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SYNTHESIS, RESOLUTION AND USE IN ENANTIOSELECTIVE CATALYSIS OF AN AXIALLY CHIRAL BINAPHTHYL-TEMPLATED P,S-HETERODONOR LIGAND (BINAPS)

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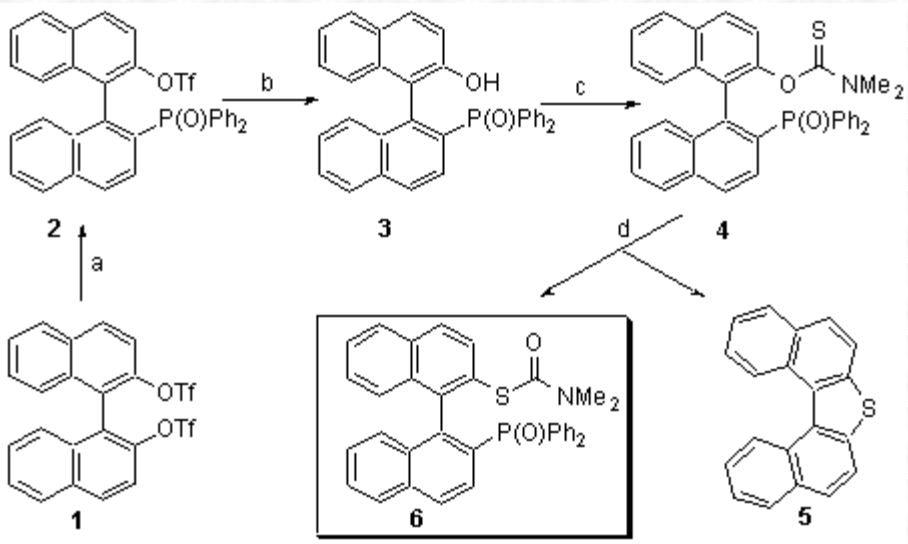
Abstract: The synthesis of racemic or enantiopure 2-diphenylphosphanyl-1,1'-binaphthalene-2'-thiol **8** (BINAPS) has been accomplished through a multistep reaction sequence from racemic or enantiopure binaphthol, respectively. The reaction sequence is completely stereoconservative. Enantiopure **8** can be alternatively obtained by resolution of *rac*-**8** using the chiral benzylaminato Pd(II)-complex **16** as the resolving agent.

The S-methyl or the S-*iso*-propyl derivatives **11** have been used as chiral ligands in the Rh(I)-catalyzed asymmetric hydroformylation of styrene and in the hydrogen transfer reduction of acetophenone with modest success (up to 20% e.e.). The same ligands provide higher e.e.'s in the hydrosilylation of styrene (50% e.e.) and in the allylic alkylation of 1,3-diphenylprop-2-enyl acetate (60% e.e.) with Pd-catalysts.

Keywords: Heterodonor ligands; Binaphthalene derivatives; Enantioselective catalysis; Transition metal catalysts; Allylic alkylation.

The synthesis of S-alkyl (2'-diphenylphosphanyl-1,1'-binapht)-2-yl sulfides **11** has been accomplished in eight steps starting from 2,2'-binaphthol.[1] Desymmetrization of the starting material is achieved in the second step through a Pd-catalyzed phosphinylation reaction (Scheme 1). The key intermediate **6** is obtained by Newmann-Kwart thermorearrangement of the thiocarbamate **4** at 260-270°C. In this reaction, the pentahelicenic thiophene **5** is formed as a by-product to a variable extent. Short reaction times and fast heating of the reactor are crucial factors for obtaining satisfactory yields in this stage. It must be stressed that, in spite of the harsh conditions required for the reaction to proceed, if properly performed the N.-K. rearrangement is completely stereoconservative. No loss of enantiomeric purity was observed when enantiopure samples of **4** were used as the starting material.

