Achiral benzophenone ligand–rhodium complex with chiral diamine activator for high enantiocontrol in asymmetric transfer hydrogenation†

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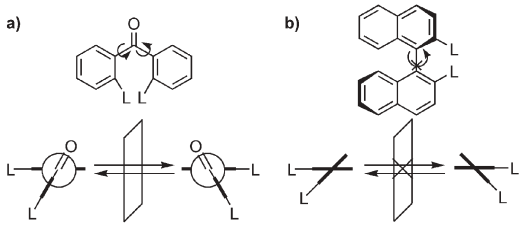
The chirality of an achiral benzophenone-based rhodium complex can be controlled by chiral diamines to afford significantly high enantioselectivity in the catalytic asymmetric transfer hydrogenation of ketones (up to 99% *ee*, 99% yield).

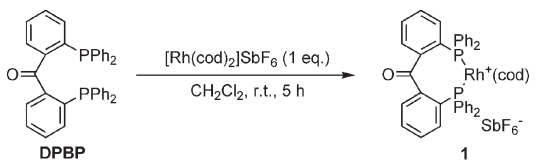
Asymmetric catalysis is one of the most important subjects in modern science and technology.[1] Asymmetric catalysts are generally metal complexes with enantiopure ligands. We report, however, the development of novel achiral benzophenone ligands for rhodium catalysts[2] in transfer hydrogenation of ketones with a significantly high level of enantioselectivity and yields (up to 99% *ee*, 99% yield). Rhodium catalyzed asymmetric transfer hydrogenation has never been described in an efficient format.[3]

Metal complexes are generally employed as asymmetric catalysts bearing chiral and atropisomeric ligands[4] (originating from *atropos* in Greek)[5] such as BINAP in enantiopure forms.[6] However, achiral and *tropos* ligands, such as benzophenone-derived diphosphine DPBP (2,2′-bis(diphenylphosphino)benzophenone), could be controlled into a single enantiomeric conformation[7,8] and hence replace the enantiopure and *atropos* ligands (Eq. 1).[9]



(1)

Upon addition of DPBP to $[Rh(cod)_2]SbF_6$, DPBP–Rh complex **1** was obtained in a pure form (Eq. 2). Not only $[Rh(cod)_2]SbF_6$ but also $[Rh(nbd)_2]SbF_6$ gave DPBP–Rh complexes in pure forms.



(2)

Unfortunately, a single crystal of $[Rh(dpbp)(cod)]SbF_6$ or $[Rh(dpbp)(nbd)]SbF_6$ could not be obtained, but $PtCl_2$(dpbp) **2** was obtained. Indeed, X-ray analysis of a single crystal of $PtCl_2$(dpbp) **2**‡ clearly shows the chiral conformation of the benzophenone skeleton of the DPBP ligand, which adopts a helical propeller conformation (Fig. 1).

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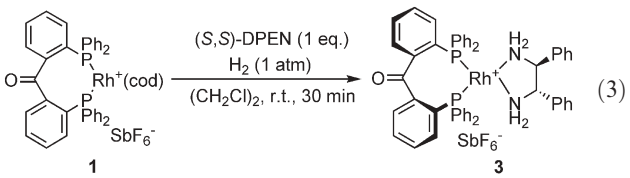
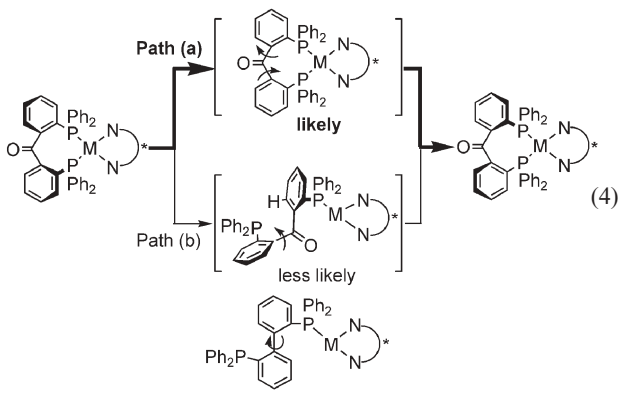
The control of the chirality of DPBP–Rh complex **1** by the addition of (*S*,*S*)-DPEN led to the formation of diastereomerically pure complex $[Rh(dpbp)\{(S,S)\text{-dpen}\}]SbF_6$ **3** (Eq. 3). This isomerization was found to be significantly fast. Upon addition of (*S*,*S*)-DPEN at room temperature, Rh(dpbp)[(*S*,*S*)-dpen] **3** was instantaneously obtained in diastereomerically pure form.[10]



