聚乙二醇 400-水介质中水溶性钌膦二胺催化茚叉丙酮的不对称加氢反应

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摘要: 在聚乙二醇 400-水绿色可循环介质中, 以手性二胺 (*S,S*)-1,2-二苯基乙二胺二磺酸钠 ((*S,S*)-DPENDS) 与非手性钌膦络合物 ($[\text{RuCl}_2(\text{TPPTS})_2]$) 原位生成的水溶性钌膦二胺为催化剂, 考察了茚叉丙酮的选择性不对称加氢反应。在优化的反应条件下, 羰基加氢产物 4-苯基-3-丁烯-2-醇的化学选择性和对映选择性分别为 98.5% 和 74.3%。经正己烷萃取后, 催化剂即可从产物中分离出来。循环使用 5 次后, 4-苯基-3-丁烯-2-醇化学选择性和对映选择性没有明显下降。

关键词: 聚乙二醇 400; 水; 不对称加氢; 水溶性钌膦二胺; 茚叉丙酮; 循环

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Green and Recyclable Medium for Asymmetric Hydrogenation of Benzalacetone Catalyzed by $\text{RuCl}_2(\text{TPPTS})_2$ -(*S,S*)-DPENDS

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Abstract: PEG400-H₂O was a green and recyclable reaction medium for asymmetric hydrogenation of benzalacetone catalyzed by ruthenium achiral monophosphine complex, $\text{RuCl}_2(\text{TPPTS})_2$ (TPPTS: $\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$), which was modified by (*S,S*)-DPENDS (disodium salt of sulfonated (*S,S*)-1,2-diphenyl-1,2-ethylene-diamine). Under the optimized conditions, the chemoselectivity for 4-phenyl-3-buten-2-ol was 98.5% with a corresponding ee value of 74.3%. The resulting products could easily be separated from the catalyst by extraction with *n*-hexane. The catalyst immobilized on PEG400-H₂O could be recycled and reused at least five times without significant loss of chemoselectivity and enantioselectivity.

Key words: polyethylene glycol 400; water; asymmetric hydrogenation; water-soluble ruthenium-phosphine-diamine; benzalacetone; recycling

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催化 α,β -不饱和酮的不对称加氢可以制备光学活性烯丙醇^[1], 后者可用于手性药物、香精香料以及其它精细化学品的合成. Noyori 型钌膦二胺均相催化剂体系成功用于 α,β -不饱和酮的不对称催化加氢^[1~5], 产物烯丙醇的对映选择性最高可达 97%, 但催化剂价格昂贵, 与产物的分离困难^[6].

为了解决催化剂的循环使用问题, 研究人员对负载型多相催化体系和均相催化剂多相化方面进行了研究. 明方永等^[7]制备了手性二胺修饰的 Ru-TPP/ γ - Al_2O_3 催化剂, 用于茚叉丙酮的不对称加氢反应, 羰基加氢的选择性在 98% 以上, 不饱和醇的对映选择性达 47%. Ohkuma 等^[8]采用均相催化剂多相化的方法, 将 Ru/BINAP/二胺均相催化剂连接到高分子树脂上, 用于 β -紫罗兰酮和 2,4,4-三甲基-2-环己烯酮的多相不对称催化加氢反应中, 产物对映选择性分别达到 94% 和 87%.

要实现循环使用, 催化剂的有效分离是关键. 在两相催化体系中, 反应后催化剂与产物分别进入水相和有机相, 通过萃取即可实现两者的分离, 从而有利于催化剂的循环使用, 因而广泛用于不对称氢化反应中. C=O 键由于在热力学上较 C=C 键难以加氢, 因此, 有关两相催化体系中 α,β -不饱和酮的不对称加氢反应鲜有报道.

我们曾研究了 $\text{RuCl}_2(\text{TPPTS})_2$ -(*S,S*)-DPENDS 催化剂在离子液体或水两相体系中催化 α,β -不饱和酮的不对称加氢反应^[9,10]. 发现催化剂分离方便, 可循环使用多次, 但离子液体价格昂贵且制备工艺复杂, 且在纯水介质中烯丙醇的 ee 值稍低.

聚乙二醇 (PEG) 是目前公认的廉价、性质稳定、无毒环保的绿色反应介质, 已应用于众多催化反应中, 但是将其作反应溶剂或共溶剂用于不对称催化反应却较少^[11~14]. 本文以 PEG400-水为反应介质, 将 $\text{RuCl}_2(\text{TPPTS})_2$ -(*S,S*)-DPENDS 用于催化茚叉丙酮的不对称加氢反应, 考察了水、溶剂、修饰剂和碱浓度、催化剂前体对反应性能的影响.

