Platinum-Catalyzed Enantioselective Aldol Addition of Ketene Silyl Acetals to Aldehydes

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Abstract: The first platinum-catalyzed enantioselective aldol reactions are reported. The catalysts are generated from chiral bisphosphine platinum acyl complexes by activation with noncoordinating or weakly coordinating strong acids and can be used to catalyze the enantioselective aldol addition of ketene silyl acetals to various aldehydes. The presence of oxygen and water during catalyst activation is required to obtain enantioselectivity. The enantioselectivities observed in the cases of aliphatic primary aldehydes are more than 90% enantiomer excess. IR and ^{31}P NMR spectroscopies were used to demonstrate the intermediacy of C-bound platinum enolate in the aldol process.

Introduction

Enantioselective aldol addition reactions are one of the most important methodologies utilized for the construction of asymmetric carbon−carbon bonds.[1] Two major approaches have been developed for the catalytic variants of this reaction. One is to employ chiral Lewis acids to activate the carbonyl compounds toward the addition of preformed latent enolates such as enol silanes. The other is to utilize chiral transition metal complexes and latent enolates to generate transition metal enolates as catalytic intermediates. Concerning the former approach, significant progress has been made in recent years.[2,3] On the other hand, the number of examples reported on aldol addition reactions involving transition metal enolates is rather limited.[4,5]

Late transition metal complexes generally show remarkable activities as Lewis acids (once they are converted to cationic form)[6,7] and may also have the potential to be metal enolate precursors.[4,8] For example, there are excellent works utilizing copper(II) complexes as Lewis acids reported by Evans[9] and a recent report by Carreira regarding the copper(II) enolate mediated asymmetric addition of dienolate to aldehydes.[5] As part of an ongoing project directed toward the development of useful catalysts for potential industrial applicability, we investigated the possibilities of platinum(II) cationic complexes serving as either Lewis acids or metal enolate precursors for catalytic enantioselective aldol reactions. Although cationic Pt complexes are known to behave as very strong Lewis acids,[10] there are no examples of the application of these complexes to reactions mediated by Lewis acids. In this paper, we report the first example of platinum-catalyzed enantioselective aldol reactions, which are considered to be mediated by platinum C-enolates. The scope and limitations of this new process will be discussed.

Results and Discussion

Preparation of the Catalyst Precursors. Platinum cationic species such as platinum triflate(II) or platinum tetrafluoborate-(II) are generally derived from K_2PtCl_4 in three steps:[11] (1) synthesis of Pt(diene)Cl_2 complexes; (2) replacement of the dienes by the desired ligands (like phosphines); and (3) halogen exchange reaction with silver salts of noncoordinating or weakly coordinating strong acids (Scheme 1). This multistep synthesis is relatively easy to perform on a laboratory scale, but several difficulties arise during large scale production. In particular, the stoichiometric use of silver salts in the last step raise the cost of catalysts for industrial processes. (The product AgCl can be recovered and converted to AgOTf or $AgBF_4$, but these additional processes also result in higher costs.)

(1) For a review of asymmetric aldol addition reactions, see: (a) Group I and II enolates: Heathcock, C H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock C. H., Eds.; Pergamon: New York, 1991; Vol. 2, pp 181−238. (b) Group III enolates: Kim, B. M.; Williams, S. F.; Masamune, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon: New York, 1991; Vol. 2, pp 239−275. (c) Transition metal enolates: Paterson, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock C. H., Eds.; Pergamon: New York, 1991; Vol. 2, pp 301−319.

(2) For a review of Lewis acid-catalyzed asymmetric aldol additions of latent enolates, including Lewis basic catalysts, see: Nelson, S. G. *Tetrahedron: Asymmetry* **1998**, *9*, 357−389.

(3) Recently, direct catalytic asymmetric aldol reactions were reported, see: Yamada, Y. M. A.; Yoshikawa, N.; Sasai, H.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1871−1873.

(4) Palladium: (a) Hagiwara, E.; Fujii, A.; Sodeoka, M. *J. Am. Chem. Soc.* **1998**, *120*, 2474−2475. (b) Sodeoka, M.; Tokunoh, R.; Miyazaki, F.; Hagiwara, E.; Shibasaki, M. *Synlett* **1997**, 463−466. (c) Sodeoka, M.; Ohrai, K.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 2648−2649.

(5) Copper: Krüger, J.; Carreira, E. M. *J. Am. Chem. Soc.* **1998**, *120*, 837−838.

(6) (a) Corey, E. J.; Imai, N.; Zhang, H. Y. *J. Am. Chem. Soc.* **1991**, *113*, 728−729. (b) Khiar, N.; Fernandez, I.; Alcudta, T. *Tetrahedron Lett.* **1993**, *34*, 123−126.

(7) (a) Evans, D. A.; Murry, J. A.; Matt, P.; Norcross, R. D.; Miller, S. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 798−800. (b) Evans, D. A.; Miller, S. J.; Lectka, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460−6461. (c) Evans, D. A.; Lectka, T.; Miller, S. J. *Tetrahedron Lett.* **1993**, *34*, 7027−7030.

(8) Slough, G. A.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, *111*, 938−949.

(9) (a) Evans, D. A.; Kozlowski, M. C.; Burgey, C. S.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **1997**, *119*, 7893−7894. (b) Evans, D. A.; Murry, J. A.; Kozlowski, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 5814−5815.

(10) (a) Longato, B.; Corain, B.; Bonora, G. M.; Pilloni, G. *Inorg. Chim. Acta* **1987,** *137*, 75−79. (b) Longato, B.; Pillioni, G.; Valle, G.; Corain, B. *Inorg. Chem.* **1988**, *27*, 956−958.

(11) Stang, P. J.; Cao, D. H.; Saito, S.; Arif, A. M. *J. Am. Chem. Soc.* **1995**, *117*, 6273−6283. See also ref 10.

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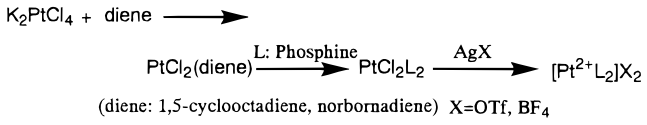
Scheme 1



To avoid these problems, we selected platinum(II) acyl complexes derived from salicylaldehyde and 2 equiv of tertiary phosphines as candidates for the catalyst precursors. These chelating acyl platinum(II) complexes were first reported by Pregosin[12] and possess several attractive features. First, they can be synthesized from commercially available starting materials in a single step. Second, they can be easily handled due to their stability toward air and moisture. Finally, the corresponding platinum cationic species are easily generated by the treatment with noncoordinating or weakly coordinating strong acids.[13] Despite these attractive features, applications of these complexes to organic synthesis have been primarily limited to the oxidation reactions developed by Strukul and co-workers.[13]

We anticipated that these complexes, once transformed to a cationic species, would be active catalysts for enantioselective aldol reactions as either Lewis acids or metal enolate precursors. To investigate these possibilities, a variety of Pt complexes were synthesized (Figure 1, Scheme 2).

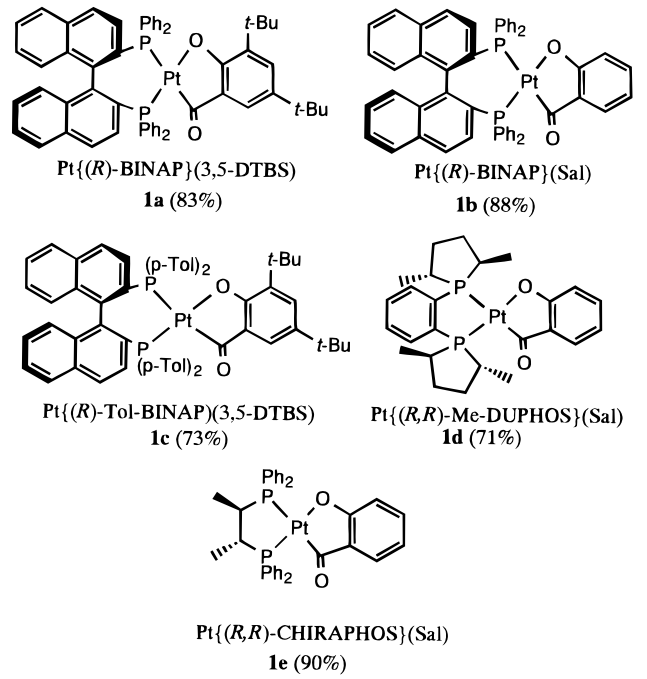


Figure 1. Catalyst precursors (isolated yields are shown in parentheses).

