Available online at www.sciencedirect.com
ScienceDirect
Journal of Molecular Catalysis A: Chemical 261 (2007) 112–119
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

# Water-tolerant enantioselective carbonyl-ene reactions with palladium(II) and platinum(II) Lewis acid catalysts bearing BINAP

He-Kuan Luo [a,*], Hai-Yan Yang [a], Tan Xiang Jie [a], Ong Siong Chiew [a], Herbert Schumann [b], Lim Bee Khim [a], Christina Lim [a]

[a] *Institute of Chemical and Engineering Sciences (ICES), 1 Pesek Road, Jurong Island, Singapore 627833, Singapore*
[b] *Institut für Chemie, Technische Universität Berlin (TU-Berlin), Straße des 17, Juni 135, D-10623 Berlin, Germany*

Received 14 June 2006; received in revised form 25 July 2006; accepted 26 July 2006
Available online 7 September 2006

**Abstract**

Palladium(II) and platinum(II) Lewis acid catalysts bearing BINAP have been proved to be water-tolerant in enantioselective carbonyl-ene reactions, thus arylglyoxal monohydrate could be used directly as substrate achieving good to excellent enantioselectivities as high as 95.4% e.e.. The enantioselective carbonyl-ene reactions using phenylglyoxal monohydrate as substrate with four alkenes including methylenecyclohexane, 2,3-dimethyl-1-butene, 2,4,4-trimethyl-1-pentene and alpha-methylstyrene, were investigated demonstrating comparable or even higher yields and enantioselectivities in comparison with the corresponding carbonyl-ene reactions using dry phenylglyoxal as substrate for both palladium(II)-BINAP catalyst and platinum(II)-BINAP catalyst. The palladium(II) and platinum(II)-BINAP catalyzed enantioselective carbonyl-ene reactions between 4-methylphenylglyoxal monohydrate and the four alkenes were also investigated affording enantioselectivities between 76.2% and 91.8% e.e.. A mechanism involving the coordination of arylglyoxal and 2,2-dihydroxy-1-phenylethanone with chiral catalyst was proposed to interpret the enantioselective carbonyl-ene reactions using arylglyoxal monohydrate as substrate.


*Keywords:* Enantioselective; Carbonyl-ene; Palladium; Platinum; Phenylglyoxal

## 1. Introduction

Water-tolerant catalysts and catalytic processes do not require dehydrative drying of substrates, solvents and reactors etc., hence they are more easily to be used in industry. Moreover, water has been reported to have beneficial effect on enantioselectivities and activities in a few Lewis acid catalyzed asymmetric catalytic reactions. For example, in hetero-Diels-Alder reaction with Danishefsky's diene using chiral lanthanide bis(bisfluoromethanesulfonyl)amide (bis-trifylamide) catalyst, the presence of a small amount of water as an additive can increase the enantioselectivity [1]. Therefore developing water-tolerant asymmetric catalysis is of general interests.

The enantioselective carbonyl-ene reaction catalyzed by chiral Lewis acid is an important methodology for carbon–carbon bond construction to prepare optically active homoallylic alcohols. For this reaction a variety of chiral Lewis acid catalysts based on various metals and ligands have been studied [2–8], some of them were reported demonstrating high efficiency and high enantioselectivity, such as organoaluminum catalyst [2], Ti-BINOL catalyst [3], Cu-BOX catalyst [5] and optically active β-ketoiminato cationic cobalt(III) catalyst [6] etc.. However all of them were reported to be water-sensitive, hence properly dried solvents, substrates and reactors have to be used. Particularly, as one of the most common substrates for enantioselective carbonyl-ene reactions, dry phenylglyoxal has to be made by drying phenylglyoxal monohydrate which is usually prepared, purified and transported as monohydrate form because phenylglyoxal monohydrate is loose white powder therefore it could be easily handled (see Picture 1A, left) [9]. Phenylglyoxal monohydrate has not been used directly in enantios-

* Corresponding author. Tel.: +65 6796 3827; fax: +65 6316 6182.
*E-mail address:* luo_hekuan@ices.a-star.edu.sg (H.-K. Luo).

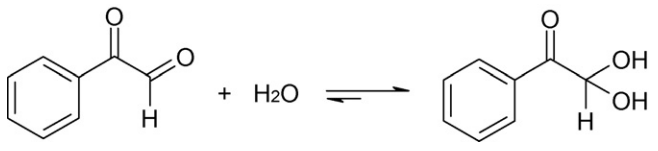
1381-1169/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2006.07.068

Picture 1. Phenylglyoxal monohydrate (A, left) and dry phenylglyoxal (B, right).

elective catalytic reactions just because all the existing chiral Lewis acid catalysts were reported to be water-sensitive and most of the phenylglyoxal is in the form of 2,2-dihydroxy-1-phenylethanone($PhC(O)CH(OH)_2$) (see Scheme 1). On the other hand, pure and dry phenylglyoxal is brown oil under high temperature, such as 90 °C, or very sticky and thick semi-solid under low temperature, such as 30 °C (see Picture 1B, right), which is much more difficult to be handled and may undergo dimerization or polymerization. Therefore phenylglyoxal has to be freshly dried prior to use. This may greatly hinder the use of phenylglyoxal in catalytic processeses in which the catalysts are water-sensitive. Therefore it is very useful to develop water-tolerant enantioselective catalytic reactions by using phenylglyoxal monohydrate directly as substrate to prepare chiral chemicals.

Palladium catalyst of bis(diphenylphosphino)-type ligand has been proved to be water-tolerant in some catalytic reactions. For example, the palladium catalyst incorporated with 1,3-bis(diphenylphosphino)propane could catalyze the alternating copolymerization of CO and ethylene in methanol–water or in acetic acid–water solvents demonstrating high activity [10]. Therefore the palladium catalyst of (*R*)/(*S*)-(+)/(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene(BINAP) could be water-tolerant catalyst for asymmetric catalysis. However, previous reports demonstrated that the enantioselective glyoxylate-ene reactions between ethyl glyoxylate and alkenes was water-sensitive, trace water ($H_2O$:ethyl glyoxylate = 2:3) could stop the reaction completely [7d].