1 实验部分

1.1 催化剂和手性修饰剂的制备

$\text{RuCl}_2(\text{TPPTS})_2$ 和 (*S,S*)-DPENDS (见图式 1)

制备参考文献 [15,16]. $\text{RuCl}_2(\text{TPPTS})_2$: ^1P NMR (D_2O , 300 MHz) δ 56.7; (*S,S*)-DPENDS: $[\alpha]_{\text{D}}^{20} = +48.1^\circ$ ($c = 0.70$, H_2O); ^1H NMR (D_2O , 300 MHz) δ 7.60–7.57 (m, 4H, aromatic H), 7.32–7.14 (m, 4H, aromatic H), 4.26 (s, 2H, 2-CH).

图式 1 手性修饰剂 (*S,S*)-DPENDS
Scheme 1. Chiral modifier (*S,S*)-DPENDS.

1.2 茚叉丙酮的选择性不对称加氢反应

向带有玻璃内衬和磁力搅拌的 60 ml 不锈钢高压釜中加入去离子水, $\text{RuCl}_2(\text{TPPTS})_2$, (*S,S*)-DPENDS, KOH 和茚叉丙酮 (Acros, >98%). 用氢气置换 5 次后, 充到指定压力, 在 40 °C 下搅拌反应一段时间后卸压, 然后加入 5 ml 正己烷萃取, 剧烈搅拌 5 min 后静置分层, 上层有机层待用, 此操作重复几次. 合并有机相, 产物用硅胶柱纯化.

经正己烷萃取后, 下层液体即为含有催化剂的聚乙二醇溶剂层, 不用任何处理直接用于下一次催化反应.

1.3 加氢产物的分析

在茚叉丙酮的加氢反应中, 可能有三种加氢产物生成: 双键加氢生成饱和酮 (记为 SK), 羰基加氢生成不饱和醇 (记为 UA), 羰基和双键全部加氢生成饱和醇 (记为 SA).

加氢产物的转化率和化学选择性用配有 β -DEX¹²⁰ 毛细管柱 (30 m $\times$ 0.25 mm, 0.25 μm) 的 GC-960 型气相色谱 (上海海欣色谱仪器有限公司) 分析, 氢气为载气, FID 检测器; 不饱和醇的对映选择性用配有 Chiralcel OD-H 手性柱 (25 cm $\times$ 4.6 mm) 的 YL9100 型高压液相色谱 (英麟机器有限公司) 分析.

产物的选择性 (以 UA 为例) 按下式计算: $X(\text{UA}) = m(\text{UA}) / (m(\text{SK}) + m(\text{SA}) + m(\text{UA}))$; 不饱和醇的 ee 值按下式计算: $\text{ee} = (c(R) - c(S)) / (c(R) + c(S))$.

图式 2 苯叉丙酮的不对称加氢

Scheme 2. Asymmetric hydrogenation of benzalacetone.

2 结果与讨论

2.1 PEG400 中水的比例对苯叉丙酮不对称加氢反应的影响

在研究离子液体中 $\text{RuCl}_2(\text{TPPTS})_2-(S,S)\text{-DPENDS}$ 催化苯叉丙酮的不对称加氢反应时发现, 离子液体中含有适量水的存在有利于提高催化性能^[9]. Wu 等^[17]在研究酮的不对称氢转移反应时发现, 水对酮的还原具有加速和促进作用. 因此, 为了进一步优化 $\text{RuCl}_2(\text{TPPTS})_2-(S,S)\text{-DPENDS}$ 在 PEG400 介质中的催化性能, 本文考察了水的加入量对苯叉丙酮的不对称加氢反应性能的影响, 结果见表 1. 可以看出, 在不加水的 PEG400 介质中, 反应的转化率、 α,β -不饱和醇的化学选择性和 ee 值分别仅为 11.5%、86.7% 和 42.5%. 随着 PEG400 中水的加入, 催化剂性能明显改善, 主产物 α,β -不饱和醇

表 1 溶剂对苯叉丙酮不对称加氢反应的影响

Table 1 Influence of water on the asymmetric hydrogenation of benzalacetone

$V(\text{PEG400})/V(\text{H}_2\text{O})$	Conversion (%)	Selectivity (%)			ee (%)
		SK	SA	UA	
PEG400	11.5	3.2	10.1	86.7	42.5
2:1	95.5	1.7	—	98.3	62.3
1.5:1	100.0	2.2	0.8	97.0	65.7
1:1	99.7	0.8	0.7	98.5	74.3
1:1.5	93.8	4.5	1.3	94.2	70.7
1:2	83.1	3.8	0.9	95.3	68.4
water	20.4	27.2	3.2	69.6	58.2

Reaction conditions: benzalacetone 0.85 mmol, $\text{Ru}/\text{benzalacetone} = 1:112$, PEG400 0.37 mL, $(S,S)\text{-DPENDS}$ 7.5×10^{-2} mol/L, KOH 0.12 mol/L, $p(\text{H}_2) = 5.0$ MPa, 40 °C, 2 h.

All products were in the *R*-configuration.

的化学选择性和对映选择性明显提高, 尤其是反应转化率, 由 11.5% 剧增至 95.5%. 这可能源于三个原因: (1) 水的加入使得水溶性催化剂在反应体系中的溶解度有所增加, 手性修饰剂 $(S,S)\text{-DPENDS}$ 对 $\text{RuCl}_2(\text{TPPTS})_2$ 的修饰作用进一步增强; (2) PEG400 和水的混合溶剂使体系中氢的浓度提高^[18]; (3) 水的加入使 PEG400 能够发挥非离子表面活性剂的作用.

