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Catalytic Enantioselective Hydrophosphonylation of Aldehydes Using the Iron Complex of a Camphor-Based Tridentate Schiff Base $[FeCl(SBAIB\text{-}d)]_2$

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Abstract: An iron(III)-Schiff base-catalyzed, highly enantioselective hydrophosphonylation of various aldehydes is described. Under the optimized reaction conditions, 5 mol% of the iron/camphor-based tridentate Schiff base complex $[FeCl(SBAIB\text{-}d)]_2$ produces high yields (up to 99%) of α-hydroxy phosphonates in excellent enantioselectivities (up to 99%). The merits of this catalytic system are an easily synthesizable catalyst, inexpensive starting materials, practically simple aerobic reaction conditions, and low catalyst loading (5 mol%).

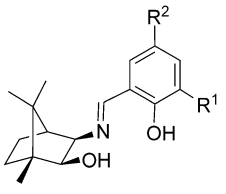
Keywords: (1*R*)-camphor-based ligands; enantioselective Pudovik reaction; hydrophosphonylation; iron-Schiff base complexes; Schiff base of aminoisoborneol

Introduction

The enantioselective synthesis of chiral α-hydroxy phosphonates is one of the rapidly growing research fields in organic chemistry[1] because of the intriguing biological properties of these compounds and their derivatives, such as antibiotics, antivirals, anticancer drugs, herbicides, insecticides, fungicides, and enzyme inhibitors.[2] Over the last two decades, considerable efforts were made to develop various methods for synthesizing chiral α-hydroxy phosphonates, including the asymmetric hydrogenation of α-keto phosphonates, the enzymatic resolution of esters of α-hydroxy phosphonates, the asymmetric α-hydroxylation of alkyl phosphonates, the asymmetric Abramov reaction, and the asymmetric Pudovik reaction.[1] Among these methods, the Pudovik reaction, which is a base-catalyzed enantioselective hydrophosphonylation of aldehydes, is the simplest reaction for forming α-hydroxy phosphonates. Substantial developments have occurred in the design and use of numerous catalytic systems for this critical enantioselective P–C bond-forming reaction.[3,4,5]

Highly enantioselective catalysts for the Pudovik reaction of aldehydes are classified into three primary types: (i) BINOL-based catalysts, namely, the tailor-made heterobimetallic catalysts ALB (alumium lithium binaphthoxide)[3f] and LLB (lathanam lithium binaphthoxide)[3h] that have been developed principally by Shibasaski's group (although they were initiated by Shibuya and Spilling independently),[3d,e] and Feng's Al(BINOL-*tert*-amine);[3p] (ii) tri-/tetradentate Schiff base catalysts, namely, Kee's Al(salcyen),[4a,b] Katsuki's Al(salalen),[4d,e,h] and Al(sal-binaphthylen),[4f] as well as Feng's tridentate Al-Schiff base obtained from L-valinol;[4g] (iii) organocatalysts, namely Wynberg's quinine,[3a,b] and Ooi's tetraaminophosphonium salt.[3q] Although the numerous catalytic systems afford excellent yields and *ee* values of chiral α-hydroxy phosphonates, they are also highly moisture-sensitive, do not perform adequately under aerobic conditions, require a high amount of catalyst loading and an extended reaction time. We studied the enantioselective reactions by using camphor-based tridentate Schiff base SBAIB ligands (Figure 1).[6]

We hypothesized that this SBAIB ligand would afford a high level of chiral induction in the hydro-



1 (+)-SBAIB-a: R^1, R^2 = H;
2 (+)-SBAIB-b: R^1, R^2 = *t*-Bu;
3 (+)-SBAIB-c: R^1, R^2 = Me;
4 (+)-SBAIB-d: R^1 = Me, R^2 = H;
5 (+)-SBAIB-e: R^1 = H, R^2 = Me;
6 (+)-SBAIB-f: R^1 = *t*-Bu, R^2 = H;
7 (+)-SBAIB-g: R^1 = H, R^2 = *t*-Bu.

Figure 1. Structures of the Schiff bases derived from aminoisoborneol.

