Synthesis and Characterisation of Activated Ruthenium Complexes Bearing a Sulfonamide EWG

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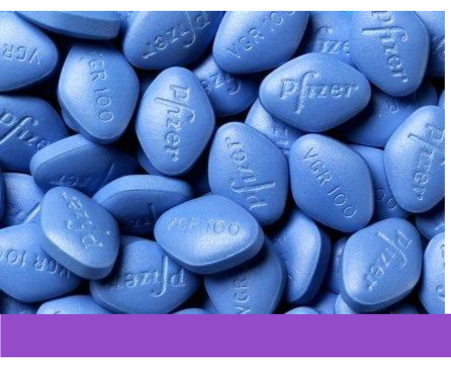
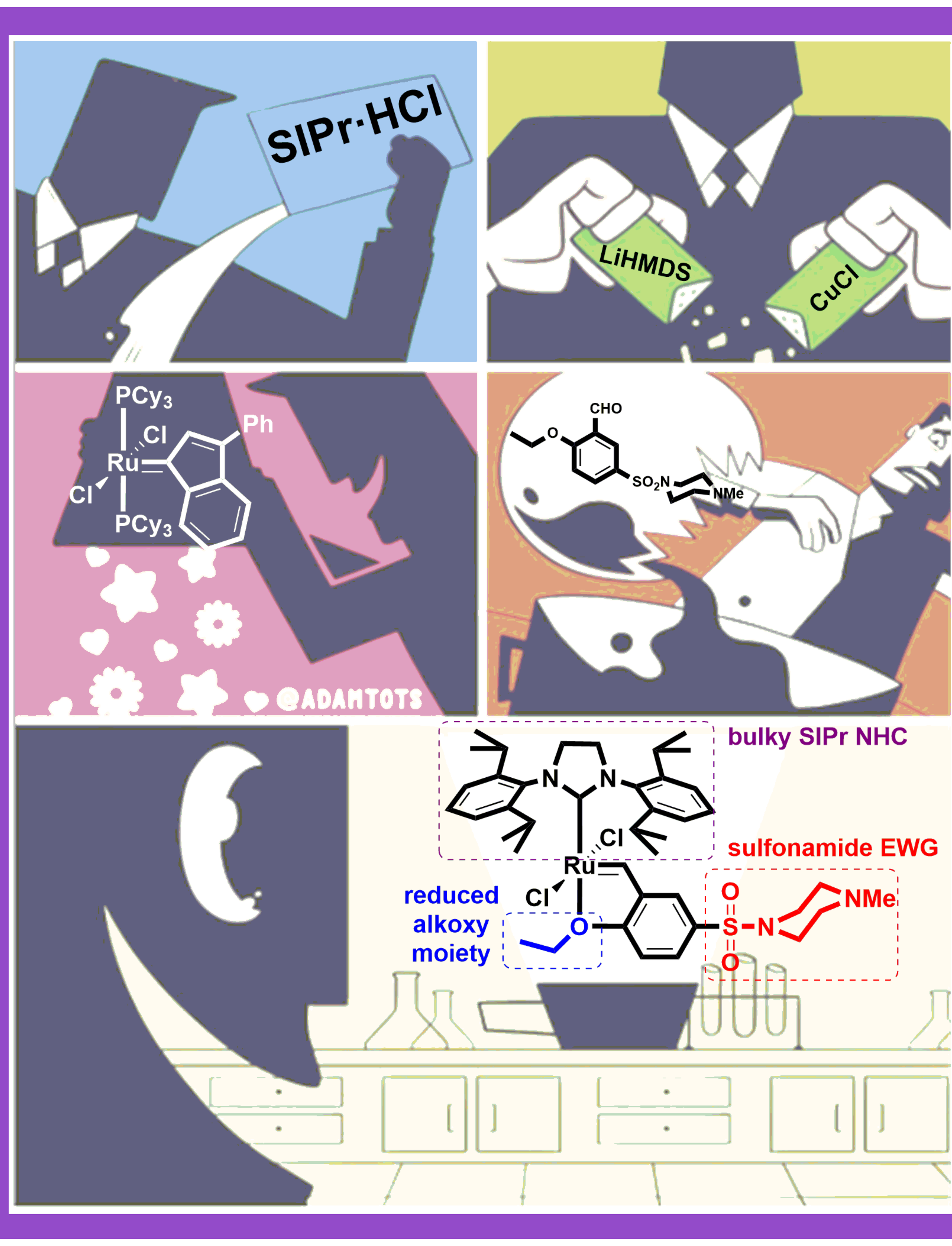