随着水量的进一步增加, 反应的转化率和主产物的化学选择性变化不大, 对映选择性有较为明显的提高; 当 PEG400 与水的比例达到 1:1 时, 反应的转化率、选择性和 ee 值分别达到了 99.7%、98.5% 和 74.3%; 继续提高反应溶剂中水的比例, 反应的转化率以及主产物 α,β -不饱和醇的化学选择性和对映选择性开始逐渐降低. 当仅用水做溶剂时, 催化剂性能较低. 这可能是由于在同样的反应压力下, 纯水中 H_2 浓度较低; 另外, 受水溶剂化效应的影响, 两种对映异构体之间的能量变小, 从而导致产物对映选择性下降^[14,19,20].

2.2 $(S,S)\text{-DPENDS}$ 和 KOH 浓度对苯叉丙酮不对称加氢反应的影响

在 PEG400-水介质中, KOH 浓度对苯叉丙酮不对称加氢反应性能的影响见表 2. 可以看出, 当体系中含有 KOH 时, 反应不能进行. 加入少量 KOH, 底物开始转化, 当 KOH 浓度达到 0.12 mol/L 时, 反应的转化率和对映选择性明显提高. 这说明 KOH 浓度的提高不仅加快了反应速率, 而且增强了 $(S,S)\text{-DPENDS}$ 对钌配合物 $\text{RuCl}_2(\text{TPPTS})_2$ 的手性

表 2 KOH 浓度对苯叉丙酮不对称加氢反应的影响

Table 2 Influence of KOH concentration on the asymmetric hydrogenation of benzalacetone

Concentration (mol/L)	Conversion (%)	Selectivity (%)			ee (%)
		SK	SA	UA	
0.000	—	—	—	—	—
0.023	5.9	—	—	100	71.4
0.060	90.6	1.9	0.4	97.7	73.7
0.120	99.7	0.8	0.7	98.5	74.3
0.180	99.6	1.2	0.9	97.9	73.9

The reaction conditions are the same as in Table 1 except PEG400:H₂O (V/V) = 1:1 and the change of KOH concentration.

修饰作用,从而提高了反应的对映选择性.继续增加 KOH 浓度至 0.18 mol/L, α,β -不饱和醇的化学选择性和对映选择性略有下降.

表 3 为水溶性手性配体 (S,S)-DPENDS 浓度对苯叉丙酮不对称加氢反应性能的影响.由表可见,与 KOH 的影响不同,未加 (S,S)-DPENDS 时,反应依然可以进行,底物转化率达到 35.1%,但只生成 C=C 加氢的副产物.在热力学上 C=O 加氢要比 C=C 的更难,因此,未加手性修饰剂 (S,S)-DPENDS 时, RuCl₂(TPPTS)₂ 催化剂仅催化苯叉丙酮中 C=C 的加氢. (S,S)-DPENDS 的加入,有效地活化了 C=O,使其比 C=C 更易于加氢,因此,产物的对映选择性较高,且显著提高了 α,β -不饱和醇的化学选择性.当 (S,S)-DPENDS 浓度达到 0.075 mol/L 时,反应转化率、化学选择性和对映选择性均较佳,且不再随手性修饰剂浓度的增加而升高.

表 3 (S,S)-DPENDS 浓度对苯叉丙酮不对称加氢反应影响

Table 3 Effect of (S,S)-DPENDS concentration on the asymmetric hydrogenation of benzalacetone

Concentration (mol/L)	Conversion (%)	Selectivity (%)			ee (%)
		SK	SA	UA	
0.0	35.1	100	—	—	—
2.5	99.4	1.4	1.0	97.6	74.4
5.0	99.2	0.8	0.7	98.5	73.8
7.5	99.7	0.8	0.7	98.5	74.3
10.0	100.0	0.7	1.0	98.3	74.2

Reaction conditions: benzalacetone 0.85 mmol, Ru/benzalacetone = 1:112, PEG400 0.37 ml, PEG400:H₂O (V/V) = 1:1, KOH 0.12 mol/L, $p(\text{H}_2)$ = 5.0 MPa, 40 °C, 2 h.

表 2 和表 3 结果还表明 KOH 和手性二胺 (S,S)-DPENDS 在苯叉丙酮不对称加氢反应中存在协同作用,即只有在二者共同存在下,反应才能高效

进行.我们在研究苯乙酮的不对称加氢反应以及在前期研究 α,β -不饱和酮的不对称加氢反应中也观察到了这种协同效应^[9,10,14,21~23].

