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[(BINAP)Re(O)Cl_3] as an efficient catalyst for olefination of chiral α-substituted aliphatic aldehydes

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ABSTRACT

A convenient one-pot preparation of [(BINAP)Re(O)Cl_3] (**6**) is described. This complex was demonstrated to be an efficient catalyst for the olefination of aldehydes by reaction with α-diazo esters, with essentially quantitative yields and up to 98:2 geometric selectivity. The potential for using enantiopure [(BINAP)Re(O)Cl_3] (**6**) to promote an asymmetric kinetic resolution of racemic α-stereogenic aldehydes was investigated, but no enantiotopic discrimination was observed. Control experiments indicate that this lack of selectivity stems from the in-situ formation of a phosphonium ylide, which accounts for product formation in a non-metal associated reaction pathway.

1. Introduction

The ability to meet an increasing demand for complex molecules in an efficient and sustainable manner relies on the development of new synthetic methods and the strategies that they inspire. Considerable efforts have been invested in the development of asymmetric reactions where new stereogenic units are created, e.g. selective bond formation to one of the enantiotopic faces of a carbonyl or enolate. A different approach, to discriminate between enantiotopic groups or enantiomers, is attractive as in principle any process, also those that do not create new chirogenic units, can be rendered enantioselective this way [1]. An example of such a process is asymmetric olefination, e.g., the asymmetric Horner–Wadsworth–Emmons (HWE) reaction. Chiral phosphonates have been used to differentiate α-stereogenic enantiotopic carbonyls, often with high yields and excellent geometric and diastereoselectivies [2,3]. This strategy has played a key role in several recent total syntheses of complex natural products with anticancer activity [4]. The utility of asymmetric olefination reactions is however currently hampered by the high cost of the most efficient chiral phosphonates as well as by expensive and sensitive additives (i.e. strong bases, crown ethers). A recent report by O'Brien and coworkers recently addressed some of these concerns by presenting a method for Wittig reactions which is catalytic in phosphine [5]. To lower the cost, and ideally improve on operational convenience and scalability, a method relying on readily available materials that recycle the expensive chiral information in a catalytic cycle is desired. Several reports on catalytic asymmetric HWE-type reactions have been published [6], but a general, cheap, convenient and efficient protocol remains elusive. The development of transition metal catalyzed olefination reactions based on metalla-carbenes, formed through catalytic decomposition of diazocompounds, suggests new entries to an asymmetric olefination reaction [7,8]. Seminal work by Herrmann on MTO (methyltrioxorhenium)-catalyzed olefinations serves as a useful starting point in this context. This reaction has been shown to proceed via a metallaoxetane intermediate, arising from cycloaddition of a Re–carbene to an aldehyde (Scheme 1, [9a,b]). The metal is thus associated with the substrate carbonyl in the proposed product-determining step. Attaching chiral ligands to the metal in this process would create a chiral environment at the reaction center that might discriminate between enantiotopic carbonyl groups, either in the same substrate molecule (asymmetric desymmetrization) or in different ones (kinetic resolution), resulting in a catalytic asymmetric olefination reaction. Chen and Zhang subsequently reported a detailed mechanistic study on a cationic Re–bipyridyl catalyst formed from decomposition of [Re_2O_7(bipy)] [9d]. With this catalyst the olefination reaction was shown to proceed via in-situ generation of a Wittig-ylide, which accounts for product formation.

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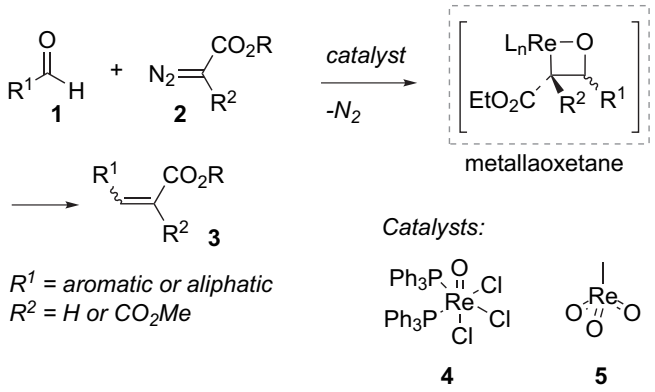

Scheme 1. Rhenium catalyzed olefination of aldehydes.