In the present studies, we proved that $[(R\text{-BINAP})Pd]^{2+}$ and $[(S\text{-BINAP})Pt]^{2+}$ are water-tolerant chiral Lewis acid catalysts for the enantioselective carbonyl-ene reactions. Here we report our studies on $[(R\text{-BINAP})Pd]^{2+}$ and $[(S\text{-BINAP})Pt]^{2+}$ catalyzed water-tolerant enantioselective carbonyl-ene reactions of phenylglyoxal monohydrate and 4-methylphenylglyoxal monohydrate with four alkenes including methylenecyclohexane, 2,3-dimethyl-1-butene, 2,4,4-trimethyl-1-pentene and alpha-methylstyrene, demonstrating good to excellent enantioselectivities with e.e. values as high as 95.4%.




Scheme 1. Equilibration between phenylglyoxal and 2,2-dihydroxy-1-phenylethanone.

## 2. Results and discussions

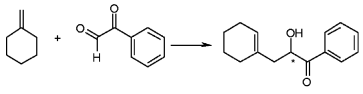
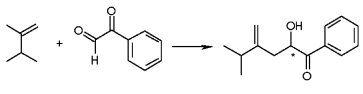
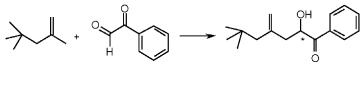
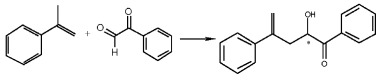
### *2.1. Enantioselective carbonyl-ene reactions between phenylglyoxal monohydrate and alkenes (see Table 1)*

The $[(R\text{-BINAP})Pd]^{2+}$ Lewis acid catalyzed enantioselective carbonyl-ene reactions using phenylglyoxal monohydrate directly as substrate were firstly studied and compared with the corresponding carbonyl-ene reactions using dry phenylglyoxal as substrate (see Table 1). The first reaction we studied was the palladium(II)-BINAP catalyzed carbonyl-ene reaction between phenylglyoxal and methylenecyclohexane. We found that phenylglyoxal monohydrate did not kill the catalyst or stop the reaction, but could give higher yield and enantioselectivity as compared with dried phenylglyoxal (see entries 1 and 2 in Table 1, 51% yield, 88.0% ee versus 36% yield and 86.5% e.e.). In order to confirm this result, we run the reaction for six times and the data presented are average values of six runs. For the palladium(II)-BINAP catalyzed carbonyl-ene reactions of the other three alkenes including 2,3-dimethyl-1-butene, 2,4,4-trimethyl-1-pentene and alpha-methylstyrene, phenylglyoxal monohydrate also demonstrated comparable or higher yields and enantioselectivities as compared with dried phenylglyoxal (see entries 7, 8, 13, 14, 19, 20) with e.e. values as high as 93.0%.

$[(S\text{-BINAP})Pt]^{2+}$ catalyst was also studied for all the four enantioselective carbonyl-ene reactions between phenylglyoxal and the four alkenes including methylenecyclohexane, 2,3-dimethyl-1-butene, 2,4,4-trimethyl-1-pentene and alpha-methylstyrene. As we expected, phenylglyoxal monohydrate also demonstrated higher yields and enantioselectivities in different degrees as compared with dried phenylglyoxal (see entries 3–6, 9–12, 15–18, 21, 22). In order to make a clear comparison, we run the reactions of phenylglyoxal monohydrate with three alkenes including methylenecyclohexane, 2,3-dimethyl-1-butene and 2,4,4-trimethyl-1-pentene for 10 min, and compared with dried phenylglyoxal. As shown in Table 1, phenylglyoxal monohydrate demonstrated higher yields and enantioselectivities than dired phenylglyoxal (51% yield and 88% e.e. versus 39% yield and 86.4% e.e.; 47% yield and 95.4% e.e. versus 45% yield and 95.0% e.e.; 59% yield and 91.0% e.e. versus 48% yield and 90.0% e.e., see entries 4, 5, 10, 11, 16, 17). For the platinium(II)-BINAP catalyzed enantioselective carbonyl-ene reactions between phenylglyoxal and alpha-methylstyrene, phenylglyoxal monohydrate also demonstrated higher yield and enantioselectivity than dried phenylglyoxal (76% yield and 78.0 % e.e. versus 43% yield and 77.1% e.e., see entries 21, 22).

The above results proved that $[(R\text{-BINAP})Pd]^{2+}$ and $[(S\text{-BINAP})Pt]^{2+}$ are water-tolerant in enantioselective carbonyl-ene reactions in dichloromethane, phenylglyoxal monohydrate could be used directly as substrate achieving good to excellent enantioselectivities.