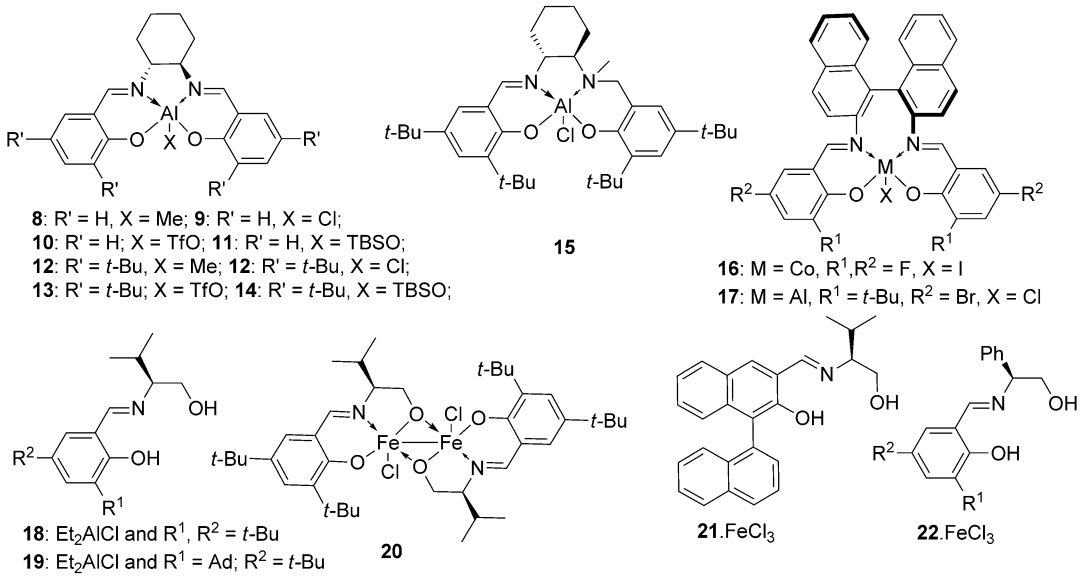


Figure 2. Metal complexes of tri-/tetradentate Schiff bases used for the catalytic enantioselective hydrophosphonylation of aldehydes.

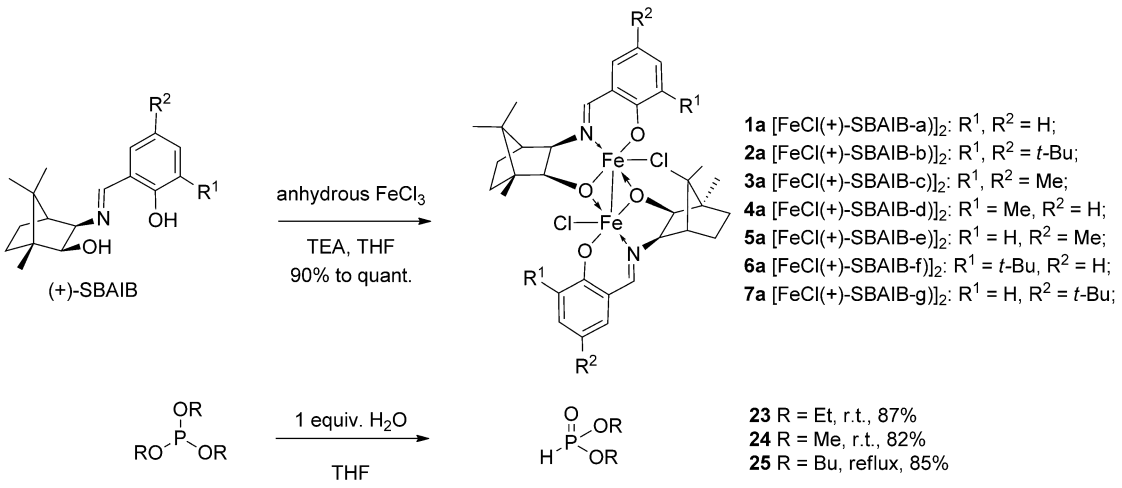
phosphonylation reactions of aldehydes because of the presence of high steric hindrances provided by both a camphor-backbone motif and electronically tunable alkyl groups in the phenol ring. Figure 2 shows the structure of various metal complexes of tri- and tetradentate Schiff bases that, to date, are used in the hydrophosphonylation of the aldehydes. Most of the Schiff bases were used either as pre-prepared aluminium complexes or as *in situ* aluminium complexes generated from Al(III) salts. Among them, Katsuki's Al(salalen) **15**[4h] and Feng's Al(Schiff base) **19**[4g] are excellent catalysts for the Pudovik reaction of various aldehydes. Al(Salcyen) complexes **8**–**14**[4a] were the first Schiff base complexes that were tested for the Pudovik reaction. Other than the aluminium-Schiff bases, cobalt-Schiff base **16**,[4f] and, more recently, an Fe(III)-Schiff base **20**[4j] were used. However, the Co(III)-Schiff base **16** showed no reactivity towards this reaction, whereas the Fe(III)-Schiff base **20**, either pre-prepared or generated *in situ*, showed a moderate *ee* (up to 71%) for several aromatic aldehydes. The iron complexes of **21** and **22** that were generated *in situ* through a reaction with $FeCl_3$ were demonstrated inferior results compared to complex **20**.[4j]

