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An efficient direct activation method transferring diastereopure platinum complex of BIPHEP to highly efficient Lewis acid catalyst for enantioselective carbonyl-ene reaction

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Abstract

An efficient direct activation method was developed to transfer diastereopure λ-[(BIPHEP)Pt(*S*-BINOL)] to highly active and selective enantiopure Lewis acid λ-[(BIPHEP)Pt]$(SbF_6)_2$ by silver hexafluoroantimonate($AgSbF_6$) for the enantioselective carbonyl-ene reactions. Both enantioselective glyoxylate-ene reactions between ethyl glyoxylate and alkenes, and enantioselective carbonyl-ene reactions between phenylglyoxal and alkenes were studied demonstrating good catalytic activity and enantioselectivity. Particularly, for the enantioselective carbonyl-ene reaction between phenylglyoxal and 2,3-dimethyl-1-butene, the Lewis acid catalyst λ-[(BIPHEP)Pt]$(SbF_6)_2$ generated with this direct activation method by silver hexafluoroantimonate($AgSbF_6$) could give excellent ee values high up to 94%.

Keywords: Enantioselectivity; Carbonyl-ene; BIPHEP; Platinum; Activation

1. Introduction

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 [1] which could then be transferred into more functionalized compounds by further reaction on its carbon–carbon double bond, hydroxyl and carbonyl groups. The key of this topic is searching for highly efficient and selective chiral catalyst to gain high ee values. Up to now, a variety of transition metal complexes have been studied involving Al [2], Ti [3], Ln [4], Cu [5], Co [6], Pd and Pt [7], etc., among which some could achieve high efficiency and enantioselectivity in the carbonyl-ene reaction. Evans et al. [5b] reported that the C_2-symmetric complex [Cu(*S*,*S*)-*tert*-butylbis(oxazolinyl)]$(SbF_6)_2$ could catalyze the glyoxylate-ene reaction between ethyl glyoxylate and methylenecyclohexane to give (*S*)-ethyl 3-(1′-cyclohexenyl)-2-hydroxypropionate with 96% ee, similarly, the complex [Cu(*S*,*S*)-*tert*-butylbis(oxazolinyl)]$(OTf)_2$ gave 86% ee for the same reaction. Optically active β-ketoiminato cationic cobalt(III) complex was reported by Yamada and co-workers [6] to be an efficient catalyst for enantioselective carbonyl-ene reaction to gave 88% ee in the carbonyl-ene reaction between phenylglyoxal and α-methylstyrene, and 94% ee in the carbonyl-ene reaction between phenylglyoxal and methylenecyclohexane. Ding and co-workers [3d] reported an extremely efficient Ti catalyst of modified BINOL ligands. Under nearly solvent-free conditions, 6,6′-I_2- or 6,6′-$(CF_3)_2$-BINOL-Ti-catalyst could catalyze the enantioselective carbonyl-ene reaction of glyoxylate ester with a variety of olefins at very low catalyst loadings (up to 0.01 mol%) affording the corresponding α-hydroxy esters in high yields and excellent enantioselectivities.

Chiral diphosphine-palladium and platinum complexes which are usually highly efficient and selective catalysts for Diels–Alder reaction [7a,8], have also been proved to be highly efficient and selective catalysts for enantioselective