Table 1
Comparison of enantioselective carbonyl-ene reactions using phenylglyoxal monohydrate and dry phenylglyoxal as substrate with four alkenes

| Catalytic reaction | Entry | Phenyl glyoxal | Product | Time | Catalayst | Yield[a] (%) | e.e.[b] (%) |
|---|---|---|---|---|---|---|---|
|  | 1[c] | Monohydrate | 1a | 1 h | Pd | 51 | 88.0(*S*)[d] |
| | 2[c] | Dried | 1a | 1 h | Pd | 36 | 86.5(*S*) |
| | 3 | Monohydrate | 1a | 30 min | Pt | 72 | 87.0(*R*) |
| | 4 | Monohydrate | 1a | 10 min | Pt | 51 | 88.0(*R*) |
| | 5 | Dried | 1a | 10 min | Pt | 39 | 86.4(*R*) |
| | 6 | Dried | 1a | 2 h | Pt | 63 | 86.4(*R*) |
|  | 7 | Monohydrate | 1b | 2 h | Pd | 50 | 93.0(*S*) |
| | 8 | Dried | 1b | 2 h | Pd | 50 | 93.0(*S*) |
| | 9 | Monohydrate | 1b | 30 min | Pt | 64 | 95.2(*R*) |
| | 10 | Monohydrate | 1b | 10 min | Pt | 47 | 95.4(*R*) |
| | 11 | Dried | 1b | 10 min | Pt | 45 | 95.0(*R*) |
| | 12 | Dried | 1b | 2 h | Pt | 66 | 94.9(*R*) |
|  | 13 | Monohydrate | 1c | 2 h | Pd | 56 | 88.0(*S*) |
| | 14 | Dried | 1c | 2 h | Pd | 50 | 87.6(*S*) |
| | 15 | Monohydrate | 1c | 30 min | Pt | 88 | 91.0(*R*) |
| | 16 | Monohydrate | 1c | 10 min | Pt | 59 | 91.0(*R*) |
| | 17 | Dried | 1c | 10 min | Pt | 48 | 90.0(*R*) |
| | 18 | Dried | 1c | 2 h | Pt | 54 | 88.2(*R*) |
|  | 19 | Monohydrate | 1d | 1 h | Pd | 40 | 80.0(*S*) |
| | 20 | Dried | 1d | 1 h | Pd | 27 | 78.8(*S*) |
| | 21 | Monohydrate | 1d | 2 h | Pt | 76 | 78.0(*R*) |
| | 22 | Dried | 1d | 2 h | Pt | 43 | 77.1(*R*) |

Reaction conditions: all the reactions were run at room temperature. Catalyst [(*R*-BINAP)Pd](SbF$_6$)$_2$ or [(*S*-BINAP)Pt](SbF$_6$)$_2$ 0.0125 mmol (5 mol%); phenylglyoxal, 0.25 mmol; alkene, 0.25 mmol.

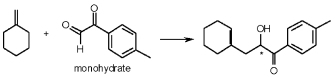
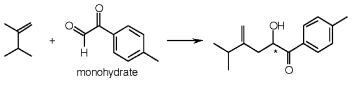
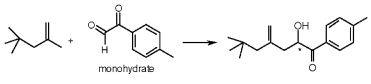
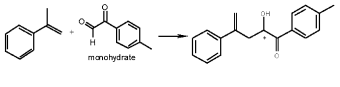
[a] Isolated yield with flash chromatography.

[b] Determined by HPLC with a Chiralcel OD-H column for products 1a, 1b and 1c, with a Chiralcel OB-H column for products 1d.

[c] Average of six runs, the others are average values of three runs.

[d] The absolute configurations of the carbonyl-ene products were determined by comparing the HPLC retention times with those reported in the literature.

Table 2
Enantioselective carbonyl-ene reactions between 4-methylphenylglyoxal monohydrate and alkenes

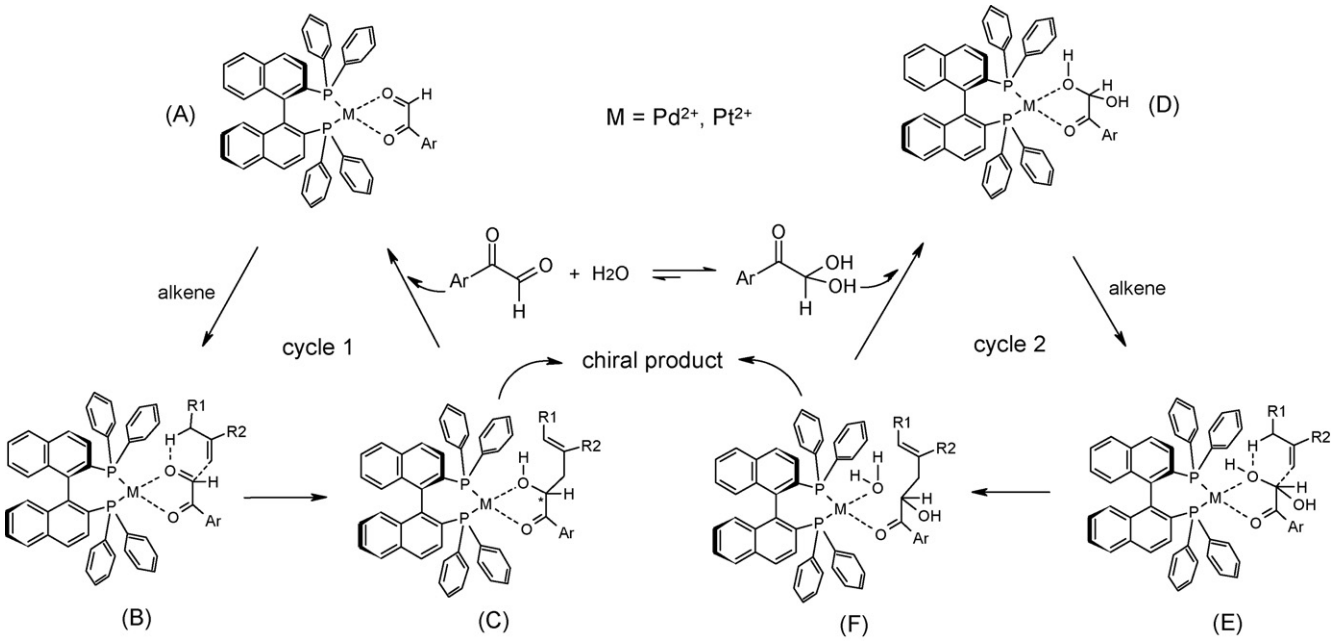
| Catalytic reaction | Entry | Product | Time (h) | Catalyst | Yield[a] (%) | e.e.[b] (%) |
|---|---|---|---|---|---|---|
|  | 1 | 2a | 1 | Pd | 47 | 85.5(*S*)[c] |
| | 2 | 2a | 2 | Pt | 75 | 87.2(*R*) |
|  | 3 | 2b | 1 | Pd | 37 | 91.8(*S*) |
| | 4 | 2b | 2 | Pt | 76 | 88.0(*R*) |
|  | 5 | 2c | 1 | Pd | 49 | 86.8(*S*) |
| | 6 | 2c | 2 | Pt | 51 | 88.2(*R*) |
|  | 7 | 2d | 1 | Pd | 32 | 82.8(*S*) |
| | 8 | 2d | 1.5 | Pt | 70 | 76.2(*R*) |