Furthermore, aluminium salts have disadvantages; for example, they need an inert atmosphere to conduct a reaction, and are highly sensitive to moisture, difficult to handle, and considerably expensive. Conversely, iron salts have apparent advantages: they are inexpensive, non-toxic, naturally abundant, environmentally benign, have a mild Lewis acidity, and are used as catalysts in many organic transformations.[7] However, their uses have rarely been investigated for the enantioselective Pudovik reaction except for **20**. Because we were inspired by the Fe(III)-Schiff base complex **20** and because one of our goals is to make stable and moisture-insensitive Schiff base SBAIB metal complexs for asymmetric synthesis,[8] we synthesized Fe(III)-SBAIB Schiff base complexes. Consequently, we report a highly enantioselective Fe(III)-tridentate Schiff base-catalyzed Pudovik reaction.

Results and Discussion

Syntheses of Iron Complexes and Dialkyl Phosphites

As shown in Scheme 1, seven iron complexes of the type $[FeCl(SBAIB)]_2$ (**1a**–**7a**) were synthesized in high yield from (+)-SBAIB (**1**–**7**) through a reaction with ferric chloride and triethylamine in tetrahydrofuran. The procedure reported by Sekar was used to obtain the stable, dark brownish-black solid Fe(III) complexes.[4j] The structures of the obtained Fe(III)-SBAIB complexes were confirmed by the paramagnetic nature of ^{1}H NMR and HR-MS results. Compared to $FeCl_3$, which became a paste or oil because HCl was released when exposed to atmospheric moisture, these Fe(III)-SBAIB complexes were highly stable under atmospheric conditions. The Schiff base of aminoisoborneol, namely, (+)-SBAIB, could be obtained easily from (1*R*)-camphor by following our previously reported procedure.[6a] We also synthesized dialkyl phosphites from trialkyl phosphites by reacting them with an equimolar mixture of water and tetrahydrofuran.[9]

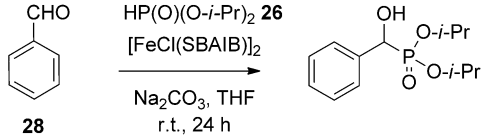


Scheme 1. Syntheses of Fe(III)-SBAIB complexes and dialkyl phosphites.

Optimization of Reaction Conditions for the Hydrophosphonylation of Benzaldehyde

After producing seven Fe(III)-SBAIB complexes, the optimization commenced by implementing a catalyst screening (Table 1). For this purpose benzaldehyde **28** was reacted with diisopropyl phosphite **26** in the presence of sodium carbonate and Fe(III)-SBAIB catalysts in THF solution. Although in all cases 5 mol% of the Fe(III)-SBAIB complexes afforded a high yield for the base-catalyzed Pudovik reaction under aerobic conditions; as expected, the $[FeCl(SBAIB\text{-}d)]_2$ (**4a**) (Table 1, entry 4) was found to be the optimal catalyst and displayed superior selectivity of 79% *ee* for the corresponding diisopropyl α-hydroxy phosphonate in 24 h at room temperature. To date, this result is the highest enantiomeric excess that has been provided by any chiral iron complex. The exact reason behind the effect of substituents and its position in the phenyl ring of SBAIB is unclear. However, the size of the methyl substituent *ortho* to the hydroxy group in **4a** might play a crucial role in keeping the phenyl ring of benzaldehyde in a certain distance and angle for the formation of better π-π stacking (*vide infra* for the proposed mechanism) than the other substituents.[10] Subsequently, we systematically explored every criterion to identify the superior optimization conditions for the $[FeCl(SBAIB\text{-}d)]_2$-catalyzed hydrophosphonylation.

Table 1. Catalyst screening and optimization.[a,b]

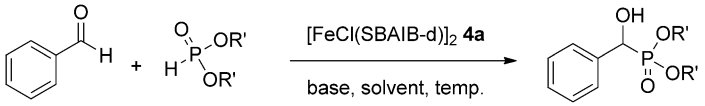


Entry	Catalyst [mol%]	Yield [%][c]	*ee* [%][d]
1	**1a** [5]	96	15
2	**2a** [5]	85	44
3	**3a** [5]	99	52
4	**4a [5]**	**99**	**79**
5	**5a** [5]	98	32
6	**6a** [5]	99	12
7	**7a** [5]	83	19

[a] All reactions were done in 8-mL screw-capped vials under aerobic conditions.
[b] Reagents ratio: PhCHO:HP(O)(O-*i*-Pr)$_2$:Na_2CO_3 = 1:1.1:1.
[c] Yields were for products purified by column chromatography.
[d] The chiral purity of the compound was checked by HPLC using Chiralcel OD-H column.