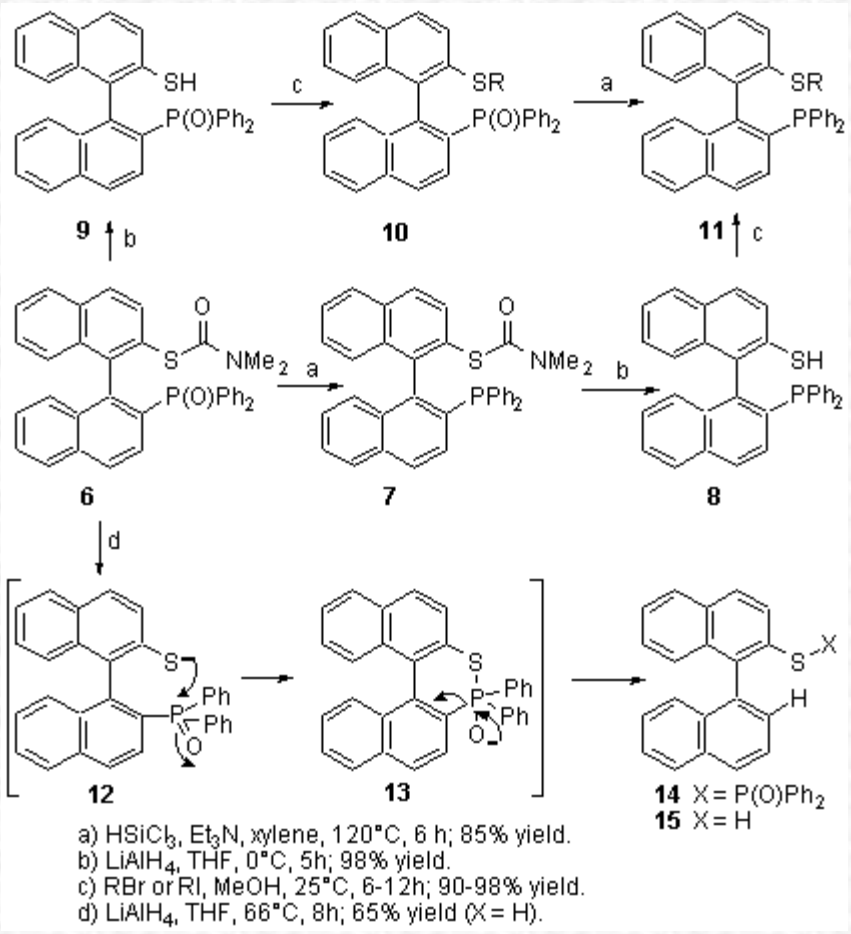


a) $Ph_2P(O)H$, Et_3N, $Pd(AcO)_2$/1,4-*bis*-diphenylphosphinobutane, DMSO, 100°C, 14 h; 78% yield.
b) NaOH, H_2O/THF, 25°C, 12 h; 98% yield.
c) $Me_2C(S)Cl$, Et_3N, DMAP, THF, 25°C, 48 h; 78% yield.
d) Neat, 260-270°C, 10'; 75% yield.

Scheme 1

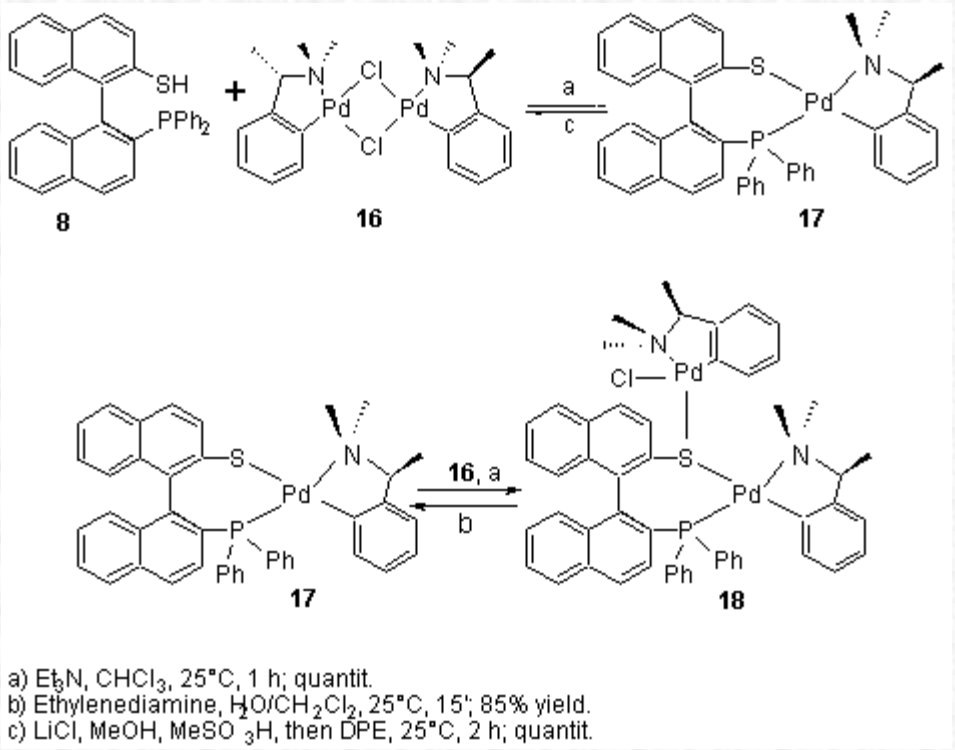
Conversion of **6** into the phosphanyl sulfides **11** has been accomplished through two different but basically equivalent three-step routes. One involves hydrolysis of the carbamate, alkylation at sulfur and deoxygenation of the phosphinyl group (Scheme 2; upper part). In the second case deoxygenation precedes hydrolysis (Scheme 2; middle part).