(3)

Two possible mechanisms can be envisaged for isomerization of DPBP–Rh complex **3**. Path (a) involves internal rotation between the two phenyl rings, and path (b) needs dissociation of one phosphine–metal (P–M) bond followed by rotation back to the enantiomeric DPBP–metal complex (Eq. 4). In the case of BIPHEP–metal complex, the single diastereomer was obtained at 80 °C over 5 h *via* path (b).[11] In sharp contrast, DPBP–metal complex was instantaneously obtained in a diastereomerically pure form at room temperature *via* path (a).[12]



(4)

The advantage of "achiral" but *tropos* benzophenone ligand over the enantiopure *atropos* BINAP for asymmetric catalysis can be seen in transfer hydrogenation of 1′-acetonaphthone (Table 2).§ At the outset, the reaction conditions were optimized using the BINAP catalysts.[13] BINAP–Rh complexes were examined by changing the chirality and aliphatic or aromatic nature of diamines complexed to give single diastereomers in all cases (Table 1).

Among diamines examined, 1,2-diphenylethylenediamine (DPEN) afforded the highest enantioselectivity, though at a moderate level (71% *ee*, 96%). It should be noted here that the matched enantiomer of DPEN for acetophenone is changed from $RuCl_2[(R)\text{-binap}][(R,R)\text{-dpen}]$[14] to $[Rh\{(R)\text{-binap}\}\{(S,S)\text{-dpen}\}]SbF_6$.

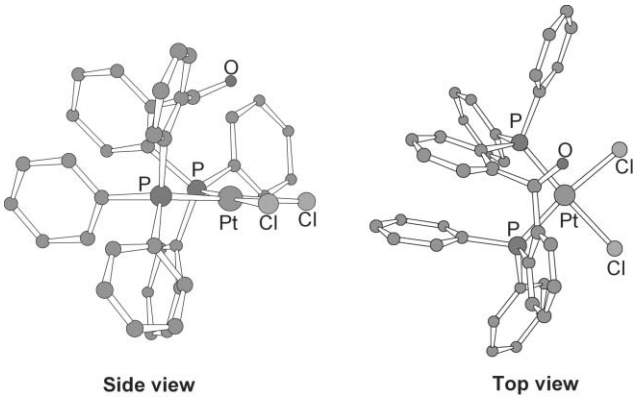


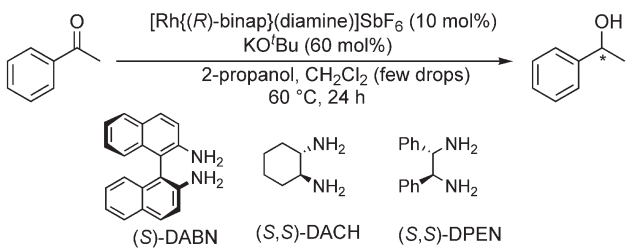
Fig. 1 3D X-ray structure of $PtCl_2$(dpbp) **2**.

With the best diamine for [Rh{(*R*)-binap}{(*S*,*S*)-dpen}]SbF_6, the reaction temperature and co-solvent were examined for [Rh(dpbp){(*S*,*S*)-dpen}]SbF_6. 1,2-Dichloroethane rather than dichloromethane was found to be the best co-solvent and room temperature was preferable to give the highest enantioselectivity (see Table S1 in supporting information).

Virtually complete (99% *ee*) enantioselectivities were thus obtained for 1′-acetonaphthone and *o*-substituted acetophenone under the optimized reaction conditions (Table 2). The benzophenone catalyst **3** gave (*R*)-1-(1′-naphthyl)ethanol and (*R*)-*o*-methylphenethyl alcohol with 99% *ee* in 99% yield, which is significantly higher than the 72% *ee* and 57% *ee* respectively obtained with enantiopure [Rh{(*R*)-binap}{(*S*,*S*)-dpen}]SbF_6.[15] [Rh{(*R*)-biphep}{(*S*,*S*)-dpen}]SbF_6 catalyst[16] also gave (*R*)-1-phenylethanol with only 59% *ee* in 12% yield.

