MEDNARODNA PODIPLOMSKA ŠOLA JOŽEFA STEFANA

JOŽEF STEFAN INTERNATIONAL POSTGRADUATE SCHOOL

Comprehensive transformation of alcohols catalyzed by *N*-halo compounds under green reaction conditions

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Amsterdam , March 2017

1. Introduction

- Methods for the transformation of organic compounds following the principles of green chemistry ⟶ challenging tasks in organic synthesis.

1. Introduction

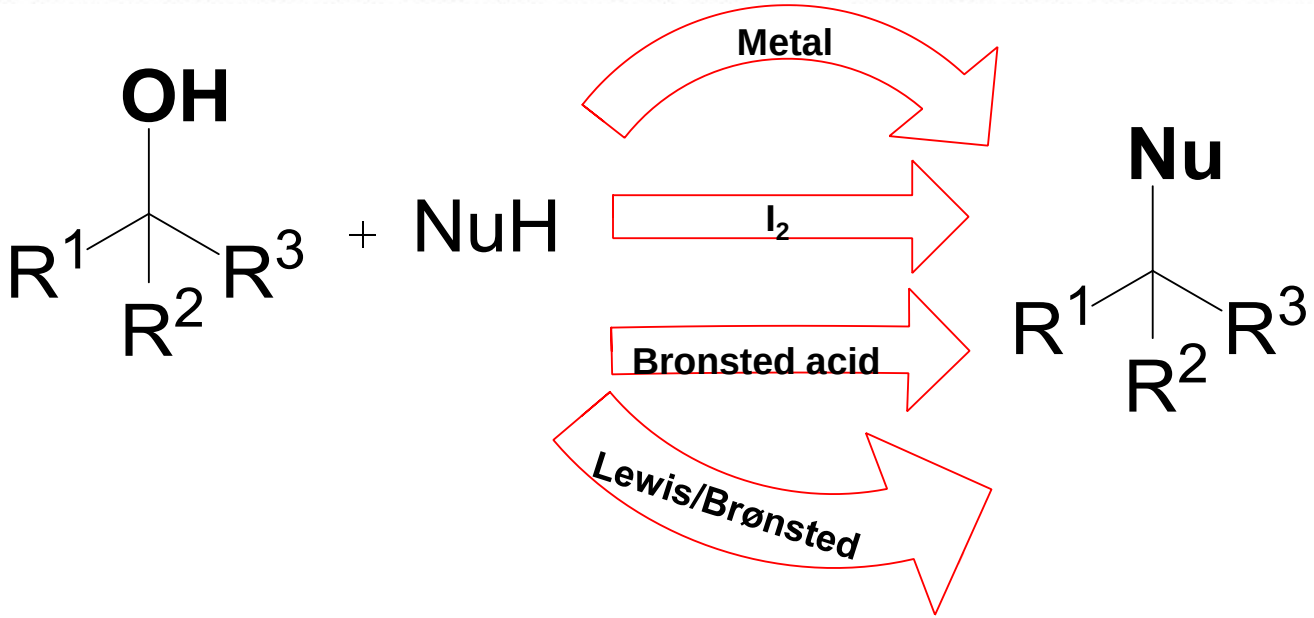
- Organic solvents-**blacklisted!!** ➡ human health and environment.

- **Solvent-free synthetic methods** - laboratory synthesis and chemical industry ➡ simplicity and cost efficiency.

1. Introduction

- Alcohols ➡ transformation under **green reaction conditions** - useful building block in organic synthesis.

1. Introduction



- **Metal**: $InCl_3$, (La, Yb, Sc, Hf triflate), $BiCl_3$
- **Brønsted acid**: TfOH, H_2SO_4, $HClO_4$
- **Lewis/Brønsted combination**: $FeCl_3 \cdot 6H_2O$ mediated by TsOH

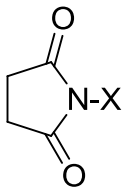
1. Introduction

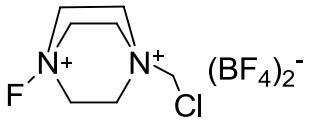
- DISADVANTAGES of general synthetic methods:
  - solvent (environmentally unfriendly)
  - high temperature
  - long reaction time
  - high amount of catalyst

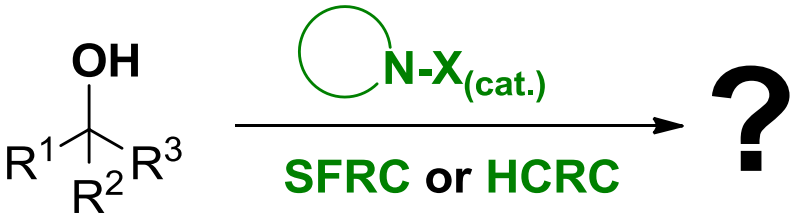
2. Aim of the work

New methodologies for comprehensive direct transformation of various alcohols ⟶ principles of green chemistry, especially catalytically supported transformations under **solvent-free reaction conditions (SFRC)** or **high substrate concentration reaction conditions (HCRC).**

