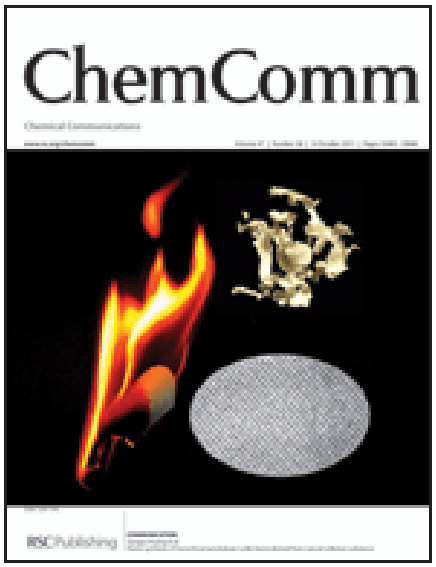

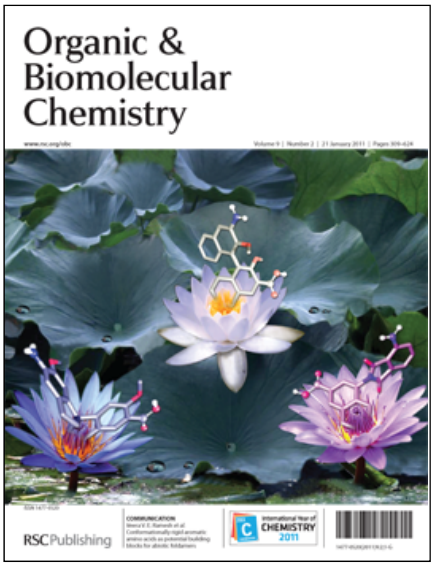

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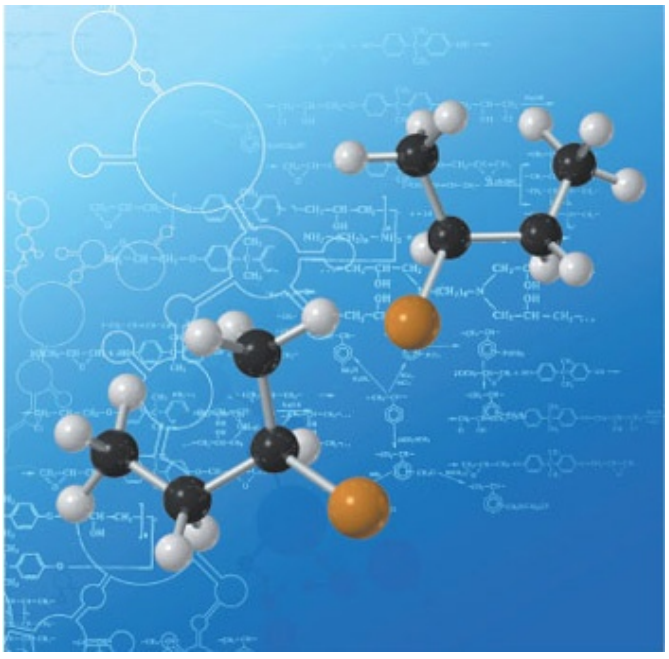

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PAPER

Synthesis of aryl group-modified DIOP dioxides (Ar-DIOPOs) and their application as modular Lewis base catalysts†

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Treatment of an optically pure tartaric acid-derived diiodide and various secondary phosphine oxides with LHMDS provides the corresponding aryl group-modified DIOP dioxides (Ar-DIOPOs). The activities of Ar-DIOPOs as Lewis base catalysts were investigated for several asymmetric transformations using chlorosilane reagents. The *p*-tolyl-substituted DIOPO (*p*-tolyl-DIOPO) was most effective for the reductive aldol reaction of chalcone and aldehydes with trichlorosilane, whereas the 2,8-dimethylphenoxaphosphine-derived DIOPO (DMPP-DIOPO) afforded the best enantioselectivity for the phosphonylation of conjugated aldehydes and the chlorinative aldol reaction of an ynone and benzaldehyde.

Introduction

Asymmetric catalysts consist of a catalytically active site, a chiral backbone, and a pendant moiety (Fig. 1). The constitution of the chiral backbone is of primary importance for the structure of the asymmetric catalyst. Kagan *et al.* first developed C_2-symmetrical diphosphine DIOP for metal-catalyzed asymmetric hydrogenation and demonstrated the importance of the backbone chirality.[1,2] The pendant moiety also plays an important role in further improving the catalytic activity and selectivity. For example, refining substituents on the phenyl groups of BINAP effectively enhances the enantioselectivity of ketone hydrogenation.[3] The modifiability of the pendant group on a catalyst is important for catalyst design.

C_2-Symmetrical chiral bisphosphine oxides have found many applications as asymmetric Lewis base catalysts for the activation of chlorosilane reagents.[4,5] We demonstrated previously that BINAP dioxide (BINAPO)[6a–k] and DIOP dioxide (DIOPO)[6l] (Fig. 2), prepared by the oxidation of BINAP and DIOP, respectively, exhibited good catalytic activities in the allylation of aldehydes,[6a,d] ring-opening of epoxides,[6b] aldol-type reactions,[6c,d,h–k] phosphonylation of aldehydes,[6e] reductive aldol reaction of enones and aldehydes,[6f,l] and reductive cyclization of *N*-acylated β-amino enones;[6g] however, low accessibility to their derivatives (synthesis of each diphosphine followed by oxidation) can hinder further optimization.

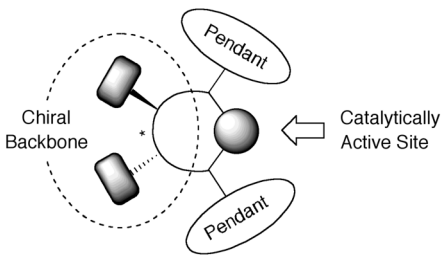

Fig. 1 Schematic diagram showing the structural components of an asymmetric catalyst.

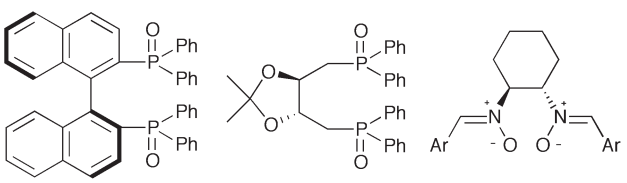

Fig. 2 The structures of BINAPO, DIOPO, and dinitrones.

In this context, we recently demonstrated that chiral dinitrones (Fig. 2), derivatives of which may be prepared in one step from a C_2-symmetrical dihydroxylamine and various aromatic aldehydes, served as effective modular Lewis base catalysts for the allylation of aldehydes using allyltrichlorosilane.[7] The aryl group may be readily modified as a pendant moiety by selecting the aromatic aldehyde used in the preparation.

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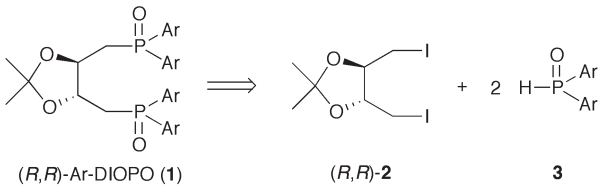


Fig. 3 Retrosynthesis of Ar-DIOPO (**1**).