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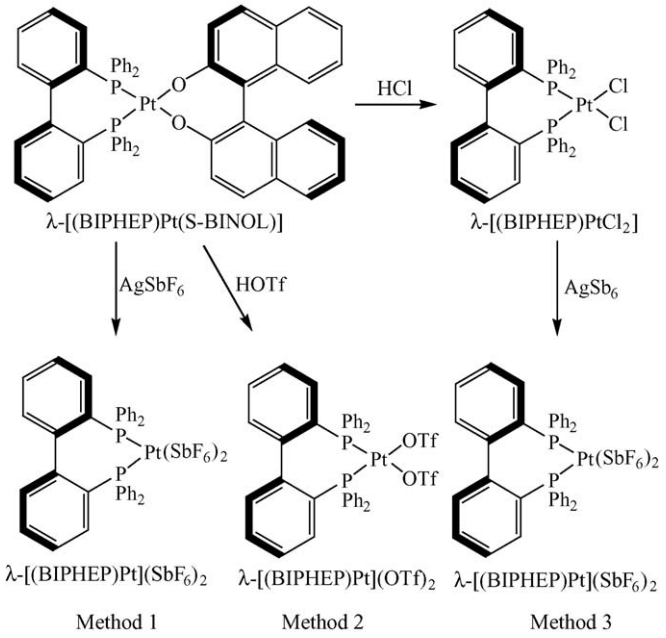
carbonyl-ene reaction. Mikami and co-workers [7b] reported that $\{Pd(CH_3CN)_2[(S)\text{-Tol-BINAP}]\}(SbF_6)_2$ could catalyze the glyoxylate-ene reaction between ethyl glyoxylate and methylenecyclohexane to give (*S*)-ethyl-3-(1′-cyclohexenyl)-2-hydroxypropionate with 78% ee and 88% yield under room temperature. More recently, $\{[(S)\text{-MeOBIPHEP}]Pt\}(SbF_6)_2$ was reported by Gagne and co-workers [7c] to be efficient and selective catalysts for the same glyoxylate-ene reaction to give 77% ee and 67% conversion under −50 °C for 5 h run.

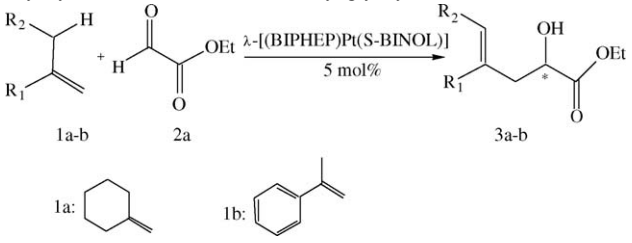
Besides BINAP (*atropos*), BIPHEP (*tropos*) is another popular diphosphine ligand with potential application in asymmetric catalysis. There are two methodologies have been reported to resolve palladium or platinum complexes of BIPHEP to chiral catalyst. Mikami et al. reported that palladium complexes of BIPHEP could be resolved with 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl (DM-DABN) [8d] to give enantiopure Lewis acid $(R)\text{-}[(BIPHEP)Pd(CH_3CN)_2](SbF_6)_2$ which was proved to be an efficient catalyst for the Hetero Diels–Alder reaction between ethyl glyoxylate and 1,3-cyclohexadiene to give 82% ee. Mikami et al. further reported that the diastereopure $(R)\text{-}[(BIPHEP)Pd(R\text{-DABN})(SbF_6)_2[R\text{-DABN}$: (*R*)-diaminobinaphthyl]] was an activated highly efficient and enantioselective catalyst [8e] for the Hetero Diels–Alder reaction between ethyl glyoxylate and 1,3-cyclohexadiene to give 92% ee and 75% yield under room temperature, the key of this catalyst is the chiral activator DABN which could completely control the BIPHEP-Pd chirality and significantly increase the catalytic activity. In another methodology, Gagne and co-workers [7a] demonstrated that platinum complex of BIPHEP could be resolved with (*S*)-BINOL, the δ- and λ-[(BIPHEP)Pt(*S*-BINOL)] could be each isolated to give corresponding single diastereoismer. After liberation of (*S*)-BINOL, the δ- or $\lambda\text{-}[(BIPHEP)Pt]^{2+}$ fragment was proved to be an efficient catalyst for Diels–Alder reaction and glyoxylate-ene reaction. In this approach BIPHEP was used as the sole source of chirality to achieve high ee in asymmetric catalysis since coordination of BIPHEP with platinum slows the atropinterconversion. After diastereopure δ- or λ-[(BIPHEP)Pt(*S*-BINOL)] is isolated, the key of this methodology is to find an efficient activator or method to liberate *S*-BINOL from platinum center to give the δ- or $\lambda\text{-}[(BIPHEP)Pt]^{2+}$ fragment and the activator should have minimum influence to the reaction. Two methods were used by Gagne. The first method (method 3 in Scheme 1) is a two-step activation, firstly to convert diastereopure δ- or λ-[(BIPHEP)Pt(*S*-BINOL)] to enantiopure δ- or $\lambda\text{-}[(BIPHEP)PtCl_2]$ which was then transferred to activated catalyst $[(BIPHEP)Pt](SbF_6)_2$ or $[(BIPHEP)Pt](OTf)_2$ by reaction with corresponding silver salt. The resulting $\lambda\text{-}[(BIPHEP)Pt](SbF_6)_2$ could catalyze the glyoxylate-ene reaction between ethyl glyoxylate and methylenecyclohexane to give 70% ee. The second method (method 2 in Scheme 1) is a treatment of δ- or λ-[(BIPHEP)Pt(*S*-BINOL)] solution with trifluoromethanesulfonic acid (HOTf) to give enantiopure catalyst δ- or $\lambda\text{-}[(BIPHEP)Pt](OTf)_2$ which could catalyze the Diels–Alder reaction between oxazolidinone and cyclopentadiene to give cycloadduct with 92–94% ee (93:7 endo: exo).