2.3 溶剂对苯叉丙酮不对称加氢反应的影响

在 PEG400 与水或有机溶剂的二元混合体系以及 PEG400 与水、有机溶剂组成的三元混和体系中,水溶性钌膦二胺 RuCl₂(TPPTS)₂-(S,S)-DPENDS 催化苯叉丙酮不对称加氢反应的结果见表 4.可以看出,在 PEG400-水或 PEG400-水-有机溶剂体系中,反应的转化率、 α,β -不饱和醇的化学选择性和对映选择性都相对较高.其中,在 PEG400-水-异丙醇的三元混合溶剂体系中催化剂性能最好.因为异丙醇既与水混溶,又可溶解部分底物,从而使催化剂与底物的接触面积增大,有利于催化剂发挥更好的性能;而在 PEG-水-正己烷的三元混合溶剂体系中,由于正己烷的疏水性强,虽然可以溶解底物,但使之与水溶性催化剂接触几率变小,从而导致反应转化率、化学选择性和对映选择性均显著下降.

表 4 溶剂对苯叉丙酮不对称加氢反应的影响

Table 4 Effect of organic solvent on the asymmetric hydrogenation of benzalacetone

Solvent	Conversion (%)	Selectivity (%)			ee (%)
		SK	SA	UA	
PEG400/H ₂ O	99.7	0.8	0.7	98.5	74.3
PEG400/ <i>i</i> -PrOH	48.7	2.0	1.2	97.8	54.9
PEG400/ <i>n</i> -hexane	25.5	5.8	—	94.2	41.1
PEG400/ <i>i</i> -PrOH/H ₂ O	99.7	0.5	0.7	98.8	76.5
PEG400/ <i>n</i> -hexane/H ₂ O	97.5	0.9	1.2	97.9	73.2

Reaction conditions: benzalacetone 0.85 mmol, Ru/benzalacetone = 1:112, PEG400 0.37 ml, PEG400:H₂O:organic solvent (V/V/V) = 1:1:1, (S,S)-DPENDS 0.075 mol/L, KOH 0.12 mol/L, $p(\text{H}_2)$ = 5.0 MPa, 40 °C, 2 h.

还可以看出,在 PEG400-有机溶剂体系中,反应转化率、化学选择性和对映选择性都相对较低.特别是在 PEG400-正己烷溶剂体系中,转化率和 ee 值分别仅为 25.5% 和 41.1%.在 PEG-异丙醇溶剂体系中,转化率和 ee 值较前者略高,但明显低于 PEG400-水-异丙醇的三元混合溶剂体系中的.由此进一步证明了反应体系中水对苯叉丙酮的不对称加氢反应的重要影响.

2.4 不同的钌催化剂前驱体对苯叉丙酮不对称加氢反应的影响

在 PEG400-H₂O 介质中,研究了不同的钌催化

表 5 不同钌催化剂前体对苯叉丙酮不对称加氢反应的影响

Table 5 Effect of different ruthenium precatalysts on the asymmetric hydrogenation of benzalacetone

Ruthenium precatalyst	Conversion (%)	Selectivity (%)			ee (%)
		SK	SA	UA	
[RuCl ₂ (TPPTS) ₂] ₂	99.7	0.8	0.7	98.5	74.3
RuCl ₃ -2TPPTS	1.3	100.0	—	—	—
RuCl ₂ (COD)-2TPPTS	13.3	79.3	—	20.7	65.2
RuCl ₂ (COD)-2TPPTS ^a	99.3	—	8.7	91.3	70.0

Reaction conditions are the same as in Table 1 except the change of ruthenium precatalysts.

^aRuCl₂(COD) and TPPTS were pretreated at $p(\text{H}_2) = 5.0 \text{ MPa}$, 40°C , 30 min.

剂前驱体对催化苯叉丙酮的不对称加氢反应性能的影响, 结果见表 5. 可以看出, 以 RuCl₂(TPPTS)₂ 为催化剂前驱体时效果最佳, 反应转化率、选择性和 ee 值分别为 99.7%, 98.5% 和 74.3%. 当 RuCl₃-2TPPTS 作为催化剂前驱体时, Ru³⁺要还原成低的氧化态才能与 TPPTS 配位生成活性物种 RuCl₂(TPPTS)₂, 因此, 反应存在较长的诱导期, 使得催化活性很低. 对于 RuCl₂(COD), 因为 COD 要与 TPPTS 交换生成活性物种, 也需要一段时间的诱导期, 所以在同样反应条件下表现出较低的催化活性.

另外, 以 RuCl₂(COD)-2TPPTS 和 RuCl₃-2TPPTS 为催化剂前驱体时, α,β -不饱和醇化学选择性也很低, 说明在形成催化活性物种前, 优先加氢 C=C 键而非 C=O 键. 为了验证 RuCl₂(COD)-2TPPTS 在形成活性物种前存在诱导周期, 我们将 RuCl₂(COD) 和 TPPTS 预先在反应温度下加热 30 min, 然后加入其余反应物进行反应, 结果发现反应的转化率、 α,β -不饱和醇的化学选择性和对映选择性均明显提高, 表明确实存在诱导期, 同时也说明 RuCl₂(TPPTS)₂ 是一种最好的催化剂前体.