Among the various solvents surveyed for this catalytic system (Table 2, entries 1–6), THF was identified as the most suitable solvent (Table 1, entry 4). The alkyl group of the dialkyl phosphites played a vital role regarding reactivity and enantioselectivity; for instance, the reaction time of the hydrophosphonylation of various aldehydes using a Yamamoto catalyst[3n] is very short because of the use of highly reactive bis(2,2,2-trifluroethyl) phosphites. Therefore, we subsequently investigated the role of dialkyl phosphites (Table 2, entries 7–10). Diethyl phosphite exhibits the same chiral induction as diisopropyl phosphite; on the other hand, dimethyl phosphite produced a corresponding phosphonate with a slightly improved *ee* (80%) but the yield was merely 50%. As anticipated, the highly reactive bis(2,2,2-trifluoroethyl) phosphite affords a high yield of the corresponding product within 5 h reaction time, but with a lower enantioselectivity (56%). We discovered that dibutyl phosphite produced excellent yields (99%) of α-hydroxy phosphonate and the highest *ee* (83%) level (Table 2, entry 9); thus, it was chosen as a suitable dialkyl phosphite for the catalytic system in this study.

Table 2. Optimization of other criteria for the hydrophosphonylation of benzaldehyde.[a]



Entry	**4a** [mol%]	R′	Base [equiv.][b]	Solvent [volume][b]	Temp. [°C]	Time [h]	Yield [%][c]	*ee* [%][d]
1	5	*i*-Pr	Na_2CO_3 [1]	DCM [40]	r.t.	24	90	65
2	5	*i*-Pr	Na_2CO_3 [1]	DCE [40]	r.t.	24	30	72
3	5	*i*-Pr	Na_2CO_3 [1]	hexane [40]	r.t.	24	88	33
4	5	*i*-Pr	Na_2CO_3 [1]	toluene [40]	r.t.	24	71	52
5	5	*i*-Pr	Na_2CO_3 [1]	dioxane [40]	r.t.	24	57	73
6	5	*i*-Pr	Na_2CO_3 [1]	Et_2O [40]	r.t.	24	95	60
7	5	Me	Na_2CO_3 [1]	THF [40]	r.t.	24	50	80
8	5	Et	Na_2CO_3 [1]	THF [40]	r.t.	24	87	79
9	**5**	**Bu**	**Na_2CO_3 [1]**	**THF [40]**	r.t.	**24**	**99**	**83**
10	5	CF_3CH_2	Na_2CO_3 [1]	THF [40]	r.t.	5	96	56
11	5	Bu	K_2CO_3[1]	THF [40]	r.t.	24	88	56
12	5	Bu	NaOMe	THF [40]	r.t.	24	trace	NA
13	5	Bu	KO-*t*-Bu [1]	THF [40]	r.t.	24	trace	NA
14	5	Bu	pyridine [1]	THF [40]	r.t.	24	45	37
15	5	Bu	DBU [1]	THF [40]	r.t.	24	82	2
16	5	Bu	DABCO [1]	THF [40]	r.t.	24	95	67
17	5	Bu	lutidine[1]	THF [40]	r.t.	24	99	63
18	**5**	**Bu**	**TEA [1]**	**THF [40]**	r.t.	**24**	**99**	**87**
19	5	Bu	TBA [1]	THF [40]	r.t.	24	99	84
20	5	Bu	DIPEA [1]	THF [40]	r.t.	24	95	86
21	5	Bu	TEA [1.5]	THF [40]	r.t.	18	90	87
22	5	Bu	TEA [0.75]	THF [40]	r.t.	24	85	80
23	5	Bu	TEA [0.5]	THF [40]	r.t.	24	87	82
24	5	Bu	none	THF [40]	r.t.	30	99	57
25	7.5	Bu	TEA [1]	THF [40]	r.t.	20	99	87
26	2.5	Bu	TEA [1]	THF [40]	r.t.	30	96	79
27	1	Bu	TEA [1]	THF [40]	r.t.	36	99	71
28	5	Bu	TEA [1]	THF [20]	r.t.	18	91	84
29	5	Bu	TEA [1]	none (neat)	r.t.	2	99	68
30	**5**	**Bu**	**TEA [1]**	**THF [60]**	**r.t.**	**24**	**99**	**89**
31	5	Bu	TEA [1]	THF [80]	r.t.	24	98	88
32	5	Bu	TEA [1]	THF [100]	r.t.	24	95	86
33	5	Bu	TEA [1]	THF [40]	45–50	14	97	86
34	5	Bu	TEA [1]	THF [40]	4	24	99	91
35	5	Bu	TEA [1]	THF [40]	−25	35	99	92
36	**5**	**Bu**	**TEA [1]**	**THF [60]**	**−25**	**35**	**99**	**93**