Reaction conditions: all the reactions were run at room temperature. Catalyst [(*R*-BINAP)Pd](SbF$_6$)$_2$ or [(*S*-BINAP)Pt](SbF$_6$)$_2$, 0.0125 mmol (5 mol%); 4-methylphenylglyoxal monohydrate, 0.25 mmol; alkene, 0.25 mmol.

[a] Isolated yield with flash chromatography.

[b] Determined by HPLC with a Chiralcel OD-H column for products 2a, 2b and 2c, with a Chiralcel OB-H column for products 2d.

[c] The absolute configurations of the carbonyl-ene products were determined by comparing with the products in Table 1. Average of three runs.




Scheme 2. Proposed catalytic mechanism for enantioselective carbonyl-ene reactions of arylglyoxal monohydrate and alkene.

### 2.2. Enantioselective carbonyl-ene reactions between 4-methylphenylglyoxal monohydrate and alkenes (see Table 2)

As a very common substrate, 4-methylphenylglyoxal has not been studied for enantioselective carbonyl-ene reactions. The development of water-tolerant enantioselective carbonyl-ene reactions provided us a convenient protocol to study the enantioselective carbonyl-ene reactions using 4-methylphenylglyoxal monohydrate as substrate with the four alkenes using [(*R*-BINAP)Pd]$^{2+}$ and [(*S*-BINAP)Pt]$^{2+}$ Lewis acid catalysts. As shown in Table 2, the results are close to the enantioselective carbonyl-ene reactions of phenylglyoxal monohydrate with alkenes. Both [(*R*-BINAP)Pd]$^{2+}$ and [(*S*-BINAP)Pt]$^{2+}$ catalysts demonstrated very high e.e. values for the carbonyl-ene reaction of 4-methylphenylglyoxal monohydrate and 2,3-dimethyl-1-butene (91.8% e.e. and 88.0% e.e., respectively), also demonstrated very good enantioselectivities for the carbonyl-ene reactions of 4-methylphenylglyoxal monohydrate with 2,4,4-trimethyl-1-pentene (86.8% e.e. and 88.2% e.e., respectively) and methylenecyclohexane (85.5% e.e. and 87.2% e.e., respectively). For the carbonyl-ene reaction of 4-methylphenylglyoxal monohydrate and alpha-methylstyrene, [(*R*-BINAP)Pd]$^{2+}$ and [(*S*-BINAP)Pt]$^{2+}$ demonstrated relatively low e.e. values (82.8% e.e. and 76.2% e.e., respectively).

### 2.3. Mechanism of [(R-BINAP)Pd]$^{2+}$ and [(S-BINAP)Pt]$^{2+}$ Lewis acid catalyzed enantioselective carbonyl-ene reactions

As shown in Tables 1 and 2, for all the enantioselective carbonyl-ene reactions of phenylglyoxal monohydrate and 4-methylphenylglyoxal monohydrate with the four alkenes, both palladium(II)-BINAP and platinum(II)-BINAP catalysts demonstrated comparable or even higher yields and enantioselectivities in comparison with the corresponding carbonyl-ene reactions using dry phenylglyoxal as substrate, clearly indicating that [(*R*-BINAP)Pd]$^{2+}$ and [(*S*-BINAP)Pt]$^{2+}$ are water-tolerant in dichloromethane for carbonyl-ene reactions. For example, for the palladium(II)-BINAP catalyzed enantioselective carbonyl-ene reaction between phenylglyoxal and methylenecyclohexane, dry phenylglyoxal demonstrated only 36% yield and 86.5% e.e. for 1 h run, however phenylglyoxal monohydrate demonstrated increased yield and enantioselectivity (51% yield and 88.0% e.e. for 1 h run). Since the increase was not significant, we run the reaction for six times to confirm the results, and the above data are average values of six runs; For the platinium(II)-BINAP catalyzed enantioselective carbonyl-ene reactions between phenylglyoxal and alkenes, phenylglyoxal monohydrate also demonstrated higher yields and enantioselectivities than dried phenylglyoxal. This result is a sharp contrast against the {[(*S*)-MeOBIPHEP]Pt}$(SbF_6)_2$ catalyzed enantioselective glyoxylate-ene reactions between ethyl glyoxylate and alkenes, in which trace water ($H_2O$:ethyl glyoxylate = 2:3) could stop the reaction completely [7d].

In order to interpret the enantioselective carbonyl-ene reactions of arylglyoxal monohydrate, here a catalytic mechanism was proposed and shown in Scheme 2. Previously it has been proposed that, in the enantioselective carbonyl-ene reactions [7a,d,e], phenylglyoxal is firstly activated by coordination with chiral catalyst to form a key intermediate (A) (see Scheme 2), which is then attacked by alkene and the carbonyl-ene reaction occurs (see intermediate B) forming intermediate (C) which is a complex of chiral catalyst and product. Finally, intermediate (C) releases chiral product and backs to intermediate (A) by subsequent coordination with the second molecule phenylglyoxal.