Herein, we report the synthesis and application of aryl group-modified DIOP dioxides (Ar-DIOPOs) (**1**) as phosphine oxide-type modular Lewis base catalysts (Fig. 3). **1** can be prepared in one step from tartaric acid-derived optically pure diiodide (*R*,*R*)-**2** (the chiral backbone) and the corresponding secondary diarylphosphine oxides **3** (the modifiable pendant moiety) in the presence of a base.[8] The activities of the Ar-DIOPOs (**1**) as Lewis base catalysts are demonstrated using the reductive aldol reaction with trichlorosilane[6f,l,9] and the phosphonylation of aldehydes with tetrachlorosilane,[6e] both of which were developed previously, and in the chlorinative aldol reaction of an ynone with benzaldehyde, which we report here for the first time.

Results and discussion

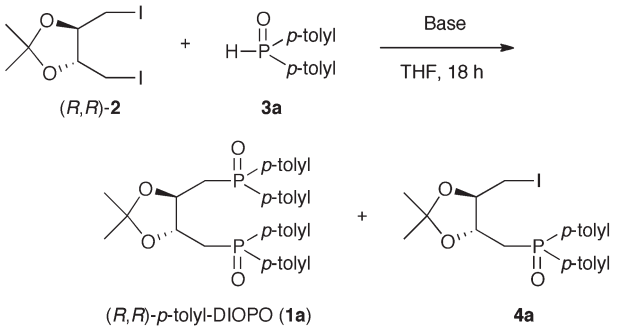
Optimization of the reaction conditions for the synthesis of *p*-tolyl-DIOPO

Our investigation began with the reaction of diiodide (*R*,*R*)-**2**[10] and bis(*p*-tolyl)phosphine oxide **3a**[11] for the preparation of *p*-tolyl-DIOPO **1a** (Table 1). Phosphine oxide **3a** was chosen as a probe substrate because it is highly crystalline, relatively stable, and, hence, easily handled. Haynes *et al.* reported the synthesis of a DIOPO-type bisphosphine oxide from a similar diiodide and *P*-chiral *tert*-butyl(phenyl)phosphine oxide with LDA at −78 °C.[12] However, the synthesis of DIOPO derivatives bearing any of a variety of diaryl groups has not been investigated.

To a solution of (*R*,*R*)-**2** (1.0 equiv) and **3a** (2.4 equiv) in THF was added LHMDS (2.4 equiv) at −20 °C, and the mixture was stirred at that temperature for 18 h. After aqueous workup, the desired *p*-tolyl-DIOPO (**1a**) was obtained in a moderate yield along with 5% monophosphine oxide **4a** (entry 1). The effect of the amide base counter cation was investigated by examining NaHMDS and KHMDS (entries 2 and 3). NaHMDS afforded a yield comparable to LHMDS, but KHMDS decreased the yield. In these cases, phosphine oxide **3a** could not be recovered.[13] In the case of LHMDS, 37% of **3a** remained. This indicated that the phosphinylide intermediate was relatively stable if the counter cation was lithium. Thus, the reaction temperature was increased to 0 °C in the presence of LHMDS to further promote the nucleophilic substitution, and the yield of **1a** increased to *ca.* 80% (entry 4). Reducing the amounts of both **3a** and LHMDS (2.2 and 2.0 equiv, respectively) at 0 °C did not decrease the yield of **1a** (entry 5).[14]

Interestingly, even when the amounts of both **3a** and LHMDS were reduced by half (1.1 and 1.0 equiv, respectively), the formation of bisphosphine oxide **1a** still dominated the formation of monophosphine oxide **4a** (entry 6). This observation suggested that coordination of the first introduced P═O group to the lithium phosphinylide intermediate may accelerate the second nucleophilic attack (Fig. 4).[15]

Table 1 Optimization of the reaction conditions for the synthesis of *p*-tolyl-DIOPO (**1a**)[a]



Entry	Base	Temperature	**1a**[b] (%)	**4a**[b] (%)	Rec. **3a**[b] (%)
1	LHMDS	−20 °C	57	5	37
2	NaHMDS	−20 °C	60	2	1
3	KHMDS	−20 °C	45	0	0
4	LHMDS	0 °C	78 (82)[c]	5	11
5[d]	LHMDS	0 °C	77 (80)[c]	6	17[c]
6[e]	LHMDS	0 °C	33	2	10

[a] Unless otherwise noted, a solution of diiodide **2** (0.5 mmol) and bis(*p*-tolyl)phosphine oxide **3a** (1.2 mmol) in THF (4 mL) was treated with a base (1.2 mmol) at −20 or 0 °C for 18 h. [b] Yields were determined by ^{1}H-NMR analysis using dibenzyl ether as an internal standard. [c] Isolated yields are given in parentheses. [d] With **3a** (1.1 mmol) and LHMDS (1.0 mmol). [e] With **3a** (0.55 mmol) and LHMDS (0.5 mmol).

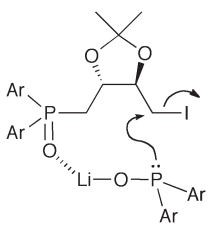
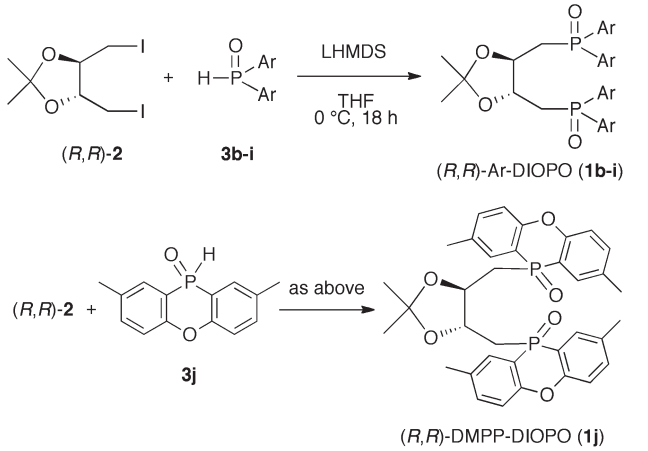


Fig. 4 Presumable directing effects of the phosphonoyl group.

Synthesis of various Ar-DIOPOs

The optimized reaction conditions for the preparation of *p*-tolyl-DIOPO (**1a**) (Table 1, entry 5) were applied to the reaction of diiodide **2** with other diarylphosphine oxides **3b–j**[11,16,17] (Table 2). An electron-rich *p*-methoxyphenyl-substituted phosphine oxide **3b** and an electron-poor *p*-chlorophenyl-substituted one **3c** afforded the desired DIOPO derivatives **1b** and **1c** in good and high yields, respectively (entries 2 and 3). The electron-donating methoxy group may lower the stability of the anionic phosphinylide intermediate, diminishing the yield of **1**.[18] A similar trend was observed for the reaction of a series of *meta*-substituted phosphine oxides **3d–f**, giving the corresponding DIOPO derivatives in moderate to good yields (entries 4–6). Despite their bulkiness, the *o*-tolyl- or *m*-xylyl-substituted phosphine oxides **3g** and **3h** reacted smoothly to afford the DIOPO

Table 2 Synthesis of various Ar-DIOPOs (**1**)[a]



Entry	Ar (**3**)	Product (**1**)[b]	Yield of **1**[c] (%)
1	*p*-Tolyl (**3a**)	*p*-Tolyl-DIOPO (**1a**)	80
2	*p*-$MeOC_6H_4$ (**3b**)	*p*-MeO-DIOPO (**1b**)	68
3	*p*-ClC_6H_4 (**3c**)	*p*-Cl-DIOPO (**1c**)	81
4	*m*-Tolyl (**3d**)	*m*-Tolyl-DIOPO (**1d**)	71
5	*m*-$MeOC_6H_4$ (**3e**)	*m*-MeO-DIOPO (**1e**)	60
6	*m*-ClC_6H_4 (**3f**)	*m*-Cl-DIOPO (**1f**)	66
7	*o*-Tolyl (**3g**)	*o*-Tolyl-DIOPO (**1g**)	70
8	3,5-$Me_2C_6H_3$ (**3h**)	*m*-Xylyl-DIOPO (**1h**)	80
9	2-Thienyl (**3i**)	Thienyl-DIOPO (**1i**)	58
10	**3j**	DMPP-DIOPO (**1j**)	57
11[d]	**3j**	DMPP-DIOPO (**1j**)	77

[a] Unless otherwise noted, a solution of diiodide **2** (0.5 mmol) and diarylphosphine oxide (**3**) (1.1 mmol) in THF (4 mL) was treated with LHMDS (1.0 mmol) at 0 °C for 18 h. [b] (*R*,*R*)-Isomers in all cases. [c] Isolated yields. [d] **3j** (1.5 mmol) and LHMDS (1.2 mmol) were used.