[a] All reactions were done in 8-mL screw-capped vials.
[b] Abbreviations: 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), triethylamine (TEA), tributylamine (TBA), diisopropylethylamine (DIPEA), dichloromethane (DCM), 1,2-dichloroethane (DCE), tetrahydrofuran (THF).
[c] Yields were for products purified by column chromatography.
[d] The chiral purity of the compound was checked by HPLC using a Chiralcel OD-H column.

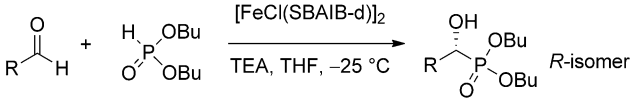
Subsequently, we focused on optimizing the base for our base-catalyzed hydrophosphonylation. Inorganic bases have been considered to facilitate the hydrophosphonylation reaction without eroding the enantioselectivity because they exhibit a relatively weak basicity and a low solubility in THF.[4k] However, the results of the base screening (Table 2, entries 11–20) showed that 1 equivalent of an organic base, such as triethylamine and diisopropylethylamine, produced a phosphonate product with a higher *ee* (87%, and 86%, respectively) than did inorganic bases, such as Na_2CO_3 and K_2CO_3. A similar characteristic of the organic bases was identified using Feng's Yb(III) complex-catalyzed hydrophosphonylation,[3r] where pyridine was determined as the superior base. The inorganic bases NaOMe and KO-*t*-Bu afford only traces of product, and the non-nucleophilic organic base DBU affords almost racemic phospho-

nate (2% *ee*). One equivalent of TEA was necessary and this was confirmed by using various amount of TEA (Table 2, entries 21–23). The higher and lower equivalents of TEA did not improve the *ee*. A high yield of phosphonate product was also obtained in a reaction time that was a slightly longer when no base was used (Table 2, entry 24); however, low enantioselectivity (57% *ee*) was observed.

When the catalyst loading was increased to 7.5 mol%, instead of 5 mol%, no change was observed in the *ee* (Table 2, entry 25); however, when it was decreased to 2.5 mol% and 1 mol% (Table 2, entries 26 and 27), a substantial decrease in the *ee* was observed. Subsequently, the volume of the solvent was examined to determine the source of improvement in the *ee*. In cases of lower volume (20 volumes with respect to benzaldehyde) and a neat reaction, despite the production of high yields in short reaction time, the *ee* decreased considerably (Table 2, entries 28 and 29). When it was increased to 60 volumes, the *ee* improved from 87% to 89% (Table 2, entry 30); however, further dilution to 80 and 100 volumes, did not increase the *ee*; rather, it decreased to 88% and 86%, respectively(Table 2, entry 31 and 32). Thus, 60 volume of THF was chosen as the optimal solvent volume. Simultaneously, the optimal temperature of the reaction was determined. When the reaction temperature was increased to 45–50 °C (Table 2, entry 33) from room temperature (Table 2, entry 18), the *ee* change in a short reaction time was insignificant (86% *ee*). However, when the reaction temperature was decreased to 4 °C, the *ee* was considerably improved (91%, Table 2, entry 34). When the reaction temperature was further reduced to −25 °C (Table 2, entry 35), the *ee* improved by merely 1% with an extended reaction time (35 h). Without further decreasing the reaction temperature, −25 °C was chosen to be the optimal temperature of the reaction.

At this optimal temperature, benzaldehyde (1 equiv.) reacted with $[FeCl(SBAIB\text{-}d)]_2$ (5 mol%), TEA (1 equiv.) and dibutyl phosphite (1.1 equiv.) in THF (60 volume) under aerobic conditions to afford dibutyl hydroxy(phenyl)methanephosphonate in an excellent *ee* (93%) and yield (99%) in 35 h (Table 2, entry 36). Thus, this was selected as the optimal set of reaction conditions to explore the $[FeCl(SBAIB\text{-}d)]_2$-catalyzed enantioselective hydrophosphonylation of various aldehydes.