$NX_{(cat.)}$:

a) X=Cl, Br, I NXS: 

b) X=NFSi: $(PhSO_2)_2NF$, FTEDA: 



R^1, R^2, R^3 = aryl, alkyl

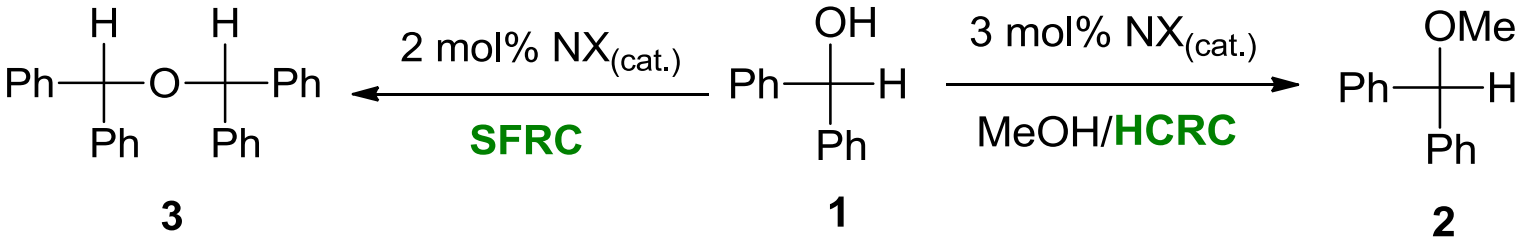
with or without **Nucleophile sources:**

Nu.sou.: MeOH, EtOH, *i*PrOH, 4-Cl-PhCH$_2$OH
(Me)$_3$Si- R', **R'** = Cl, Br, OEt, NCS, O*i*Pr
R''COCH$_2$COR'''
4-Br-PhNH$_2$, MeCN/H$_2$O
(C$_6$H$_5$)$_2$C=CH$_2$, CH$_3$C(C$_6$H$_5$)$_2$OH, electron rich benzo-cyclenes

[1] (a) B. P. Bandgar, L. S. Uppalla, V. S. Sadavarte, *Synlett* **2001**, *2001*, 1715-1718; (b) S. T. Kadam, S. S. Kim, Catal. Commun. 2008, 9, 1342-1345; (c) B. Karimi, G. R. Ebrahimian, H. Seradj, Org. Lett. 1999, 1, 1737-1739.

3. Various transformations of alcohols catalytically supported by *N*-halo organic compounds

C-O bond formation



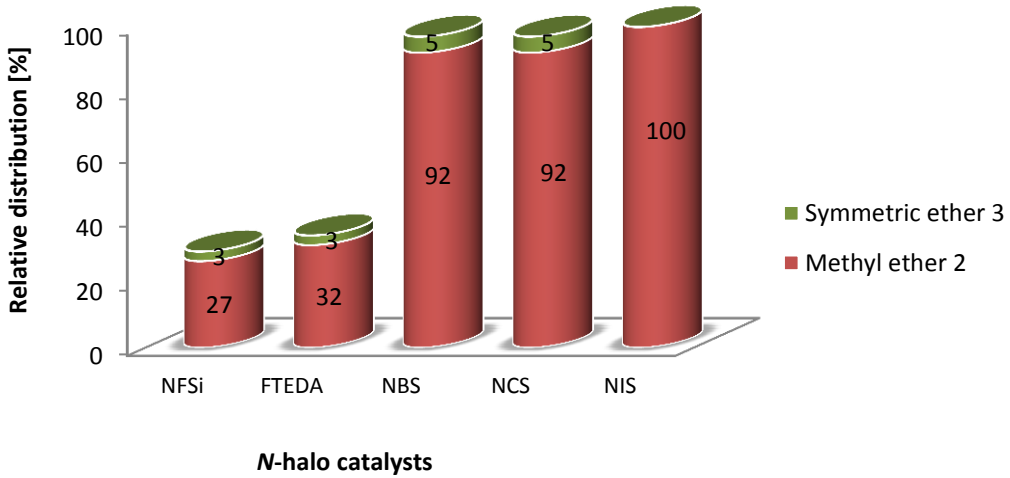
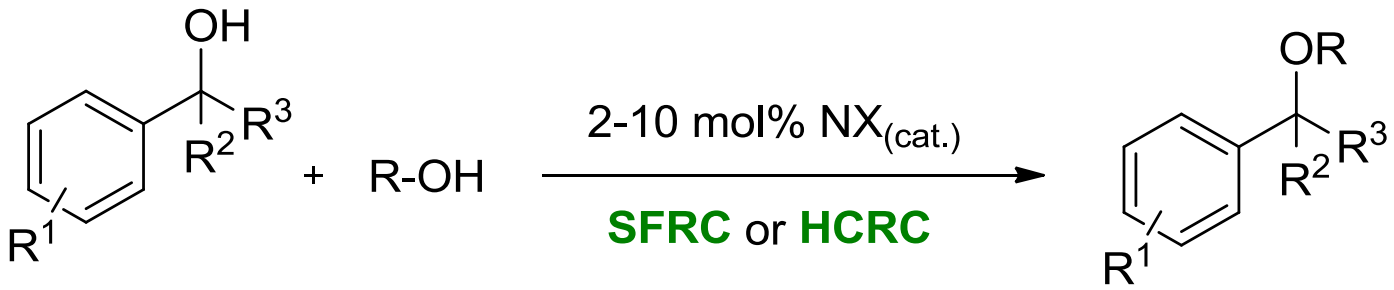
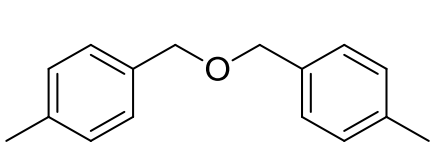