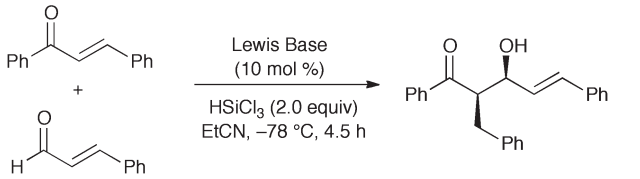
derivatives (entries 7 and 8). Di(2-thienyl)phosphine oxide (**3i**)[16] and 2,8-dimethylphenoxaphosphine oxide (**3j**, DMPP)[17] provided the desired products in moderate yields (entries 9 and 10).[19] As with the methoxy-substituted phosphine oxides, the low stabilities of the electron-rich heterocyclic phosphinylide anions may have accounted for the moderate yields. Indeed, the phosphine oxides **3i** and **3j** could not be recovered after workup. Therefore, an excess amount (three equiv) of **3j** was used for the synthesis of DMPP-DIOPO, and the yield increased to 77% (entry 11).

Application of Ar-DIOPOs to reductive aldol reaction

The conjugate reduction of α,β-unsaturated carbonyl compounds, followed by the aldol reaction of the resulting enolates with aldehydes (the reductive aldol reaction) is a powerful synthetic tool in organic synthesis.[20] We recently reported the first organocatalytic variant of this transformation, in which BINAPO and DIOPO as chiral Lewis base catalysts provided high diastereo- and enantioselectivies.[6l]

With the new DIOPO derivatives **1a–j** in hand, we investigated the reductive aldol reaction of chalcone and cinnamaldehyde with trichlorosilane (Table 3). We chose these substrates because the enantioselectivity obtained with DIOPO required

Table 3 Ar-DIOPOs-catalyzed reductive aldol reaction of chalcone and cinnamaldehyde[a]

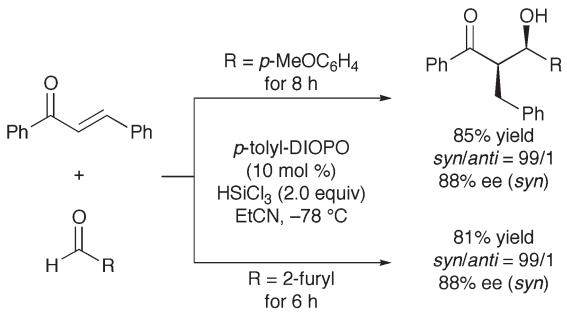


Entry	Lewis base[b]	Yield (%)	*syn*/*anti*[c]	Ee[d] (%)
1	BINAPO	91	95/5	51
2	DIOPO	71	95/5	85
3	*p*-Tolyl-DIOPO (**1a**)	78	99/1	91
4	*p*-MeO-DIOPO (**1b**)	86	96/4	89
5	*p*-Cl-DIOPO (**1c**)	80	97/3	78
6	*m*-Tolyl-DIOPO (**1d**)	81	94/6	89
7	*m*-MeO-DIOPO (**1e**)	88	99/1	88
8	*m*-Cl-DIOPO (**1f**)	75	96/4	76
9	*o*-Tolyl-DIOPO (**1g**)	54	48/52	73
10	*m*-Xylyl-DIOPO (**1h**)	97	96/4	87
11	Thienyl-DIOPO (**1i**)	67	94/6	76
12	DMPP-DIOPO (**1j**)	0	—	—

[a] All reactions were performed using chalcone (0.25 mmol), cinnamaldehyde (0.3 mmol), and a DIOPO derivative **1** (10 mol%) in propionitrile (1 mL) at −78 °C for 4.5 h. [b] (*S*)-BINAPO or (*R*,*R*)-DIOPO derivatives were used in this study. [c] Determined by ^{1}H-NMR analysis of the crude product. [d] The ee of the *syn*-isomer. Determined by HPLC analysis. The (2*R*,3*S*)-isomer was the major enantiomer in all cases.

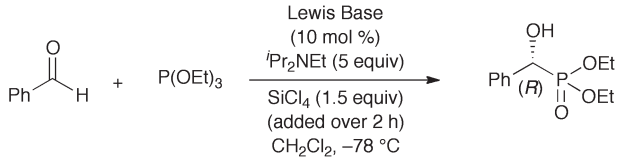
further improvements, although the enantioselectivity exceeded that resulting from BINAPO (entries 1 and 2).[6l] The experiments were performed under the conditions as previously optimized. To our delight, *p*-tolyl-DIOPO (**1a**) provided higher diastereo- and enantioselectivities than DIOPO (entry 3). The effect of the *para*-substituents on the phenyl groups was next investigated (entries 4 and 5). A more electron-donating *p*-MeO-DIOPO (**1b**) gave a higher yield and resulted in a comparable enantioselectivity (entry 4). A less electron-donating *p*-Cl-DIOPO **1c** decreased both the diastereo- and enantioselectivities (entry 5). We postulate that a catalyst with an appropriately high Lewis basicity could coordinate strongly to the trichlorosilyl enol ether intermediate and stabilize the transition structure of the aldol reaction, leading to a high selectivity. A similar trend was observed for the *meta*-substituted series (**1d–f**, entries 6–8). *m*-Tolyl- and *m*-MeO-DIOPOs gave higher enantioselectivities than DIOPO, whereas *m*-Cl-DIOPO showed a lower selectivity. Sterically congested *o*-tolyl-DIOPO (**1g**) gave an inferior result (entry 9). In this case, nearly racemic *anti*-aldol product was prevalent, implying that the catalyst did not effectively promote the reaction due to its bulkiness. Dimethyl-substituted *m*-xylyl-DIOPO (**1h**) afforded the highest yield, but the selectivity was less than 90% (entry 10). Although thienyl-DIOPO (**1i**) moderately promoted the reaction (entry 11), DMPP-DIOPO (**1j**) did not give the aldol product at all (entry 12). **1j** did not catalyze the conjugate reduction of chalcone with trichlorosilane even in the absence of the aldehyde. **1j** might strongly coordinate the silicon atom due to its high basicity and disturb the catalyst turnover.

p-Tolyl-DIOPO was then applied to the reaction of chalcone with *p*-anisaldehyde and that with 2-furfural (Scheme 1) and



Scheme 1 *p*-Tolyl-DIOPO-catalyzed reactions of chalcone with other aldehydes.