Enantioselective Aldol Addition of Ketene Silyl Acetals to Aldehydes. When complex **1a** (5 mol %) was activated by the addition of HOTf (5 mol %) in dry CH_2Cl_2 under Ar, the resulting solution catalyzed the reaction between methyl trimethylsilyl dimethylketene acetal and benzaldehyde at −25 °C in 16 h. The desired aldol product was obtained in 99% yield. We chose triflic acid because it can be easily handled and obtained as neat. To avoid the influences of residual acid, 2,6-lutidine was added as a proton scavenger.[14,15] The complexes did not catalyze the reaction without activation by triflic acid. Although the reaction proceeded cleanly and very efficiently, the enantiomer excess observed for the product was 0%.

After examining various reaction and activation conditions, we discovered that the conditions under which **1** was activated have significant effects on asymmetric induction. For example, when the activation of complex **1a** was conducted in the presence of oxygen (i.e. air), the reaction proceeded to yield a product with an enantiomer excess of 35%! Furthermore, addition of 2 equiv of water to the Pt complex in the presence of oxygen increased the enantiomer excess to 59%.

When hydrocinnamaldehyde was used as substrate, only 16% ee was observed for the reaction product when the catalyst was activated under Ar in dry CH_2Cl_2. This was improved to 77% ee when the activation was carried out under air in dry CH_2Cl_2, and an enantiomer excess of 95% was realized when the activation was carried out under air in the presence of 2 equiv of water. Water itself improved the enantioselectivity to a small extent (3−5% ee), but excess water resulted in the deactivation of the catalyst.

The presence of oxygen is only required in the catalyst activation stage, and replacement of the reaction atmosphere by Ar after activation slightly improved the enantiomer excess of the product (3−5% ee). Activation of the catalyst under Ar followed by exposure to air resulted in the loss of reactivity as well as the loss of enantioselectivity.

After establishment of the optimized activation conditions, a series of complexes are screened with benzaldehyde as a substrate, which enabled rapid screening (Table 1, entries 1 and 3−6). The best results were obtained with **1a** and **1b**. The difference in the substitution patterns on the salicyl group seemed to have almost no effect on the reaction. Various aldehydes were also screened as reaction substrates with **1a** and **1b** as catalyst precursors. The results are shown in Table 1.

Aromatic and α,β-unsaturated aldehydes showed almost the same reactivities and degrees of enantioselectivities. Primary aliphatic aldehydes showed high enantioselectivities around 90% ee. Though the reaction rate became slower, a 70−80% conversion of the starting aldehydes was observed in 20 h at −25 °C, and around 90% conversion was observed in 40 h. On the contrary, secondary and tertiary aldehydes showed almost no reactivity under these conditions.

The reaction temperature has significant effects on the reaction rate and enantioselectivity. Reactions were faster at 0 °C, but enantioselectivity diminished more than 20% in enantiomer excess (entries 2 and 10). Reactions were too sluggish to proceed at −78 °C.

As previously mentioned, addition of base to scavenge trace amounts of acid is critical in maintaining the high enantiomer excess. Without addition of base, the reaction proceeded very rapidly, but resulted in diminished enantioselectivity (entry 11). It is most likely that a catalytic amount of trimethylsilyltriflate was formed and catalyzed the nonstereoselective aldol reaction.[16,17]

(12) (a) Anklin, C.; Pregosin, P. S.; Bachechi, F.; Mura, P.; Zambonelli, L. *J. Organomet. Chem.* **1981**, *222*, 175−185. (b) Motschi, H.; Pregosin, P. S.; Ruegger, H. *J. Organomet. Chem.* **1980**, *193*, 397−405.

(13) (a) Baccin, C.; Gusso, A.; Pinna, F.; Strukul, G. *Organometallics* **1995**, *14*, 1161−1167. (b) Gusso, A.; Baccin, C.; Pinna, F.; Strukul, G. *Organometallics*, **1994**, *13*, 3442−3451.

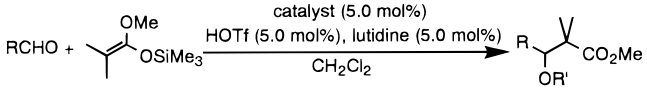
(14) (a) Singer, R. A.; Carreira, E. M. *J. Am. Chem. Soc.* **1995**, *117*, 12360−12361. (b) Carreira, E. M.; Lee, W.; Singer, R. A. *J. Am. Chem. Soc.* **1995**, *117*, 3649−3650.

(15) HOTf (5.0 mol %) catalyzed the reaction to be completed at −78 °C in 30 min.

(16) The aldol addition of ketene silyl acetals to aldehydes is catalyzed by silyl triflates. See: Carreira, E. M.; Singer, R. A. *Tetrahedron Lett.* **1994**, *35*, 4323−4326.

(17) Similer formation of trimethylsilyl tetrafluoborate is reported in ref 4a.

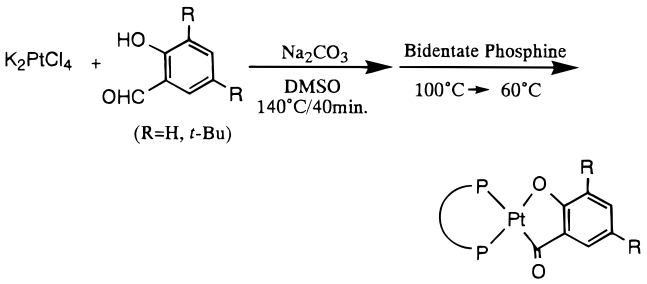
Table 1. Platinum-Catalyzed Enantioselective Aldol Addition of Ketene Silyl Acetal to Aldehydes[a]



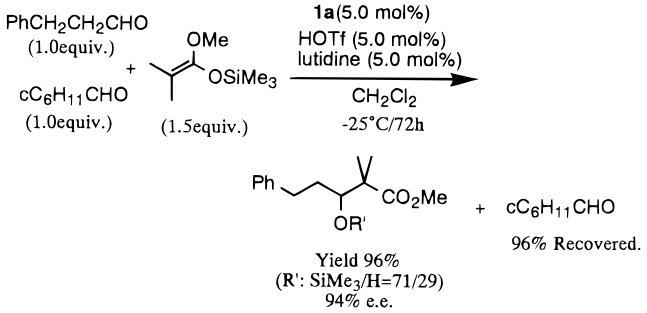
entry	RCHO	catalyst	temp (°C)/time (h)	yield (%)[b]	R′:SiMe$_3$/H[c]	ee[d–f]
1	PhCHO	**1a**	−25/21	99 (99)	65/35	59
2			0/19	99 (99)	82/18	30
3		**1b**	−25/19	99 (99)	82/18	56
4		**1c**	−25/17.5	97 (95)	75/25	26
5		**1d**	−25/20.5	99 (99)	71/29	41
6		**1e**	−25/27	82 (85)	86/14	10
7	(*E*)-PhCH═CHCHO	**1a**	−25/144	90 (86)	65/35	46
8		**1b**	−25/143	92 (94)	84/16	46
9	PhCH$_2$CH$_2$CHO	**1a**	−25/168	94 (96)	51/49	95
10			0/17	95 (96)	90/10	74
11[g]			−78 to −25/5	94 (93)	72/28	43
12		**1b**	−25/170	96 (95)	84/16	91
13	(CH$_3$)$_2$CHCH$_2$CHO	**1a**	−25/140	92 (87)	55/45	91
14		**1b**	−25/144	99 (98)	91/9	90
15	(CH$_3$)$_3$CCH$_2$CHO	**1a**	−25/171	96 (94)	82/18	88
16		**1b**	−25/171	66 (77)	94/6	80
17	cC_6H_{11}CHO	**1a**	−25/98	(7)	65/35	ND[h]
18		**1b**	−25/98	(5)	>99/1	ND[h]
19	t-BuCHO	**1a**	−25/120	NR[i]		ND[h]
20		**1b**	−25/120	NR[i]		ND[h]

[a] Catalyst activation and substrates addition was performed under air, then the reaction was performed under Ar (H_2O equivalent to Pt = 2.0). [b] Isolated yield, yields in parentheses are determined by GC. [c] Determined by GC. [d] Observed ee values for R′ = SiMe$_3$ and R′ = H were identical. [e] ee values for R′ = SiMe$_3$ were determined by chiral HPLC (CHIRALPAK-AD, Daicel Co.) after deprotection by TBAF. [f] ee values for R′ = H were determined by chiral HPLC (CHIRALPAK-AD, Daicel Co.). [g] Lutidine was not added. [h] Not determined. [i] No reaction.