*Figure 1.1 The catalytic effect of N-halo catalysts on conversion of diphenylmethanol **1** with MeOH under HCRC.*

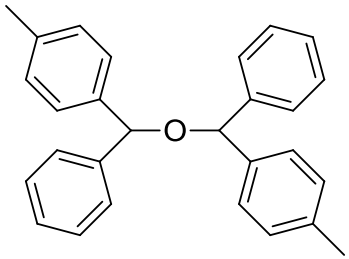
Scheme 1.1: Transformation of benzyl and tertiary alkyl alcohols with alkyl or benzyl alcohols in the presence of N-halo catalysts under SFRC or under HCRC.



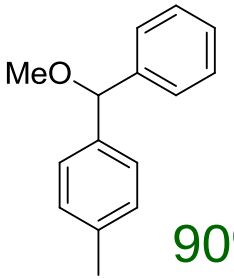
- Structures and yields [%] of products:



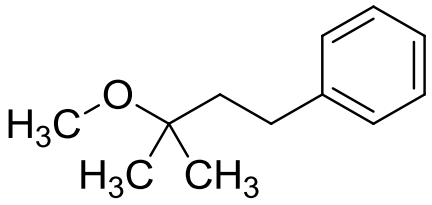
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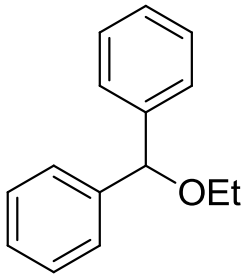
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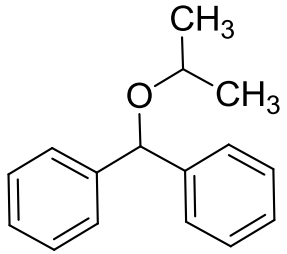
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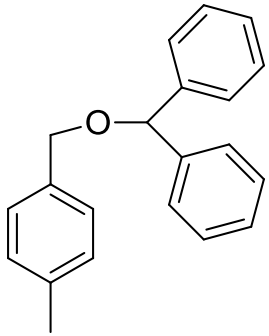
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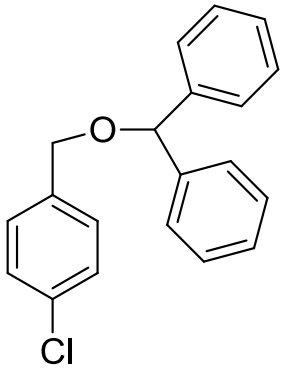
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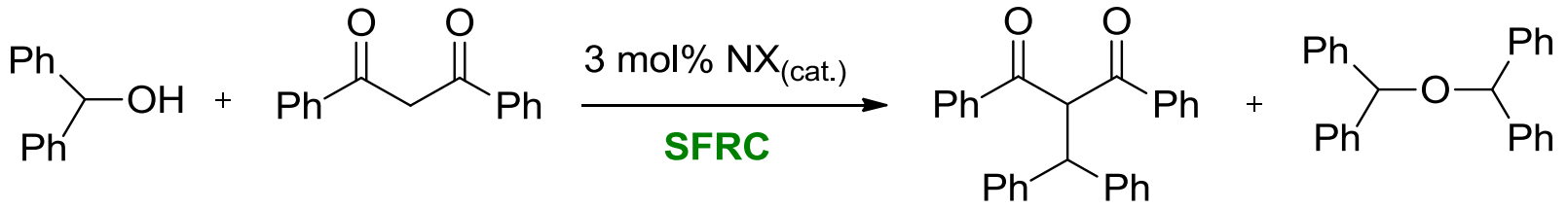