Table 4 Ar-DIOPO-catalyzed phosphonylation of benzaldehyde with triethyl phosphite[a]



Entry	Lewis base[b]	Yield[c] (%)	Ee[d] (%)
1	BINAPO	86	41
2	DIOPO	57	10
3	*p*-Tolyl-DIOPO (**1a**)	94	12
4	*m*-Tolyl-DIOPO (**1d**)	84	14
5	*o*-Tolyl-DIOPO (**1g**)	76	20
6	*m*-Xylyl-DIOPO (**1h**)	88	21
7	DMPP-DIOPO (**1j**)	90	44

[a] All reactions were performed using benzaldehyde (0.25 mmol), triethyl phosphite (0.375 mmol), tetrachlorosilane (0.375 mmol), diisopropylethylamine (1.25 mmol), and a DIOPO derivative **1** (10 mol %) in CH_2Cl_2 (1 mL) at −78 °C. [b] (*S*)-BINAPO or (*R*,*R*)-DIOPO derivatives were used in this study. [c] Isolated yields. [d] Determined by HPLC analysis. The (*R*)-isomer was the major enantiomer in all cases.

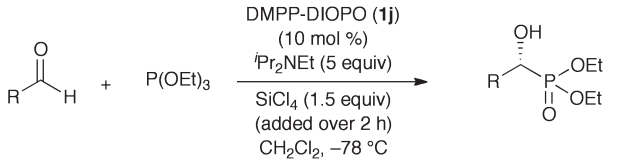
gave comparable stereoselectivities as BINAPO[6l] [72%, *syn*/*anti* = 95/5, 85% ee (*syn*) for the reaction with *p*-anisaldehyde; 84%, *syn*/*anti* = 99/1, 90% ee (*syn*) for that with 2-furfural]. Considering the availability of both the enantiomers of tartaric acid, Ar-DIOPOs can be simple and inexpensive Lewis base catalysts.

Application of Ar-DIOPOs to phosphonylation of aldehydes

Phosphonylation of aldehydes with dialkyl or trialkyl phosphites provides synthetically useful and biologically active α-hydroxyphosphonates, and several successful asymmetric metal catalysts have been developed.[21] We reported the first organocatalytic Abramov-type phosphonylation of aldehydes with trialkyl phosphite and tetrachlorosilane;[6e] however, the selectivity has remained modest yet.

Ar-DIOPOs (**1a–j**) were applied toward the phosphonylation of benzaldehyde with triethyl phosphite (Table 4). In the previous study, BINAPO provided the best results among the Lewis bases tested, whereas DIOPO resulted in a low selectivity (entries 1 and 2).[6e] Experiments were performed under the

Table 5 Ar-DIOPO-catalyzed phosphonylation of various aldehydes



		DMPP-DIOPO[a]		BINAPO[b]	
Entry	R	Yield[c] (%)	Ee[d] (%)	Yield[c] (%)	Ee[d] (%)
1	Ph	90	44	91	41
2	*p*-$MeOC_6H_4$	80	49	90	40
3	*p*-BrC_6H_4	71	41	87	22
4[e]	2-Naphthyl	63	40	98	33
5	1-Naphthyl	83	22	83	9
6	(*E*)-PhCH=CH	72	17	89	49

[a] The reactions were conducted using an aldehyde (0.25 mmol), triethyl phosphite (0.375 mmol), tetrachlorosilane (0.375 mmol), diisopropylethylamine (1.25 mmol), and (*R*,*R*)-DMPP-DIOPO (**1j**) (10 mol%) in CH_2Cl_2 (1 mL) at −78 °C. [b] The results obtained in the previous study (ref. 6*e*) with an aldehyde (0.5 mmol), triethyl phosphite (0.75 mmol), tetrachlorosilane (0.75 mmol), diisopropylethylamine (0.75 mmol), and (*S*)-BINAPO (10 mol%) in CH_2Cl_2 (2 mL). [c] Isolated yields. [d] Determined by HPLC analysis. [e] After addition of tetrachlorosilane, the mixture was stirred for 1 h before workup.

conditions investigated previously: tetrachlorosilane was added over 2 h by a syringe pump to a mixture of benzaldehyde, triethyl phosphite, diisopropylethylamine,[22] and catalyst **1** in a CH_2Cl_2 at −78 °C.

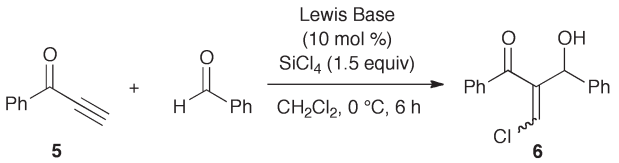
p-Tolyl-DIOPO (**1a**), the most effective promoter of the reductive aldol reaction described in the previous section, and *m*-tolyl-DIOPO (**1d**) gave selectivities as low as that of DIOPO (entries 3 and 4). *o*-Tolyl-DIOPO (**1g**) and *m*-xylyl-DIOPO (**1h**) gave slightly better enantioselectivities (entries 5 and 6). DMPP-DIOPO (**1j**), having a phenoxaphosphine ring, achieved a selectivity higher than that of BINAPO (entry 7).

To compare DMPP-DIOPO with BINAPO, the phosphonylation of other aldehydes was next investigated (Table 5). Previous studies of the BINAPO catalyst are summarized on the right hand side of Table 5. Interestingly, DMPP-DIOPO showed a low dependence on the electronics of the aldehyde (entries 1–4), giving similar enantioselectivities, whereas the steric factor of the aldehyde significantly affected the selectivity (entries 5 and 6). In most cases, the substrate scope appeared to complement that of BINAPO (entries 3–6).

Development of chlorinative aldol reaction of ynone with aldehyde and application of Ar-DIOPOs

The conjugate addition of a halide anion to α,β-unsaturated carbonyl compounds, followed by the aldol reaction with aldehydes, namely the *halogenative* aldol reaction, can provide synthetically useful α-(1-haloalkyl or 1-haloalkylidene)-β-hydroxy carbonyl compounds.[23] Several effective non-enantioselective methods have been developed for achieving this transformation, although enantioselective methods are limited.[24]

Table 6 Ar-DIOPO-catalyzed chlorinative aldol reaction of ynone **5** and benzaldehyde[a]



5 **6**

Entry	Lewis base[b]	Yield (%)	*E*/*Z*[c]	Ee[d] (%)	Ee[e] (%)
1	BINAPO	23	44/56	18	19
2	—	0	—	—	—
3	DIOPO	60	47/53	0	0
4	*p*-Tolyl-DIOPO (**1a**)	67	48/52	8	8
5	*p*-MeO-DIOPO (**1b**)	71	46/50	10	10
6	*p*-Cl-DIOPO (**1c**)	52	47/53	6	6
7	*m*-Tolyl-DIOPO (**1d**)	54	45/55	6	6
8	*o*-Tolyl-DIOPO (**1g**)	50	44/56	6	6
9	*m*-Xylyl-DIOPO (**1h**)	73	46/54	20	19
10	DMPP-DIOPO (**1j**)	35	48/52	37	37
11[f]	DMPP-DIOPO (**1j**)	46	48/52	37	37
12[g]	DMPP-DIOPO (**1j**)	89	46/54	28	28
13[h]	DMPP-DIOPO (**1j**)	80	49/51	29	29

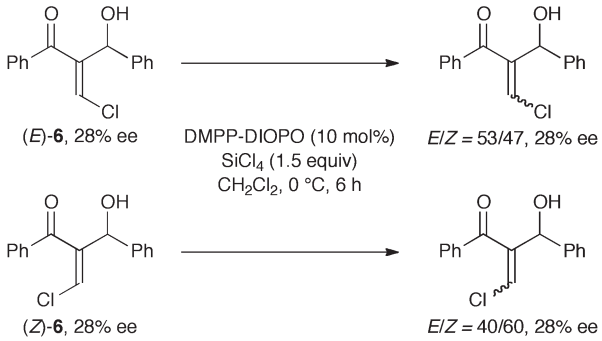
[a] All reactions were performed by the addition of tetrachlorosilane (0.375 mmol) to a mixture of ynone **5** (0.25 mmol) and benzaldehyde (0.375 mmol), a Lewis base catalyst (10 mol%) in CH_2Cl_2 (1 mL) at 0 °C with stirring for 6 h. [b] (*S*)-BINAPO or (*R*,*R*)-DIOPO derivatives were used in this study. [c] Determined by ^{1}H-NMR analysis of the crude product. [d] The ee of (*E*)-**6**. [e] The ee of (*Z*)-**6**. [f] For 19 h. [g] With 2,6-lutidine (0.25 mmol) for 12 h. [h] With 2,6-lutidine (0.25 mmol) at −20 °C for 19 h.