Scheme 2. Preparation of Catalyst Precursors



Scheme 3. Chemoselective Asymmetric Aldol Reaction



Taking advantage of the reactivity differences outlined above, a chemoselective asymmetric aldol addition was performed. In the presence of both primary and secondary aliphatic aldehydes, only the primary aldehyde was selectively reacted to give the desired aldol product in 94% ee and 96% yield, while the secondary aldehyde was recovered unchanged (Scheme 3).

NMR Studies and Mechanistic Considerations. NMR studies were conducted, together with the synthesis and reactivity trials of known authentic platinum cationic complexes, to elucidate the nature of the reactive species involved in this system.

(1) Effect of O_2 and Water on the Activation of Complex 1. To observe the activation process of complex **1** by TfOH, three NMR experiments were conducted with complex **1a**. Sample a was prepared in dry CD_2Cl_2 and the activation process was carried out under an N_2 atmosphere. Sample b was prepared in dry CD_2Cl_2 and the activation process was carried out in an atmosphere of air. Sample c was prepared in wet CD_2Cl_2 (containing 2 equiv of water to complex **1a**) and the activation process was carried out under air.

Very rapid conversion of starting complex **1a** was observed in sample c and evolution of a new phosphine−platinum species (complex **A**) was observed by ^{31}P NMR at δ 3.25 (J_{Pt-P} = 3674 Hz). Figure 2 shows ^{31}P NMR spectra of **1a** and complex **A**. In sample b, the conversion of starting **1a** is much slower but after a long period of time (22 h) it became almost identical to the spectrum of sample c. In the case of sample a, the conversion of the starting **1a** was very slow and complex **A**, observed in the case of samples b and c, was never observed. NMR samples b and c were used in sample reactions. Reactions proceeded without any problem with these NMR sample solutions and nearly the same reactivity and enantioselectivity were observed. We have concluded that platinum phosphine complex **A** is the actual catalytic species, that the presence of oxygen is necessary for its formation, and that the presence of water accelerates the rate of its formation.[18] The salicylaldehyde part of **1a** was transformed and observed as 2,4-di-*tert*-butylphenol by ^{1}H NMR, consistent with the activation scheme shown in Scheme 4 (as suggested by Strukul and co-workers).[13]

The exact nature of complex **A** is still unknown, since we could not isolate the complex. However, judging from the Pt−P coupling constant and symmetric nature of the complex (only one phosphorus peak was observed), we assume that complex **A** has an OH group in the position trans to the phosphorus.[19] We synthesized two known platinum cationic complexes [Pt((*R*)-BINAP)(H_2O)][OTf]$_2$ (**2**)[20] and [Pt((*R*)-BINAP)(μ-OH)]$_2$(BF_4)$_2$(**3**),[19,21] which are considered to be similar to complex

(18) The exact role of oxygen and water is still under investigation.

(19) Strukul, G.; Varagnolo, A.; Pinna, F. *J. Mol. Catal. A: Chem.* **1997**, *117*, 413−423.

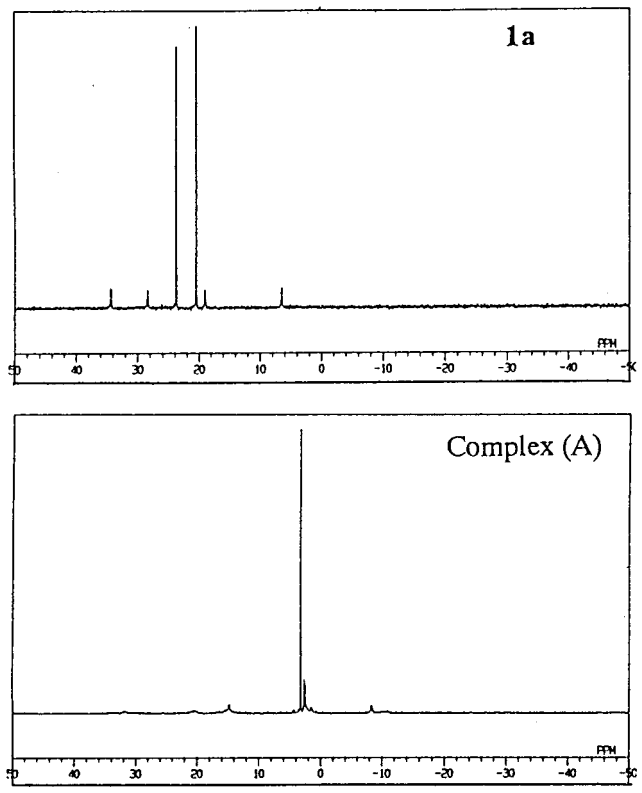
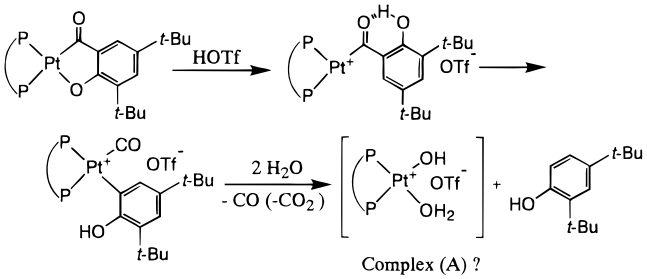


Figure 2. ^{31}P NMR of **1a** in CD_2Cl_2 (top) and complex **A** (bottom).

Scheme 4



A, and tested their reactivities in aldol addition reactions. The results are shown in Table 2.

Complex **2** catalyzed the reaction efficiently, but the resultant product was racemic. Complex **3** catalyzed the reaction but with a much lower activity and a low level of enantioselectivity. Thus, complex **A** appears to be a different platinum species. There is a possibility that the phosphine ligand (BINAP) was oxidized to form the corresponding phosphine oxides (i.e. BINAP dioxide[22] or BINAP monoxide[23]); however, they were not observed by the ^{31}P NMR monitoring of the activation process.

(2) The Role of Platinum Complex A as a Lewis Acid or a Platinum Enolate Precursor. To elucidate the role of complex **A**, 3 equiv of hydrocinnamaldehyde were added to the CD_2Cl_2 solution of complex **A** at room temperature. However, no change of the chemical shifts of the aldehyde was observed by ^{1}H and ^{13}C NMR, and no change was observed for complex **A** by ^{31}P NMR. If complex **A** has a Lewis acidic nature, it is likely that a change would be observed for one or more of these chemical shifts. Therefore, it is unlikely that complex **A** is acting as a Lewis acid.

Next, methyl trimethylsilyl dimethylketene acetal (KSA) was added to the CD_2Cl_2 solution of complex **A** at room temperature. With addition of up to 3 equiv of KSA, no change in complex **A** was observed by ^{1}H or ^{31}P NMR and little hydrolysis of the KSA was observed. But the addition of excess KSA (10 equiv) resulted in the formation of a new Pt−phosphine complex (complex **B**) in the ^{31}P NMR spectrum that has two nonequivalent phosphorus shifts at δ 26.8 and 9.5. These resonances have a common phosphorus−phosphorus coupling constant (J_{P-P} = 19 Hz) and platinum−phosphorus coupling constants of J_{Pt-P} = 1904, and 4789 Hz, respectively. The amount of complex **B** increased over time and after addition of another 18 equiv of KSA, complex **A** was completely consumed and exclusive formation of complex **B** was observed (Figure 3). ^{1}H NMR was not informative as many small ambiguous peaks started to appear.

It is reasonable to assume that complex **B** is a platinum enolate, as this is formed by the reaction of complex **A** and KSA (excess). However, there could be possibilities of the O-bound enolate (**4a,b**), or the C-bound enolate (**5a,b**) for complex **B** (Figure 4).