In addition to Re, several other metals like Mo, Co, Rh, and Fe [10], exhibit catalytic activity in similar reactions. These processes are typically described as proceeding through generation of ylides [9,11].

Getting access to chiral analogs of MTO (**5**) is a synthetically challenging task [12]. An alternative Re complex, also shown by Herrmann to be an efficient catalyst of olefination reactions, is $[(PPh_3)_2Re(O)Cl_3]$ [9b,13] (**4**). A protocol for olefinations catalyzed by $[(PPh_3)_2Re(O)Cl_3]$ (**4**) using $(EtO)_3P$ as the reducing agent instead of PPh_3 was shown to simplify the workup as the solvents and byproducts of this procedure are either volatile or water-soluble [14]. The high stability of **4**, paired with good behavior in catalysis including low catalyst loadings, simple workups, good yields and geometric selectivities makes it an attractive catalyst.

We hypothesized that $[(BINAP)Re(O)Cl_3]$ (**6**) might serve as a chiral homolog of **4** in asymmetric olefination reactions (Fig. 1). This complex is a known, air and shelf stable compound, previously shown to exhibit good catalytic activity in oxidations of sulfides to sulfoxides [15], and more recently in hydrosilylations of aldehydes [16]. The X-ray structure of *rac*-**6** was published by Parr et al. in 2005 [17].

An achiral complex with a bidentate phosphine ligand, $[(DPPE)Re(O)Cl_3]$ (**7**) was previously shown to be inactive in olefination reactions [18], but given that the electronic properties of **6** would resemble those of **4** more closely than those of the bisphenyl-alkyl ligands of **7**, this precedent was not decisive.

2. Experimental

2.1. General methodology

Tetrahydrofuran (THF) was distilled from sodium/benzophenone under a nitrogen atmosphere. Dichloromethane (CH_2Cl_2) was distilled form CaH_2 under a nitrogen atmostphere. All reactions were carried out in oven-dried glassware. Commercially available compounds were used without further purification unless otherwise indicated. TLC analyses were performed on aluminium-backed F_{254} gel plates, using UV and a solution of 5% phosphomolybdic acid in ethanol for visualization. Flash chromatography was performed using silica gel 60 (40–63 μm). Proton ^1H and carbon ^{13}C NMR spectra were recorded on a 400 or 500 MHz instrument using the residual signals from $CHCl_3$ at δ7.26 and δ77.0 as internal references, respectively. ^{31}P NMR was recorded on a 500 MHz instrument using phosphoric acid as external reference. Optical rotations were determined using the sodium-D line (589 nm).

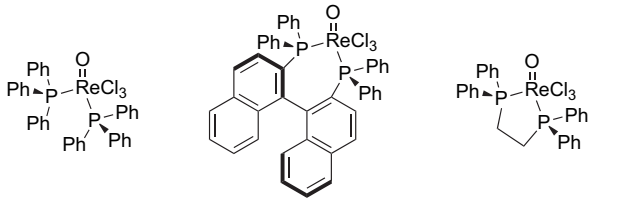

Fig. 1. Re (V) complexes with phosphine ligands.

2.2. Representative procedure for Re-catalyzed olefinations

To a stirred solution of acrolein dimer **10** (54 μl, 0.53 mmol), triphenylphosphine (46 mg, 0.18 mmol) and (+)-$[(BINAP)Re(O)Cl_3]$ (**6**) (9 mg, 0.009 mmol) in refluxing CH_2Cl_2 (2 mL) was added ethyldiazoacetate (EDA) (22 μl, 0.21 mmol) dissolved in CH_2Cl_2 (1 mL) over 4 hours using a syringe pump, during which time the reaction slowly turned brown. The reaction was refluxed a further 20 minutes and then cooled to room temperature. The volatiles were removed under reduced pressure and the crude residues were purified by flash chromatography (eluting with 3.13–6.25% EtOAc/pentane) to give alkene **11** as a separable mixture of (*E*)- and (*Z*) isomers, as a clear oil (27.5 mg, 84%).