In the course of our study of the Lewis base-catalyzed reductive aldol reactions of α,β-enones and aldehydes with trichlorosilane,[6f,l] we tested α,β-*ynone* as a substrate in place of the enone. Surprisingly, rather than conjugate reduction, we observed a chlorinative aldol reaction.

Thus, tetrachlorosilane instead of trichlorosilane was subjected to a mixture of ynone **5**, benzaldehyde (1.5 equiv), and BINAPO (10 mol%) in CH_2Cl_2 at 0 °C (Table 6, entry 2). Although the yield and enantioselectivity were low, the chlorinative aldol product **6** was obtained enantioselectively as a mixture of the *E*/*Z*-isomers. Lewis base catalyst is indispensable for the reaction, because no desired product was obtained in its absence (entry 2). The use of DIOPO as a catalyst improved the yield to a large extent, but no enantioselectivity was observed (entry 3).

Selected Ar-DIOPOs were next examined in an attempt to enhance the enantioselectivity further (entries 4–10). Among those tested, DMPP-DIOPO (**1j**) provided the highest enantioselectivity (37% ee), although the yield decreased to 35% (entry 10). *p*-MeO-DIOPO (**1b**) and *m*-xylyl-DIOPO (**1h**) bearing electron-donating groups tended to give high yields, but the ee of the product was still less than 20% (entries 5 and 9). Prolonging the reaction time using DMPP-DIOPO did not improve the yield significantly (entry 11). The addition of 2,6-lutidine (1.0 equiv) was found to increase the yield dramatically, although the enantioselectivity was reduced to 28% ee (entry 12).[25] Lowering the reaction temperature to −20 °C did not improve the selectivity, even with 2,6-lutidine (entry 13).

Interestingly, the enantiomeric excesses of the (*E*)- and (*Z*)-products **6** were nearly identical. This suggested that



Scheme 2 Geometrical isomerization of enone **6**.

interconversion between these isomers occurred during the reaction. To confirm this possibility, (*E*)- and (*Z*)-**6**, isolated by column chromatography on silica gel, were subjected to the reaction conditions (Scheme 2). Rapid geometrical isomerization but no racemization was observed in both cases. Isomerization averaged the enantiomeric excesses of (*E*)- and (*Z*)-**6**, which would have differed prior to isomerization. The conjugate addition of a chloride anion to the enone product **6**, followed by C–C bond rotation and elimination of one of the two chloride anions, likely explains the isomerization mechanism.[26]

Extensive studies of the catalyst structure and reaction mechanism[27] would be necessary to further improve the yield and selectivity.

Conclusions

We demonstrated a divergent synthetic approach to aryl group-modified DIOP dioxides (Ar-DIOPOs) and their utility as Lewis base catalysts for reductive aldol reaction, phosphonylation, and chlorinative aldol reaction with chlorosilane reagents. Refining the aryl group (the pendant moiety) effectively enhanced the reactivity and selectivity. Further systematic studies in which the chiral backbone is tuned along with the pendant moiety and application to other reactions are currently in progress.

Experimental section

General

Melting points were uncorrected. ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were measured in $CDCl_3$ with a JEOL JNM-ECX400 spectrometer unless otherwise noted. Tetramethylsilane (TMS) (δ = 0 ppm), $CDCl_3$ (δ = 77.0 ppm), and aq. phosphoric acid sealed in a glass capillary (δ = 0 ppm) were used for internal standards for ^{1}H, ^{13}C, and ^{31}P NMR analyses, respectively. Infrared spectra were recorded on JIR-6500W. Mass spectra were measured with JEOL JMS-DX303HF mass spectrometer. Optical rotations were recorded on a JASCO P-1010 polarimeter. High pressure liquid chromatography (HPLC) was performed with a JASCO P-980 and UV-1575. Thin-layer chromatography (TLC) analysis was carried out using Merk silica gel plates. Visualization was accomplished with UV light and/or phosphomolybdic acid. Column chromatography

was performed using Kanto Chemical Silica Gel 60N (spherical, neutral. 63–210 μm). All reactions were performed under argon atmosphere using oven- and heating gun-dried glassware equipped with a rubber septum and a magnetic stirring bar.

THF and CH_2Cl_2 (dehydrated) were purchased from Kanto Chemical. All other solvents were purified based on standard procedures. Trichlorosilane and tetrachlorosilane were purchased from Tokyo Kasei Kogyo (TCI) and used without further purification. LHMDS (1.0 M THF solution) was purchased from Aldrich. Triethyl phosphite was distilled from sodium. Diisopropylethylamine and 2,6-lutidine were distilled from calcium hydride. All other chemicals were purified based on standard procedures.

General procedure for preparation of Ar-DIOPOs

To a solution of a diarylphosphine oxide (1.1 mmol, 2.2 equiv) and (4*R*,5*R*)-4,5-bis(iodomethyl)-2,2-dimethyl-1,3-dioxolane (191.0 mg, 0.5 mmol) in THF (4.0 mL) was added dropwise LHMDS (1.0 M THF solution, 1.0 mL) at 0 °C. The mixture was stirred for 18 h at 0 °C, quenched with sat. aq. NH_4Cl, and extracted with AcOEt (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified with silica gel column chromatography with AcOEt only and then CH_2Cl_2–EtOH (10 : 1–6 : 1) to give the corresponding Ar-DIOPO.

(*R*,*R*)-*p*-Tolyl-DIOPO (1a)

TLC: R_f 0.63 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 223–225 °C; $[\alpha]_D^{27}$ +14.8 (*c* 1.16, $CHCl_3$); IR (KBr, cm^{-1}) 1603, 1178, 1119, 1099, 806, 651, 539; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 6H), 2.37 (s, 12H), 2.55 (ddd, *J* = 15.1, 9.8, 6.6 Hz, 2H), 2.76 (ddd, *J* = 15.1, 13.2, 3.9 Hz, 2H), 4.03–4.16 (m, 2H), 7.23 (brd, *J* = 7.2 Hz, 8H), 7.65 (dd, *J* = 11.5, 7.8 Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 26.8, 33.2 (d, *J* = 70.6 Hz), 76.5 (brd, *J* = 10.5 Hz), 109.1, 129.1 (d, *J* = 12.4 Hz), 129.2 (d, *J* = 13.3 Hz), 129.6 (d, *J* = 103.0 Hz), 130.1 (d, *J* = 103.0 Hz), 130.7 (d, *J* = 9.5 Hz), 131.0 (d, *J* = 9.5 Hz), 141.9, 142.0; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 29.7; LR-FABMS ($CHCl_3$ + NBA) *m*/*z* 587 (M + H^+, 78), 529 (M + H^+ − Me_2CO, 13), 299 (M + H^+ − Me_2CO − Ar_2POH, 18), 229 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA + NaI) *m*/*z* calcd for $C_{35}H_{40}O_4P_2Na$ (M + Na^+) 609.2300, found 609.2317.