In the case of the O-bound enolate, the J_{Pt-P} observed for the trans position of the enol alkoxide should be larger than 4000 Hz.[24] As the other coordination site is considered to be occupied by OH or the chelating methoxy group of the enolate, the other J_{Pt-P} also should be larger than 3700 Hz.[25] In this way, the assumed structure for the O-bound enolate could not account for the ^{31}P NMR spectrum of complex **B**. On the other hand, in the case of the C-bound enolate, the J_{Pt-P} observed for the δ 26.8 peak (1904 Hz) is within the typical J_{Pt-P} values for the phosphorus trans to the Pt−C σ-bond (1800−2000 Hz).[26,27] The other peak at δ 9.5 (J_{Pt-P} = 4789 Hz) could be the other phosphorus trans to OH or chelating carbonyl group. According to the ^{31}P NMR data for platinum homoenolate, C-bound enolate,[26] and BINAP dimethyl complex,[27] we feel it reasonable to assume that complex **B** is C-bound enolate **5a** or **5b**.

In addition, we observed a strong infrared stretching absorption at 1594 cm^{-1}, which is consistent with the organic carbonyl absorption strongly chelating to platinum, supporting the C-bound enolate structure **5b**.[26,28]

The proposed catalytic cycle of the asymmetric reaction is shown in Scheme 5. The requirement for excess KSA *to generate complex* **B** for the successful enantioselective aldol reaction is also confirmed by the following experiments.

When the reaction was carried out with 2 equiv of hydrocinnamaldehyde and 2.8 equiv of methyl trimethylsilyl dimethylketene acetal, the reaction did not proceed even with

(20) Stang, P. J.; Olenyuk, B.; Arif, A. M. *Organometallics* **1995**, *14*, 5281−5289.

(21) Since a very small amount of μ-OH by integration compared with aromatic protons was observed by ^{1}H NMR of complex **A** at δ = −0.65 ppm, the structure of **A** is not the μ-OH bridged binuclear platinum hydroxy complex like **3**.

(22) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S. *J. Org. Chem.* **1986**, *51*, 629−635.

(23) Ozawa, F.; Kubo, A.; Hayashi, T. *Chem. Lett.* **1992**, 2177−2180.

(24) The phosphorus trans to alkenoxy (aryloxy) groups have J_{Pt-P} of 4100−4600 Hz. See refs 12b and 13b.

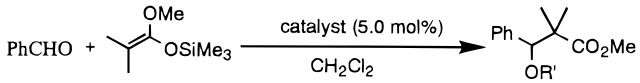
(25) The typical J_{Pt-P} value for the phosphorus trans to hydroxyl group is 3600−4000 Hz. See ref 19 and related references cited therein.

(26) Mhinzi, G. S.; Crascall, L. E.; Spencer, J. L. *Inorg. Chim. Acta* **1997,** *265*, 83−87.

(27) Nozaki, K.; Sato, N.; Tonomura, Y.; Yasutomi, M.; Takaya, H.; Hiyama, T.; Matsubara, T.; Koga, N. *J. Am. Chem. Soc.* **1997**, *119*, 12779−12795.

(28) After confirmation of the formation of complex **B**, solvents, excess KSA, and hydrolyzed methyl isobutyrate were removed in vacuo and residual solid was analyzed by IR. Very weak absorption at 1605 cm^{-1} from 2,4-di-*tert*-butylphenol seemed to be overlapped by this strong C=O absorption.

Table 2. Aldol Reaction by Platinum Cation Complexes



entry	catalyst	additive	temp (°C)/time (h)	yield (%)[a]	R′:$SiMe_3$/H[b]	ee[c−e]
1	[Pt((*R*-BINAP)(H_2O)][$OTf]_2$	none	−78/0.5	99 (99)	91/9	4
2		lutidine (5.0 mol %)	−25/17	99 (99)	98/2	4
3	[Pt((*R*-BINAP)(μ-OH)]$_2$(BF_4)$_2$	none	−25/18	27 (32)	54/44	16
4		lutidine (5.0 mol %)	−25/20	11 (10)	52/48	20

[a] Isolated yield, yields in parentheses are determined by GC. [b] Determined by GC. [c] Observed ee values for R′ = $SiMe_3$ and R′ = H were identical. [d] ee values for R′ = $SiMe_3$ were determined by chiral HPLC (CHIRALPAK-AD, Daicel Co.) after deprotection by TBAF. [e] ee values for R′ = H were determined by chiral HPLC (CHIRALPAK-AD, Daicel Co.).

catalyst loadings as high as 50 mol %. GC analysis showed no conversion of either aldehyde or ketene silyl acetal. By increasing the KSA amount to 28 equiv, reaction ensued and after 69 h yielded the product in quantitative yield and 95% ee.

Conclusion

Chiral bisphosphine platinum acyl complexes generate useful catalysts for the enantioselective aldol addition of ketene silyl acetal to various aldehydes via activation with noncoordinating or weakly coordinating strong acids. The presence of oxygen and water significantly improves the enantioselectivity and in the cases of aliphatic primary aldehydes, an enantiomer excess of more than 90% is realized. The reaction is sensitive to the substitution pattern of the substrate aliphatic aldehydes and only primary aldehydes are capable of reaction with the current system. The reaction is proposed to be mediated by a C-bound platinum enolate, based on ^{31}P NMR and IR spectroscopic data. The platinum species are not acting as Lewis acids. Further studies concerning the reaction intermediates, the addition mode of platinum−enolate and aldehydes, the improvement of enantiomer excess, and the development of improved catalyst systems are currently underway.

Experimental Section

General Methods. ^{1}H NMR spectra were recorded on a JEOL GX270 spectrometer or a EX400 spectrometer at ambient temperature. Data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale) with the solvent resonance employed as an internal standard (CD_2Cl_2 at δ 5.31, C_6D_6 at δ 7.15, $CDCl_3$ at δ 7.26), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (Hz), integration, and assignment.

^{13}C NMR spectra were recorded on a JEOL GX270 spectrometer or a EX400 spectrometer at ambient temperature. ^{13}C NMR chemical shifts are reported in parts per million downfield from tetramethylsilane (δ scale) with the solvent resonance employed as an internal standard (C_6D_6 at δ 128.0, $CDCl_3$ at δ 77.0). All ^{13}C NMR spectra were determined with complete proton decoupling.

^{31}P NMR spectra were recorded on a JEOL EX400 spectrometer at ambient temperature. All ^{31}P NMR were determined with complete proton decoupling and are reported in parts per million relative to external 85% H_3PO_4 (δ scale).

Infrared spectra were obtained on a BIO-RAD Laboratories FTS-65A FTIR. High-resolution mass spectra were provided by UBE Scientific Analysis Laboratory. Analytical thin-layer chromatography was accomplished with EM Reagents 0.25 mm silica gel 60 plates. Flash chromatography was performed on Wakogel (silica gel) 200. Elemental analysis was performed at UBE Scientific Analysis Laboratory. Optical rotations were obtained on a JASCO DIP-370 digital polarimeter.

GLC analysis was performed on a Shimadzu GC-14A gas chromatograph.

HPLC analysis was performed on a Shimadzu LC10 high performance liquid chromatograph with a chiral column (CHIRALPAK AD, 0.46 cm ϕ X 25 cm, Daicel Chemical Co.).

H_2O concentration in organic solvents was determined by a Kyoto Electronics MKC-210 Karl Fischer moisture titrator.

All manipulations involving air-sensitive materials were performed under an argon atmosphere with standard Schlenk techniques with a double-manifold vacuum line or in a N_2 filled drybox, using oven-dried glassware with magnetic stirring.

Materials. Commercial reagents were used as received, with the following exceptions. Diethyl ether and THF were vacuum transferred from sodium-benzophenone ketyl, degassed by freeze−pump−thaw (FPT) three times, and stored under argon in a Schlenk flask. Dichloromethane was dried over CaH_2, vacuum transferred to a Schlenk flask, degassed by FPT, and stored under argon. 2,6-Lutidine was dried over CaH_2, distillated to a Schlenk flask, degassed by FPT, and stored under argon. DMSO was dried over MS4A, filtered, distillated to a Schlenk flask, and stored under argon. [Pt((*R*)-BINAP)(H_2O)][$OTf]_2$[20] and [Pt((*R*)-BINAP)(μ-OH)]$_2$(BF_4)$_2$[19] were prepared according to the literature.