In our studies, since we are using phenylglyoxal monohydrate as substrate, in dichloromethane solution there is a equilibration

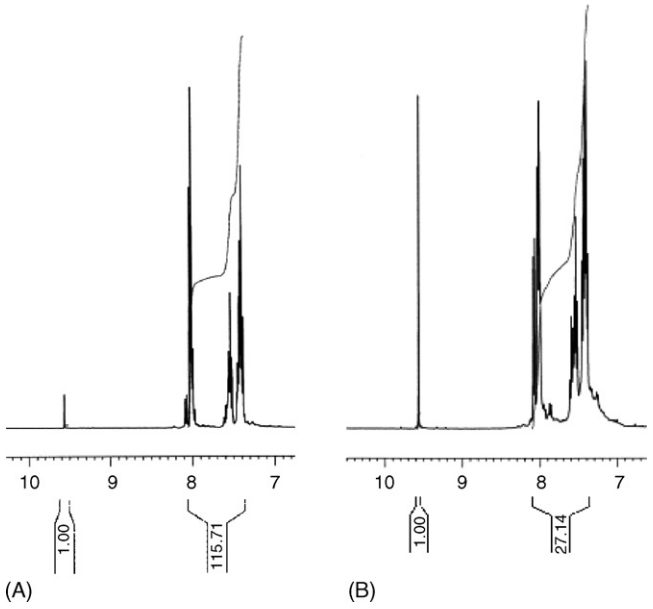
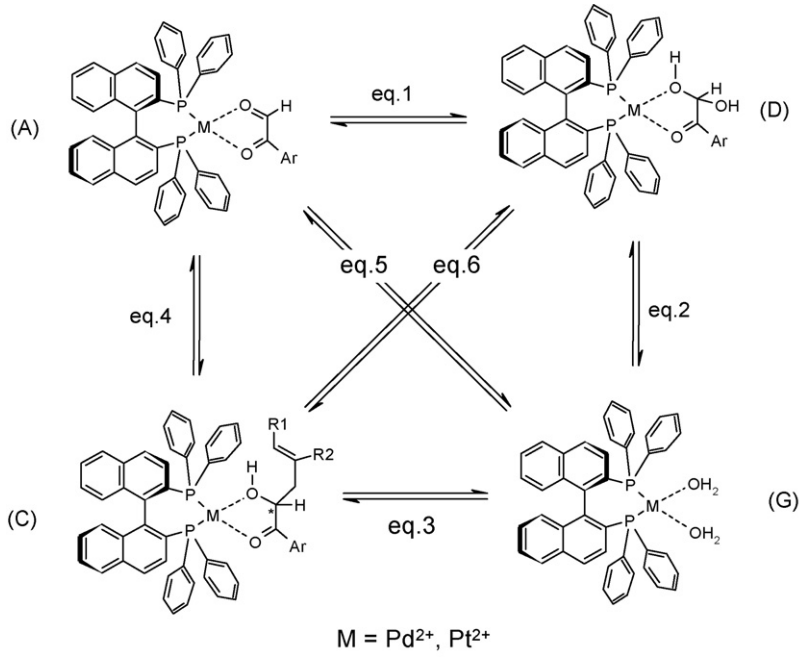



Fig. 1. Comparison of $^1$H NMR($CD_2Cl_2$, 400 MHz) of phenylglyoxal monohydrate (A) and dried phenylglyoxal (B).

between phenylglyoxal and 2,2-dihydroxy-1-phenylethanone, the $^1$H-NMR($CD_2Cl_2$, 400 MHz) of phenylglyoxal monohydrate revealed that the peak of aldehyde-H at 9.57 ppm is very small and the ratio of phenyl-H to aldehyde-H is 115.71:1.00(see A in Fig. 1). After phenylglyoxal was dried under 90 °C in vacuum, the peak of aldehyde-H was significantly enhanced, and the ratio of phenyl-H to aldehyde-H was decreased to 27.14:1.00 (see B in Fig. 1). Theoretically, in the $^1$H-NMR of free phenylglyoxal, the ratio of phenyl-H to aldehyde-H is 5:1. Therefore the $^1$H-NMR of phenylglyoxal monohydrate clearly showed that in dichloromethane solution, only a small amount of the compound is in the form of free phenylglyoxal, most of the compound should be in the form of 2,2-dihydroxy-1-phenylethanone. Under such conditions, if only pure phenylglyoxal could undergo carbonyl-ene reaction, 2,2-dihydroxy-1-phenylethanone will shift to phenylglyoxal during the reaction. Obviously, this process may result in low activity. More importantly, beside 2,2-dihydroxy-1-phenylethanone, using phenylglyoxal monohydrate as substrate introduces some water into the reaction system, water could coordinate with palladium(II) and platinum(II) [11], therefore it is considered as a competitive inhibitor for catalysis to decrease the catalytic activity or even stop a reaction completely [7d] (see Scheme 3). But in fact, for some of the carbonbyl-ene reactions using phenylglyoxal monohydrate, the isolated yield was higher than the corresponding reaction using dry phenylglyoxal. Therefore here we propose the second catalytic cycle (see cycle 2 in Scheme 2). Acetal-ene reaction was also reported to occur easily when promoted with Lewis acid catalyst [12]. Since 2,2-dihydroxy-1-phenylethanone is structurally similar to acetal, here we propose that 2,2-dihydroxy-1-phenylethanone may also undergo enantioselective reaction with alkene as shown in cycle 2 like acetal-ene reaction. Firstly, intermediate (D) was formed by coordination of chiral catalyst with 2,2-dihydroxy-1-phenylethanone. Then the alkene may approach the coordinated 2,2-dihydroxy-1-phenylethanone (see intermediate E) and form the product, meanwhile one molecule $H_2O$ is given out (see intermediate F). After releasing the product and subsequent coordination with the second molecule of 2,2-dihydroxy-1-phenylethanone, the catalyst backs to intermediate (D). In summary, the palladium(II) and platinum(II)-BINAP catalyzed enantioselective carbonyl-ene reaction involves catalytic cycle 1 and cycle 2. This mechanism could help us to understand the enantioselec-




Scheme 3. Competitive coordination on the metal center of the chiral catalyst.

tive carbonyl-ene reaction using phenylglyoxal monohydrate as substrate. In dried phenylglyoxal, the ratio of phenyl-H to aldehyde-H is 27.14:1.00 which is still higher than the ratio of 5:1 for free phenylglyoxal. This may indicate that it is very hard to remove all the water from the system by heating at 90 °C in vacuum, therefore small amount of water is always existing in the system. Although the exact amount of water is not known, it may play a beneficial role in the reaction according to the proposed mechanism shown in Scheme 2.