In summary, we have succeeded in the development of achiral benzophenone ligands for rhodium catalysts in transfer hydrogenation of ketones with virtually perfect enantiocontrol. The enantiopure benzophenone complex affords much higher enantioselectivity than those attained by the enantiopure BINAP counterpart.

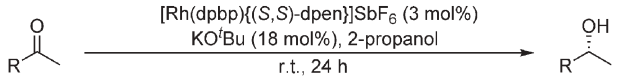
Table 1 Transfer hydrogenation catalyzed by BINAP–Rh/diamines

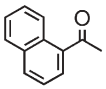
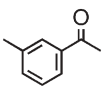


Entry	Diamine	Product conv. (%)	*ee* (%)
1	(*R*)-DABN	58	12 (*S*)
2	(*S*)-DABN	73	0
3	(*R*,*R*)-DACH	37	10 (*S*)
4	(*S*,*S*)-DACH	81	57 (*R*)
5	(*R*,*R*)-DPEN	93	0
6	**(*S*,*S*)-DPEN**	**96**	**71 (*R*)**
cf.[a]	$RuCl_2$[(*R*)-tol-binap][(*R*,*R*)-dpen]	> 99	80 (*S*)

[a] Ref. 14.

Table 2 Transfer hydrogenation catalyzed by DPBP–Rh complex



Entry	Substrate	Diphosphine	Product conv. (%)	*ee* (%)
1[a]		(*R*)-BINAP	98	72
2		**DPBP**	**> 99**	**99**
3[a]		(*R*)-BINAP	61	57
4		**DPBP**	**99**	**99**
5[a]		(*R*)-BINAP	97	68
6[b]		**DPBP**	**95**	**91**
7[a]		(*R*)-BINAP	96	71
8[c]		**DPBP**	**97**	**89**

[a] At 60 °C, with CH_2Cl_2 (few drops). [b] For 48 h. [c] With $(CH_2Cl)_2$ (2-propanol : $(CH_2Cl)_2$ = 18 : 1).

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Notes and references

‡ *Crystal data for PtCl₂(dpbp) (**2**)*: formula $C_{37}H_{28}Cl_2OP_2Pt\cdot2(CH_2Cl_2)$, one of these dichloromethanes is disordered over two sites, Triclinic, space group *P*-1(#2), a = 11.1806(4) Å, b = 11.2602(4) Å, c = 16.3715(5) Å, α = 83.78(10)°, β = 85.79(10)°, γ = 67.10(10)°, V = 1886.46(11) Å^3, Z = 2 and D = 1.736 Mg/m^3. X-ray diffraction data were collected on a Bruker APEX2 with graphite-monochromated Mo-Kα (λ = 0.7107 Å) at 100 K and the structure was solved by direct methods (SHELXL-97). The final cycle of full-matrix least-squares on $F2$ was based on 8833 observed reflections and converged to R = 0.0204 and Rw = 0.0513. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 293556. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b517585b).

§ *Typical procedure for Rh-catalyzed hydrogenation of ketones. Table 2, entry 3*: To a solution of [Rh(dpbp){(*S*,*S*)-dpen}]SbF_6 (11.0 mg, 0.01 mmol) in 2-propanol (3.6 ml) was added 0.1 M of ^{t}BuOK/2-propanol (0.6 ml, 0.06 mmol) at room temperature under argon atmosphere in a Schlenk tube. After being stirred for 20 min at room temperature, the reaction mixture was treated with *o*-methylacetophenone (43 µl, 0.33 mmol) and stirred for 24 h at room temperature under Ar atmosphere. After the reaction mixture was concentrated under reduced pressure, the residue was filtered through a short column of silica gel (hexane/ethyl acetate = 1/3) to give alcohol products.

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15 In this asymmetric transfer hydrogenation, chiral phosphine parts quite affect the yields and enantiomeric excesses of the products. In transfer hydrogenation, [Rh(cod){(*S*,*S*)-dpen}]SbF_6 gave (*R*)-1-(1′-naphthyl)-ethanol with only 43% *ee* in 7% yield.
16 [Rh{(*R*)-BIPHEP}{(*S*,*S*)-dpen}]SbF_6 was obtained by the addition of (*S*,*S*)-DPEN to the diastereomerically pure [Rh{(*R*)-BIPHEP}-{(*R*)-dabn}]SbF_6 complex in methanol.