2.5 循环使用性能

以苯叉丙酮不对称加氢为例, 考察了 RuCl₂(TPPTS)₂-(S,S)-DPENDS 催化剂的循环使用性能, 结果见表 6. 反应后通过正己烷萃取即可将催化剂从产物中分离出来, 直接用于下一次反应. 可以看出, 该催化剂循环使用 5 次后, 其催化活性、化学选择性以及对映选择性下降得非常缓慢. 经 ICP 分析发现, 钌金属催化剂的流失量仅为 0.1%. 可见, 该催化剂具有一定的重复使用性能.

表 6 RuCl₂(TPPTS)₂-(S,S)-DPENDS 催化剂循环使用性能
Table 6 Reuse of catalyst RuCl₂(TPPTS)₂-(S,S)-DPENDS in PEG-H₂O

Run	Conversion (%)	Selectivity (%)			ee (%)
		SK	SA	UA	
1	99.7	0.8	0.7	98.5	74.3
2	98.5	0.9	0.6	98.5	73.9
3	94.6	1.1	0.8	98.1	73.2
4	92.1	1.3	0.9	97.8	72.6
5	90.2	1.7	1.1	97.2	72.1
6	85.4	2.0	1.3	96.7	71.4

Reaction conditions: benzalacetone 0.85 mmol, Ru/benzalacetone = 1:112, PEG400 0.37 ml, PEG400:H₂O (V/V) = 1:1, (S,S)-DPENDS 0.075 mol/L, KOH 0.12 mol/L, $p(\text{H}_2) = 5.0 \text{ MPa}$, 40°C , 2 h.

3 结论

在绿色可循环的反应介质 PEG400-H₂O 中, 将水溶性催化剂 RuCl₂(TPPTS)₂-(S,S)-DPENDS 成功用于两相体系中苯叉丙酮的不对称催化加氢反应中, 在优化的反应条件下, 反应转化率、产物化学选择性和对映选择性分别达 99.7%, 98.5% 和 74.3%. 实验发现, PEG 介质中适量水的存在有利于提高催化剂性能, KOH 和 (S,S)-DPENDS 存在协同作用. PEG400-H₂O 对催化剂具有良好的固载作用, 经正己烷萃取即可实现催化剂和产物的有效分离, 并可循环使用 5 次. 在后续工作中, 将开展配体和修饰剂方面的研究, 进一步提高产物的对映选择性.

参 考 文 献

- Ohkuma T, Ooka H, Ikariya T, Noyori R. *J Am Chem Soc*, 1995, **117**: 10417
- Lindner E, Ghanem A, Warad I, Eichele K, Mayer H A, Schurig V. *Tetrahedron: Asymmetry*, 2003, **14**: 1045
- Peach P, Cross D J, Kenney J A, Mann I, Houson I, Campbell L, Walsgrove T, Wills M. *Tetrahedron*, 2006, **62**: 1864
- Ohkuma T, Hattori T, Ooka H, Inoue T, Noyori R. *Org Lett*, 2004, **6**: 2681
- Wu J, Ji J X, Guo R W, Yeung C H, Chan A S C. *Chem Eur J*, 2003, **9**: 2963
- Ngo H L, Hu A, Lin W. *Tetrahedron Lett*, 2005, **46**: 595
- 明方永, 王金波, 付海燕, 陈骏, 陈华, 李贤均. 催化学报 (Ming F Y, Wang J B, Fu H Y, Chen J, Chen H, Li X J. *Chin J Catal*), 2007, **28**: 1057
- Ohkuma T, Takeno H, Honda Y, Noyori R. *Adv Synth Catal*, 2001, **343**: 369
- Wang J B, Feng J, Qin R X, Fu H Y, Yuan M L, Chen H, Li X J. *Tetrahedron: Asymmetry*, 2007, **18**: 1643
- 王金波, 秦瑞香, 熊伟, 贾云, 刘德蓉, 陈华. 催化学报