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90%

C-C bond formation



1 **4** **5** **3**

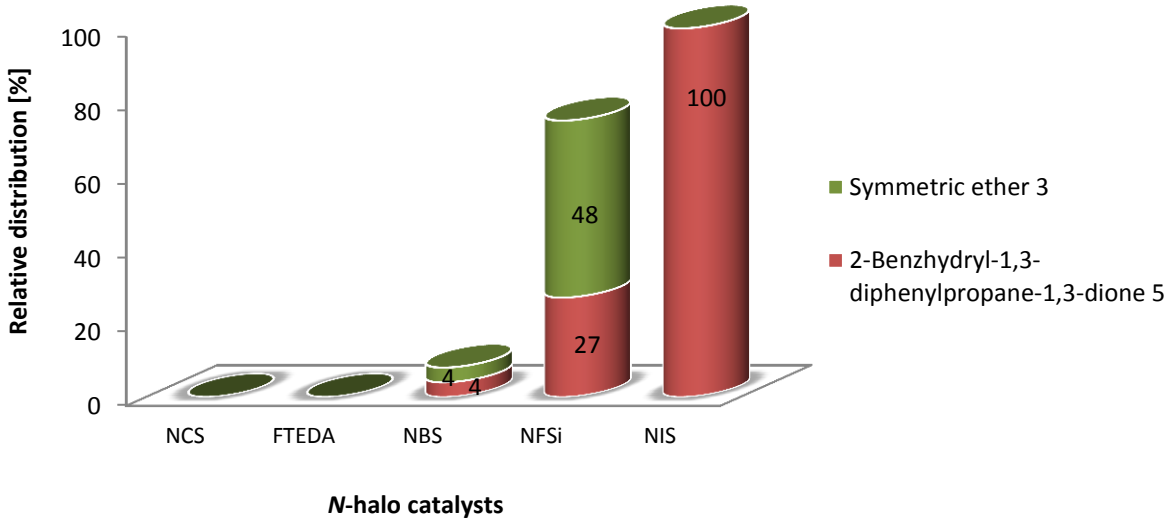
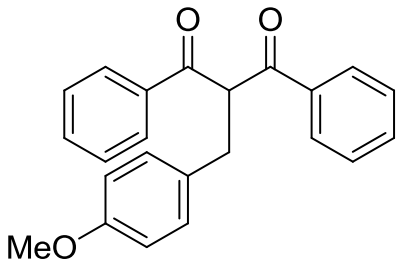


*Figure 1.2: The effect of substoichiometric amount of N-halo catalysts on conversion of diphenylmethanol **1** with dibenzoylmethane **4** under SFRC.*

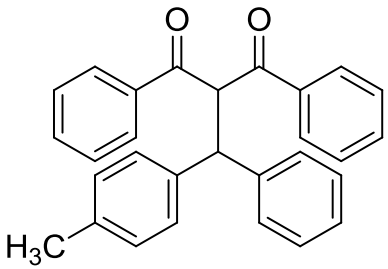
Scheme 1.2: Reactions of β-dicarbonyl compounds with different alcohols catalyzed by NIS under SFRC.



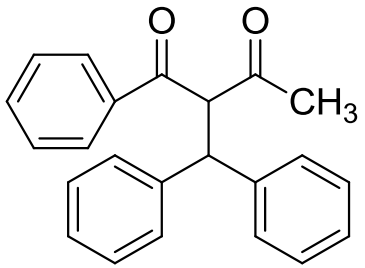
- Structures and yields [%] of products:



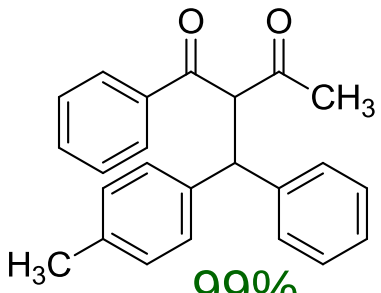
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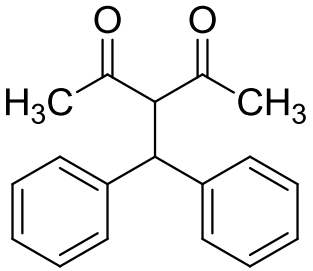
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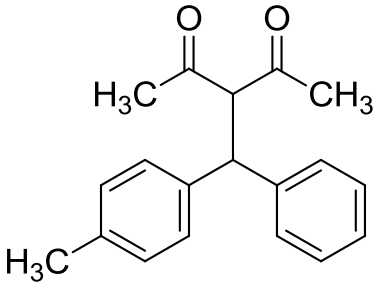
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C-C bond formation