Scheme 1. Three activation methods transferring λ-[(BIPHEP)Pt(*S*-BINOL)] to activated catalyst.

In the enantioselective glyoxylate-ene reaction studies between ethyl glyoxylate and methylenecyclohexane using λ-[(BIPHEP)Pt(*S*-BINOL)] as catalyst precursor, we found that the in situ activated catalyst system by treatment of λ-[(BIPHEP)Pt(*S*-BINOL)] solution with stoichiometric amount of HOTf, demonstrated unexpected low enantioselectivity and low yield (see Table 1, entry 3, 10% ee, 25% yield), fur-

Table 1
Glyoxylate-ene reactions between ethyl glyoxylate and alkenes



Entry	Alkene	Activator	Yield[a] (%)	ee[b] (%)
1	1a	$AgSbF_6$	88	70
2	1a	AgOTf	52	76
3	1a	HOTf	25	10
4	1b	$AgSbF_6$	85	52
5	1b	AgOTf	73	58
6	1b	HOTf	7	1
7[c]	1a	HOTf	0	–
8[d]	1a	HCl	16	Racemic

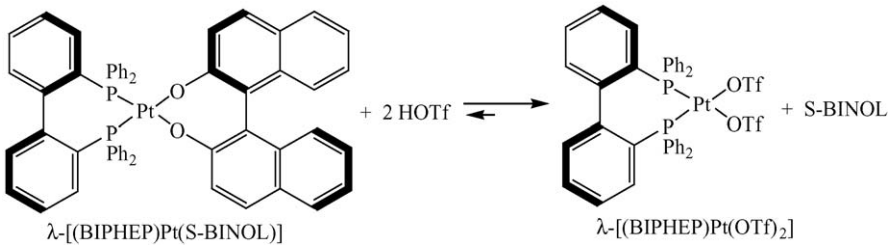
Reaction conditions: all reactions were run at room temperature for 5 h. Catalyst, 0.0125 mmol (5 mol%); ethyl glyoxylate, 0.5 mmol; alkene, 0.25 mmol.

[a] Isolated yield with flash chromatography.

[b] Determined by GC with a CYCLODEX-B column in case of methylenecyclohexane, by HPLC with a Chiracel AS column in case of α-methylstyrene.

[c] λ-[(BIPHEP)Pt(*S*-BINOL)] was not added, only 0.025 mmol HOTf was used to carry out the reaction.

[d] 0.025 mmol HCl was used as catalyst instead of platinum catalyst.