The attempt to prepare the phosphanyl thiol **8** directly from **6** by performing hydrolysis and deoxygenation in a single step by treatment with an excess of $LiAlH_4$ in boiling THF was not successful. The product isolated at the end of this reaction did not contain anymore phosphorus and was identified as 1,1'-binaphthyl-2-thiol **15**. Its formation could proceed through an intramolecular nucleophilic attack of an intermediate thiolate anion at the phosphinyl centre (as in **12**), leading to the cyclic species **13** (Scheme 2; lower part). Ring-opening of **13** results in the transfer of the phosphinyl group to the sulfur to give the thiol phosphonite **14** which is readily cleaved to the relevant thiol by $LiAlH_4$.



Scheme 2

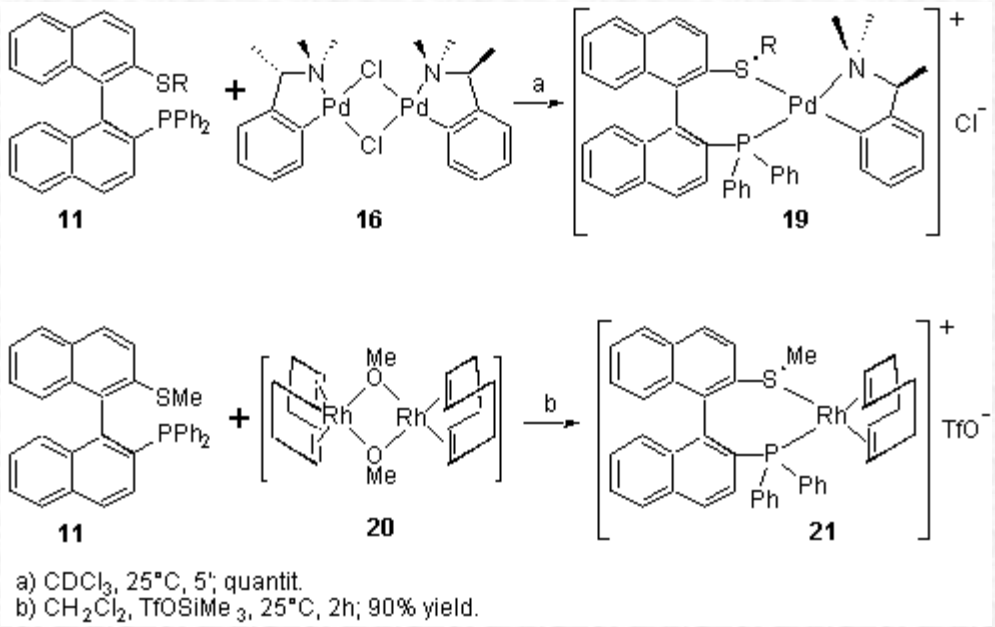
The enantiopure phosphane thiol **8** is accessible as illustrated above from enantiopure binaphthol. The (+)-(*R*)-enantiomer could be as well obtained by resolution of the racemic compound with N,N-dimethyl-(S)-a-methylbenzylaminato Pd-complex **16**. While the mononuclear derivatives **17** could not be separated by chromatography or fractional crystallization, the dinuclear thiolato bridged species **18**, obtained by addition of one more equivalent of **16** to **17**, could be separated by chromatography. Sequential treatment of the less polar isomer of **18** (*Rax,S,S*-configurations) with ethylenediamine in biphasic chloroform/water system, followed by reaction with diphenylphosphinoethane in acidic methanol allowed to recover the enantiopure ligand (*R*)-**8**, [a]D25 + 31.4 (c = 1; CHCl3). (Scheme 3)**.**



Scheme 3

(*R*)-Configured enantiopure sulfides **11** (R = Me or *i.*-Pr) have been obtained by S-alkylation of (*R*)-**8** obtained from the resolution. They have been as well prepared from (*R*)-binaphthol according to the synthetic procedure outlined in Schemes 1 and 2.

The enantomeric purity of (*R*)-**11** was determined by ^{31}P-NMR of the cationic Pd(II) complexes **19** obtained by reaction with **16** in the NMR tube (one single peak detectable at 48.9 ppm) and confirmed by HPLC on chiral phase.