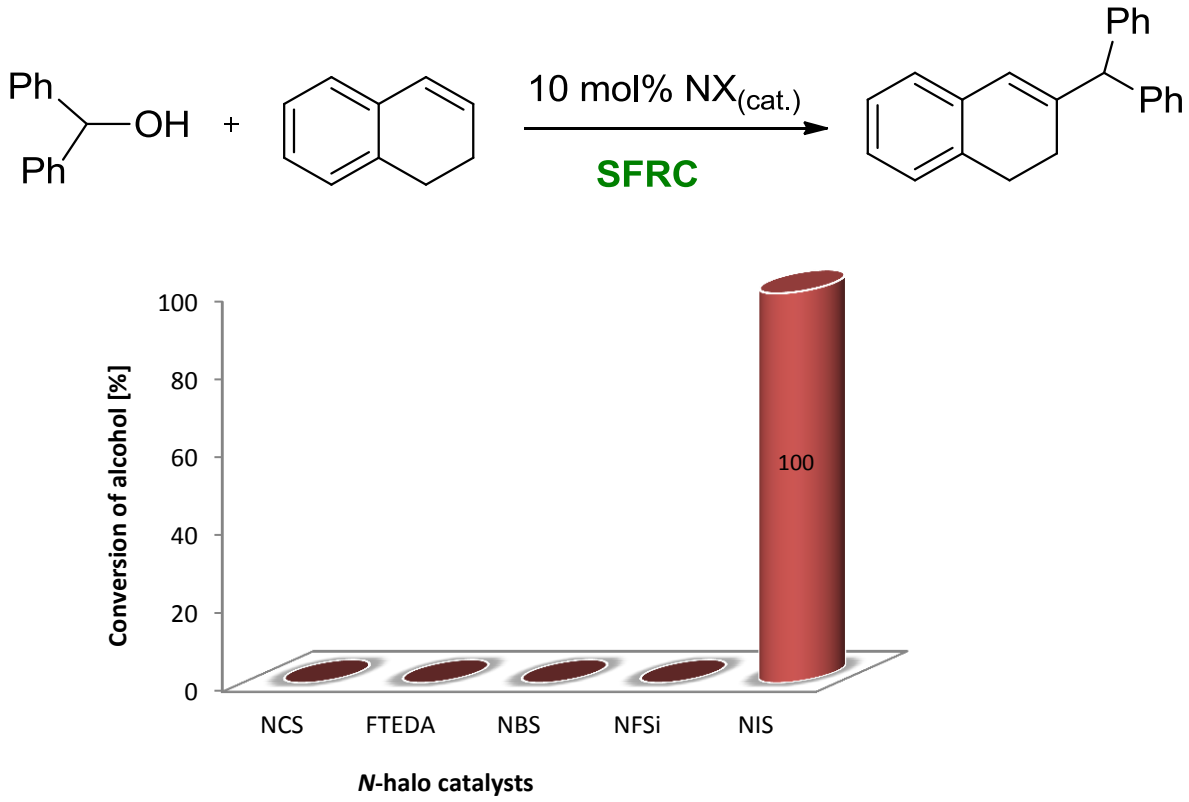
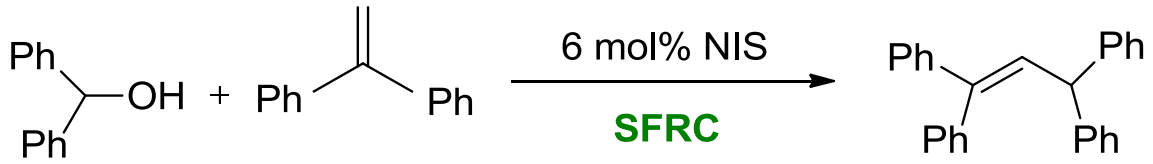


Figure 1.3: The catalytic effect of N-halo catalysts on conversion of diphenylmethanol with1,2-dihydronaphthalene under SFRC.