(*R*,*R*)-*p*-MeO-DIOPO (1b)

TLC: R_f 0.23 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid/EtOH); mp 170–172 °C; $[\alpha]_D^{27}$ +17.0 (*c* 0.995, $CHCl_3$); IR (KBr, cm^{-1}) 1599, 1504, 1294, 1255, 1173, 1122, 1026, 802, 550; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 6H), 2.52 (ddd, *J* = 15.1, 9.6, 6.4 Hz, 2H), 2.75 (ddd, *J* = 15.1, 13.3, 3.7 Hz, 2H), 3.83 (s, 12H), 4.02–4.12 (m, 2H), 6.94 (brd, *J* = 7.3 Hz, 8H), 7.68 (dd, *J* = 11.0, 8.7 Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 33.5 (d, *J* = 70.6 Hz), 55.3, 76.6 (brd, *J* = 10.5 Hz), 109.1, 113.9 (d, *J* = 12.4 Hz), 114.1 (d, *J* = 13.4 Hz), 124.1 (d, *J* = 105.8 Hz), 124.7 (d, *J* = 106.8 Hz), 132.7 (d, *J* = 11.5 Hz), 132.9 (d, *J* = 70.6 Hz), 162.2; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 29.5; LR-FABMS ($CHCl_3$ + NBA) *m*/*z* 651 (M + H^+, 43), 593 (M + H^+ − Me_2CO, 7), 331 (M + H^+ − Me_2CO − Ar_2POH, 14), 261 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) *m*/*z* calcd for $C_{35}H_{41}O_8P_2$ (M + H^+) 651.2277, found 651.2305.

(*R*,*R*)-*p*-Cl-DIOPO (1c)

TLC: R_f 0.71 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 253–255 °C; $[\alpha]_D^{24}$ +17.5 (*c* 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 1583, 1483, 1390, 1188, 1088, 1014, 754; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 6H), 2.61 (ddd, *J* = 15.1, 9.2, 6.0 Hz, 2H), 2.79 (ddd, *J* = 15.1, 13.8, 3.7 Hz, 2H), 4.10–4.20 (m, 2H), 7.45 (brd, *J* = 6.9 Hz, 8H), 7.68 (ddd, *J* = 11.0, 8.7, 2.8 Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 32.8 (d, *J* = 71.5 Hz), 76.1 (d, *J* = 9.5 Hz), 109.5, 129.1 (d, *J* = 12.4 Hz), 129.2 (d, *J* = 12.4 Hz), 130.8 (d, *J* = 101.1 Hz), 131.5 (d, *J* = 103.0 Hz), 132.2 (d, *J* = 10.5 Hz), 132.5 (d, *J* = 10.5 Hz), 138.8 (d, *J* = 2.9 Hz), 138.8 (d, *J* = 2.9 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 28.5; LR-FABMS ($CHCl_3$ + NBA) *m*/*z* 667 (M + H^+, 45), 609 (M + H^+ − Me_2CO, 14), 339 (M + H^+ − Me_2CO − Ar_2POH, 29), 269 (Ar_2PO^+,100); HR-FABMS ($CHCl_3$ + NBA) *m*/*z* calcd for $C_{31}H_{29}Cl_4O_4P_2$ (M + H^+) 667.0295, found 667.0267.

(*R*,*R*)-*m*-Tolyl-DIOPO (1d)

TLC: R_f 0.66 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 65–68 °C; $[\alpha]_D^{27}$ +14.9 (*c* 0.90, $CHCl_3$); IR (KBr, cm^{-1}) 1596, 1225, 1161, 769, 695, 565, 485; ^{1}H-NMR (400 MHz, $CDCl_3$) 1.20 (s, 6H), 2.36 (s, 12H), 2.58 (ddd, *J* = 15.1, 9.2, 6.9 Hz, 2H), 2.73 (ddd, *J* = 15.1, 13.8, 4.1 Hz, 2H), 4.08–4.18 (m, 2H), 7.27–7.36 (m, 8H), 7.52 (dd, *J* = 11.5, 6.9 Hz, 4H), 7.63 (dd, *J* = 12.1, 5.3 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 26.8, 33.1 (d, *J* = 70.6 Hz), 76.5 (d, *J* = 11.4 Hz), 109.2, 127.7 (d, *J* = 9.5 Hz), 128.0 (d, *J* = 9.5 Hz), 128.2 (d, *J* = 12.4 Hz), 129.4 (d, *J* = 12.4 Hz), 131.3 (d, *J* = 8.6 Hz), 131.6 (d, *J* = 9.5 Hz), 132.4, 132.5, 132.6 (d, *J* = 101.1 Hz), 133.1 (d, *J* = 101.1 Hz), 138.2 (d, *J* = 11.4 Hz), 138.4 (d, *J* = 12.4 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 29.7; LR-FABMS ($CHCl_3$ + NBA) *m*/*z* 587 (M + H^+, 43), 529 (M + H^+ − Me_2CO, 11), 299 (M + H^+ − Me_2CO − Ar_2POH, 15), 229 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) *m*/*z* calcd for $C_{35}H_{41}O_4P_2$ (M + H^+) 587.2480, found 587.2480.

(*R*,*R*)-*m*-MeO-DIOPO (1e)

TLC: R_f 0.54 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 96–99 °C; $[\alpha]_D^{18}$ +22.1 (*c* 0.995, $CHCl_3$); IR (KBr, cm^{-1}) 1592, 1575, 1484, 1422, 1252, 1180, 1041, 783, 695, 500; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 6H), 2.60 (ddd, *J* = 15.1, 9.6, 6.0 Hz, 2H), 2.79 (ddd, *J* = 15.1, 13.8, 3.7 Hz, 2H), 3.80 (s, 6H), 3.82 (s, 6H), 4.10–4.17 (m, 2H), 7.02 (dd, *J* = 8.2, 1.8 Hz, 4H), 7.25–7.40 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 33.2 (d, *J* = 70.6 Hz), 55.38, 55.43,

76.5 (brd, J = 10.5 Hz), 109.3, 115.5 (d, J = 10.5 Hz), 115.8 (d, J = 10.5 Hz), 118.1, 122.8 (d, J = 9.5 Hz), 123.1 (d, J = 9.5 Hz), 129.6 (d, J = 14.3 Hz), 129.8 (d, J = 14.3 Hz), 134.0 (d, J = 99.2 Hz), 134.5 (d, J = 99.2 Hz), 159.5 (d, J = 10.5 Hz), 159.6 (d, J = 10.5 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 29.7; LR-FABMS ($CHCl_3$ + NBA) m/z 651 (M + H^+, 61), 593 (M + H^+ − Me_2CO, 17), 331 (M + H^+ − Me_2CO − Ar_2POH, 31), 261 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) m/z calcd for $C_{35}H_{41}O_8P_2$ (M + H^+) 651.2277, found 651.2294.

