Tsuji-Trost Allylation Reaction: Applications towards the Total Synthesis of *(+)-Zoapatanol*

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Introduction

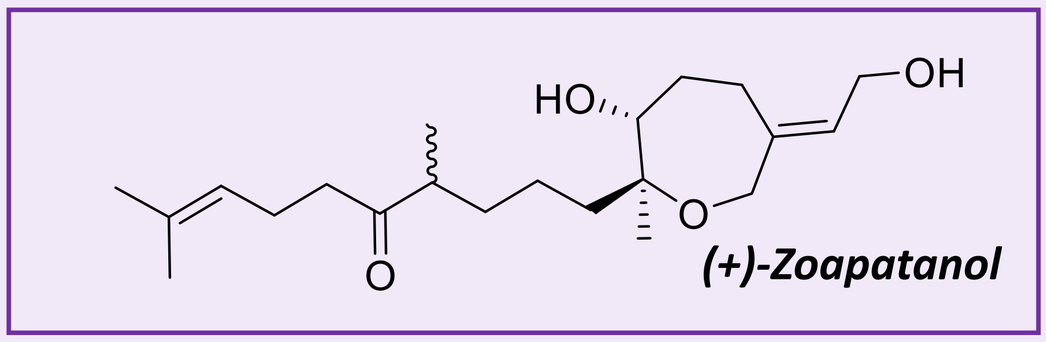
- In 1979, Levine and co-workers isolated and identified bioactive diterpenoid **'zoapatanol'** from the zoapatle plant, ***Montanoa Tomentosa*** [1]
- Prepared in the form of tea and is used by Mexican women for several **gynaecological/obstetrical applications**[2]
- Extracts of zoapatle was tested in human and animal subjects, thereby prompting an extensive research[2]
- Biological applications evoked interest in the compound. The structure of zoapatanol spurred synthetic attempts to access them for further biological assessment[2]

