Waihoensene was isolated from the New Zealand podocarp in 1997. It is a tetracyclic diterpene containing an angular triquinane.

The whole structure contains a highly congested and cis-fused tetracyclic core decorated with 6 contiguous stereogenic centers, 4 of them are contiguous quaternary carbon.

First total synthesis of Waihoensene was achieved by Lee and co-workers in 2017 in 18 steps, featuring a tandem [2+3] cycloaddition to construct BCD ring.

Here, they achieved the asymmetric total synthesis with 15 steps and 3.8% overall yield.
Retro-synthetic Analysis

(+)-Waihoensene 1

Asymmetric conjugate addition

Conia-ene reaction

Pauson-Khand reaction

Conjugate addition

TS_{D-E}
Grignard Nucleophilic addition:

Asymmetric conjugate addition/ Enolate trapping/ Cope elimination
OTMSMe(-)\textsubscript{4}d) AllylTMS, BF\textsubscript{3}Et\textsubscript{2}O (89%)

DCM, –78 °C to RT

O, DCM, –78 °C

PPh\textsubscript{3}, RT

Sakurai Reaction

Ozonomolysis
Forming diyne 7 and *in situ* desilylation

Diastereoselective Conia-ene type cyclization

yield as a single diastereomer
b) \( \text{Co}_2(\text{CO})_8, \text{N}_2 \text{O} \)

DCE, 80 °C, 22 h

(59%, 93% ee)

c) \( \text{Ni(acac)}_2 \) (10 mol%),

LiBr, \( \text{Me}_2\text{Zn} \), Et\text{O},

0 °C to RT, 48 h

(81%)

Pauson-Khand reaction

Nickel catalyzed conjugate addition of organozinc reagents

as a single diastereomer
Ketal Formation

Wittig reaction and ketal deprotection

\[
\text{BrCH}_3\text{PPh}_3 \xrightarrow{\text{base}} \text{Me,} \quad \text{PPh}_3\text{Me}_2
\]

\[
\text{Ph}_3\text{P}^+\text{MeBr}, \text{tBuOK (78%)} \quad \text{MeBr}
\]

\[
\text{HCl (89%)} \quad \text{MeH}
\]
Hydrogen Atom Transfer (HAT) for olefin hydrogenation

C3 methylation and another Wittig reaction