Introduction and Outline

Olefin metathesis (OM) reaction catalyzed by ruthenium alkylidene complexes is one of the most powerful tools in C(sp^2)-C(sp^2) bond creation in the modern organic synthesis.[1] This important organic transformation found plenty of applications in a directed synthesis of chemical compounds ranging from industrial fine chemicals, through structurally-advanced active pharmaceutical ingredients (APIs) to natural products.[2]

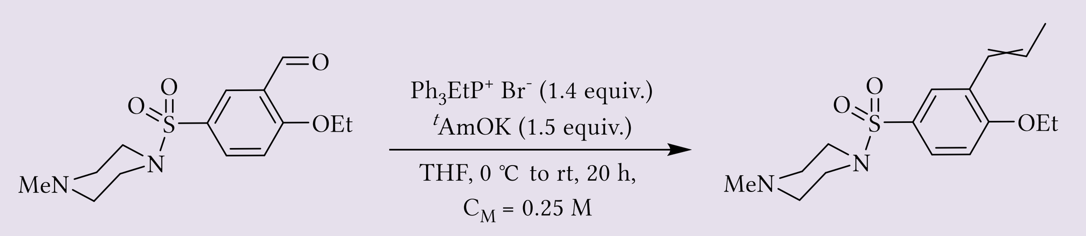
In order to develop the complexes with significantly higher tolerance towards ambient conditions and enhanced activity in metathetical transformations, a series of structural modifications has been performed.[3] One of the most game-changing adjustments of organic ligands is based on the introduction of electron-withdrawing group (EWG) in benzylidene ligand.[4] Such modification dramatically influences the electronic properties of the chelating ether moiety. The bond between the ruthenium metallic centre and the chelating oxygen atom weakens due to the decrease of electron density in the ether environment. The abovementioned effect accounts for the poor chelation so the activation of the pre-catalyst in metathesis reactions occurs more rapidly. The most dramatic consequences were noticeable when nitro substituent was introduced.[5]

Over the period of time, a series of ruthenium catalyst employing a plethora of EWG groups was synthesized.[6] Despite the activity benefits, the syntheses of such catalysts are more complex and very often different retrosynthetical approaches have to be taken into consideration.[7] This problem can be circumvented through appropriate building blocks that are routinely used in the multi-scale synthesis processes or are their by-products.

The aim of the current research was the development and thorough characterisation of two alkylidene ruthenium complexes bearing the electron-withdrawing (EWG) sulfonamide group in benzylidene ligand. The chelating part of the obtained catalysts is a simple derivative of Sildenafil aldehyde – the intermediate in the synthesis of a medication commonly used in erectile disfunction treatment.[8]

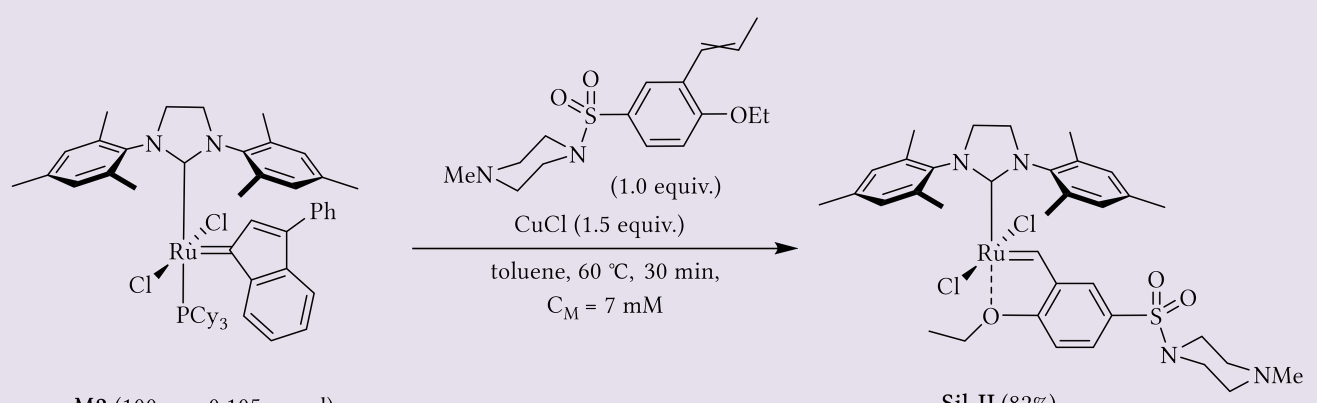
The synthesized ruthenium complexes were examinated and compared with commercially available OM catalysts with respect to stability and activity in metathetical transformations. They were fully characterised using spectroscopic (^{1}H and ^{13}C NMR, IR), analytic (EA, HR-MS) and crystallographic (XRD) techniques. Moreover, kinetic experiments using UV-Vis were also carried out and revealed the alternative activation mechanism of one of the obtained complexes.