## 3. Summary

Both palladium(II) and platinum(II)-BINAP Lewis acid catalysts have been demonstrated to be water-tolerant in enantioselective carbonyl-ene reactions between arylglyoxals and alkenes. Thus arylglyoxal monohydrate could be used directly as substrate achieving comparable or even higher yields and enantioselectivities as compared with the corresponding carbonyl-ene reactions using dry phenylglyoxal as substrate. The enantioselective carbonyl-ene reactions using phenylglyoxal monohydrate and 4-methylphenylglyoxal monohydrate as substrates with four alkenes including methylenecyclohexane, 2,3-dimethyl-1-butene, 2,4,4-trimethyl-1-pentene and alpha-methylstyrene, were investigated affording good to excellent enantioselectivities between 76.2% and 95.4% e.e.. A mechanism involving the coordination of arylglyoxal and 2,2-dihydroxy-1-phenylethanone with chiral catalyst was proposed to interpret the enantioselective carbonyl-ene reaction using arylglyoxal monohydrate as substrate. To the best of our knowledge, this is the first report on water-tolerant enantioselective carbonyl-ene reactions using arylglyoxal monohydrate as substrate.

The development of water-tolerant enantioselective carbonyl-ene reactions using arylglyoxal monohydrate as substrate provided us a convenient and versatile protocol to study the enantioselective carbonyl-ene reactions between various arylglyoxals and alkenes. The studies on enantioselective carbonyl-ene reactions using more substituted and functionalized aryglyoxals monohydrate are in process. meanwhile we are also studying the catalyst recycle of palladium(II)-BINAP catalyst in ionic liquid. All these research works will be published later in due course.

## 4. Experimental

### 4.1. General considerations

In case of water-free reactions, the manipulations were carried out under an atmosphere of nitrogen or argon by using standard Schlenk line techniques in dried glassware. $^{1}$H-NMR and $^{13}$C-NMR were recorded in $CDCl_3$ on a BRUCKER 400 spectrometer. Analytical high-performance liquid chromatography (HPLC) was performed on an Agilent 110 Series HPLC equipped with a UV detector using a Chiralcel OD-H or Chiralcel OB-H column. Elemental analysis was performed on a EuroEA3000 Series Elemental Analyzer. Purification of reaction products was carried out by flash column chromatography on silica gel. Dry dichloromethane was purified using MBRAUN-SPS solvent purification system. 0.25 mM phenylglyoxal solution of dichloromethane was prepared by dissolving freshly dried phenylglyoxal (under 90 °C in vacuum) in dry dichloromethane. Phenylglyoxal monohydrate and alkenes were purchased from Sigma–Aldrich. 4-Methylphenylglyoxal monohydrate was purchased from SynChem. *R*-BINAP((*R*)-(+)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene) and *S*-BINAP((*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene) were purchased from Sigma–Aldrich. (*R*-BINAP)$PdCl_2$ and (*S*-BINAP)$PtCl_2$ were prepared according to a reported method [13] by reaction of BINAP (1 equiv.) in dichloromethane with dichloro($\eta^4$-1,5-cyclooctadiene)palladium(II) or dichloro($\eta^4$-1,5-cyclooctadiene)platinum(II) (1 equiv.) which were also prepared according to reported methods [14].

### 4.2. Catalyst activation

A small Schlenk flask was charged with 0.0125 mmol (*R*-BINAP)$PdCl_2$ or (*S*-BINAP)$PtCl_2$ and $AgSbF_6$ (2.5–3.0 equiv), after 2 mL dichloromethane was added, the resulting mixture was stirred for 30 min under nitrogen or argon atmosphere at room temperature, giving in situ activated catalyst solution of [(*R*-BINAP)Pd]$(SbF_6)_2$ or [(*S*-BINAP)Pt]$(SbF_6)_2$.

### 4.3. General procedure for enantioselective carbonyl-ene reactions

To a solution of the in situ prepared catalyst in dichloromethane according to the above described activation method, was added 0.25 mmol corresponding arylglyoxal monohydrate and 0.25 mmol alkene. The resulting mixture was stirred for required time at room temperature. Then the mixture was loaded onto a silica gel, and eluted with hexane/ethyl acetate mixture to give the corresponding compound. The isolated product was characterized with $^{1}$H-NMR and $^{13}$C-NMR($CDCl_3$, 400 MHz). Enantiomeric excess was determined by HPLC with a chiral column.

### 4.4. Preparation of 3-(1′-cyclohexenyl)-2-hydroxy-1-phenylpropan-1-one (1a)

The title compound was prepared according to the general procedure using 0.25 mmol phenylglyoxal monohydrate and 0.25 mmol methylenecyclohexane. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). The obtained product was checked with $^{1}$H-NMR and $^{13}$C-NMR($CDCl_3$, 400 MHz), which is consistent with the reported results. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (1.0% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 13.2 min(major), (*R*)enantiomer RT = 20.1 min(minor)).

