Catalytic Asymmetrization of *meso*-3,7-Bis-siloxycycloheptene by Chiral Rhodium(I)–binap [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] Catalyst: the Enantiocontrolled Asymmetric Synthesis of (−)-(*S*)-Physoperuvine

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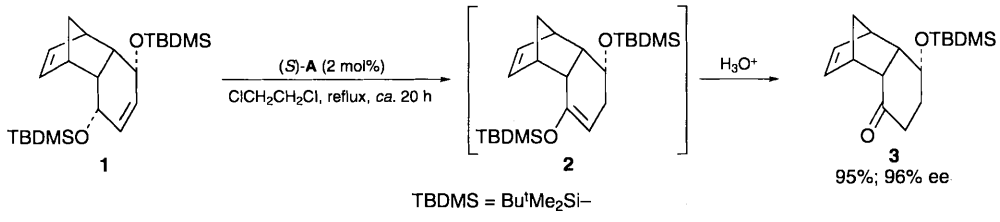
Catalytic asymmetrization of *meso*-3,7-bis-*tert*-butyldimethylsiloxycycloheptene occurs in the presence of a chiral rhodium(I) binap catalyst to give optically active 4-*tert*-butyldimethylsiloxycycloheptanone in 70% ee after hydrolytic workup, the (*R*)-enantiomer of which has been transformed into (−)-(*S*)-physoperuvine, the major alkaloid of *Physalis peruviana*.

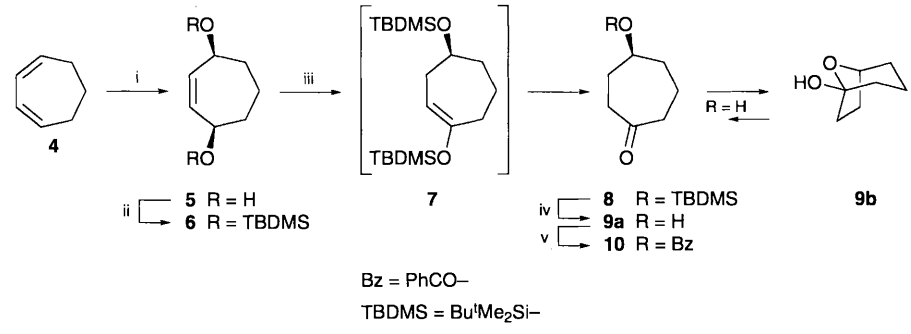
The chiral Rh^{I}–binap catalysed enantiospecific isomerization has so far been limited to allyl amines for practical use.[1] However, quite recently, we have succeeded in a catalytic asymmetrization[2] of a series of tricyclic *meso*-1,4-diol bis-ethers using [Rh{(*S*)-binap}(cod)]$^{+}ClO_4^{-}$ (*S*)-**A** (cod = cycloocta-1,5-diene) as catalyst as represented by the reaction of the tricyclic *meso*-bis-silyl ether **1**. Thus, treatment of **1** with a catalytic amount (2 mol%) of (*S*)-**A** in refluxing 1,2-dichloroethane furnished the siloxy ketone **3** in excellent chemical and optical yields comparable to those in the enzymatic procedure[3] after hydrolytic workup of the enol ether intermediate **2** (Scheme 1). We report here an extension of this catalytic procedure to a monocyclic *meso*-substrate, *cis*-3,7-bis-*tert*-butyldimethylsiloxycycloheptene **6**, to produce a new useful chiral building block.

[Rh{(*S*)-binap}(cod)]$^{+}$ ClO_4^{-} (*S*)-**A**

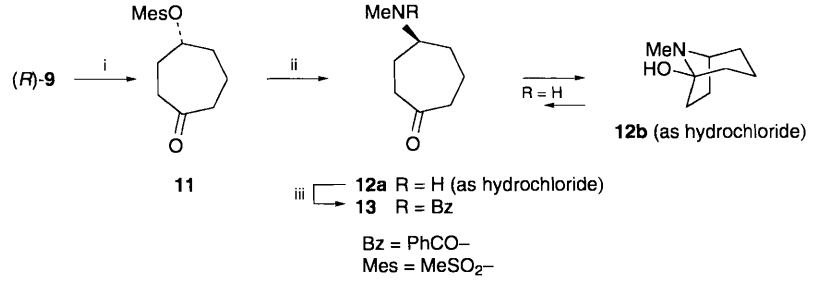
The monocyclic *meso*-ene-1,4-diol bis-silyl ether† **6** was prepared without difficulty from cyclohepta-1,3-diene **4** *via* the *cis*-ene-1,4-diol **5** by following the established procedure.[4] When **6** was refluxed with a catalytic amount (2 mol%) of (*S*)-**A** catalyst[5] in 1,2-dichloroethane, the starting material disappeared after 24 h to give a mixture (*ca.* 4 : 1) of the silyl enol ether **7** and the siloxy ketone **8** which without separation was briefly exposed to tetrabutylammonium fluoride (TBAF) to yield the siloxy ketone **8**, $[\alpha]_D^{31}$ −8.69 (*c* 1.05, $CHCl_3$), in 96%