Ligand and Complexes' Syntheses



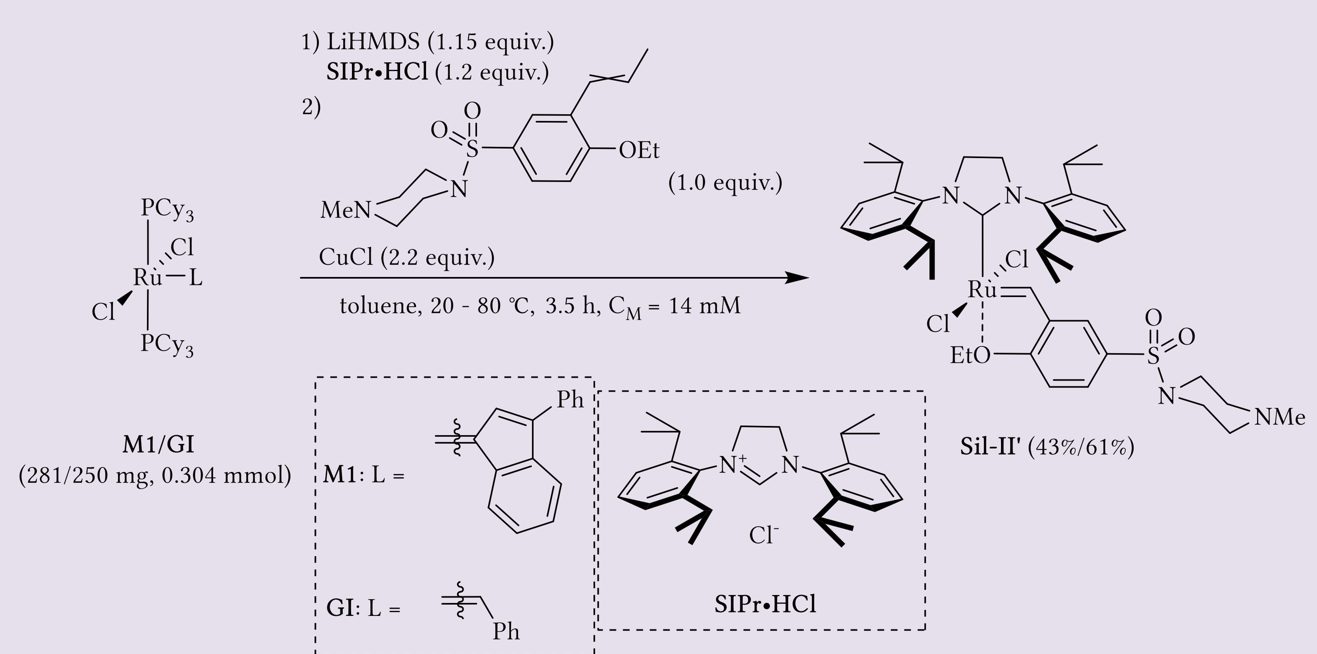
L1 (3.12 g, 10 mmol) L2 (71%, E/Z =88/12)

Scheme 1. Synthesis of the Sildenafil-based sulfonamide ligand.



M2 (100 mg, 0.105 mmol) Sil-II (82%)

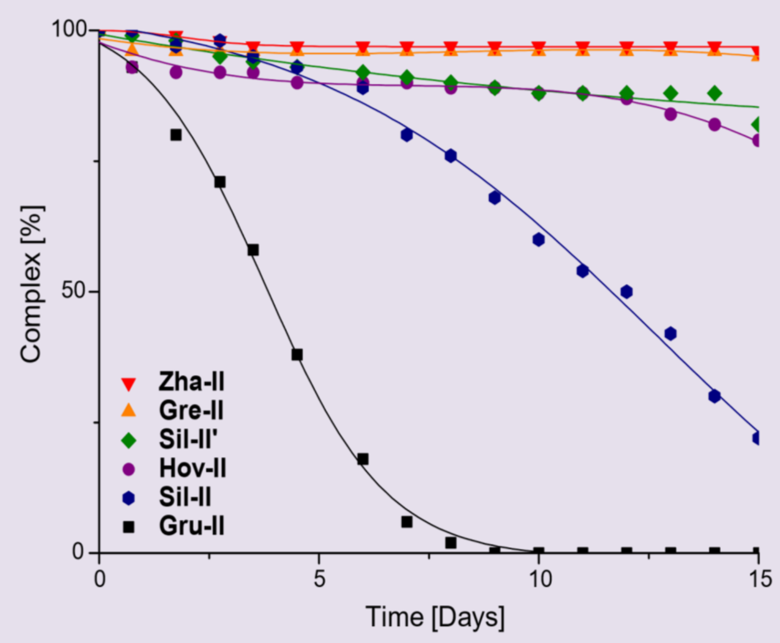
Scheme 2. Synthesis of the **Sil-II** ruthenium complex.