(2*E*)-Ethyl 3-(3,4-Dihydro-2*H*-pyran-2-yl)acrylate (**11**) [19]. IR (film) 2942 (m), 1720 (s), 1303 (m), 1180 (m), 1033 (m); ^1H NMR (500 MHz, $CDCl_3$) 6.94 (dd, $J = 15.7$, 4.3 Hz, 1H major isomer), 6.41 (td, $J = 6.6$, 1.9 Hz, 1H), 6.08 (dd, $J = 15.7$, 1.8, Hz, 1H), 4.77–4.70 (m, 1H), 4.55–4.49 (tdd, $J = 8.7$, 4.3, 2.3 Hz, 1H), 4.22 (q, $J = 7.1$ Hz, 2H), 2.17–2.06 (m, 1H), 2.05–1.95 (m, 2H), 1.77–1.66 (m, 1H), 1.31 (t, $J = 7.2$ Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$), 166.8, 146.7, 143.7, 121.3, 101.1, 73.6, 60.9, 27.7, 19.5, 14.6; HPLC e.r. = 50:50, Chiracel OD-RH column, 60–25% MeCN/H_2O over 30 min., 0.5 mL/min; $t_{R1} = 14.38$ min, $t_{R2} = 14.90$ min; MS (ESI, $M + H^+$) = calcd' for $C_{10}H_{15}O_3$ 183.1, found 183.

(2*E*)-Ethyl 3-(1-Tosylpiperidin-2-yl)acrylate (**13**). IR (film) 2942 (m), 1720 (s), 1446 (m), 1263 (m), 1155 (s); ^1H NMR (500 MHz, $CDCl_3$) 7.72–7.66 (m, 2H), 7.32–7.27 (m, 2H), 6.77 (dd, $J = 15.8$, 5.3 Hz, 1H), 5.90 (dd, $J = 15.8$, 1.9 Hz, 1H major isomer), 4.79–4.29 (m, 1H), 4.19 (q, $J = 7.1$, 2H), 3.80–3.75 (d, $J = 13.4$ Hz, 1H), 3.06–2.96 (m, 1H), 2.43 (s, 3H), 1.80–1.68 (m, 2H), 1.64–1.40 (m, 4H) (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 145.3, 143.3, 137.4, 129.6, 127.2, 123.3, 60.5, 53.9, 41.8, 29.6, 24.7, 21.5, 19.3, 14.2; HPLC e.r. = 50:50, Chiracel, OD-J column, 3% *i*PrOH/Hexanes, 0.9 mL/min; $t_{R1} = 29.46$ min, $t_{R2} = 35.76$ min; MS (ESI, $M + H^+$) calcd' for $C_{17}H_{24}NO_4S$ 338.1, found 338.

rac-$[BINAP]Re(O)Cl_3$ (*rac*-**6**). Perrhenic acid (224 mg, 53% in H_2O, 0.537 mmol) was dissolved in HCl (200 μL, conc.), and the resulting solution was added dropwise to a stirred suspension of BINAP (318 mg, 0.426 mmol) in AcOH (6 mL). The resulting mixture immediately turned green and a dark green precipitate was formed. After 1 h, the reaction mixture was filtered and the filtrate washed repeatedly with Et_2O (3x) and cold CH_2Cl_2 (2x) to give **6**, as dark green microcrystals (205 mg, 41%): IR (KBr) 3054 (m), 2954 (m), 2856 (m), 1722 (m), 1434 (s); ^1H NMR (500 MHz, $CDCl_3$) 7.80–7.73 (m, 3H), 7.71–7.59 (m, 5H), 7.56–7.39 (m, 11H), 7.36 (ddd, $J = 8.2$, 6.8, 1.2 Hz, 1H), 7.30–7.18 (m, 4H), 7.09–7.03 (m, 1H), 6.90 (d, $J = 8.7$ Hz, 1H), 6.87–6.76 (m, 4H), 6.59 (dt, $J = 8.1$, 2.4 Hz, 2H); ^{31}P NMR (202 MHz, $CDCl_3$), −17.8, −21.0.

(+)-$[BINAP]Re(O)Cl_3$ (**6**) [20]. To a stirred solution of $[(AsPh_3)_2Re(O)Cl_3]$ (**9**) (590 mg, 0.643 mmol) in CH_2Cl_2 (5 mL) was added (+)-(*R*)-BINAP (405 mg, 0.650 mmol). The resulting bright green solution was stirred for 3 h after which it was concentrated to 0.5 mL. Addition of hexanes (7 mL) resulted in precipitation of **6**, which was collected by filtration. The solid was washed repeatedly