### 4.5. Preparation of 4-isopropyl-2-hydroxy-1-phenyl-4-penten-1-one (1b)

The title compound was prepared according to the general procedure using 0.25 mmol phenylglyoxal monohydrate and

0.25 mmol 2,3-dimethyl-1-butene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). The obtained product was checked with $^{1}$H-NMR and $^{13}$C-NMR($CDCl_3$, 400 MHz), which is consistent with the reported results. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (0.8% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 27.5 min(major), (*R*)enantiomer RT = 58.6 min(minor)).

### *4.6. Preparation of 6,6-dimethyl-2-hydroxy-4-methylene-1-phenylheptan-1-one (1c)*

The title compound was prepared according to the general procedure using 0.25 mmol phenylglyoxal monohydrate and 0.25 mmol 2,4,4-trimethyl-1-pentene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). The obtained product was checked with $^{1}$H-NMR and $^{13}$C-NMR($CDCl_3$, 400 MHz), which is consistent with the reported results. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (1.0% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 10.2 min(major), (*R*)enantiomer RT = 14.3 min(minor)).

### *4.7. Preparation of 1,4-diphenyl-2-hydroxy-4-penten-1-one (1d).*

The title compound was prepared according to the general procedure using 0.25 mmol phenylglyoxal monohydrate and 0.25 mmol alpha-methylsyrene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). The obtained product was checked with $^{1}$H-NMR and $^{13}$C-NMR($CDCl_3$, 400 MHz), which is consistent with the reported results. Enantiomeric excess was determined by HPLC with a Chiralcel OB-H column (3.0% 2-propanol in hexane, flow 1.0 mL/min, (*R*)enantiomer RT = 20.5 min(minor), (*S*)enantiomer RT = 27.4 min(major)).

### *4.8. Preparation of 3-(1′-cyclohexenyl)-2-hydroxy-1-(4-methylphenyl)-propan-1-one (2a)*

The title compound was prepared according to the general procedure using 0.25 mmol 4-methylphenylglyoxal monohydrate and 0.25 mmol methylenecyclohexane. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). $^{1}$H-NMR($CDCl_3$, 400 MHz, $\delta$): 1.532–1.587(m) and 1.602–1.639(m) (–C$H_2$C$H_2$–, 4H), 2.036–2.042(m, –C$H_2$–C=C–, 4H), 2.110, 2.131, 2.146, 2.167(dd, –C$H_2$CH(OH)–, 1H), 2.430(S, Ph-C$H_3$, 3H), 2.459, 2.495(d, –C$H_2$CH(OH)–, 1H), 3.660, 3.677(d, –O$H$, 1H), 5.133–5.179(m, –C$H$(OH)–, 1H), 5.475(s, –C=C$H$–, 1H), 7.283, 7.303(d) and 7.806, 7.826(d)(Ph-$H$, 4H). $^{13}$C-NMR($CDCl_3$, 400 MHz, $\delta$): 21.74, 22.16, 22.83, 25.28, 28.79, 44.66, 72.03, 124.89, 128.72, 129.51, 131.33, 133.36, 144.87, 201.54. $C_{16}H_{20}O_2$ (244.34): Calcd. C 78.65%, H 8.25%; found C 78.24%, H 8.06%. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (1.0% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 8.3 min(major), (*R*)enantiomer RT = 11.2 min(minor)).

### *4.9. Preparation of 4-isopropyl-2-hydroxy-1-(4-methylphenyl)-4-penten-1-one (2b)*

The title compound was prepared according to the general procedure using 0.25 mmol 4-methylphenylglyoxal monohydrate and 0.25 mmol 2,3-dimethyl-1-butene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). $^{1}$H-NMR($CDCl_3$, 400 MHz, $\delta$): 1.020, 1.029(d), 1.037, 1.046(d) (–C$H_3$, 6H), 2.161, 2.184, 2.199, 2.222(dd, –C$H_2$CH(OH)–, 1H), 2.282–2.350(m, –C$H$(C$H_3$)$_2$, 1H), 2.433(S, Ph-C$H_3$, 3H), 2.585, 2.591, 2.623, 2.629(dd, –C$H_2$CH(OH)–, 1H), 3.687, 3.704(d, –O$H$, 1H), 4.901, 4.936(s, s, –C=C$H_2$, 2H), 5.169–5.216(m, –C$H$(OH)–, 1H), 7.292, 7.312(d), 7.817, 7.838(d) (Ph-$H$, 4H). $^{13}$C-NMR($CDCl_3$, 400 MHz, $\delta$): 21.56, 21.78, 33.57, 41.14, 72.16, 109.63, 128.69, 129.40, 129.59, 131.13, 145.01, 151.37, 201.28. $C_{15}H_{20}O_2$ (232.33): Calcd. C 77.55%, H 8.68%; found C 77.22%, H 8.97%. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (1.0% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 7.2 min(major), (*R*)enantiomer RT = 9.5 min(minor)).

### *4.10. Preparation of 6,6-dimethyl-2-hydroxy-4-methylene-1-(4-methylphenyl)-heptan-1-one (2c)*

The title compound was prepared according to the general procedure using 0.25 mmol 4-methylphenylglyoxal monohydrate and 0.25 mmol 2,4,4-trimethyl-1-pentene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). $^{1}$H-NMR($CDCl_3$, 400 MHz, $\delta$): 0.882(s, –C(C$H_3$)$_3$, 9H), 1.963, 1.996, 2.016, 2.049(q, –C$H_2$C(C$H_3$)$_3$, 2H), 2.197, 2.219, 2.234, 2.256(dd, –C$H_2$CH(OH)–, 1H), 2.434(s, Ph-C$H_3$, 3H), 2.599, 2.606, 2.636, 2.642(dd, –C$H_2$CH(OH)–, 1H), 3.676, 3.693(d, –O$H$, 1H), 4.868, 5.012(s, s, –C=C$H_2$, 2H), 5.154–5.200(m, –C$H$(OH)–, 1H), 7.290, 7.310(d) and 7.818, 7.839(d) (Ph-$H$, 4H). $^{13}$C-NMR($CDCl_3$, 400 MHz, $\delta$): 21.76, 29.88, 31.61, 44.24, 49.49, 72.44, 116.31, 128.70, 129.56, 131.14, 143.05, 145.02, 201.20. $C_{17}H_{24}O_2$ (260.38): Calcd. C 78.42%, H 9.29%; found C 78.76%, H 9.11%. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (1.0% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 6.1 min(major), (*R*)enantiomer RT = 8.0 min(minor)).