Pt{O(3,5-*t*Bu$_2$C$_6$H$_2$)CO}{(*R*)-BINAP}; [Pt{(*R*)-BINAP}(3,5-DTBS)] (1a). To a 50 mL Schlenk flask were added K_2PtCl_4 (0.67 g, 1.6 mmol), Na_2CO_3 (0.81 g, 4.8 mmol), 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (0.38 g, 1.6 mmol), and DMSO (25 mL) under argon. The reaction mixture was heated to 140 °C. After the mixture was stirred for 40 min at the same temperature, the resulting yellow green suspension was slowly cooled to 100 °C and (*R*)-BINAP (1.0 g, 1.6 mmol) was added. The yellow suspension was further cooled to 60 °C and DMSO was removed in vacuo. The dry residue was extracted by CH_2Cl_2 and filtered. The yellow filtrate was reduced in volume to a few milliliters, followed by the addition of EtOH. The yellow microcrystals were precipitated out and collected, washed by EtOH, and dried in vacuo at 50 °C for 3 h (yield of **1**, 1.4 g, 83%).

Pt{O(3,5-*t*Bu$_2$C$_6$H$_2$)CO}{(*R*)-BINAP} (**1a**): IR (KBr) 1623, 1437, 1426, 744, 696, 523 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.86 (m, 4H, aromatic), 7.55−6.98 (m, 22H, aromatic), 6.75−6.72 (m, 4H, aromatic), 6.60−6.57 (m, 4H, aromatic), 1.20 (s, 9H, *t*Bu), 1.03 (s, 9H, *t*Bu); ^{31}P NMR (160 MHz, $CDCl_3$) δ 23.7 (d, J_{P-P} = 10.7, J_{Pt-P} = 1512, trans to C), 20.4 (d, J_{P-P} = 10.7, J_{Pt-P} = 4474, trans to O); $[\alpha]^{25}_D$ +582° (*c* 0.44, CH_2Cl_2). Anal. Calcd for $C_{59}H_{52}O_2P_2Pt$: C, 67.48; H, 4.99. Found: C, 66.38; H, 4.94.

Pt(OC$_6$H$_4$CO){(*R*)-BINAP}; [Pt{(*R*)-BINAP}(Sal)] (1b). The procedure used for the preparation of complex **1a** was followed except salicylaldehyde (0.20 g, 1.6 mmol) was used instead of 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (0.38 g, 1.6 mmol), giving 1.3 g (88%) of complex **1b** as yellow orange microcrystals.

Pt(OC$_6$H$_4$CO){(*R*)-BINAP} (**1b**): IR (KBr) 1627, 1456, 1436, 877, 743, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−7.97 (m, 4H, aromatic), 7.53−7.25 (m, 17H, aromatic), 7.13−6.98 (m, 5H, aromatic), 6.79−6.57 (m, 9H, aromatic), 6.36 (dd, *J* = 7.3, 7.3, 1H, aromatic); ^{31}P NMR (160 MHz, $CDCl_3$) δ 24.4 (d, J_{P-P} = 11.6, J_{Pt-P} = 1491, trans to C), 19.2 (d, J_{P-P} = 11.6, J_{Pt-P} = 4536, trans to O). Anal. Calcd for $C_{51}H_{36}O_2P_2Pt$: C, 65.31; H, 3.87. Found: C, 64.88; H, 3.96.

Pt{O(3,5-*t*Bu$_2$C$_6$H$_2$)CO}{(*R*)-Tol-BINAP}; [Pt{(*R*)-Tol-BINAP}-(3,5-DTBS)] (1c). The procedure used for the preparation of complex **1a** was followed, starting from K_2PtCl_4 (0.31 g, 0.74 mmol), Na_2CO_3 (0.23 g, 2.2 mmol), and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (0.17 g, 0.74 mmol), and (*R*)-Tol-BINAP (0.50 g, 0.74 mmol) was used instead of (*R*)-BINAP, giving 0.59 g (73%) of complex **1c** as yellow microcrystals.

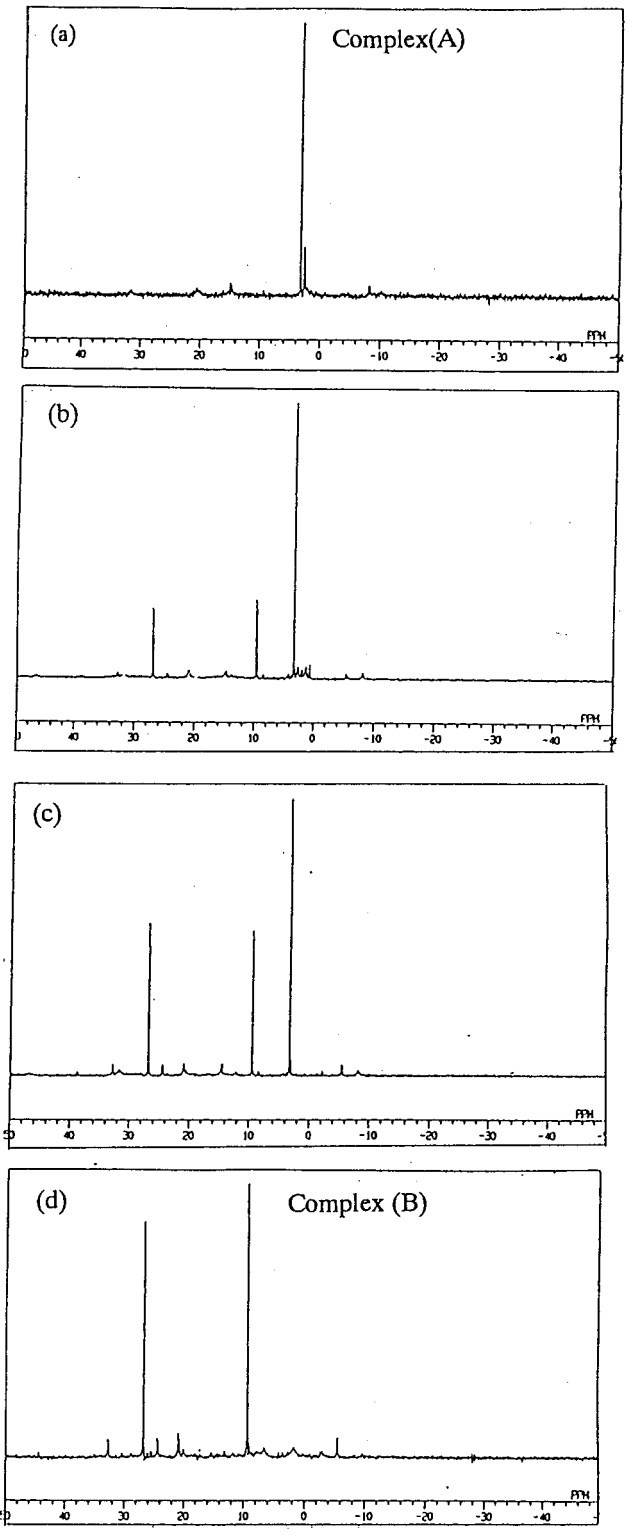


Figure 3. ^{31}P NMR of complex **A** [**1a** was activated by HOTf (1 equiv) in the presence of H_2O (2 equiv) under air; then the atmosphere of the NMR tube was replaced by Ar] in CD_2Cl_2 at 25 °C (a). KSA (10 equiv) was introduced and ^{31}P NMR was taken after 30 min (b) and 24 h (c). Additional KSA (18 equiv) was introduced and ^{31}P NMR was taken after 4 h (d).

Pt{O(3,5-*t*Bu$_2$C$_6$H$_2$)CO}{(*R*)-Tol-BINAP} (**1c**): IR (KBr) 1625, 1439, 1246, 805 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.71 (m, 4H, aromatic), 7.53 (d, J = 8.3, 1H, aromatic), 7.47−7.17 (m, 15H, aromatic), 7.09−7.00 (m, 4H, aromatic), 6.71 (dd, J = 8.8, 8.8, 2H, aromatic), 6.36 (d, J = 7.8, 4H, aromatic), 2.39 (s, 3H, C*H*$_3$C$_6$H$_4$), 2.35 (s, 3H, C*H*$_3$C$_6$H$_4$), 1.95 (s, 3H, C*H*$_3$C$_6$H$_4$), 1.94 (s, 3H, C*H*$_3$C$_6$H$_4$), 1.20 (s, 9H, *t*Bu), 1.01 (s, 9H, *t*Bu); ^{31}P NMR (160 MHz, $CDCl_3$) δ 21.8 (d, J_{P-P} = 10.4, J_{Pt-P} = 1517, trans to C), 18.6 (d, J_{P-P} = 10.4, J_{Pt-P} = 4455, trans to O). Anal. Calcd for $C_{63}H_{60}O_2P_2Pt$: C, 68.40; H, 5.47. Found: C, 67.70; H, 5.35.