Scheme 2. Proposed equilibration in the reaction of λ-[(BIPHEP)Pt(*S*-BINOL)] with HOTf.

thermore, side reactions were always found to give impurities. The reason is probably because when the molar ratio of HOTf/Pt is approaching to 2, the reaction of λ-[(BIPHEP)Pt(*S*-BINOL)] with HOTf is not complete and is slightly reversible (see Scheme 2), which may result in the existence of a small amount of HOTf. A small amount of free HOTf could significantly influence this reaction. In fact, a comparative reaction by using the same amount of HOTf showed that no product was found, but only some impurities were formed (see Table 1, entry 7). While, inorganic acid HCl could catalyze the glyoxylate-ene reaction between ethyl glyoxylate and methylenecyclohexane to give clean product, of course the product is racemic (see Table 1, entry 8). Therefore, it is necessary to find an alternative efficient activator or method to transfer λ-[(BIPHEP)Pt(*S*-BINOL)] directly to highly efficient and highly enantioselective catalyst λ-$[(BIPHEP)Pt]^{2+}$ for the enantioselective carbonyl-ene reaction, and the activator should has no evident negative influence on the reaction.

Here, we report an efficient direct activation method using hexafluoroantimonate ($AgSbF_6$) or silver trifluoromethanesulfonate (AgOTf) as activators to transfer diastereopure λ-[(BIPHEP)Pt(*S*-BINOL)] to highly active and selective enantiopure Lewis acid for enantioselective carbonyl-ene reactions with ee values as high as 94%.

2. Results and discussions

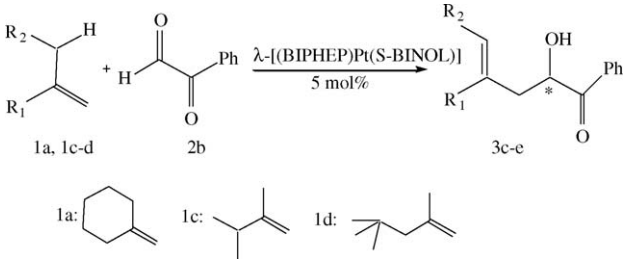
2.1. Enantioselective glyoxylate-ene reactions between ethyl glyoxylate and alkenes

Instead of HOTf, the λ-[(BIPHEP)Pt(*S*-BINOL)] solution was treated with two equivalent silver hexafluoroantimonate ($AgSbF_6$) or silver trifluoromethanesulfonate (AgOTf). After 25 min stirring under room temperature, a purple solution was given, then 0.50 mmol ethyl glyoxylate and 0.25 mmol methylenecyclohexane were added. After routine work up, we surprisingly found that both catalytic activity and enantioselectivity were enhanced significantly relative to HOTf activation method. The isolated yield was increased from 25% to 88% and 52%, respectively; the enantioselectivity was increased from 10% ee to 70% ee and 76% ee, respectively (see Table 1, entries 1–3). For the glyoxylate-ene reaction between ethyl glyoxylate and α-methylstyrene, the isolated yield was increased from 7% to 85% and 73%, respectively; the enantioselectivity was increased from 1% ee to 52% ee and 58% ee, respectively (see Table 1, entries 4–6). These results clearly indicate that $AgSbF_6$ and AgOTf are efficient activators for λ-[(BIPHEP)Pt(*S*-BINOL)].

2.2. Enantioselective carbonyl-ene reactions between phenylglyoxal and alkenes

So far, the platinum complexes of BIPHEP have been shown to be efficient catalyst for the glyoxylate-ene reactions between ethyl glyoxylate and alkenes, but this catalyst has not been explored for the enantioselective carbonyl-ene reaction of phenylglyoxal. The significant improvement with $AgSbF_6$/AgOTf activation method encouraged us to carry out the enantioselective carbonyl-ene reactions between phenylglyoxal and various alkenes, including methylenecyclohexane, 2,3-dimethyl-1-butene and 2,4,4-trimethyl-1-pentene. As expected a significant improvement was also achieved for both catalytic activity and enantioselectivity. For all the three carbonyl-ene reactions between phenylglyoxal and the three alkenes, the $AgSbF_6$ activation method gives the best results (see Table 2, entry 1 corresponding to methylenecyclohexane, 80% yield, 83% ee; entry 4 corresponding to 2,3-dimethyl-1-butene, 73%