### *4.11. Preparation of 4-phenyl-1-(4-methylphenyl)-2-hydroxy-4-penten-1-one (2d)*

The title compound was prepared according to the general procedure using 0.25 mmol 4-methylphenylglyoxal monohydrate and 0.25 mmol alpha-methylsyrene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). $^{1}$H-NMR($CDCl_3$, 400 MHz, $\delta$): 2.419(s, Ph-C$H_3$, 3H), 2.605, 2.626, 2.641, 2.663(dd, –C$H_2$CH(OH)–, 1H), 3.046, 3.053,

3.082, 3.090(dd, –C$H_2$CH(OH)–, 1H), 3.657, 3.674(d, –O*H*, 1H), 5.067–5.114(m, –C*H*(OH)–, 1H), 5.165, 5.346(s, s, –C=C$H_2$, 2H), 7.240–7.353(m) and 7.684, 7.704(d), (Ph-H, 9H). $^{13}$C-NMR($CDCl_3$, 400 MHz, $\delta$): 21.76, 42.18, 71.50, 116.07, 126.63, 127.71, 128.39, 128.67, 129.52, 131.24, 140.67, 144.14, 145.01, 201.13. $C_{18}H_{18}O_2$ (266.34): Calcd. C 81.17%, H 6.81%; found C 80.76%, H 6.52%. Enantiomeric excess was determined by HPLC with a Chiralcel OB-H column (3.0% 2-propanol in hexane, flow 0.5 mL/min, (*S*)enantiomer RT = 21.7 min(major), (*R*)enantiomer RT = 28.8 min(minor)).

## Acknowledgement

This work was supported by Institute of Chemical and Engineering Sciences (ICES) A-STAR, Singapore.

## References

[1] K. Mikami, O. Kotera, Y. Motoyama, H. Sakaguchi, Synlett (1995) 975.
[2] For catalysts based on Al, see;
K. Maruoka, Y. Hoshino, T. Shirasaka, H. Yamamoto, Tetrahedron Lett. 29 (1988) 3967.
[3] For catalysts based on Ti, see;
(a) K. Mikami, M. Terada, T. Nakai, J. Am. Chem. Soc. 111 (1989) 1940;
(b) K. Mikami, M. Terada, T. Nakai, J. Am. Chem. Soc. 112 (1990) 3949;
(c) K. Mikami, Pure Appl. Chem. 68 (1996) 639;
(d) Y. Yuan, X. Zhang, K. Ding, Angew. Chem. Int. Ed. 42 (2003) 5478;
(e) H. Guo, X. Wang, K. Ding, Tetrahedron Lett. 45 (2004) 2009.
[4] For catalysts based on Ln, see;
(a) C. Qian, T. Huang, Tetrahedron Lett. 38 (1997) 6721;
(b) C. Qian, L. Wang, Tetrahedron: Asymmetry 11 (2000) 2347.
[5] For catalysts based on Cu, see;
(a) D.A. Evans, C.S. Burgey, N.A. Paras, T. Vojkovsky, S.W. Tregay, J. Am. Chem. Soc. 120 (1998) 5824;
(b) D.A. Evans, S.W. Tregay, C.S. Burgey, N.A. Paras, T. Vojkovsky, J. Am. Chem. Soc. 122 (2000) 7936.
[6] For catalysts based on Co, see;
S. Kezuka, T. Ikeno, T. Yamada, Org. Lett. 3 (2001) 1937.
[7] For catalysts based on Pd and Pt, see;
(a) J. Hao, M. Hatano, K. Mikami, Org. Lett. 2 (2000) 4059;
(b) K. Aikawa, S. Kainuma, M. Hatano, K. Mikami, Tetrahedron Lett. 45 (2004) 183;
(c) J.J. Becker, P.S. White, M.R. Gagne, J. Am. Chem. Soc. 123 (2001) 9478;
(d) J.H. Koh, A.O. Larsen, M.R. Gagne, Org. Lett. 3 (2001) 1233;
(e) H.-K. Luo, H. Schumann, J. Mol. Catal. A: Chem. 248 (2006) 42.
[8] For catalysts based on Sc, see;
D.A. Evans, J. Wu, J. Am. Chem. Soc 127 (2005) 8006.
[9] R. Bousset, Bull. Soc. Chim. 6 (1939) 986.
[10] (a) A. Vavasori, L. Toniolo, G. Cavinato, F. Vistentin, J. Mol. Catal. A: Chem. 204 (2003) 295;
(b) A. Vavasori, L. Toniolo, G. Cavinato, J. Mol. Catal. A: Chem. 215 (2004) 63.
[11] P.J. Stang, D.H. Cao, G.T. Poulter, A.M. Arif, Organometallics 14 (1995) 1110.
[12] A. Ladepeche, E. Tam, J.-E. Ancel, L. Ghosez, Synthesis (2004) 1375.
[13] P. Gugger, S.O. Limmer, A.A. Watson, A.C. Willis, S.B. Wild, Inorg. Chem. 32 (1993) 5692.
[14] (a) D. Drew, J.R. Doyle, Inorg. Synth. (1990) 346;
(b) J. Chatt, L.M. Vallarino, L.M. Venanzi, J. Chem. Soc. (1957) 2496.