Table 3. Enantioselective hydrophosphonylation of various aldehydes using $[FeCl(SBAIB\text{-}d)]_2$.[a]



Entry	Aldehyde	Product	Time [h]	Yield [%][b,d]	*ee* [%][c,d]	Sign/Configuration[g]
1	PhCHO **28**	**28a**	35	86 (99)	96 (93)	+/*R*
2	4-$MeOC_6H_4CHO$ **29**	**29a**	72	81 (90)	>99 (95)	+/*R*
3	3-$MeOC_6H_4CHO$ **30**	**30a**	55	99[e]	91	+/*R*
4	2-$MeOC_6H_4CHO$ **31**	**31a**	72	83 (92)	95 (85)	+/*R*
5	4-PhC_6H_4CHO **32**	**32a**	50	85 (97)	99 (88)	+/*R*
6	4-$Me_2NC_6H_4CHO$ **33**	**33a**	72	77 (87)	>99 (94)	+/*R*
7	4-MeC_6H_4CHO **34**	**34a**	60	86 (99)	93 (88)	+/*R*
8	3-MeC_6H_4CHO **35**	**35a**	60	83(99)	92 (85)	+/*R*
9	2-MeC_6H_4CHO **36**	**36a**	60	88 (99)	92 (83)	+/*R*
10	4-FC_6H_4CHO **37**	**37a**	48	80(90)	91 (83)	+/*R*
11	4-BrC_6H_4CHO **38**	**38a**	48	90[e]	85	+/*R*
12	2-naphthaldehyde **39**	**39a**	55	79 (93)	>99 (88)	+/*R*
13	pyrrole-2-carboxaldehyde **40**	**40a**	72	86[e]	87	+/*R*
14	furfural **41**	**41a**	72	91[e]	84	+/*R*
15	thiophene-2-carboxaldehyde **42**	**42a**	73	92[e]	89	+/*R*
16	α-methyl-*trans*-cinnamaldehyde **43**	**43a**	72	70 (80)	>99 (89)	+/*R*
17	butyraldehyde **44**	**44a**	96	90[e]	83[f]	−/*R*
18	valeraldehyde **45**	**45a**	90	94[e]	79[f]	−/*R*

[a] The reactions were carried out with reagent ratio of $RCHO:HP(O)(OBu)_2:[FeCl(SBAIB\text{-}d)]_2:TEA = 1:1.1:0.05:1$
[b] Yields obtained after a single recrystallization from hexane/ether.
[c] The chiral purity of the compound after a single recrystallization from ether/hexane that checked by HPLC using Chiralcel OD-H and Chiralpak AD columns.
[d] Values in parenthesis are before recrystallization.
[e] Physical state of the product is an oil.
[f] The chiral purity was determined for the corresponding benzoates.
[g] Configuration was assigned on the basis of a thorough literature survey.

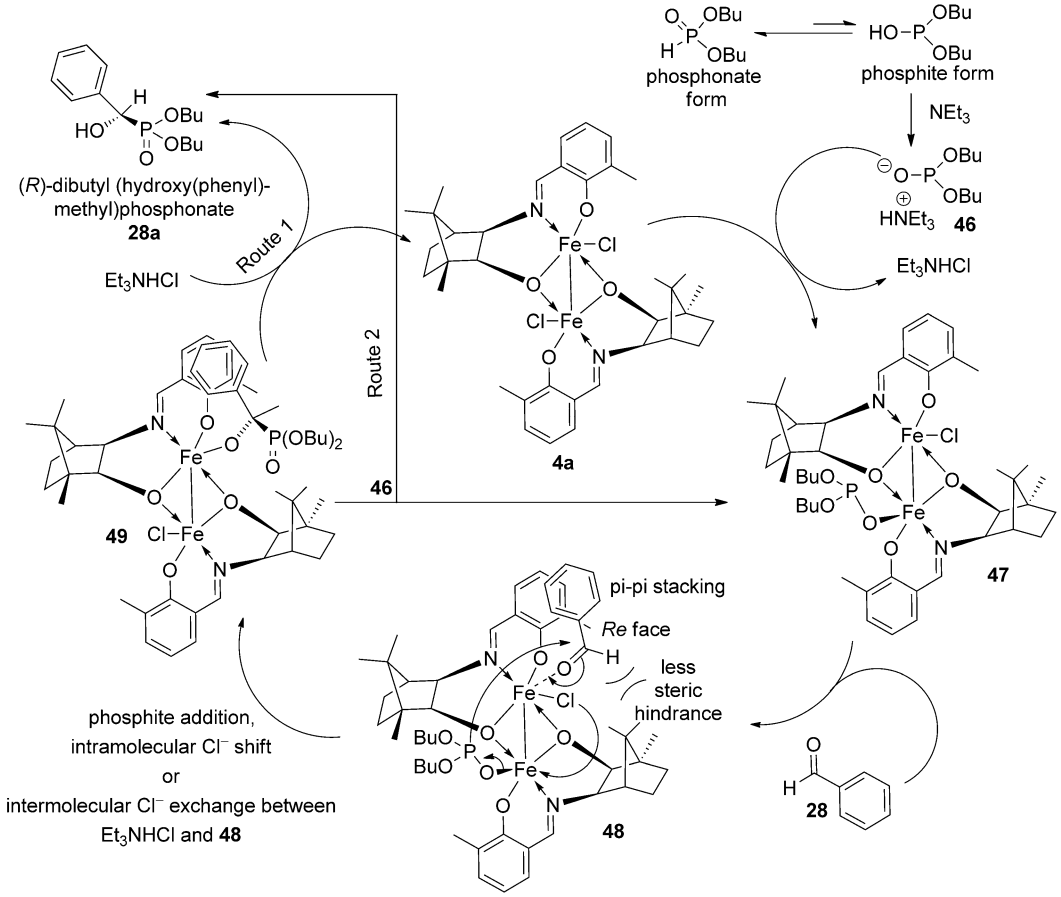
Scope of this Catalytic System for Other Aldehydes