(*R*,*R*)-*m*-Cl-DIOPO (1f)

TLC: R_f 0.71 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 72–74 °C; $[\alpha]_D^{17}$ +14.8 (c 1.03, $CHCl_3$); IR (KBr, cm^{-1}) 1566, 1469, 1403, 1186, 1134, 685; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 6H), 2.64 (ddd, J = 15.1, 9.2, 6.9 Hz, 2H), 2.76 (ddd, J = 15.1, 14.7, 4.1 Hz, 2H), 4.10–4.22 (m, 2H), 7.43 (dddd, J = 8.2, 7.8, 3.4, 2.3 Hz, 4H), 7.51 (brd, J = 8.2 Hz, 4H), 7.63 (dd, J = 11.0, 7.8 Hz, 4H), 7.78 (brd, J = 11.9 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 32.8 (d, J = 71.5 Hz), 76.1 (d, J = 10.5 Hz), 109.7, 128.6 (d, J = 9.5 Hz), 129.0 (d, J = 9.5 Hz), 130.1 (d, J = 12.4 Hz), 130.3 (d, J = 13.4 Hz), 130.6 (d, J = 10.5 Hz), 131.1 (d, J = 10.5 Hz), 132.2 (d, J = 2.9 Hz), 132.3 (d, J = 1.9 Hz), 134.4 (d, J = 98.2 Hz), 135.0 (d, J = 99.2 Hz), 135.1 (d, J = 15.3 Hz), 135.3 (d, J = 16.2 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 27.8; LR-FABMS ($CHCl_3$ + NBA) m/z 667 (M + H^+, 34), 609 (M + H^+ − Me_2CO, 23), 339 (M + H^+ − Me_2CO − Ar_2POH, 54), 269 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) m/z calcd for $C_{31}H_{29}Cl_4O_4P_2$ (M + H^+) 667.0295, found 667.0325.

(*R*,*R*)-*o*-Tolyl-DIOPO (1g)

TLC: R_f 0.71 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 61–63 °C; $[\alpha]_D^{28}$ −4.0 (c 0.98, $CHCl_3$); IR (KBr, cm^{-1}) 1593, 1453, 1178, 750; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.15 (s, 6H), 2.30 (s, 12H), 2.67–2.77 (m, 4H), 4.20–4.30 (m, 2H), 7.12–7.20 (m, 4H), 7.20–7.30 (m, 4H), 7.33–7.42 (m, 4H), 7.71 (dd, J = 12.8, 7.8 Hz, 2H), 7.84 (dd, J = 13.3, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 26.7, 31.9 (d, J = 71.5 Hz), 76.2 (dd, J = 11.9, 3.3 Hz), 109.0, 125.3 (d, J = 12.4 Hz), 125.6 (d, J = 11.5 Hz), 131.2 (d, J = 97.3 Hz), 131.5 (d, J = 10.5 Hz), 131.63, 131.66 (d, J = 10.5 Hz), 131.7, 131.8 (d, J = 10.5 Hz), 132.0 (d, J = 97.3 Hz), 132.4 (d, J = 10.5 Hz), 141.3 (d, J = 8.6 Hz), 141.7 (d, J = 9.5 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 31.8; LR-FABMS ($CHCl_3$ + NBA) m/z 587 (M + H^+, 100), 529 (M + H^+ − Me_2CO, 13), 299 (M + H^+ − Me_2CO − Ar_2POH, 24), 229 (Ar_2PO^+, 90); HR-FABMS ($CHCl_3$ + NBA) m/z calcd for $C_{35}H_{41}O_4P_2$ (M + H^+) 587.2480, found 587.2465.

(*R*,*R*)-*m*-Xylyl-DIOPO (1h)

TLC: R_f 0.71 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 156–158 °C; $[\alpha]_D^{27}$ +24.8 (c 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 1601, 1454, 1419, 1377, 1273, 1182, 1128, 1043, 852, 694, 571; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 6H), 2.31 (s, 24H), 2.50–2.67 (m, 4H), 4.08–4.16 (m, 2H), 7.09 (d, J = 3.7 Hz, 4H), 7.37 (dd, J = 11.7, 2.5 Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 26.9, 33.2 (d, J = 70.6 Hz), 76.6 (d, J = 10.5 Hz), 109.2, 128.3 (d, J = 9.5 Hz), 128.7 (d, J = 9.5 Hz), 132.7 (d, J = 99.2 Hz), 133.20 (d, J = 99.2 Hz), 133.25 (d, J = 1.9 Hz), 133.4 (d, J = 1.9 Hz), 137.9 (d, J = 12.4 Hz), 138.2 (d, J = 12.4 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 29.8; LR-FABMS ($CHCl_3$ + NBA) m/z 643 (M + H^+, 74), 585 (M + H^+ − Me_2CO, 13), 327 (M + H^+ − Me_2CO − Ar_2POH, 18), 257 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) m/z calcd for $C_{39}H_{49}O_4P_2$ (M + H^+) 643.3106, found 643.3124.

(*R*,*R*)-Thienyl-DIOPO (1i)

TLC: R_f 0.57 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 171–173 °C; $[\alpha]_D^{28}$ +3.2 (c 1.01, $CHCl_3$); IR (KBr, cm^{-1}) 1502, 1406, 1188, 1176, 1095, 1016, 714, 536; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 6H), 2.66 (ddd, J = 15.1, 10.1, 6.9 Hz, 2H), 2.86 (ddd, J = 15.1, 14.7, 4.6 Hz, 2H), 4.17–4.27 (m, 2H), 7.17–7.20 (m, 4H), 7.63–7.68 (m, 4H), 7.70–7.74 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 37.0 (d, J = 79.1 Hz), 76.2 (d, J = 11.4 Hz), 109.6, 128.2 (d, J = 11.4 Hz), 128.4 (d, J = 10.5 Hz), 133.50 (d, J = 4.8 Hz), 133.58 (d, J = 4.6 Hz), 133.64 (d, J = 114.4 Hz), 134.2 (d, J = 114.4 Hz), 135.6 (d, J = 9.5 Hz), 135.9 (d, J = 10.5 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 18.8; LR-FABMS ($CHCl_3$ + NBA) m/z 555 (M + H^+, 99), 497 (M + H^+ − Me_2CO, 18), 283 (M + H^+ − Me_2CO − Ar_2POH, 24), 213 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) m/z calcd for $C_{23}H_{25}O_4P_2S_4$ (M + H^+) 555.0111, found 555.0107.

(*R*,*R*)-DMPP-DIOPO (1j)

TLC: R_f 0.23 (AcOEt–EtOH = 10 : 1, stained blue with phosphomolybdic acid–EtOH); mp 120–124 °C; $[\alpha]_D^{20}$ −21.0 (c 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 2981, 1612, 1587, 1473, 1396, 1281, 1230, 1163, 822, 762; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 6H), 2.07–2.12 (ddd, J = 15.1, 9.6, 9.6 Hz, 2H), 2.31 (ddd, J = 16.1, 15.1, 2.8 Hz, 2H), 2.37 (s, 6H), 2.39 (s, 6H), 3.70–3.80 (m, 2H), 7.12 (ddd, J = 8.2, 6.4, 2.3 Hz, 4H), 7.35 (ddd, J = 8.4, 4.1, 2.1 Hz, 4H), 7.72 (brd, J = 13.3 Hz, 2H), 7.77 (dd, J = 13.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 26.6, 37.2 (d, J = 79.1 Hz), 76.3 (dd, J = 14.3, 4.8 Hz), 109.1, 113.6 (d, J = 99.2 Hz), 114.4 (d, J = 99.2 Hz), 117.73 (d, J = 5.7 Hz), 117.79 (d, J = 5.7 Hz), 130.0 (d, J = 3.8 Hz), 131.1 (d, J = 3.8 Hz), 133.1 (d, J = 10.5 Hz), 133.4 (d, J = 10.5 Hz), 134.7, 153.22 (d, J = 3.8 Hz), 153.31 (d, J = 3.8 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 5.2; LR-FABMS ($CHCl_3$ + NBA) m/z 615 (M + H^+, 75), 557 (M + H^+ − Me_2CO, 9), 313 (M + H^+ − Me_2CO − Ar_2POH, 12), 243 (Ar_2PO^+, 100); HR-FABMS ($CHCl_3$ + NBA) m/z calcd for $C_{35}H_{37}O_6P_2$ (M + H^+) 615.2065, found 615.2067.