Pt(OC$_6$H$_4$CO){(*R*,*R*)-Me-DUPHOS}; [Pt{(*R*,*R*)-Me-DUPHOS}-(Sal)] (1d). The procedure used for the preparation of complex **1b** was followed, starting from K_2PtCl_4 (0.14 g, 0.33 mmol), Na_2CO_3 (0.10 g, 0.98 mmol), and salicylaldehyde (40 mg, 0.33 mmol), and (*R*,*R*)-Me-DUPHOS (0.10 g, 0.33 mmol) was used instead of (*R*)-BINAP, giving 0.14 g (71%) of complex **1d** (recrystallized from *n*-hexane) as yellow microcrystals.

Pt(OC$_6$H$_4$CO){(*R*,*R*)-Me-DUPHOS} (**1d**): IR (KBr) 1612, 1574, 1455, 1314, 1274, 882, 758, 655, 551 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68−7.66 (m, 2H, aromatic), 7.56−7.54 (m, 2H, aromatic), 7.30 (d, J = 7.8, 1H, aromatic), 7.18 (dd, J = 8.3, 7.8, 1H, aromatic), 6.91 (d, J = 8.3, 1H, aromatic), 6.45 (dd, J = 7.8, 7.8, 1H, aromatic), 3.55−3.25 (m, 1H, C*H*CH$_3$), 3.00−2.78 (m, 2H, C*H*CH$_3$), 2.60−2.20 (m, 5H, C*H*CH$_3$, C*H*$_2$C*H*$_2$), 2.00−1.60 (m, 4H, C*H*$_2$C*H*$_2$), 1.49 (dd, J = 19.5, 6.8, 3H, CHC*H*$_3$), 1.27 (dd, J = 19.1, 6.4, 3H, CHC*H*$_3$), 0.85 (dd, J = 14.7, 7.3, 3H, CHC*H*$_3$), 0.84 (dd, J = 16.6, 7.3, 3H, CHC*H*$_3$); ^{31}P NMR (160 MHz, $CDCl_3$) δ 66.0 (d, J_{P-P} = 4.6, J_{Pt-P} = 1530, trans to C), 52.7 (d, J_{P-P} = 4.6, J_{Pt-P} = 3935, trans to O). Anal. Calcd for $C_{25}H_{32}O_2P_2Pt$: C, 48.31; H, 5.19. Found: C, 47.47; H, 5.10.

Pt(OC$_6$H$_4$CO){(*R*,*R*)-CHIRAPHOS}; [Pt{(*R*,*R*)-CHIRAPHOS}-(Sal)] (1e). The procedure used for the preparation of complex **1b** was followed, starting from K_2PtCl_4 (0.97 g, 2.3 mmol), Na_2CO_3 (0.75 g, 7.0 mmol), and salicylaldehyde (0.29 g, 2.3 mmol), and (*R*,*R*)-CHIRAPHOS (1.0 g, 2.3 mmol) was used instead of (*R*)-BINAP, giving 1.6 g (90%) of complex **1e** (recrystallized from ether) as orange yellow microcrystals.

Pt(OC$_6$H$_4$CO){(*R*,*R*)-CHIRAPHOS} (**1e**): IR (KBr) 1612, 1577, 1457, 1320, 1278, 1102, 881, 756, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.75 (m, 8H, aromatic), 7.52−7.35 (m, 12H, aromatic), 7.12 (d, J = 7.8, 1H, aromatic), 7.08 (dd, J = 7.8, 7.8, 1H, aromatic), 6.81 (d, J = 8.3, 1H, aromatic), 6.34 (dd, J = 8.3, 7.8, 1H, aromatic), 2.45−2.32 (m, 1H, C*H*CH$_3$), 2.30−2.15 (m, 1H, C*H*CH$_3$), 1.02 (dd, J = 11.2, 6.8, 3H, CHC*H*$_3$), 0.97 (dd, J = 13.2, 6.8, 3H, CHC*H*$_3$); ^{31}P NMR (160 MHz, $CDCl_3$) δ 45.7 (s, J_{Pt-P} = 1482, trans to C), 35.9 (s, J_{Pt-P} = 4162, trans to O). Anal. Calcd for $C_{35}H_{32}O_2P_2Pt$: C, 56.68; H, 4.35. Found: C, 55.79; H, 4.19.

A Typical Experimental Procedure for Platinum-Catalyzed Enantioselective Aldol Reactions. (1) Catalyst Activation. To complex **1a** (26 mg, 0.025 mmol) in wet CH_2Cl_2 (2.2 mL, H_2O 320 ppm, 0.05 mmol) was added HOTf (2.2 μL, 0.025 mmol) with a microsyringe and stirring was continued at ambient temperature for 15 min under air.

(2) Aldol Reaction. The activated catalyst solution was cooled to −78 °C and 2,6-lutidine (2.9 μL, 0.025 mmol) was added. To this yellow solution was added hydrocinnamaldehyde (67 mg, 0.5 mmol), followed by the dropwise addition of methyl trimethylsilyl dimethylketene acetal (122 mg, 0.7 mmol). The reaction atmosphere was replaced by argon via freeze−pump−thaw (FPT) of the reaction mixture. The reaction mixture was kept in a −25 °C freezer for 168 h at which time GC showed 96% of the starting aldehyde was consumed. Then, the reaction mixture was poured into ice-cooled water and extracted by CH_2Cl_2 (10 mL × 3). The CH_2Cl_2 extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (Wakogel (silica gel) 200, Hexane/EtOAc = 100/0−20/1−5/1) yielded 85 mg (0.28 mmol) of methyl 2,2-dimethyl-5-phenyl-3-trimethylsiloxypentanoate and 46 mg (0.19 mmol) of methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate (desilylated product) in 94% combined yield.

The products were further quantitatively deprotected by treatment with tetrabutylammonium fluoride/THF solution (1.0 M) to give methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate. The ee of the product was then determined by chiral HPLC analysis (CHIRALPAK AD (Daicel Chemical Co.)) to be 95% ee (see Supporting Information for further details).

Methyl 2,2-dimethyl-5-phenyl-3-trimethylsiloxypentanoate: IR (neat) 2955, 1729, 1251, 1132, 1101, 840, 751, 699 cm^{-1}; ^{1}H NMR (270 MHz, C_6D_6) δ 7.18−7.03 (m, 5H, aromatic), 4.06 (dd, J = 8.1,

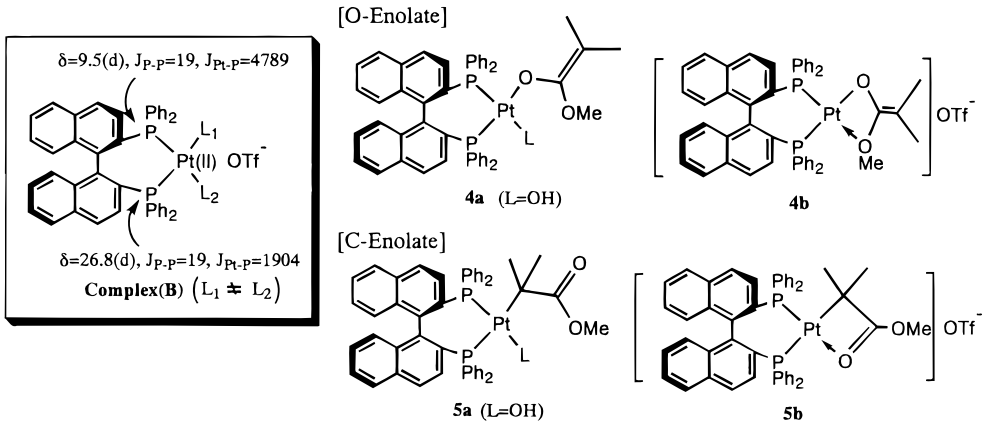
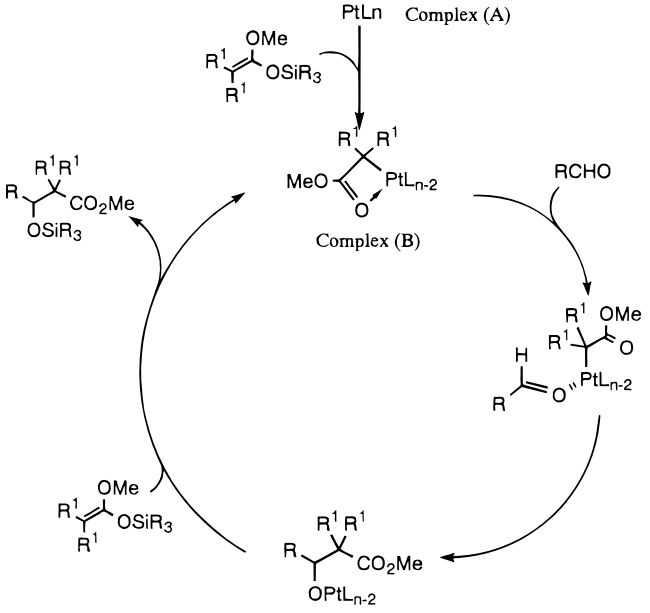


Figure 4. Complex B (^{31}P NMR data) and possible structures.

