The Beneficial Use of Prenyl Groups in Ring-Closing Metathesis

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Introduction

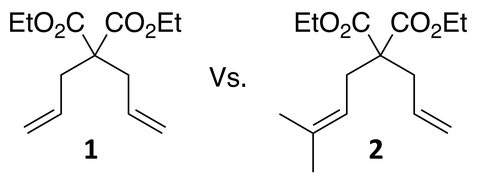
The prenyl moiety is present in vast numbers of naturally occurring compounds.[1] Many of these are commercially available and very cheap, therefore, if they can be incorporated as a building block for organic syntheses, they can add great value. Furthermore, the synthesis of more structurally complex natural products, particularly those with a terpenoid framework, may proceed *via* compounds that contain the prenyl grouping.

A plethora of metathesis reactions are used in natural product synthesis,[2] despite this, there are limited examples of use of the prenyl moiety in ring-closing metathesis (RCM) reactions, particularly in the synthesis of natural products.[3]

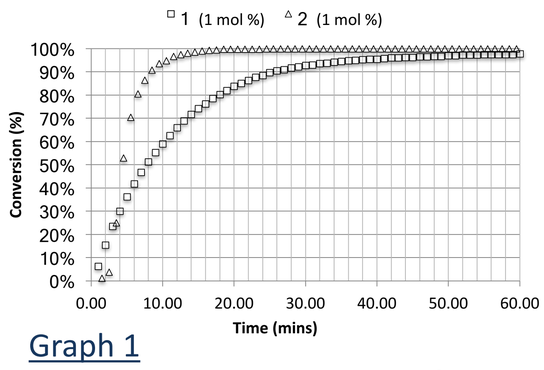
Using well-established benchmarks for comparison,[4] a thorough investigation and kinetic analysis into the use of the prenyl moiety in ring-closing metathesis (Section 1) and their utility in controlling the outcome of dienyne metathesis (Section 2) is presented.[5]

1. 'Allyl' Vs. 'Prenyl' RCM

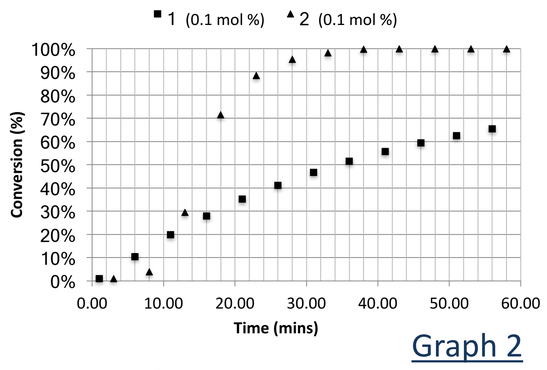
All reactions were conducted in CD_2Cl_2 in a sealed NMR tube, using Grubbs 2nd Generation catalyst, at a substrate concentration of 0.1 M*, and monitored by ^1H NMR.[4]



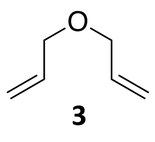
Vs.



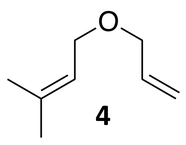
Graph 1

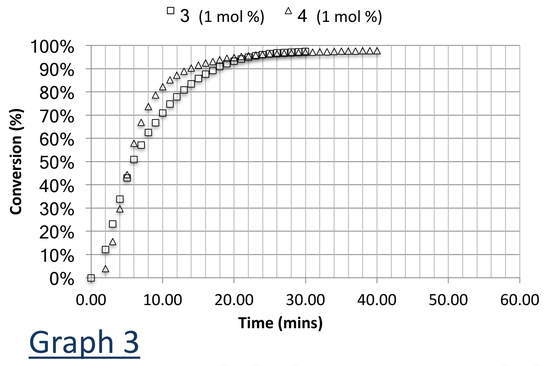


Graph 2

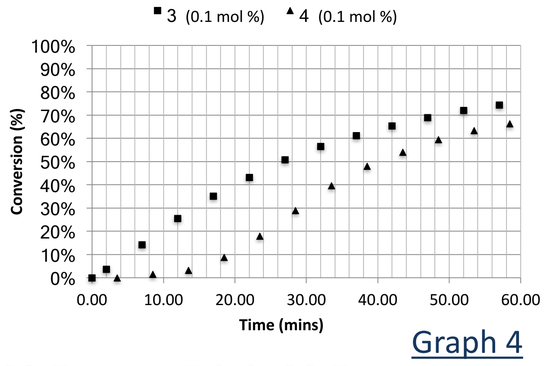


Vs.