General procedure for reductive aldol reaction of chalcone and aldehydes catalyzed by Ar-DIOPO

To a solution of Ar-DIOPO (10 mol%), chalcone (0.25 mmol) and an aldehyde (0.3 mmol, 1.2 equiv) in dry propionitrile (2 mL) was added dropwise trichlorosilane (*ca*. 3 M CH_2Cl_2 solution, 0.5 mmol) at −78 °C. The mixture was stirred for the

indicated time at that temperature and quenched with sat. aq. $NaHCO_3$ (1.5 mL). After addition of AcOEt (5 mL), the mixture was stirred for 1 h, filtered through a Celite pad, and extracted with AcOEt (3×). The combined organic layers were washed with brine (1×), dried over anhydrous $MgSO_4$, filtered, and evaporated. The residue was purified by silica gel column chromatography with hexane–AcOEt (15 : 1–3 : 1) to give a reductive aldol product. After separation of the product, the Lewis base could be recovered by eluting with CH_2Cl_2–EtOH (10 : 1) without loss of the optical purity. For physical data and HPLC analysis of the products, see ref. 6*l*.

General procedure for phosphonylation of aldehydes catalyzed by Ar-DIOPO

Triethyl phosphite (0.375 mmol) was added to a solution of an aldehyde (0.25 mmol), $^{i}Pr_2NEt$ (0.375 mmol) and Ar-DIOPO (10 mol%) in CH_2Cl_2 (1 mL) at −78 °C and then tetrachlorosilane (0.75 M CH_2Cl_2 solution, 0.5 mL) was introduced over 2 h using a syringe pump. After checking completion of the reaction by TLC analysis, deionized water (1 mL), sat. aq. $NaHCO_3$ (2.5 mL), and AcOEt (2.5 mL) were added in turn to the reaction mixture. After being stirred for 1 h, the mixture was filtered *via* a Celite pad and extracted with AcOEt (3 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified with silica gel column chromatography with hexane–acetone (2 : 1–1 : 1) to give the corresponding α-hydroxyphosphonate. After separation of the product, the Lewis base could be recovered by eluting with CH_2Cl_2–EtOH (10 : 1) without loss of the optical purity. For physical data and HPLC analysis of the products, see ref. 6*e*.

General procedure for chlorinative aldol reaction of a ynone and benzaldehyde catalyzed by Ar-DIOPOs

To a solution of ynone **5** (32.5 mg, 0.25 mmol), benzaldehyde (38 μL, 0.375 mmol) and Ar-DIOPO (10 mol%) in CH_2Cl_2 (1.0 mL) was added tetrachlorosilane (43 μL, 0.375 mmol) at 0 °C. After being stirred for 6 h, the mixture was quenched with sat. aq. $NaHCO_3$. The mixture was stirred for 30 min, filtered through a Celite pad, and extracted with AcOEt (3×). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated. The residue was purified by silica gel column chromatography with hexane–AcOEt (15 : 1–5 : 1) to give (*E*)-**6** (less polar isomer) and (*Z*)-**6** (polar isomer).

(*E*)-3-Chloro-2-(hydroxy(phenyl)methyl)-1-phenylprop-2-en-1-one ((*E*)-6)

TLC: R_f 0.39 (hexane–AcOEt = 5 : 1, stained green with phosphomolybdic acid in EtOH); mp 89–91 °C; $[\alpha]_D^{21}$ −42.6 (*c* 1.325, $CHCl_3$, for 28% ee); IR (KBr, cm^{-1}) 3477, 3061, 1633, 1593, 1446, 1336, 1039, 841, 731, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 4.65 (d, J = 10.8 Hz, 1H), 6.12 (d, J = 10.8 Hz, 1H), 7.00 (s, 1H) 7.25–7.62 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.5, 125.3, 127.6, 128.5, 128.6, 129.6, 133.3, 135.2, 137.2, 141.3, 141.9, 196.7; LR-FABMS ($CHCl_3$ + NBA + NaI) *m*/*z* 295 ($M + Na^+$, 64), 105 ($PhCO^+$, 100); HR-FABMS ($CHCl_3$ + NBA + NaI) *m*/*z* calcd for $C_{16}H_{13}ClO_2Na$ ($M + Na^+$) 295.0502, found 295.0507; HPLC (CHIRALPAK AS-H, hexane/2-propanol = 39 : 1, flow rate 1.0 mL min^{-1}, UV detection at 254 nm): t_R = 23.6 min (major), 36.8 min (minor).

(*Z*)-3-Chloro-2-(hydroxy(phenyl)methyl)-1-phenylprop-2-en-1-one ((*Z*)-6)

TLC: R_f 0.28 (hexane–AcOEt = 5 : 1, stained green with phosphomolybdic acid in EtOH); $[\alpha]_D^{22}$ +12.3 (*c* 1.17, $CHCl_3$, for 28% ee); IR (neat, cm^{-1}) 3446, 3064, 1662, 1653, 1595, 1450, 1323, 1228, 700; ^1H NMR (400 MHz, $CDCl_3$) δ 2.88 (dd, J = 1.4, 3.2 Hz, 1H), 5.65 (d, J = 3.2 Hz, 1H), 6.45 (d, J = 1.4 Hz, 1H), 7.26–7.80 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.1, 120.5, 126.5, 128.4, 128.6, 128.7, 129.5, 133.8, 135.8, 139.7, 143.8, 196.0; LR-FABMS ($CHCl_3$ + NBA + NaI) *m*/*z* 295 ($M + Na^+$, 100), 105 ($PhCO^+$, 52); HR-FABMS ($CHCl_3$ + NBA + NaI) *m*/*z* calcd for $C_{16}H_{13}ClO_2Na$ ($M + Na^+$) 295.0502, found 295.0504; HPLC (CHIRALPAK AS-H, hexane–2-propanol = 39 : 1, flow rate 1.0 mL min^{-1}, UV detection at 254 nm): t_R = 42.8 min (major), 46.4 min (minor).

Notes and references

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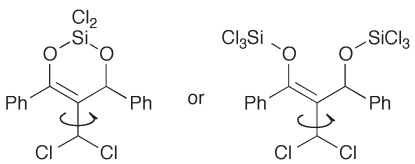
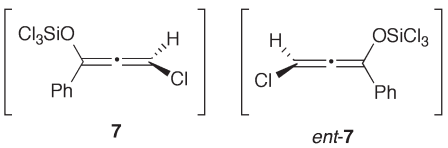
26 Plausible intermediates for the geometrical isomerization are shown below.



27 The following reaction pathway for the current chlorinative aldol reaction is proposed. First, the conjugate addition of a chloride anion to the ynone **5** generates a pair of chiral allenylic trichlorosilyl enol ethers **7** and *ent*-**7**, depicted below (the chlorination step). Second, these intermediates react with benzaldehyde *via* six-membered cyclic transition states to give the product **6** (the aldol step). This aldol step is controlled by the chiral Lewis base catalyst and may generate all four stereoisomers of product **6** from either **7** or *ent*-**7**. The geometrical isomerization of product **6** complicates the identification of the stereochemical course.



7 *ent*-**7**