Scheme 5



2.9, 1H, C*H*OSiMe$_3$), 3.29 (s, 3H, CO$_2$C*H*$_3$), 2.88−2.78 (m, 1H, PhCH$_2$C*H*H), 2.55−2.37 (m, 1H, PhCH$_2$CH*H*), 1.75−1.60 (m, 2H, PhC*H*$_2$), 1.20 (s, 3H, C(C*H*$_3$)), 1.06 (s, 3H, C(C*H*$_3$)), 0.13 (s, 9H, Si*Me*$_3$); ^{13}C NMR (67.5 MHz, C$_6$D$_6$) δ 177.0, 142.5, 128.7, 128.6, 126.2, 77.9, 51.2, 48.4, 35.4, 33.9, 21.3, 20.9, 0.9; mass spectrum (CI) *m*/*z* (rel intensity) 309 (MH$^+$, 40), 219 (98), 159 (45), 117 (100), 91 (96), 73 (70); HRMS, *m*/*z* calcd for C$_{16}$H$_{25}$O$_3$Si (M − CH$_3^+$) 293.1589, found 293.1591.

Methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate: IR (neat) 3512 (br), 2951, 1723, 1455, 1275, 1135, 1076, 750, 701 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.31−7.19 (m, 5H, aromatic), 3.68 (s, 3H, CO$_2$C*H*$_3$), 3.63 (m, 1H, C*H*OH), 3.05−2.90 (m, 1H, PhCH$_2$C*H*H), 2.72−2.59 (m, 1H, PhCH$_2$CH*H*), 2.58 (d, *J* = 7.3, 1H, O*H*), 1.86−1.52 (m, 2H, PhC*H*$_2$), 1.18 (s, 3H, C(C*H*$_3$)), 1.16 (s, 3H, C(C*H*$_3$)); ^{13}C NMR (75 MHz, CDCl$_3$) δ 178.2, 142.1, 128.5, 128.4, 125.9, 76.1, 51.9, 47.1, 33.6, 32.9, 22.5, 20.4; mass spectrum (CI) *m*/*z* (rel intensity) 237 (MH$^+$, 20), 219 (50), 159 (65), 117 (100), 91 (80), 70 (30); HRMS, *m*/*z* calcd for C$_{14}$H$_{20}$O$_3$ (M$^+$) 236.1412, found 236.1412.

Reaction Products from Benzaldehyde and Methyl Trimethylsilyl Dimethylketene Acetal. Methyl 2,2-dimethyl-3-phenyl-3-trimethylsiloxypropanoate: IR (neat) 2954, 1743, 1727, 1252, 1133, 1094, 1068, 881, 843 cm^{-1}; ^{1}H NMR (270 MHz, C$_6$D$_6$) δ 7.28−7.27 (m, 2H, aromatic), 7.15−7.05 (m, 3H, aromatic), 5.12 (s, 1H, C*H*OSiMe$_3$), 3.39 (s, 3H, CO$_2$C*H*$_3$), 1.30 (s, 3H, C(C*H*$_3$)), 1.03 (s, 3H, C(C*H*$_3$)), 0.00 (s, 9H, Si*Me*$_3$); ^{13}C NMR (67.5 MHz, C$_6$D$_6$) δ 176.6, 141.3, 128.2, 127.8, 127.6, 79.7, 51.3, 49.3, 22.0, 19.5, 0.0; mass spectrum (CI) *m*/*z* (rel intensity) 281 (MH$^+$, 5), 265 (10), 191 (100), 73 (90).

Methyl 3-hydroxy-2,2-dimethyl-3-phenylpropanoate (desilylated product): IR (neat) 3454 (br), 2978, 1705, 1472, 1293, 1276, 1161, 1052, 771, 706 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.25−7.22 (m, 2H, aromatic), 7.25−7.07 (m, 3H, aromatic), 4.86 (d, *J* = 4.4, 1H, C*H*OH), 3.30 (s, 3H, CO$_2$C*H*$_3$), 2.83 (d, *J* = 4.4, O*H*), 1.19 (s, 3H, C(C*H*$_3$)), 1.02 (s, 3H, C(C*H*$_3$)); ^{13}C NMR (75 MHz, CDCl$_3$) δ 177.6, 141.0, 128.1, 127.8, 127.7, 78.7, 51.5, 48.1, 22.6, 19.5; mass spectrum (CI) *m*/*z* (rel intensity) 209 (MH$^+$, 5), 191 (100), 102 (76), 73 (74).

Reaction Products from Cinnamaldehyde and Methyl Trimethylsilyl Dimethylketene Acetal. Methyl (*E*)- 2,2-dimethyl-5-phenyl-3-trimethylsiloxy-4-pentenoate: IR (neat) 2954, 1740, 1251, 1135, 1066, 892, 877, 842, 745, 694 cm^{-1}; ^{1}H NMR (400 MHz, C$_6$D$_6$) δ 7.24−7.01 (m, 5H, aromatic), 6.51 (d, *J* = 16.0, 1H, PhC*H*), 6.22 (dd, *J* = 16.0, 7.3, 1H, PhCHC*H*), 4.63 (d, *J* = 7.3, 1H, C*H*OSiMe$_3$), 3.39 (s, 3H, CO$_2$C*H*$_3$), 1.34 (s, 3H, C(C*H*$_3$)), 1.16 (s, 3H, C(C*H*$_3$)), 0.13 (s, 9H, Si*Me*$_3$); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ 176.5, 137.1, 132.6, 128.2, 128.1, 126.8, 110.6, 79.1, 51.3, 48.7, 21.6, 20.1, 0.4; mass spectrum (CI) *m*/*z* (rel intensity) 307 (MH$^+$, 1), 205 (100), 157 (46), 73 (55); HRMS, *m*/*z* calcd for C$_{16}$H$_{23}$O$_3$Si (M − CH$_3^+$) 291.1427, found 291.1428.

Methyl (*E*)-3-hydroxy-2,2-dimethyl-5-phenyl-4-pentenoate (desilylated product): IR (neat) 3483 (br), 2980, 1725, 1470, 1270, 1136, 1100, 970, 750, 695 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34−7.10 (m, 5H, aromatic), 6.58 (d, *J* = 16.1, 1H, PhC*H*), 6.16 (dd, *J* = 16.1, 6.8, 1H, PhCHC*H*), 4.30 (d, *J* = 6.8, 1H, C*H*OH), 3.67 (s, 3H, CO$_2$C*H*$_3$), 3.00−2.40 (br s, 1H, O*H*), 1.19 (s, 3H, C(C*H*$_3$)), 1.18 (s, 3H, C(C*H*$_3$)); ^{13}C NMR (100 MHz, CDCl$_3$) δ 177.8, 136.6, 132.9, 128.5, 127.8, 127.4,126.5, 77.8, 52.0, 47.2, 22.7, 20.0; mass spectrum (EI) *m*/*z* (rel intensity): 234 (MH$^+$, 2), 157 (4), 133 (100), 102 (45), 77 (20), 55 (30); HRMS, *m*/*z* calcd for C$_{14}$H$_{18}$O$_3$ (M$^+$) 234.1255, found 234.1255.