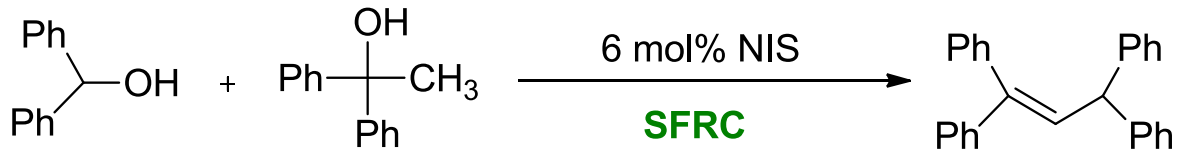
C-C bond formation

Scheme 1.3: Direct coupling of diphenylmethanol and 1,1 diphenylethene catalyzed by NIS under SFRC.



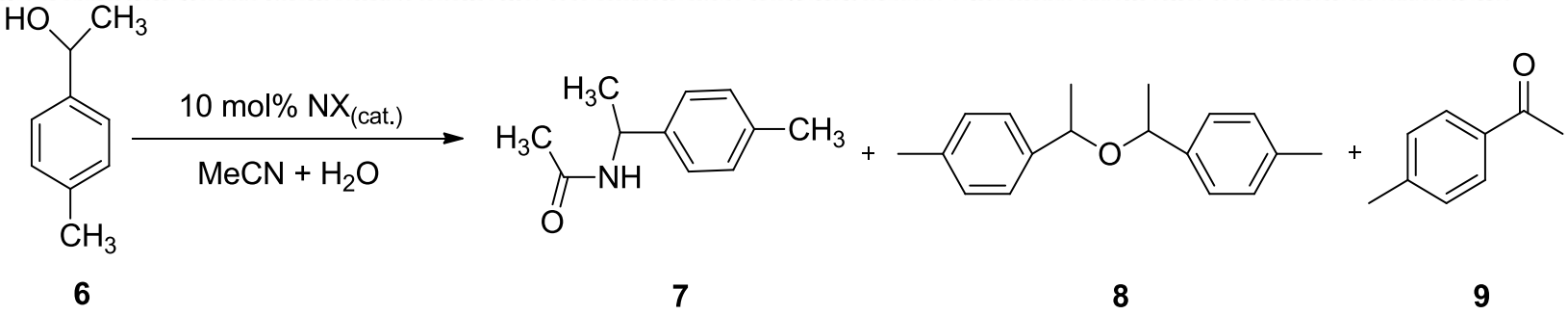
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Scheme 1.4: Direct coupling of secondary and tertiary alcohol catalyzed by NIS under SFRC.



92%

C-N bond formation



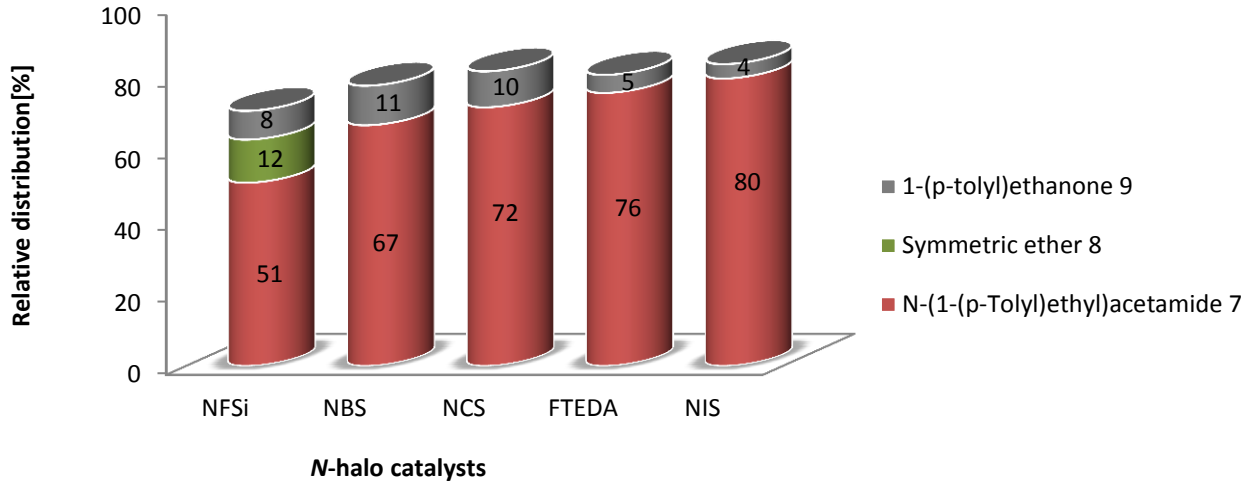
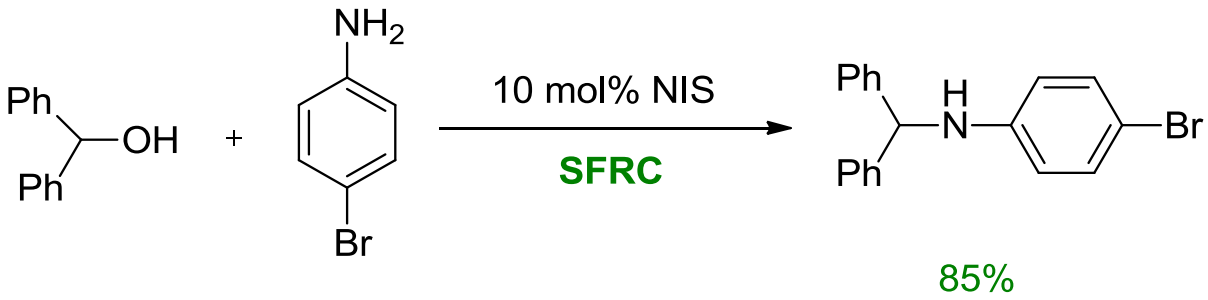


