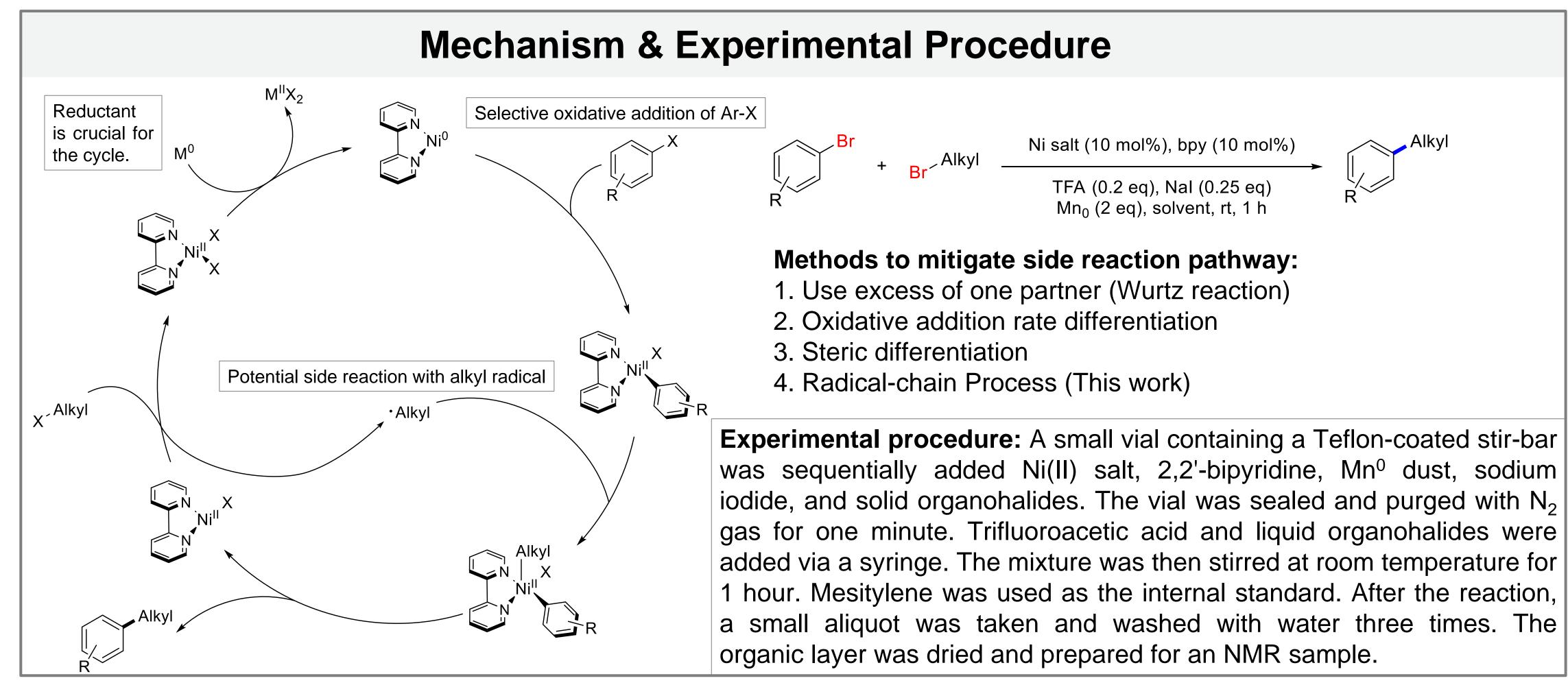
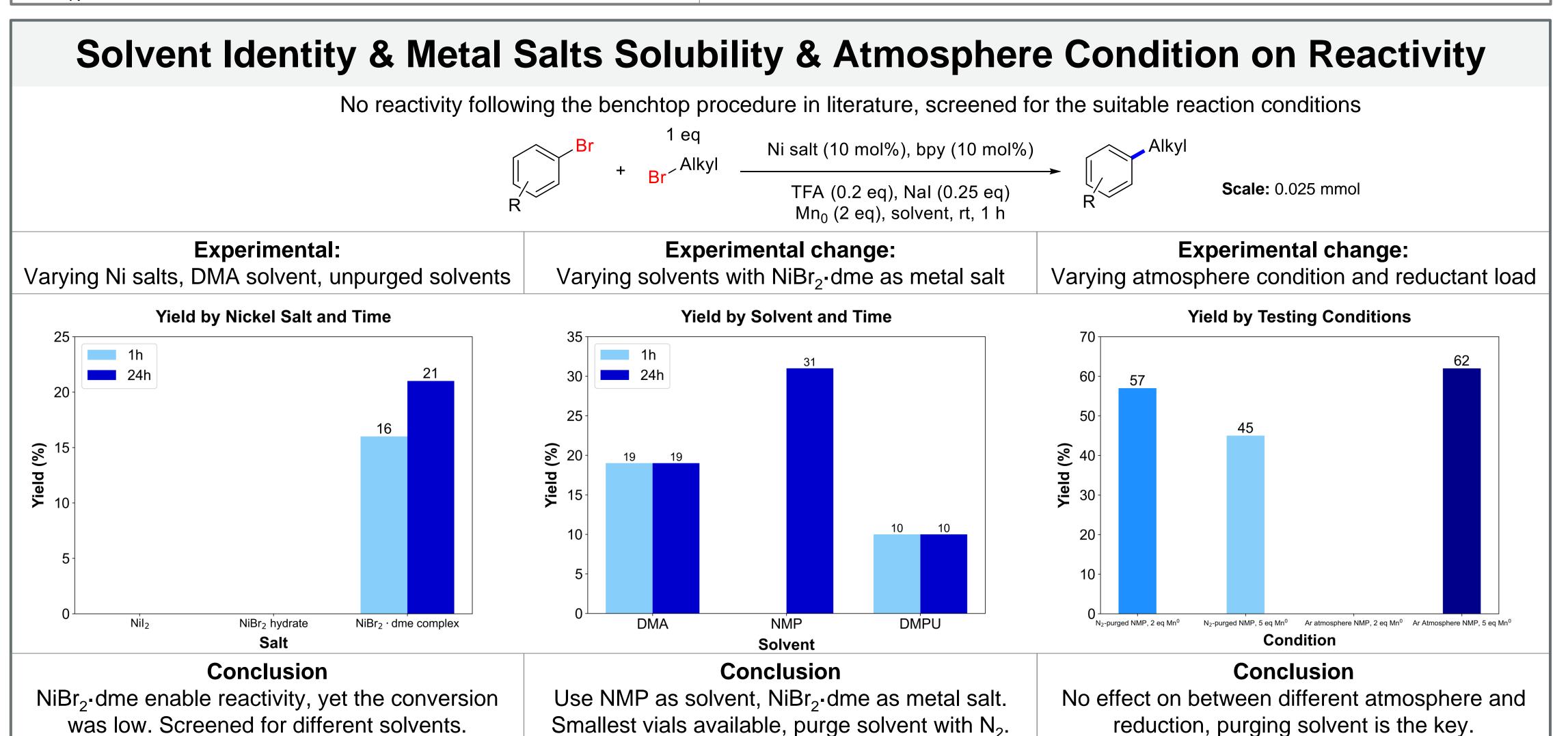
Screening of a Ni-Catalyzed Cross-Electrophile Coupling of Aryl Halides with Alkyl Halides