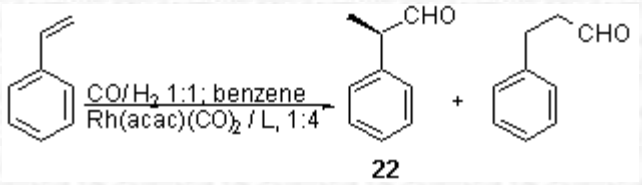
Scheme 4

Reaction of (R)-**11** with **20** produced the cationic Rh(I)-complex **21**. Given that the sulfur becomes sterogenic upon coordination to the metal, the formation of more than one stereoisomer is possible. In this complex, the

chelate coordination of the ligand was confirmed in the ^{13}C-NMR by the presence of a coupling (J = 10.2 Hz) between the S-methyl group and the phosphorus. Notably, the ^{1}H-NMR showed the S-methyl peak as a sharp singlet. This indicates that: a) the binding of the Rh to the sulfur centre has proceeded with complete stereoselectivity affording only one diastereoisomer; b) at room temperature inversion of configuration at the S-stereocentre, if occurring, is slow on the NMR time scale; c) at room temperature the complex **21** is locked in a single conformation, where most probably the methyl takes up an equatorial position in the puckered seven-membered ring. All these facts have signifcant bearings in view of the use of this complex in asymmetric catalysis.

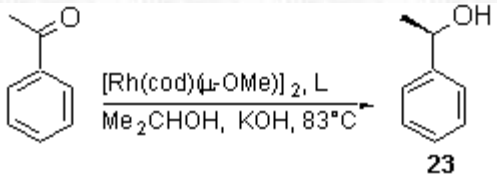
Both the preformed derivative **21** or other Rh(I)-complexes prepared *in situ* from (*R*)-**11** (R = *i.*-Pr) have been inspected for their catalytic activity in the asymmetric hydroformylation of styrene and in the H-transfer reduction of acetophenone.

In the hydroformylation at 40°C (Scheme 5) the *in situ* catalyst obtained from [Rh(acac)(CO)$_2$] and the *i.*-Pr sulfide produced the branched aldehyde **22** in quite high regioselectivity (96% at 100% conversion), but in insignificant e.e. (14%).



Scheme 5

Comparable e.e.'s (20 %) but lower conversions were observed after 1 h in the hydrogen transfer reduction of acetophenone in boiling 2-propanol (Scheme 6). Prolonged reaction times led to higher conversions, but the e.e. decreased due to the concurrent racemization sufferred by the chiral carbinol **23** in the presence of base. In this reaction the *in situ* Ir(I)-based complex displayed a lower catalytic activity and stereoselectivity (11% e.e.).

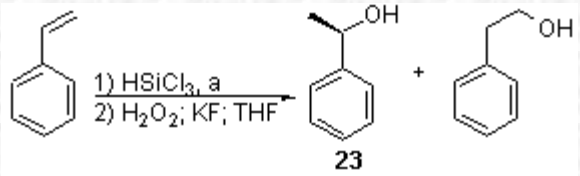


Ligand (*R*)-**11**	t (h)	conv.(%)	e.e.(%)
R = Me	1 (12)	12 (55)	14 (3)
R = *i*Pr	1 (14)	21 (75)	20 (5)
R = *i*Pr[a]	1	6	11

a) Catalyst prepared from [Ir(cod)Cl]$_2$

Scheme 6

Better performances were obtained in the Pd-catalyzed asymmetric processes. In the hydrosilylation of acetophenone, the (*R*)-*i.*-Pr derivative **11** led to the branched derivative in more than 90% regioselectivity and 50% stereoselectivity (Scheme 7).

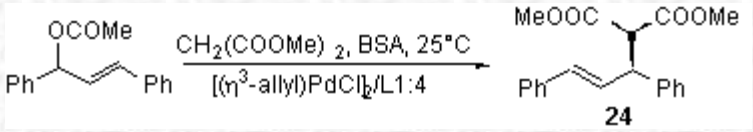


Ligand (*R*)-**11**	t (h)	conv.(% **23**)	e.e.(config.)
R = Me	39	41 (82)	4 (*S*)
R = *i*Pr	41	72 (91)	51 (*R*)

a) [(η^3-allyl)PdCl]$_2$/L1:4; Styrene/Pd 1000:1; 25°C

Scheme 7

The same ligand In the Pd-catalyzed allylic alkylation of 1,3-diphenyl allyl acetate with dimethylmalonate gave the (*R*)-configured alkylated product **24** in up to 60% e.e. (Scheme 8). Higher e.e.'s (up to 91%) have been reported in this process by korean researchers using the methyl sulfide **11**.[2]



Scheme 8

References

1) S. Gladiali, A. Dore and D. Fabbri *Tetrahedron : Asymmetry*, **1994**, *5*, 1143.

2) J. Kang, S. Hoon Yu, J. I. Kim, H. G. Cho, *Bull Korean Chem. Soc.* , **1995**, *16*, 439.

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