- (Wang J B, Qin R X, Xiong W, Jia Y, Liu D R, Chen H. *Chin J Catal*), 2010, **31**: 273
- 11 Zhou H F, Fan Q H, Tang W J, Xu L J, He Y M, Deng G J, Zhao L W, Gu L Q, Chan A S C. *Adv Synth Catal*, 2006, **348**: 2172
 - 12 Zhou H F, Fan Q H, Huang Y Y, Wu L, He Y M, Tang W J, Gu L Q, Chan A S C. *J Mol Catal A*, 2007, **275**: 47
 - 13 Zhou Z Q, Sun Y. *React Kinet Mech Catal*, 2010, **99**: 391
 - 14 秦瑞香, 王金波, 熊伟, 刘德蓉, 冯建, 陈华. 催化学报 (Qin R X, Wang J B, Xiong W, Liu D R, Feng J, Chen H. *Chin J Catal*), 2011, **32**: 1490
 - 15 陈华. [博士学位论文]. 成都: 四川大学 (Chen H. [PhD Dissertation]. Chengdu: Sichuan Univ), 1999
 - 16 Ma Y P, Liu H, Chen L, Cui X, Zhu J E, Deng J G. *Org Lett*, 2003, **5**: 2103
 - 17 Wu X F, Wang C, Xiao J L. *Platinum Metals Rev*, 2010, **54**: 3
 - 18 Pugin B, Studer M, Kuesters E, Sedelmeier G, Feng X. *Adv Synt Catal*, 2004, **346**: 1481
 - 19 Laghmari M, Sinou D. *J Mol Catal*, 1991, **66**: L15
 - 20 Sandoval C A, Ohkuma T, Munlz K, Noyori R. *J Am Chem Soc*, 2003, **125**: 13490
 - 21 Wang J B, Qin R X, Fu H Y, Chen J, Feng J, Chen H, Li X J. *Tetrahedron: Asymmetry*, 2007, **18**: 847
 - 22 熊伟, 杨朝芬, 袁茂林, 陈华, 李贤均. 催化学报 (Xiong W, Yang Ch F, Yuan M L, Chen H, Li X J. *Chin J Catal*), 2005, **26**: 1093
 - 23 Xiong W, Lin Q, Ma H X, Zheng H J, Chen H, Li X J. *Tetrahedron: Asymmetry*, 2005, **16**: 1959

英 译 文

English Text

Catalytic asymmetric hydrogenation of α,β -unsaturated ketones is a powerful method for the synthesis of optically active allylic alcohols [1]. These allylic compounds are important materials for the preparation of chiral pharmaceuticals, flavors, and fine chemicals. In the past chiral ruthenium-phosphate-diamine, Noyori's type homogeneous catalyst, was successfully applied to the asymmetric hydrogenation of α,β -unsaturated ketones [1–5]. This method increased the selectivity of allylic alcohols by up to 97%. However, the drawback of this method is that homogeneous catalysts are expensive and difficult to recycle and reuse [6].

The utilization of either the supported heterogeneous catalyst or the heterogenized homogeneous catalyst for the reuse of the catalyst has been reported previously. Ming et al. [7] developed a chiral diamine modified Ru-TPP/ γ -Al₂O₃ catalyst for asymmetric hydrogenation of benzalacetone where the selectivity of C=O hydrogenation was 98% and the enantioselectivity for unsaturated alcohol was 47%, as well. In addition to the supported heterogeneous catalytic system modified by chiral compounds, Ohkuma et al. [8] demon-

strated a polymer-bonded heterogeneous catalyst with Ru/BINAP/diamine for enantioselective hydrogenation of β -ionone and 2,4,4-trimethyl-2-cyclohexenone, and reported ee values of 94% and 87%, respectively.

It is important that catalyst can be easily separated from their products for future usage. A biphasic catalytic system has become a very active field of research recently due to the easy separation of chiral catalysts from the organic products and is an interesting approach for catalyst recycle and reuse [13,14]. However, the preferential hydrogenation of C=C bond over the coexisting C=O bond makes this approach unattractive. Hence, limited research has been done on the asymmetric hydrogenation of α,β -unsaturated ketones in biphasic reaction systems.

In our previous work, a RuCl₂(TPPTS)₂-(*S,S*)-DPENDS catalyst for asymmetric hydrogenation of α,β -unsaturated ketones was reported in ionic liquids and water diphase system [9–10]. The catalyst could be reused seven times and easily separated from the product. However, ionic liquids had disadvantages because of their high price and tedious preparation. The enantioselectivity was slightly lower in pure water media.

Polyethylene glycols (PEGs) are inexpensive and low toxicity. Recently, liquid PEGs have been attracting increasing interest as novel solvents for organic reactions due to benign characteristics. However, PEGs as reaction medium for asymmetric hydrogenation have rarely been reported [11–14]. Here, we report the asymmetric hydrogenation of benzalacetone catalyzed by a RuCl₂(TPPTS)₂-(*S,S*)-DPENDS complex in water media, and the influences of the ruthenium complexes, solvents, concentrations of (*S,S*)-DPENDS, and KOH, temperature, and pressure on the asymmetric hydrogenation of benzalacetone were investigated.

1 Experimental

1.1 Synthesis of catalyst and modifier

RuCl₂(TPPTS)₂ and chiral modifier (*S,S*)-DPENDS (Scheme 1) were synthesized according to known methods in our laboratory [15,16]. RuCl₂(TPPTS)₂: ¹P NMR (D₂O, 300 MHz) δ 56.7; (*S,S*)-DPENDS: [α]_D²⁰ = +48.1° (*c* = 0.70, H₂O); ¹H NMR (D₂O, 300 MHz) δ 7.60–7.57 (m, 4H, aromatic H), 7.32–7.14 (m, 4H, aromatic H), 4.26 (s, 2H, 2-CH).