Tom Tan*, Brett Akana-Schneider

Department of Chemistry, University of Wisconsin-Madison, 1101 University Ave., Madison, WI 53706-1322 USA

Introduction Cross-electrophile coupling (XEC) reactions Conventional cross-coupling reactions Challenge: Possible self-coupling due to similar preference Self-coupling unlikely, due to different reaction preference Electrophile X = halogen, pseudohalogen 1. Fewer steps, excellent function groups compatibility 1. Reactive nucleophiles lead to selectivity issues and function group limitation. M^0 reductant = Zn^0 , Mn^0 2. Better commercial availability with only halogen electrophiles 2. Inert atmosphere and water-free conditions are often required; unstable reagents. X = halogen, pseudohalogen M = Mg, Li, Zn, Sn, Si, B 3. Significant difference in commercial availability between the two coupling partners This project: Assess how reaction parameters affect on yield and side reaction pathways

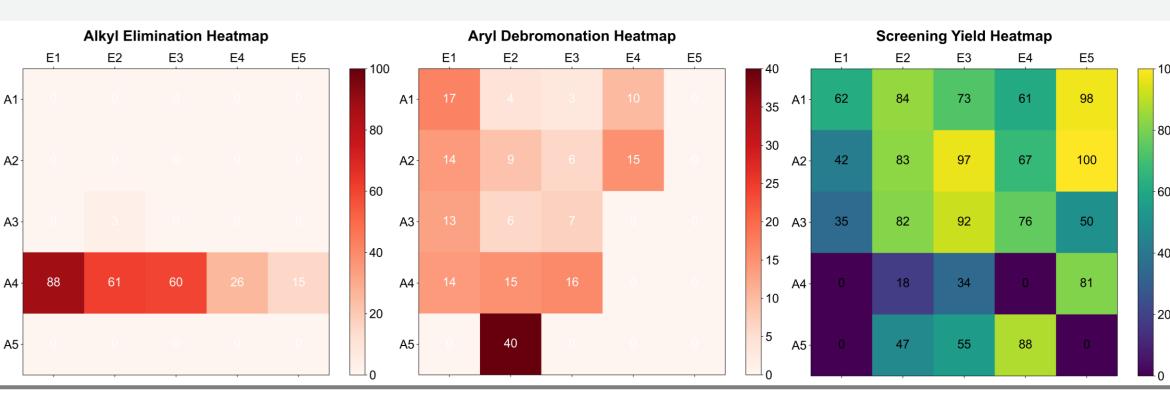




Results: Substrate stereoelectronic effect on reactivity Hypothesis: more electron-poor & less sterically hindered substrates promote reactivity **Experimental improvement:** 1.5 equivalent alkyl bromide, N₂ purged solvent, smaller vial Mn₀ (2 eq), NMP, rt, 3 h **E3** more electron poor, higher yield higher yield 73 % (31 %, 3 %) 97 % (7 %, 6 %) 35 % (64 %, 13 %) 76 % (8 %, 21 %) 50 % (59 %) elimination to cyclopentene CO₂Et CO₂Et CO₂Et F_2C_2 CO₂Et MeO. CO₂Et lower yield increased side reactivity 0 % (91 %) 55 % (48 %) 0 % (100 %) 58 % (29 %, 10 %) 47 % (13 %, 40 %) Substrate reactivity 1. Good reactivity across primary alkyl halides 2. Secondary and tertiary halides had lower yield 3. Electron withdrawing group promote reactivity Possible causes: steric hinderence, intermediate radical stability 1. Higher yield with more electron-poor aryl halides 2. Lower yield with ortho substituted substrates 3. High yield with ortho small substituents substrate Possible cause: aryl halides electron density, steric hinderence

Summary & Conclusions

This study underscores the critical role of metal solubility and solvent preparation in cross-electrophile coupling reactions between aryl halides ^ with alkyl halides, with NMP solvent and N₂-purged conditions _{A2} significantly increased yields. Less sterically hindered primary alkyl halides and electron-poor aryl halides were the more reactive. Steric As hindered second and tertiary alkyl substrates also exhibited reactivity albeit with lower yield. These data can provide helpful information regarding substrate selection in future synthesis using this reaction.



Literature cited & Acknowledgement

Conclusion: Steric hindrance of alkyl halides & electrons density of aryl halides are the major factor in affecting reactivity

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