Table 2
Carbonyl-ene reactions between phenylglyoxal and alkenes



Entry	Alkene	Activator	Yield[a] (%)	ee[b] (%)
1	1a	$AgSbF_6$	80	83
2	1a	AgOTf	45	69
3	1a	HOTf	Little[c]	–
4	1c	$AgSbF_6$	73	94
5	1c	AgOTf	22	93
6	1c	HOTf	12	78
7	1d	$AgSbF_6$	65	86
8	1d	AgOTf	44	67
9	1d	HOTf	23	35

Reaction conditions: all the reactions were run at room temperature for 5 h. Catalyst, 0.0125 mmol (5 mol%); phenylglyoxal, 0.5 mmol; alkene, 0.25 mmol.
[a] Isolated yield with flash chromatography.
[b] Determined by HPLC with a Chiralcel OD-H column.
[c] Not pure enough to get ee.

Table 3
Effect of catalyst loading in the enantioselective carbonyl-ene reaction between phenylglyoxal and 2,3-dimethyl-1-butene

Entry	Catalyst loading (mol%)	Yield[a] (%)	ee[b] (%)
1	5	73	94
2	2	72	94
3	1	64	94
4	0.5	54	93
5	0.2	53	91
6	0.1	40	91

All the reactions were run for 5 h under room temperature.
[a] Isolated yield with flash chromatography.
[b] Determined by HPLC with a Chiralcel OD-H column.

yield, 94% ee; entry 7 corresponding to 2,4,4-trimethyl-1-pentene, 65% yield, 86% ee). The AgOTf activation method gives lower yield and ee's (see Table 2, entry 2 corresponding to methylenecyclohexane, 45% yield, 69% ee; entry 5 corresponding to 2,3-dimethyl-1-butene, 22% yield, 93% ee; entry 8 corresponding to 2,4,4-trimethyl-1-pentene, 44% yield, 67% ee). Obviously both of $AgSbF_6$ and AgOTf activations are much better than the HOTf activation method (see Table 2, entries 3, 6 and 9 corresponding to methylenecyclohexane, 2,3-dimethyl-1-butene and 2,4,4-trimethyl-1-pentene, respectively).

2.3. Study on catalyst loading

In order to test the capability of this unique catalyst activation method and the catalyst system generated, the catalyst loading was dropped from 5 mol% down to 0.1 mol% for the carbonyl-ene reaction between phenylglyoxal and 2,3-dimethyl-1-butene, see Table 3. It was found that the isolated yield was decreased from 73% to 40%, while the enantioselectivity was only slightly dropped, even at 0.1 mol% catalyst loading, the ee is still excellent (91%), demonstrating a highly efficient and highly enantioselective catalyst system. It is very important for industrial applications by using low catalyst loading while the enantioselectivity is still excellent because the chiral platinum catalyst is expensive.

2.4. The effect of anions

Generally, for all the enantioselective carbonyl-ene reactions including ethyl glyoxylate and phenylglyoxal, λ-[(BIPHEP)Pt]$(SbF_6)_2$ gave better yield than λ-[(BIPHEP)Pt]$(OTf)_2$. This result is consistent with the result of $\{[(S)\text{-MeOBIPHEP}]Pt\}^{2+}$ catalyst [7c]. The reason is probably because SbF_6 is a good leaving group, while OTf has relatively stronger coordination capability with platinum center, which may result in the decrease of coordination opportunities between platinum center and phenylglyoxal (see Scheme 3).