1.2 Typical procedure for asymmetric hydrogenation of aromatic ketones

PEG400, H₂O, RuCl₂(TPPTS)₂, (*S,S*)-DPENDS, KOH, and benzalacetone (Acros, >98%) were added to a 60 ml

stainless autoclave with a glass linear and magnetic stirrer was introduced to the desired pressure after the reaction mixture had been purged with H₂ five times. The mixture was stirred at 40 °C for a predetermined time. After the hydrogen was vented, *n*-hexane (5 ml) was added to extract the organic product. The resulting two layers were mixed thoroughly by vigorous stirring for 5 min. The upper layer was separated by decantation. This procedure was repeated one more time. The two extracts containing the product were combined and purified by silica gel technique. The reaction mixture was extracted with *n*-hexane under Ar atmosphere. The organic layer was siphoned from the PEG400 and the residual *n*-hexane was removed by blowing the Ar gas before the addition of a new substrate.

1.3 Product analysis

The conversion and selectivity were determined by GC-960 (Shanghai Haixin Chromatographic Instrument Co.) with a β -DEX¹²⁰ column (25 m $\times$ 0.25 mm) and FID detector using hydrogen gas as a carrier. The ee values were determined by YL HPLC (Young Lin Instrument Co.) with a Chirasil OD-H column (25 cm $\times$ 4.6 mm).

The selectivity and ee values of unsaturated alcohol were calculated from the equations: $X(\text{UA}) = m(\text{UA}) / (m(\text{SK}) + m(\text{SA}) + m(\text{UA}))$ and $\text{ee} (\%) = (c(\text{R}) - c(\text{S})) / (c(\text{R}) + c(\text{S}))$, respectively.

2 Results and discussion

2.1 Influence of water on asymmetric hydrogenation of benzalacetone

Our previous report [9] indicated that the influence of water on the asymmetric hydrogenation of benzalacetone catalyzed by a RuCl₂(TPPTS)₂-(*S,S*)-DPENDS was crucial, as appropriate amount of water was beneficial to enhanced the catalytic property. Furthermore, it was reported by Wu et al. [17] that water had the ability to accelerate the reduction of ketones in the asymmetric transfer hydrogenation. In view of the beneficial effect of water to improve the performance of RuCl₂(TPPTS)₂-(*S,S*)-DPENDS catalyst in PEG400, we added some water to evaluate its effect on the asymmetric hydrogenation of benzalacetone, and the results are listed in Table 1. The data shown in Table 1 indicated that the addition of appropriate amount of water was not only beneficial to exerting the catalytic activity and chemoselectivity of the catalyst, but also helped improve the enantioselectivity.

In pure PEG400, the conversion, chemoselectivity of the allylic alcohol, and the ee value were only 11.5%, 86.7%, and 42.5%, respectively (Table 1, entry 1). With the addition of water, the catalytic performance is obviously enhanced, as

indicated by an increase in conversion from 11.5% to 95.5%. There are three possible reasons that can attribute to this phenomenon. First, the addition of water enhanced solubility of the water-soluble catalyst and chiral modification of (*S,S*)-DPENDS to Ru catalyst is increased. Second, the concentration of H₂ is increased as a result of the PEG400 and water mixed solvent [18], and finally, PEG400 might exert the role of non-ionic surfactant.

When the amount of water was equal to that of PEG400, the conversion, chemoselectivity of allylic alcohol, and ee value reached 99.7%, 98.5%, and 74.3%, respectively (Table 1, entry 4). However, continuous increase of the amount of water resulted in lower enantioselectivity. When only water was used as solvent, there is reduction in activity and chemoselectivity. Also low H₂ concentration resulted in decrease conversion in pure water. By altering the water solvation effect, the energy difference between the two enantiomers as well as their enantioselectivities declined [14,19,20].

2.2 Influence of (*S,S*)-DPENDS and KOH concentration on asymmetric hydrogenation of benzalacetone

The influence of KOH concentration on the asymmetric hydrogenation of benzalacetone was investigated and the results are summarized in Table 2. It could be seen that KOH concentration had a profound effect on the conversion, chemoselectivity, and enantioselectivity. The reaction was unable to proceed in the absence of KOH (Table 5, entry 1). With the addition of KOH, there was a reduction in the reactant with subsequent increase in the product indicating some conversion of the reactant to the products. When the concentration of KOH was raised up to 0.12 mol/L, the conversion and enantioselectivity of α,β -unsaturated alcohol obviously increased. The increase of KOH concentration did not only accelerate the rate of the reaction but also facilitated the chiral conversion of (*S,S*)-DPENDS to the ruthenium complex. Thereafter the chemoselectivity and enantioselectivity of α,β -unsaturated alcohol began to decreased slightly with further increase in KOH concentration.

The influence of (*S,S*)-DPENDS on asymmetric hydrogenation of benzalacetone was observed in Table 3. Unlike KOH, there is no allylic alcohol detected in the absence of (*S,S*)-DPENDS, while the hydrogenation of C=C was observed and the conversion of benzalacetone was 35.1%. It was probably because the C=O bond is difficult to hydrogenate than the C=C bond, so the RuCl₂(TPPTS)₂ catalyst could only hydrogenate C=C bond of benzalacetone in the absence of (*S,S*)-DPENDS. When (*S,S*)-DPENDS was added, C=O bond can be effectively activated and easier to hydrogenate than C=C bond. Therefore, the addition of

(*S,S*)-DPENDS not only gave a higher enantioselectivity, but also increased the chemoselectivity for the α,β -unsaturated alcohol. When the concentration of (*S,S*)-DPENDS was 7.5×10^{-2} mol/L, the conversion, chemoselectivity, and enantioselectivity were good, and remain constant upon increasing the concentration of (*S,S*)-DPENDS.