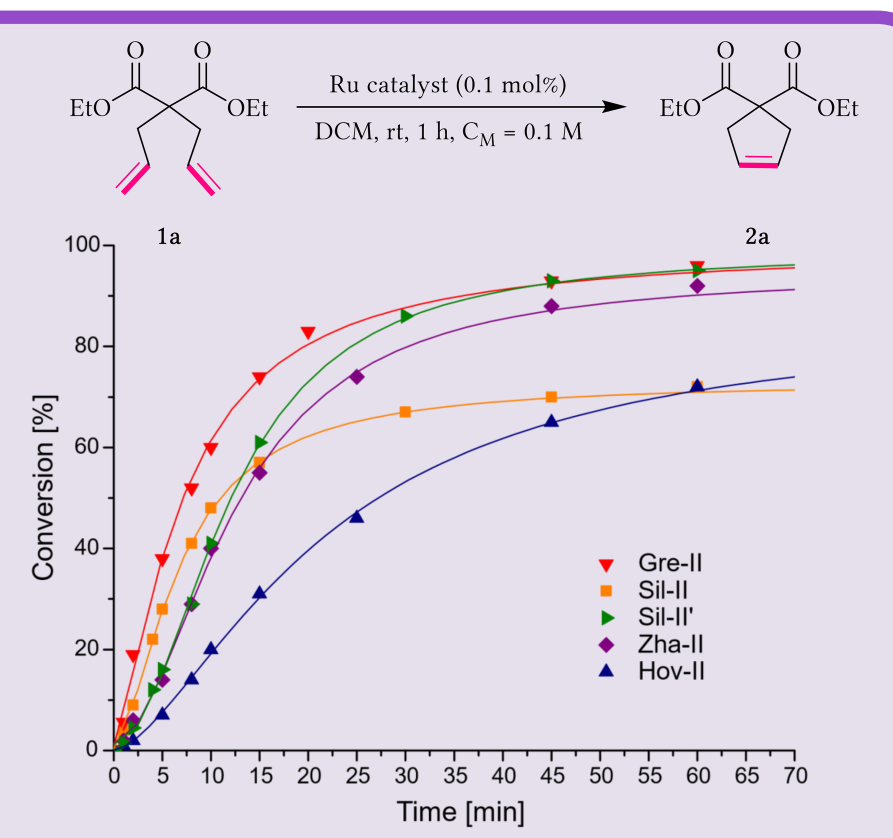
M1/GI (281/250 mg, 0.304 mmol) Sil-II' (43%/61%)

Scheme 3. Synthesis of the **Sil-II'** ruthenium complex.