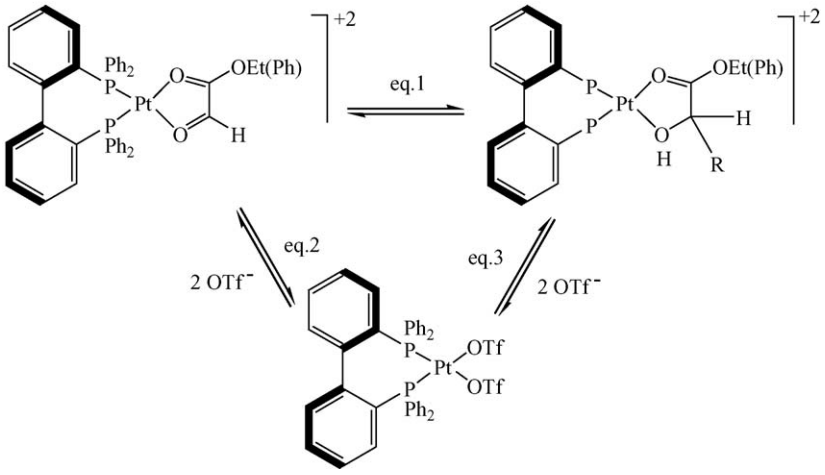
3. Summary

An efficient direct activation method was developed to transfer diastereopure λ-[(BIPHEP)Pt(*S*-BINOL)] to highly active and selective enantiopure Lewis acid λ-[(BIPHEP)Pt]$(SbF_6)_2$ by silver hexafluoroantimonate ($AgSbF_6$). With this activation method the enantioselective glyoxylate-ene reactions between ethyl glyoxylate and alkenes, and the carbonyl-ene reactions between phenylglyoxal and alkenes were studied. λ-[(BIPHEP)Pt]$(SbF_6)_2$ was proved to be particularly highly efficient and enantioselective catalyst for the carbonyl-ene reaction between phenylglyoxal and 2,3-dimethyl-1-butene with ee as high as 94%, even at very low catalyst loading (0.1 mol%), the ee% was still as high as 91%. This efficient activation method made the methodology to resolve racemic catalyst with *S*-BINOL more valuable, and provided an alternative activation way in the asymmetric catalysis when using diastereopure diphosphine/platinum/*S*-BINOL complex as catalyst precursor.

4. Experimental

4.1. General considerations

All manipulations involving air and/or moisture sensitive materials were carried out under an atmosphere of nitrogen



Scheme 3. Ligand/counterion exchange equilibrations.

by using standard Schlenk line techniques in dried glassware. Dichloromethane was distilled from CaH_2. Ethyl glyoxylate was freshly distilled prior to use. Pure phenylglyoxal was obtained by drying phenylglyoxal hydrate at 90 °C under vacuum and was used freshly. λ-[(BIPHEP)Pt(*S*-BINOL)] was prepared according to a reported method [7a].

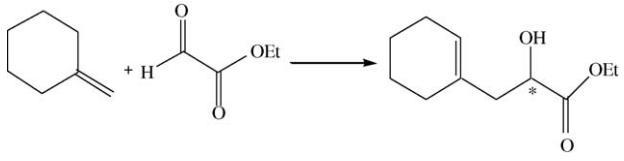
4.2. Catalyst activation

Two methods of catalyst activation were used and compared. In method A, a small Schlenk was charged with 12.5 mg (0.0125 mmol) λ-[(BIPHEP)Pt(*S*-BINOL)] and $AgSbF_6$ (or AgOTf) (2.0 equiv.), after 2 mL dichloromethane was added, the resulting mixture was stirred for 25 min under nitrogen atmosphere at room temperature, the color changed from pale yellow to deep purple gradually. In method B, a small Schlenk was firstly charged with 12.5 mg (0.0125 mmol) λ-[(BIPHEP)Pt(*S*-BINOL)], then 2 mL dichloromethane was added and stirred until platinum complex λ-[(BIPHEP)Pt(*S*-BINOL)] was dissolved completely, the solution was then treated with HOTf (2.2 μL, 2.0 equiv.), resulting in an immediate color change from light yellow to near colorless. The resulting mixture was stirred for 5 min under nitrogen atmosphere at room temperature before substrates were added.