Reaction Products from 3-Methylbutanal and Methyl Trimethylsilyl Dimethylketene Acetal. Methyl 2,2,5-trimethyl-3-trimethylsiloxyhexanoate: IR (neat) 2957, 1742, 1469, 1251, 1132, 1096, 1032, 911, 841 cm^{-1}; ^{1}H NMR (400 MHz, C$_6$D$_6$) δ 4.13 (dd, *J* = 9.8, 2.0, 1H, C*H*OSiMe$_3$), 3.36 (s, 3H, CO$_2$C*H*$_3$), 1.79−1.72 (m, 1H, CH$_3$C*H*CH$_3$), 1.54−1.48 (m, 1H, CH$_3$CH(CH$_3$)C*H*H), 1.26 (s, 3H, C(C*H*$_3$)), 1.14 (s, 3H, C(C*H*$_3$)), 1.08−1.01 (m, 1H, CH$_3$CH(CH$_3$)CH*H*), 0.89 (d, 6H, *J* = 6.8, C*H*$_3$CHC*H*$_3$), 0.15 (s, 9H, Si*Me*$_3$); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ 177.0, 76.0, 51.2, 48.4, 42.7, 24.8, 24.3, 21.5, 21.4, 20.5, 0.9; mass spectrum (CI) *m*/*z* (rel intensity) 261 (MH$^+$, 20), 245 (10), 171 (100), 139 (10), 111 (12); HRMS, *m*/*z* calcd for C$_{12}$H$_{25}$O$_3$Si (M − CH$_3^+$) 245.1576, found 245.1576.

Methyl 3-hydroxy-2,2,5-trimethylhexanoate (desylilated product): IR (neat) 3512 (br), 2951, 1723, 1469, 1265, 1142, 1074 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 3.70 (s, 3H, CO$_2$C*H*$_3$), 3.73−3.66 (m, 1H, C*H*OH), 2.35 (d, *J* = 7.3, 1H, O*H*), 1.88−1.80 (m, 1H, CH$_3$C*H*CH$_3$), 1.40−1.08 (m, 2H, CH$_3$CH(CH$_3$)C*HH*), 1.18 (s, 3H, C(C*H*$_3$)), 1.17 (s, 3H, C(C*H*$_3$)), 0.95 (d, 3H, *J* = 6.6, CHC*H*$_3$), 0.91 (d, 3H, *J* = 6.6, CHC*H*$_3$); ^{13}C NMR (67.5 MHz, CDCl$_3$) δ 178.3, 74.7, 51.9, 47.2, 41.0, 24.9, 24.0, 22.2, 21.4, 20.4; mass spectrum (CI) *m*/*z* (rel intensity) 189 (MH$^+$, 40), 171 (100), 157 (28), 139 (25), 102 (97); HRMS, *m*/*z* calcd for C$_{10}$H$_{19}$O$_2$ (M − OH$^+$) 171.1382, found 171.1382.

Reaction Products from 3,3-Dimethylbutanal and Methyl Trimethylsilyl Dimethylketene Acetal. Methyl 2,2,5,5-tetramethyl-3-trimethylsiloxyhexanoate: IR (neat) 2955, 1741, 1262, 1252, 1131, 1098, 841 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 4.26 (dd, J = 7.3, 1.5, 1H, C*H*OSiMe_3), 3.35 (s, 3H, CO_2CH_3), 1.46 (dd, J = 14.7, 7.3, 1H, $CH_3C(CH_3)_2CHH$), 1.33 (dd, J = 14.7, 1.5, 1H, $CH_3C(CH_3)_2CHH$), 1.24 (s, 3H, $C(CH_3)CO_2CH_3$), 1.10 (s, 3H, $C(CH_3)CO_2CH_3$), 0.93 (s, 9H, $C(CH_3)_3$), 0.19 (s, 9H, SiMe_3); ^{13}C NMR (100 MHz, C_6D_6) δ 177.0, 75.2, 51.2, 49.4, 47.7, 30.4, 30.2, 21.1, 21.0, 1.5; mass spectrum (CI) *m*/*z* (rel intensity) 275 (MH^+, 9), 259 (20), 185 (100), 117 (25), 73 (25); HRMS, *m*/*z* calcd for $C_{13}H_{27}O_3Si$ ($M - CH_3^+$) 269.1733, found 259.1733.

Methyl 3-hydroxy-2,2,5,5-tetramethylhexanoate (desilylated product): IR (neat) 3526 (br), 2954, 1720, 1470, 1366, 1134,1074, 994 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 3.76 (dd, J = 7.3, 7.3, 1H, C*H*OH), 3.70 (s, 3H, CO_2CH_3), 1.36−1.16 (m, 2H, CCH_2CH), 1.16 (s, 6H, $C(CH_3)_2$), 0.96 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 176.8, 72.6, 50.4, 46.5, 44.7, 28.6, 20.6, 19.1; mass spectrum (CI) *m*/*z* (rel intensity) 204 (MH^+, 45), 185 (100), 170 (12), 102 (8); HRMS, *m*/*z* calcd for $C_{11}H_{21}O_2$ ($M - OH^+$) 185.1567, found 185.1570.

Chemoselective Platinum-Catalyzed Enantioselective Aldol Reaction. To complex **1a** (26 mg, 0.025 mmol) in wet CH_2Cl_2 (2.2 mL, H_2O 320 ppm, 0.05 mmol) was added HOTf (2.2 μL, 0.025 mmol) with a microsyringe with stirring at ambient temperature for 15 min under air. The activated catalyst solution was cooled to −78 °C and 2,6-lutidine (2.9 μL, 0.025 mmol) was added. To this yellow solution were added hydrocinnamaldehyde (67 mg, 0.5 mmol) and cyclohexanecarboxaldehyde (56 mg, 0.5 mmol), followed by the dropwise addition of methyl trimethylsilyl dimethylketene acetal (131 mg, 0.75 mmol). The reaction atmosphere was replaced by argon via freeze−pump−thaw (FPT) of the reaction mixture. The reaction mixture was kept in a −25 °C freezer for 72 h at which time GC showed 96% of the starting hydrocinnamaldehyde was consumed while less than 3% of the cyclohexanecarboxaldehyde was consumed. Then, the reaction mixture was poured into ice-cooled water and extracted by CH_2Cl_2 (10 mL × 3). The CH_2Cl_2 extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (Wakogel (silica gel) 200, hexane/EtOAc = 100/0−20/1−5/1) yielded 108 mg (0.34 mmol) of methyl 2,2-dimethyl-5-phenyl-3-trimethylsiloxypentanoate and 35 mg (0.14 mmol) of methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate (desilylated product) in 94% combined yield together with 54 mg of unreacted cyclohexanecarboxaldehyde (96% recovered).

The aldol products were further quantitatively deprotected by treatment with tetrabutylammonium fluoride/THF solution (1.0 M) to give methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate. The ee of the product was then determined by chiral HPLC analysis (CHIRALPAK AD (Daicel Chemical Co.)) to be 94% ee.

NMR Experiments for Catalyst Activation. (a) Sample preparation was performed in a drybox under nitrogen atmosphere. A solution of platinum complex **1a** (26 mg, 0.025 mmol) in dry CD_2Cl_2 (1 mL) was transferred into a dry 5-mm NMR tube. HOTf (2.2 μL, 0.025 mmol) was added with a microsyringe and thoroughly mixed. The reaction progress was monitored by NMR.

(b) Sample preparation was performed in open air. A solution of platinum complex **1a** (26 mg, 0.025 mmol) in dry CD_2Cl_2 (1 mL) was transferred into a dry 5-mm NMR tube and sealed with a rubber septa. HOTf (2.2 μL, 0.025 mmol) was added with a microsyringe and thoroughly mixed. The reaction progress was monitored by NMR.

(c) Sample preparation was performed in open air. A solution of platinum complex **1a** (26 mg, 0.025 mmol) in wet CD_2Cl_2 (1 mL) (H_2O, 660 ppm, 0.05 mmol) was transferred into a 5-mm NMR tube and sealed with a rubber septa. HOTf (2.2 μL, 0.025 mmol) was added with a microsyringe and thoroughly mixed. The reaction progress was monitored by NMR.

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Supporting Information Available: The proof of the enantiomer excess determination of all the reaction products and chiral HPLC analysis conditions as well as ^1H NMR spectra for all aldol products (15 pages print/PDF). See any current masthead page for ordering information and Web access instructions.

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