*Figure 1.4: The catalytic effect of N-halo catalysts on conversion of 1-(p-tolyl)ethan-1-ol **6** in acetonitrile solution.*

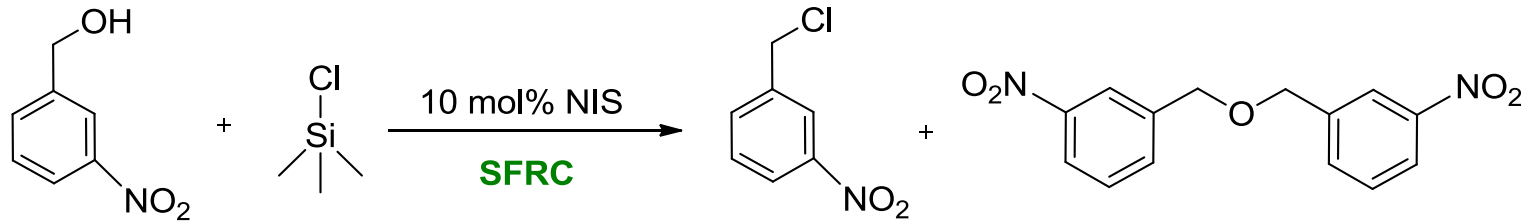
C-N bond formation

Scheme 1.4: Direct coupling of diphenylmethanol with 4-bromoaniline catalyzed by NIS under SFRC.



C-Cl bond formation

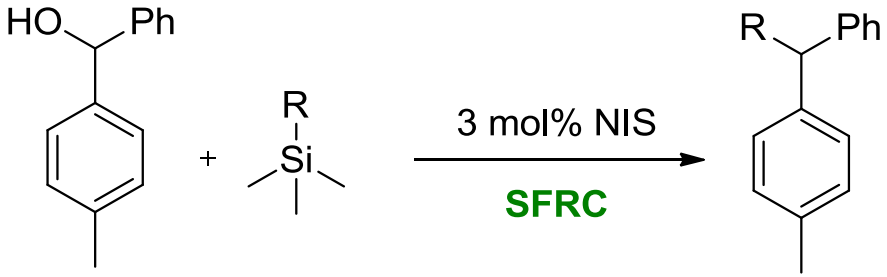
Scheme 3.3: Chlorination of 4-nitrobenzyl alcohol with TMSCl catalyzed by NIS under SFRC.



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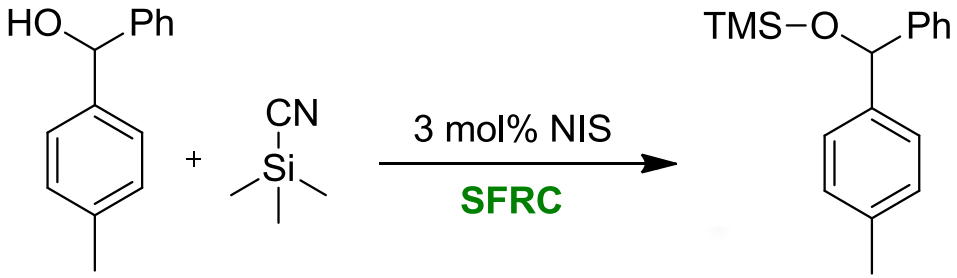
Scheme 1.5: Isothiocyanation or ethoxylation of phenyl(p-tolyl)methanol with TMSNCS or TMSOEt catalyzed by NIS under SFRC.