4.3. General procedure for enantioselective carbonyl-ene reactions

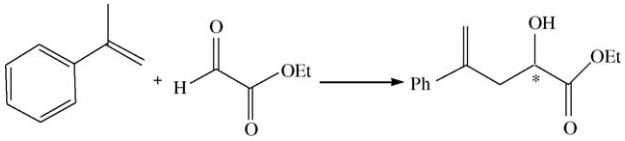
To a solution of the in situ prepared catalyst in dichloromethane according to activation method A or B, was added 0.5 mmol freshly distilled ethyl glyoxylate or freshly dried phenyloxal and 0.25 mmol alkylene. The resulting mixture was stirred for 5 h at room temperature, then the mixture was directly loaded onto a silica gel, and eluted with hexane/ethyl acetate mixture to give the corresponding compound [5,6].

4.4. Preparation of ethyl 3-(1′-cyclohexenyl)-2-hydroxypropionate (3a)



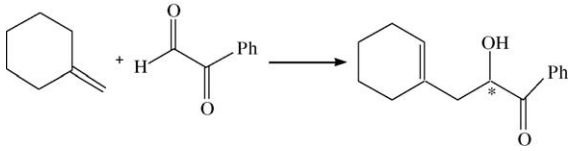
The title compound was prepared according to the general procedure using 0.5 mmol freshly distilled ethyl glyoxylate and 0.25 mmol methylenecyclohexane. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (4:1). ^{1}H NMR ($CDCl_3$, 300 MHz, *δ*): 1.31 (t, $–CH_2CH_3$), 1.58–1.63 (m, $–CH_2CH_2–$), 1.95–2.05 (m, $–CH_2–C{=}C–$), 2.30, 2.45 (dd,dd, $–CH_2CH(OH)$), 2.76 (O*H*), 4.23–4.28 (m, $–OCH_2CH_3$ and $–CH(OH)–$), 5.55 (s, $–C{=}CH–$). ^{13}C NMR ($CDCl_3$, 300 MHz, *δ*): 14.2, 22.2, 22.8, 25.3, 28.4, 43.2, 61.4, 69.2, 125.3, 133.0, 174.9. Enantiomeric excess was determined by GC with a CYCLODEX-B column (10.8 psi, 107 °C, at t = 50 min, rate 5 °C/min, final T = 160 °C, (*R*)enantiomer t_r = 25 min (minor), (*S*)enantiomer t_r = 26 min (major)).

4.5. Preparation of ethyl 2-hydroxy-4-phenyl-4-pentenoate (3b)



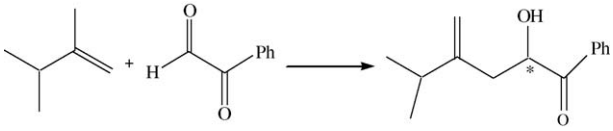
The title compound was prepared according to the general procedure using 0.5 mmol freshly distilled ethyl glyoxylate and 0.25 mmol α-methylstyrene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (5:1). ^{1}H NMR ($CDCl_3$, 300 MHz, *δ*): 1.26 (t, $–CH_2CH_3$), 2.79 (O*H*), 2.90, 3.10 (dd,dd, $–CH_2–$), 4.05–4.15 (m, $–OCH_2CH_3$), 4.28–4.32 (m, $–CH(OH)$), 5.25, 5.44 (s,s, $–C{=}CH_2$), 7.31–7.47 (m, Ph–*H*). ^{13}C NMR ($CDCl_3$, 300 MHz, *δ*): 14.5, 41.0, 62.0, 69.6, 116.6, 126.9, 128.1, 128.8, 140.8, 144.0, 174.8. Enantiomeric excess was determined by HPLC with a Chiralcel AS column (5.0% 2-propanol in hexane, flow 1.0 mL/min, (*S*)enantiomer RT = 11 min (major), (*R*)enantiomer RT = 17 min (minor)).