Stability and Activity

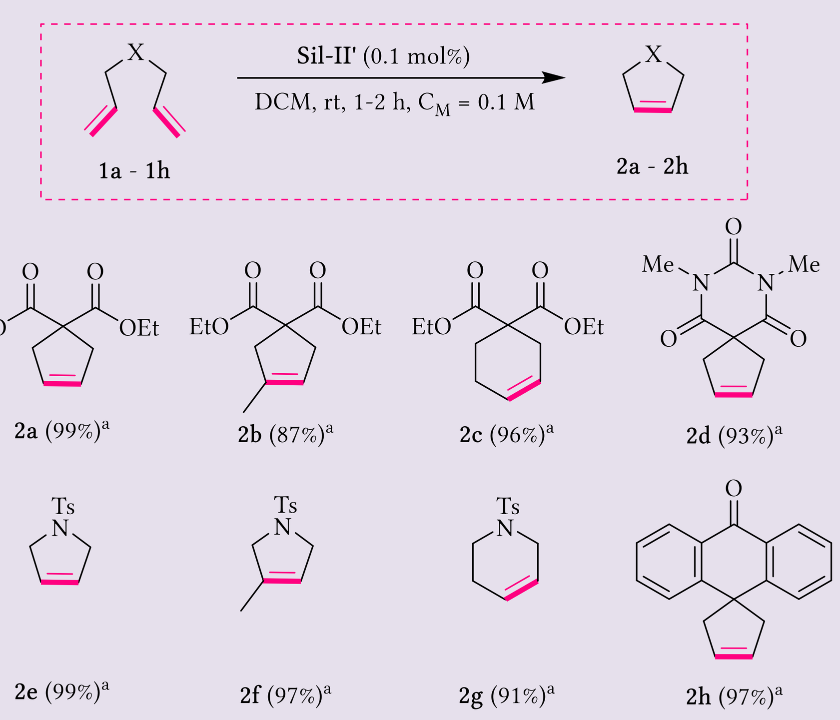


Scheme 4. Stability curves obtained from ^{1}H NMR experiments using trimethoxybenzene as internal standard (SIMes catalysts: **Zha-II** — Zhan catalyst, **Gre-II** — NitroGrela catalyst, **Hov-II** — Hoveyda-Grubbs catalyst, **Gru-II** — Grubbs catalyst).

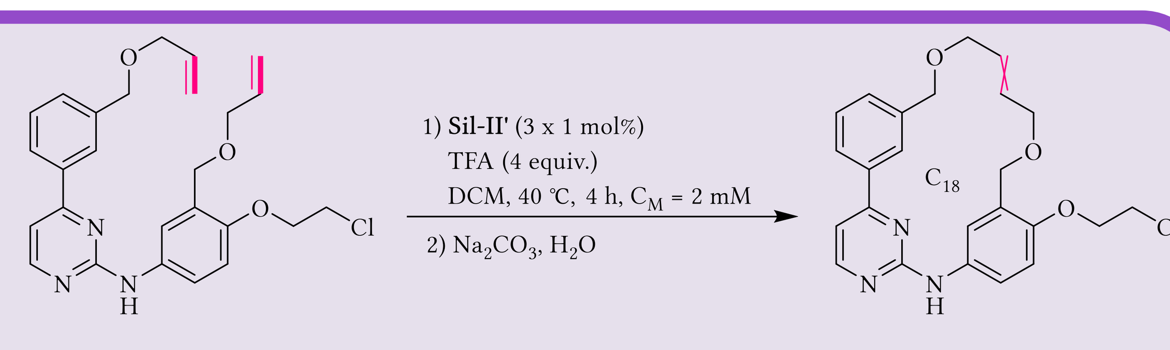


Scheme 5. Activity assessment obtained from ^{1}H NMR experiments for SIMes catalysts in RCM of **1a**.

Scope and Limitations

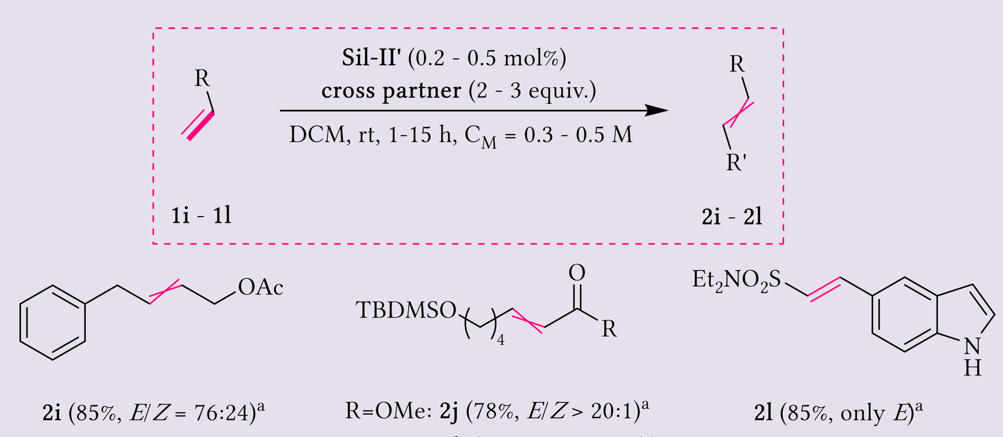


Scheme 6. Activity of **Sil-II'** catalyst in RCM reactions (^{a}isolated yield).



1m (47 mg, 0.1 mmol) 2m (73%, E/Z = 76:24)^a

Scheme 7. Activity of **Sil-II'** catalyst in macrocyclisation reaction (^{a}isolated yield).



Scheme 8. Activity of **Sil-II'** catalyst in CM reactions (^{a}isolated yield).

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