Scheme 1



Scheme 2 *Reagents and conditions*: i, ref. 4; ii, $Bu^{t}Me_2SiCl$, imidazole, DMF (86%); iii, (*S*)-**A** (2 mol%), $ClCH_2CH_2Cl$, reflux, 24 h, then Bu_4NF, THF, 0 °C (96%); iv, HF–MeCN (1 : 19); v, PhCOCl, 4-*N*,*N*-dimethylaminopyridine (cat.), pyridine (78% from **8**)



Scheme 3 *Reagents and conditions*: i, methanesulfonyl chloride, pyridine, 0 °C → room temp. (82%); ii, 40% aq. $MeNH_2$–MeOH, room temp. (57%); iii, benzoyl chloride, Et_3N, CH_2Cl_2

yield as a single product. Further treatment of **8** with hydrofluoric acid yielded (*S*)-4-hydroxycycloheptenone **9a** quantitatively, which existed as the bicyclic hemiketal **9b**. The optical purity of **9** was determined to be 71% ee by HPLC analysis using a chiral column (CHIRALCEL OJ, elution with 5% Pr^{i}OH–hexane) after transformation into the ketobenzoate **10**. The absolute configuration was determined to be *S* by transformation of the siloxy ketone **8** into (*S*)-4-acetoxy-2-cycloheptenone,[6] $[\alpha]_D^{30}$ −79.55 (*c* 0.26, $CHCl_3$) {lit.[6b] $[\alpha]_D^{23}$ −98.3 (*c* 5.0, $CHCl_3$)}, which has been obtained by an enzymatic procedure, *via* a sequence of reactions involving the Saegusa olefination,[7]‡ desilylation, and acetylation. The observed stereospecificity exerted by (*S*)-**A** was found to be in the same direction as that observed in the asymmetrization of the tricyclic *meso*-substrate **1**. The same treatment of **6** in the presence of (*R*)-**A** catalyst[5] afforded the enantiomeric (*R*)-siloxy ketone **8** in comparable chemical and optical yields.

Having established the absolute configuration, we next examined the transformation of the (*R*)-hydroxy ketone **9** into (−)-(*S*)-physoperuvine[8] **12**, the major alkaloid isolated from *Physalis peruviana*, which has not been synthesised enantiotopically.[9] Thus, (*R*)-**9** was first transformed into the mesylate **11** employing standard conditions. Upon treatment with aqueous methanolic methylamine, **11** furnished (−)-physoperuvine§ **12** as the hydrochloride, mp 152.5–153.0 °C, $[\alpha]_D^{32}$ −0.98 (*c* 1.28, MeOH) {lit.[8c] mp 153 °C; $[\alpha]_D$ −0.8 (*c* 1.0, MeOH)} in 57% yield. Its structure was further confirmed by transformation into the benzoate **13**,§ mp 135–136 °C, $[\alpha]_D^{30}$ +78.0 (*c* 0.44, $CHCl_3$) {lit.:[8d] mp 136 °C; $[\alpha]_D^{24}$ +95.6 (*c* 1.3, $CHCl_3$)} >95% ee (HPLC: CHIRALCEL OD, elution with 10% Pr^{i}OH–hexane).

In conclusion we have expanded the chiral Rh^I–binap asymmetrization reaction established in a rigid tricyclic *meso*-ene-1,4-diol bis-ether system to a more flexible monocyclic *meso*-bis-ether system with acceptable optical induction leading to a new chiral building block convertible to a naturally occurring alkaloid (−)-physoperuvine.

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Footnotes

† Satisfactory analytical (combustion and/or high resolution MS) and spectral data (IR, ^{1}H NMR, and MS) data were obtained for all new compounds.

‡ The Saegusa reaction gave two isomeric enones as a 1:1 separable mixture.

§ Spectroscopic data (IR, ^{1}H NMR and MS) were identical with those reported.[8b]

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