4.6. Preparation of 3-(1′-cyclohexenyl)-2-hydroxy-1-phenylpropan-1-one (3c)



The title compound was prepared according to the general procedure using 0.5 mmol freshly dried phenylglyoxal 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 ($CDCl_3$, 300 MHz, *δ*): 1.57–1.63 (m, $–CH_2CH_2–$), 2.01–2.03 (m, $–CH_2–C{=}C–$), 2.18, 2.50 (dd,dd, $–CH_2CH(OH)$), 3.67 (O*H*), 5.20–5.26 (m, $–OCH_2CH_3$ and $–CH(OH)$), 5.50 (s, $–C{=}CH–$), 7.53 (t), 7.65 (t), 7.95 (d) (Ph–*H*). ^{13}C NMR ($CDCl_3$, 300 MHz, *δ*): 22.6, 23.2, 25.7, 29.2, 45.0, 72.6, 125.5, 129.0, 129.2, 133.7, 134.3, 134.4, 202.4. 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 min (major), (*R*)enantiomer RT = 20 min (minor)).

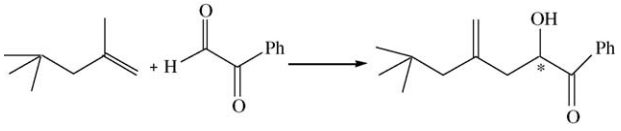
4.7. Preparation of 2-hydroxy-4-isopropyl-1-phenyl-4-penten-1-one (3d)



The title compound was prepared according to the general procedure using 0.5 mmol freshly dried phenylglyoxal and

0.25 mmol 2,3-dimethyl-1-butene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (5:1). ^{1}H NMR ($CDCl_3$, 300 MHz, δ): 1.05, 1.07 (d,d, –CH_3), 2.23 (dd, –CH_2CH(OH)), 2.34 (m, –CH(CH_3)$_3$), 2.65 (dd, –CH_2CH(OH)), 3.71 (OH), 4.93, 4.97 (s, s, –C=CH_2), 5.23–5.29 (m, –CH(OH)), 7.53 (t), 7.65 (t), 7.95 (d) (Ph–H). ^{13}C NMR ($CDCl_3$, 300 MHz, δ): 22.0, 22.2, 34.0, 41.4, 72.8, 110.2, 129.0, 129.3, 134.2, 134.4, 151.7, 202.2. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (0.8% 2-propanol in hexane, flow 0.5 mL/min, (*S*)enantiomer RT = 28 min (major), (*R*)enantiomer RT = 59 min (minor)).

4.8. Preparation of 6,6-dimethyl-2-hydroxy-4-methylene-1-phenylheptan-1-one (3e)



The title compound was prepared according to the general procedure using 0.5 mmol freshly dried phenylglyoxal and 0.25 mmol 2,4,4-trimethyl pentene. Pure product was obtained by column chromatography over silica gel eluted with hexane/ethyl acetate (9:1). ^{1}H NMR ($CDCl_3$, 300 MHz, δ): 0.90 (s, –CH_3), 2.02, 2.04 (d, –CH_2C(CH_3)$_3$), 2.26, 2.65 (dd,dd, –CH_2CH(OH)), 3.72 (OH), 4.90, 5.04 (s,s, –C=CH_2), 5.21–5.26 (m, –CH(OH)), 7.53 (t), 7.65 (t), 7.95 (d) (Ph–H). ^{13}C NMR ($CDCl_3$, 300 MHz, δ): 30.3, 32.0, 44.5, 49.9, 73.0, 116.8, 129.0, 129.3, 134.2, 134.4, 143.4, 202.1. 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 min (major), (*R*)enantiomer RT = 14 min (minor)).

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