxidative Asymmetric Michael Reaction using Diphenylprolinol Silyl Ether and DDQ in Catalytic Amounts (Table 7, Entry 1, Conditions B)

To a solution of 3-phenylpropanal (53.6 mg, 0.4 mmol), diphenylprolinol silyl ether (13.0 mg, 0.04 mmol) and MnO$_2$ (69.5 mg, 0.8 mmol) in THF (1.6 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (9.0 mg, 0.04 mmol) at room temperature. After stirring the reaction mixture at room temperature for 6 h, sodium acetate (3.3 mg, 0.04 mmol) was added to the resulting mixture. The reaction mixture was stirred for additional 5 min. Then, MeOH (800 μL) and nitromethane (214 μL, 4.0 mmol) were added to the reaction mixture. The resulting solution was stirred for 24 h at room temperature. The reaction was quenched with saturated aqueous NaHCO$_3$, and then filtered to remove MnO$_2$. The organic materials were extracted with ethyl acetate three times, and then washed with brine. The combined organic extracts were dried over anhydrous Na$_2$SO$_4$, and concentrated under vacuum after filtration. Purification by column chromatography (ethyl acetate:hexane = 1:6) gave (*S*)-4-nitro-3-phenylbutanal; yield: 55.6 mg (0.28 mmol, 72%).

Acknowledgements

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