Table 3 shows the result of the hydrophosphonylation of various aldehydes under our optimal conditions. All of the aldehydes rendered adequate to excellent yields (up to 99%) of α-hydroxy phosphonates and an excellent *ee* (up to 99%). The aromatic aldehydes possessing a strong electron-donating group at the *para*-position showed a high enantioselectivity; for instance, 4-methoxybenzaldehyde (**29**) and 4-*N,N*-dimethylaminobenzaldehyde (**33**) showed a 95% *ee* for **29a**, and a 94% *ee* for **33a**, respectively (Table 3, entries 2 and 6). Electron-withdrawing halogen substituents slightly reduce the enantioselectivity (Table 3, entries 10 and 11). However, most of the obtained aromatic phosphonates **28a**–**38a** were solids or low-melting point solids except for **30a** and **38a**; an excellent enantioselectivity was induced by recrystallization from the ether-hexane solvent mixture at either room temperature or low temperature. A polycyclic aromatic aldehyde, (i.e., 2-naphthaldehyde **39**) is also a suitable substrate that renders **39a** in high *ee* (88%), and its recrystallization produced the highest *ee* (> 99%) without substantially reducing the yield. The heteroaromatic aldehydes **40**, **41**, and **42** were also adequate substrates for the present catalytic system, all of which afforded **40a**, **41a**, and **42a** in high *ee* (84–89%, Table 3, entries 13–15). In addition, *N*-non-protected pyrrole-2-carboxaldehyde (**40**) was a new substrate for the hydrophosphonylation reaction. The α,β-unsaturated aldehyde, *trans*-α-methylcinnamaldehyde (**43**), was also examined, found to be a suitable substrate for this reaction, and produced highly enantioselective (>99% *ee*) phosphonate **43a**. Good to excellent enantioselectivities were also observed for the aliphatic aldehydes **44** and **45**.

Proposed Mechanism for Chiral Induction

The configuration of obtained phosphonates was assigned as *R* by conducting a detailed comparison study with the corresponding analogues.[11] The most probable mechanism is proposed for the **4a**-catalyzed enantioselective hydrophosphonylation of benzaldehyde in Scheme 2. It was suspected to be a bimetallic process, which was supported by the study of nonlinear effect (NLE) with various % *ee* of **4a**.

This catalytic system found to have a (−) NLE (see the Supporting Information). The catalytic cycle begins by substituting one of the chloride ions on **4a** by a phosphite anion **46**, which could be easily gener-



Scheme 2. Proposed mechanism for **4a**-catalyzed asymmetric hydrophosphonylation.

ated through a reaction of TEA with the highly reactive phosphite form of the equilibrium mixture of phosphonate and phosphite to produce an intermediate **47**. Subsequently, the benzaldehyde coordinates to another Lewis acidic iron in the manner shown in **48**. Presumably, **48** is a favorable intermediate because of the presence of π-π stacking between the phenyl rings of benzaldehyde and one of the Schiff base phenyl rings. In addition, **48** displays less substantial steric hindrance between the phenyl ring of the benzaldehyde and the bridgehead methyl and the bridge dimethyl group of the camphor moiety. The addition of the phosphite group on the *Re*-face of the benzaldehyde, concurrent formation of the Fe−O bond, and the chloride shift from one Fe to another produces intermediate **49**. The chloride shift would possibly happen by both intramolecular or by intermolecular chloride exchange between **48** and triethylammonium chloride generated from step 1. Consequently, the (*R*)-dibutyl hydroxy(phenyl)methanephosphonate **28a** is easily obtained from **48** by two routes: the one by abstracting the proton from triethylammonium chloride, regeneration of **4a** and the other by reaction with phosphite anion **46** and regeneration of intermediate **47**.