***Montanoa Tomentosa*[1]**

Key Structural features

- Oxepane ring
- Side chain
- Double bond configuration

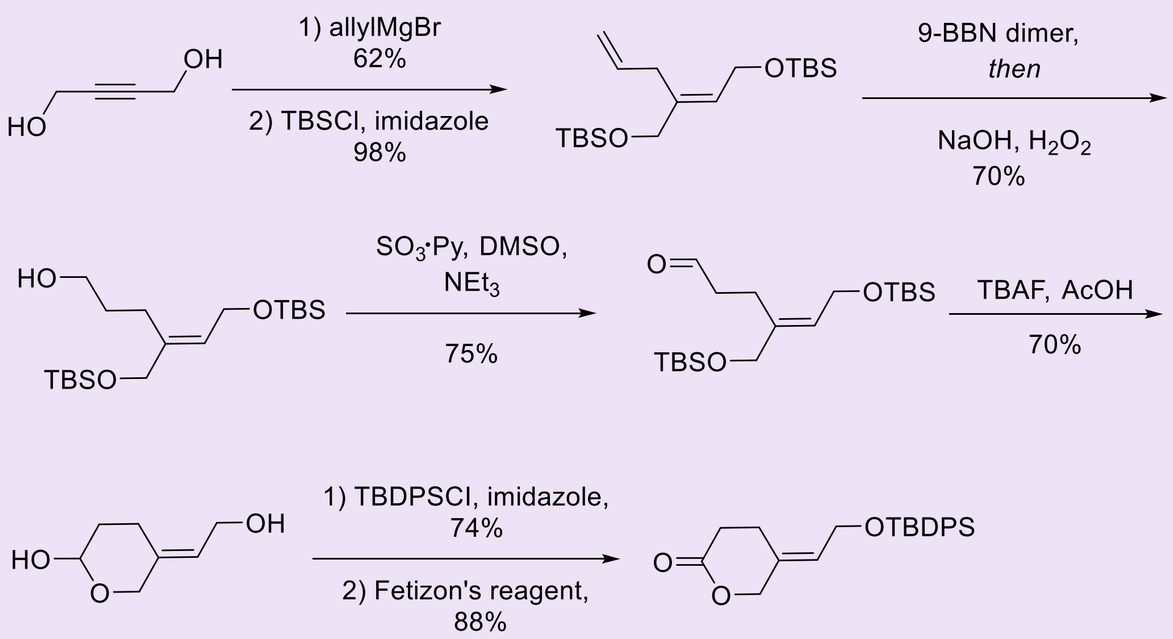
Molecular formula: $C_{20}H_{34}O_4$



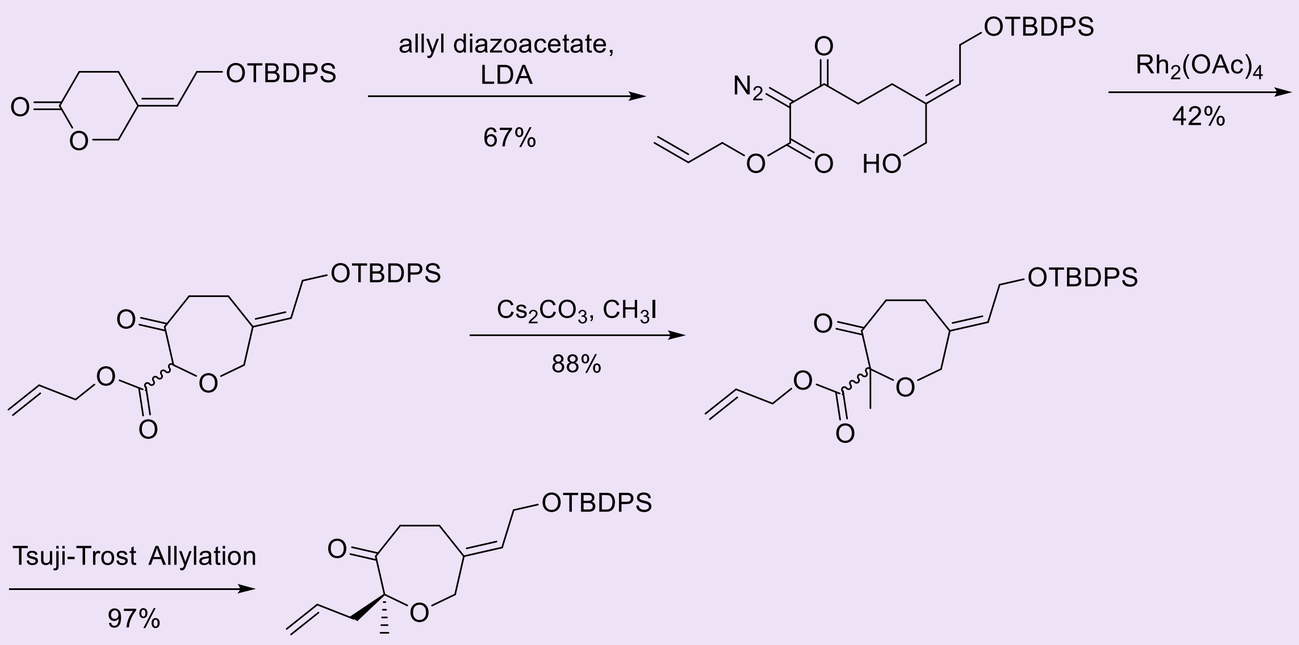
Aim

- Develop and optimise methods for the total synthesis of zoapatanol
- Application of Tsuji-Trost reaction methodology as a part of the total synthesis of zoapatanol
- Attachment of the side chain to the oxepane ring

Lactone Formation



OH – Insertion Strategy



Conclusion and Future Work

Conditions have been developed for lactone formation. OH- insertion strategy was explored as part of the synthetic efforts. The key Tsuji-Trost Allylation methodology occurred smoothly in an excellent yield.

The target is to build methodology towards the total synthesis of zoapatanol whilst ensuring an efficient and inexpensive approach.

Further biological testing of zoapatanol can be carried out once synthesis has been achieved.

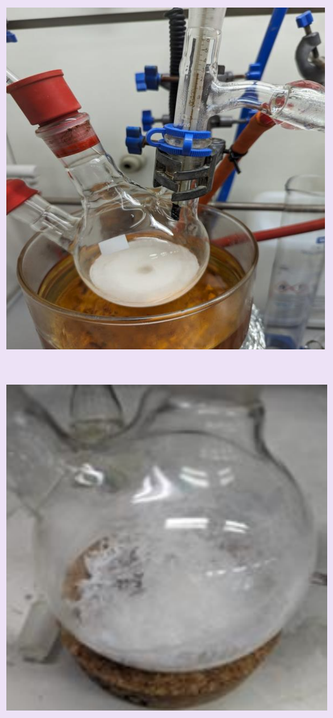
Tsuji-Trost Allylation

- Adapted from literature by Stoltz and colleagues[3]
- Facilitated by using a ligand and palladium catalyst for reaction to occur
- Research carried out by Clark, James and coworkers demonstrate the functionalization of medium-sized (seven and eight-membered) cyclic ethers with excellent results[5]

Illustrative Scheme

Typical set-up of a reaction in the lab.

A- Reaction is usually done in a round-bottomed flask, connected to a stream of argon flow to keep dry conditions in the flask, obtaining crude sample
B- Purification via chromatography is employed to obtain pure material within a collection of 'fractions'
C- Collected fractions in a flask are concentrated over reduced pressure to obtain 'sample'
D- Sample obtained after drying and can now be sent for further confirmatory tests



A

B

D

C

References & Acknowledgements

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5. J. Skardon-Duncan, M. Sparenberg, A. Bayle, S. Alexander, J. S. Clark, *Org. Lett.* **2018**, 20, 2782-2786.

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