The results shown in Tables 2 and 3 indicated that there was a synergistic effect between (*S,S*)-DPENDS and KOH. A similar phenomenon in our previous research work was observed in the asymmetric hydrogenation of acetophenone and α,β -unsaturated ketones [9,10,14,21–23].

2.3 Effect of organic solvent on the asymmetric hydrogenation of benzalacetone

The effect of organic solvent on the asymmetric hydrogenation of benzalacetone was investigated in three media of PEG400/H₂O, PEG400/organic solvent, and PEG400/H₂O/organic solvent mixed media. The data from the conversion, chemoselectivity, and enantioselectivity were higher in PEG400/H₂O and PEG400/H₂O/organic solvent. Moreover, the catalyst exhibited the best optimum activity in PEG400/*i*-PrOH/H₂O. This is because *i*-PrOH could mix with H₂O and also partially dissolve the substrate, to create contact between the catalyst and substrate. However, in PEG400/*n*-hexane/H₂O, the values were lower because the hydrophobicity of hexane was not favorable to create contact between the water-soluble catalyst and substrate.

From the results in Table 1, it was known that influence of water on asymmetric hydrogenation of benzalacetone was obvious. The data shown in Table 4 demonstrate that the values of conversion, chemoselectivity, and enantioselectivity were lower in PEG400/organic solvent. Especially in PEG400/*n*-hexane, the conversion and ee value were only 25.5% and 41.1%, respectively. In addition, the results were higher than the former but lower than those in PEG400/*i*-PrOH/H₂O. These further studies proved the significance of water in the asymmetric hydrogenation of benzalacetone.

2.4 Effects of different ruthenium precatalysts on asymmetric hydrogenation of benzalacetone

The asymmetric hydrogenation of benzalacetone catalyzed by different ruthenium precatalysts was investigated in PEG400-H₂O and the results are summarized in Table 5. The influences of the different ruthenium catalyst precursors on the activity, chemoselectivity, and enantioselectivity were evident and showed that RuCl₂(TPPTS)₂ was the most efficient precursor with conversion, chemoselectivity of allylic alcohol, and ee value reaching 99.7%, 98.5%, and 74.3%,

respectively (Table 5, entry 1). For RuCl₃-2TPPTS as a precursor, the trivalent ruthenium was reduced to a low oxidation state, RuCl₂(TPPTS)₂ and then coordinated with TPPTS to form an active catalyst. This resulted in longer induction period for RuCl₃-2TPPTS, leading to very low activity. For RuCl₂(COD)-2TPPTS the low activity could be due to the exchange between COD and TPPTS leading to an active catalyst. The chemoselectivity of allylic alcohol was lower using RuCl₂(COD)-2TPPTS and RuCl₃-2TPPTS as precursors, indicating that the precatalysts would hydrogenate C=C before forming the catalytic active species. RuCl₂(COD) and TPPTS was pretreated for 30 min at 40 °C, and then added to the reaction. The result indicated that both chemoselectivity and enantioselectivity of allylic alcohol were also apparently enhanced, which proved that there was an induction period for RuCl₂(COD)-2TPPTS, and further testified that RuCl₂(TPPTS)₂ was the most efficient catalyst precursor.

2.5 Catalyst recycling

The recycling and reuse of water soluble RuCl₂(TPPTS)₂-(*S,S*)-DPENDS catalyst was investigated in a PEG400-H₂O media using benzalacetone as the standard substrate. The data demonstrated that the chiral alcohol 4-phenyl-3-buten-2-ol could easily be separated by extraction with *n*-hexane, while the catalyst and modifiers immobilized in PEG400 could be recycled and reused several times. The catalyst exhibited good catalytic performance, and could be reused five times without a loss of activity, chemoselectivity and enantioselectivity. The loss of ruthenium was minimal, and was only 0.1% from ICP analysis.

3 Conclusions

PEG400-H₂O, was successfully used as a green and recyclable reaction medium in which the asymmetric hydrogenation of benzalacetone was catalyzed by RuCl₂(TPPTS)₂-(*S,S*)-DPENDS. The high activity, excellent chemoselectivity, and good enantioselectivity were 99.7%, 98.5%, and 74.3%, respectively, under optimized reaction conditions. It was discovered that appropriate amount of water was beneficial to enhance the catalytic activity and the synergistic effect between (*S,S*)-DPENDS and KOH. The catalyst immobilized in PEG400-H₂O can easily be separated from the products by extraction with *n*-hexane, and reused several times. In the follow up work, excellent ligand and modifier will be considered to further improve the enantioselectivity.

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