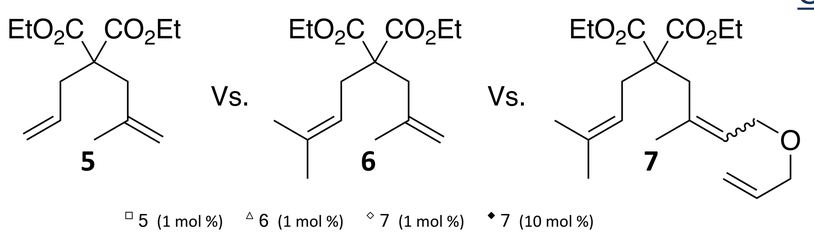


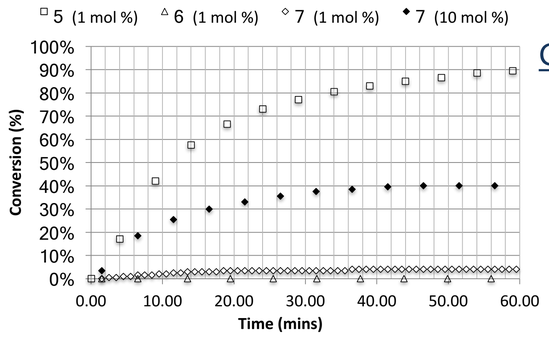


Graph 3

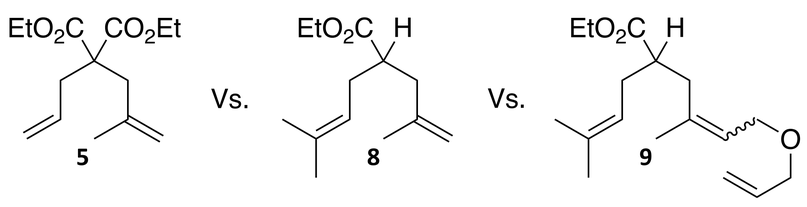


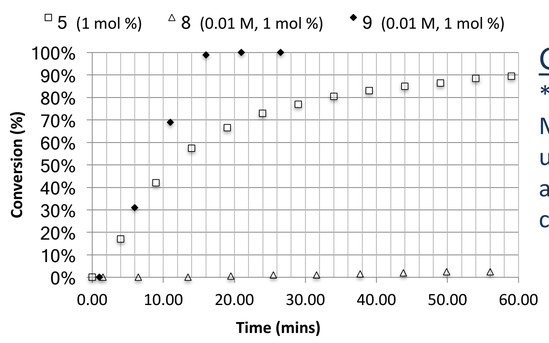
Graph 4





Graph 5



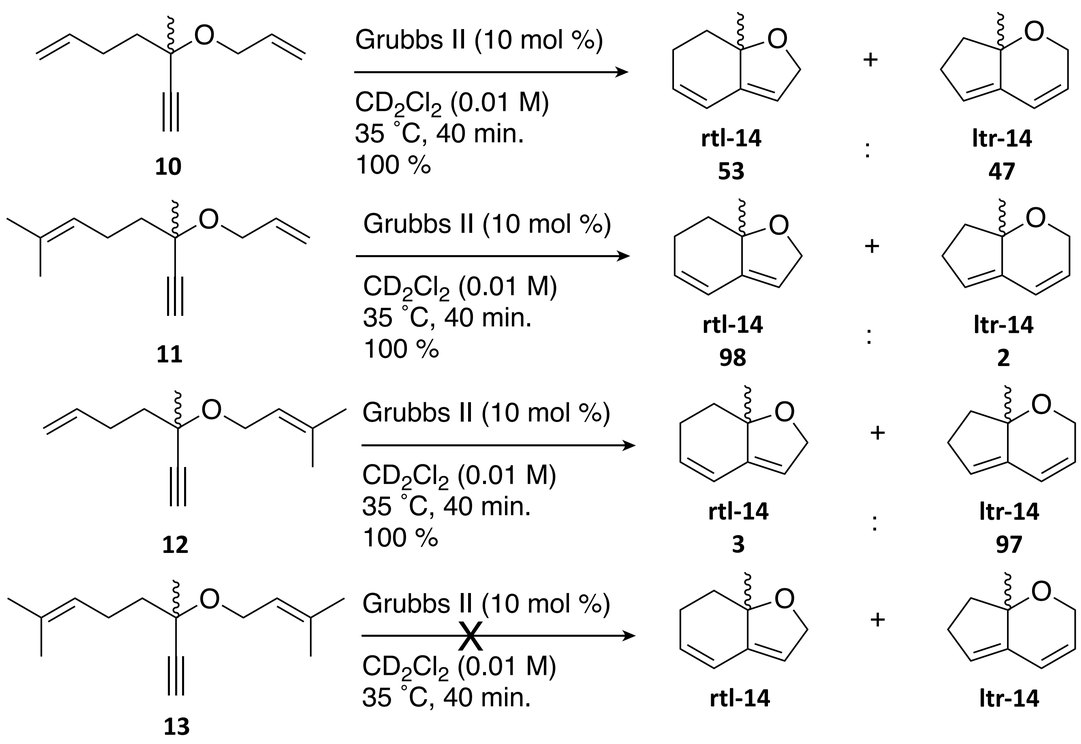


Graph 6

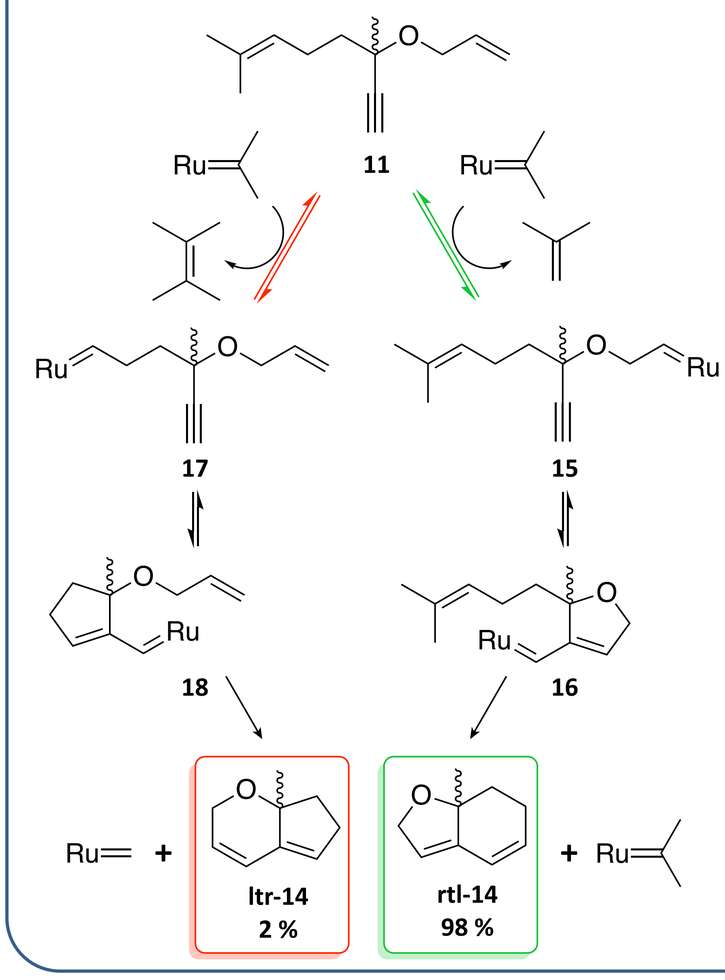
*Reactions conducted at 0.01 M for substrates **9** (to avoid undesired homodimerisation) and **8** (to allow direct comparison of rates).

2. Dienyne Metathesis Under Substrate Control

All reactions conducted in CD_2Cl_2 in a sealed NMR tube, using Grubbs 2nd Generation catalyst, at a substrate concentration of 0.01 M. Product ratios were determined by ^1H NMR.[6]



Reaction sequence for substrate **11**:



Initiation occurs readily at the lesser-substituted olefin.

The formation of the tetra substituted olefin is heavily disfavoured under these conditions.

First ene-yne metathesis occurs readily – forming the first ring.

Second metathesis step occurs readily – forming the second ring.

High selectivity observed in the formation of the two constitutional isomers **rtl-14** and **ltr-14**.

Conclusions

By using simple substrates and comparing against well-established benchmarks the beneficial use of the prenyl moiety has been demonstrated in both RCM and dieneyne metatheses. It therefore follows that in general the 'prenyl grouping' can be used interchangeably in these metathesis types with an 'allyl grouping' (providing that there is a position in the molecule where the catalyst is able to initiate); and indeed under certain circumstances there is an added benefit to doing so (i.e. an observed rate enhancement or control over product distribution).

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References and Acknowledgments

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