R: NCS
R: OEt

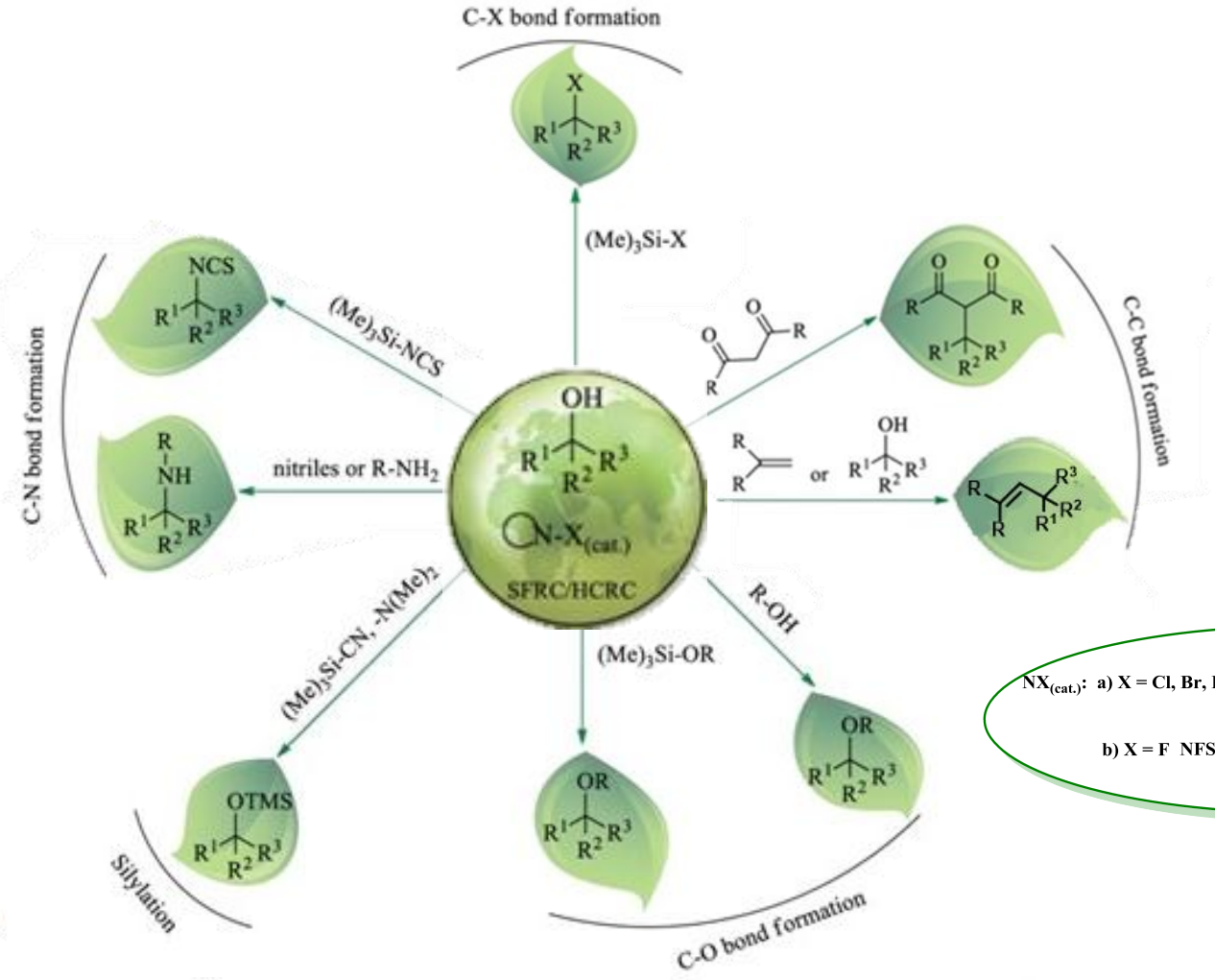
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Scheme 1.6: Trimethylsilylation of phenyl(p-tolyl)methanol with TMSCN catalyzed by NIS under SFRC.

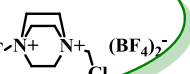


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8. Conclusions



$NX_{(cat.)}$: a) X = Cl, Br, I NXS:

b) X = F NFSi: $(PhSO_2)_2NF$, FTEDA: 

The presented methodology is new, highly efficient and easy to perform approach to the synthesis of comprehensive type of derivatives starting from hydroxyl functional group targets and applying **solvent-free reaction conditions** or **high substrate concentration reaction conditions** as green chemical reaction protocol.

Acknowledgments

- Slovene Human Resources Development and Scholarship Fund and the Slovenian Research Agency through the programme Chemistry for Sustainable Development
- Prof. Dr. Stojan Stavber
- Slovenian NMR Centre at the National Institute of Chemistry, Ljubljana, Slovenia

THANK YOU FOR YOUR ATTENTION!