Conclusions

In conclusion, we have synthesized new camphor-based Fe(III)-Schiff base complexes derived from aminoisoborneol and implemented an catalytic asymmetric hydrophosphonylation reaction. In the optimized reaction conditions, 5 mol% of **4a** was determined to be the optimal catalyst for producing hydrophosphonylation products in good to excellent levels of enantioselectivity (up to 99%) and in excellent yields (up to 99%) for various aldehydes. The catalytic systems used in this study provide several advantages. The Schiff base ligands are easily synthesizable in a few steps by using an inexpensive starting materials (1*R*)-camphor. Iron sources were $FeCl_3$, which is also inexpensive. The synthesized Fe(III)-SBAIB complexes, which are air- and moisture-stable, can be used under aerobic reaction conditions. The optimal reaction conditions are extremely practical. The starting materials can be stirred in a vial and preventing exposure to air and moisture is not required. The catalytic system produced a high *ee* level for various aromatic, polycyclic aromatic, heteroaromatic, α,β-unsaturated, and aliphatic aldehydes. Furthermore, $[FeCl(SBAIB\text{-}d)]_2$ is the first iron-Schiff base complex that affords a high level of *ee* for the hydrophosphonylation reaction. A detailed literature survey comparison provided additional useful information for assigning the configuration of the α-hydroxy phosphonates. The possible bimetallic catalytic cycle mechanism is proposed. The applications of this catalytic system to other substrates, such as ketones and imines, is currently under study.

Experimental Section

General Procedure for Synthesis of Iron(III) Complexes $[FeCl(SBAIB)]_2$

A mixture of anhydrous $FeCl_3$ (1.2 equiv.) and (+)-SBAIB (1 equiv,) in THF (75 volumes) was stirred under an argon atmosphere for 1 h at room temperature. Subsequently, to this mixture the triethylamine (2.5 equiv) was added, and stirred for 12 h at room temperature. The THF was evaporated; water was added and extracted with DCM (5 times). The combined DCM layer was dried over anhydrous Na_2SO_4 and concentrated to afford a brownish-black solid.

General Procedure for Synthesis of Dialkyl Phosphites

To an ice-cooled solution of trialkyl phosphite (10 g, 1 equiv.) in THF (30 mL) was added a mixture of water (1 equiv.) in THF (5 mL) under an argon atmosphere. The resulting solution was stirred for overnight, at either room temperature or reflux. Subsequently, the evaporation of the THF by using a rotary evaporator and high-vacuum distillation afforded the dialkyl phosphite as a colorless liquid.

General Procedure for Catalytic Enantioselective Hydrophosphonylation using 4a

Dibutyl phosphite (**25**, 1.1 equiv.) was added to a stirred THF (60 volumes) solution of $[FeCl(SBAIB\text{-}d)]_2$ **4a** (0.05 equiv., 5 mol%) and TEA (1 equiv.) in an 8-mL screw-capped vial and stirred for 1 h. The reaction mixture was cooled to −25 °C for 15 min, aldehyde (1 equiv., 100 mg) was added, and the mixture was continually stirred at the same temperature for the mentioned time (Table 3). Subsequently, the THF was evaporated to obtain a residue that was purified using column chromatography. The reported yields are for products purified by column chromatography and the *ee* of the obtained products were verified before and after recrystallization from ether/hexane through the chiral HPLC by using Chiralcel OD-H, and Chiralpak AD columns.

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[9] Recently, in Taiwan, many of the phosphorus compounds have been banned by UN due to considerations of safety and environment pollution, therefore, chemicals that are needed for research, must be prepared in laboratory from the available resources. Diisopropyl phosphite was available, and we synthesized dibutyl, diethyl and dimethyl phosphites from available trialkyl phosphites. We have also synthesized bis(2,2,2-trifluoroethyl) phosphite **27** from 2,2,2-trifluoroethanol under the reported reaction conditions: S. D. Broady, J. E. Rexhausen, E. J. Thomas, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1083–1094.

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[11] Refer to the Supporting Information for the detailed literature survey to assign the configurations of the obtained phosphonates.

Catalytic Enantioselective Hydrophosphonylation of Aldehydes Using the Iron Complex of a Camphor-Based Tridentate Schiff Base $[FeCl(SBAIB\text{-}d)]_2$

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