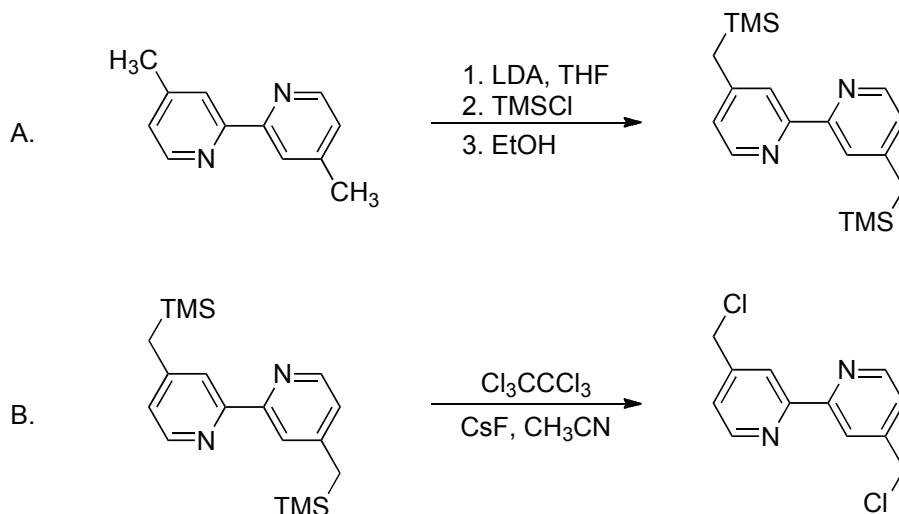


**Discussion Addendum for:
Efficient Synthesis of Halomethyl-2,2'-Bipyridines: 4,4'-
Bis(Chloromethyl)-2,2'-Bipyridine**



Prepared by Tiandong Liu and Cassandra L. Fraser*.¹

Original article: Smith, A. P.; Lamba, J. J. S.; Fraser, C. L. *Org. Synth.* **2002**, *78*, 82.

Halogenation of dimethyl-2, 2'-bipyridines via trimethylsilyl (TMS) intermediates and electrophilic halide reagents, CX_3CX_3 ($X = Cl, Br$ or F), is a very useful method for bipyridine (bpy) derivation.²⁻⁴ This approach benefits from nearly quantitative yields, few by-products, and low cost reagents. In the past decade, there have been only a few improvements reported for this reaction, but many bipyridine derivatives have been prepared using this method. Many bipyridine analogues have been accessed via TMS-bpy intermediates.

Monohalogenation of Dimethyl-Bipyridine

Other common methods for methylpyridine halogenation involve radical reactions or hydroxymethylbipyridine precursors. The radical method suffers from high reactivity and poor selectivity, often generating mixtures of halogenated species, whereas hydroxyl halogenations typically involve multi-step processes.

Monohalogenation of dimethyl-bipyridine may be performed by the TMS procedure with a reduced amount of lithium diisopropylamide (LDA). The reported yields were nearly quantitative (~99%)⁶ for 5-bromomethyl-5'-methyl-2,2'-bipyridine and over 60% for 5-chloromethyl-5'-methyl-2,2'-bipyridine⁵ and. However, the same reaction with 4,4'-dimethyl-2,2'-bipyridine generated the monobromo product in only 35% yield.⁷

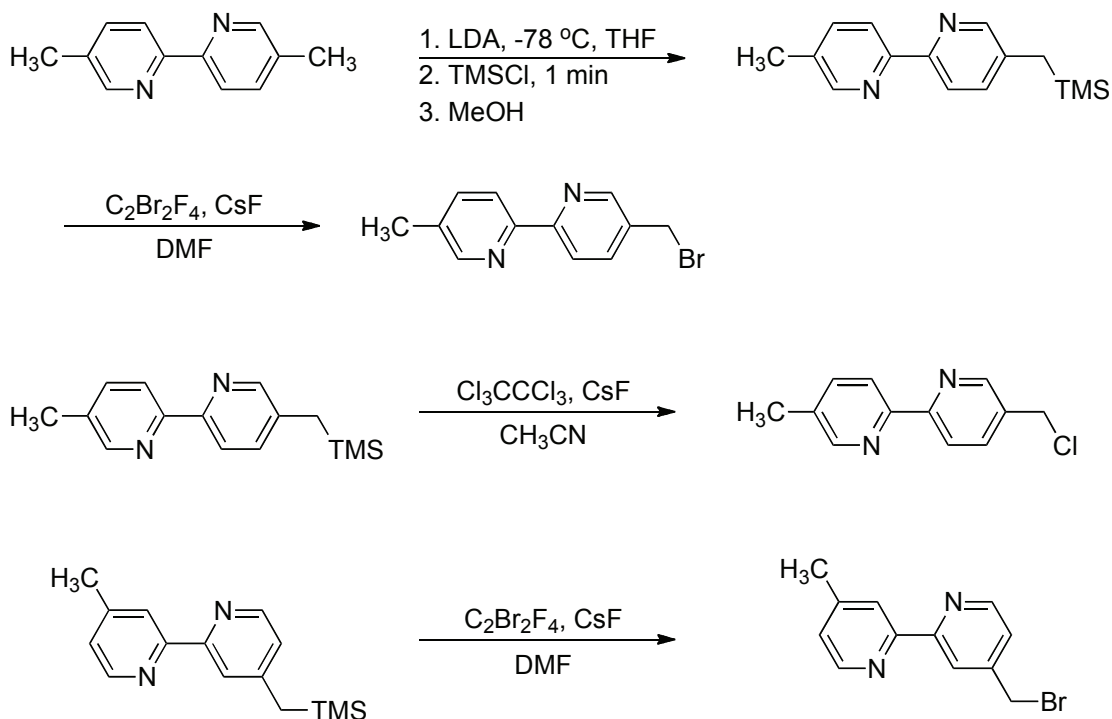


Figure 1. Monohalogenation of dimethyl-bipyridines.

Bipyridine Derivatization via Silane Reagents

Given that the trimethylsilyl-bpy reagents were good nucleophile precursors in the halogenation of dimethylbipyridine, their reactivity was extended to other electrophilic substrates, such as aldehydes² and alkylhalides.⁸ Tetrachlorosilane can also be used to trap lithium intermediates and generate reactive trichlorosilane species, which have been reacted with alcohols to generate trialkoxysilylmethyl bipyridines or hydroxyl groups on zeolite surfaces for catalysis.⁹ New derivatives are accessible via these approaches using various reagents and substrates.

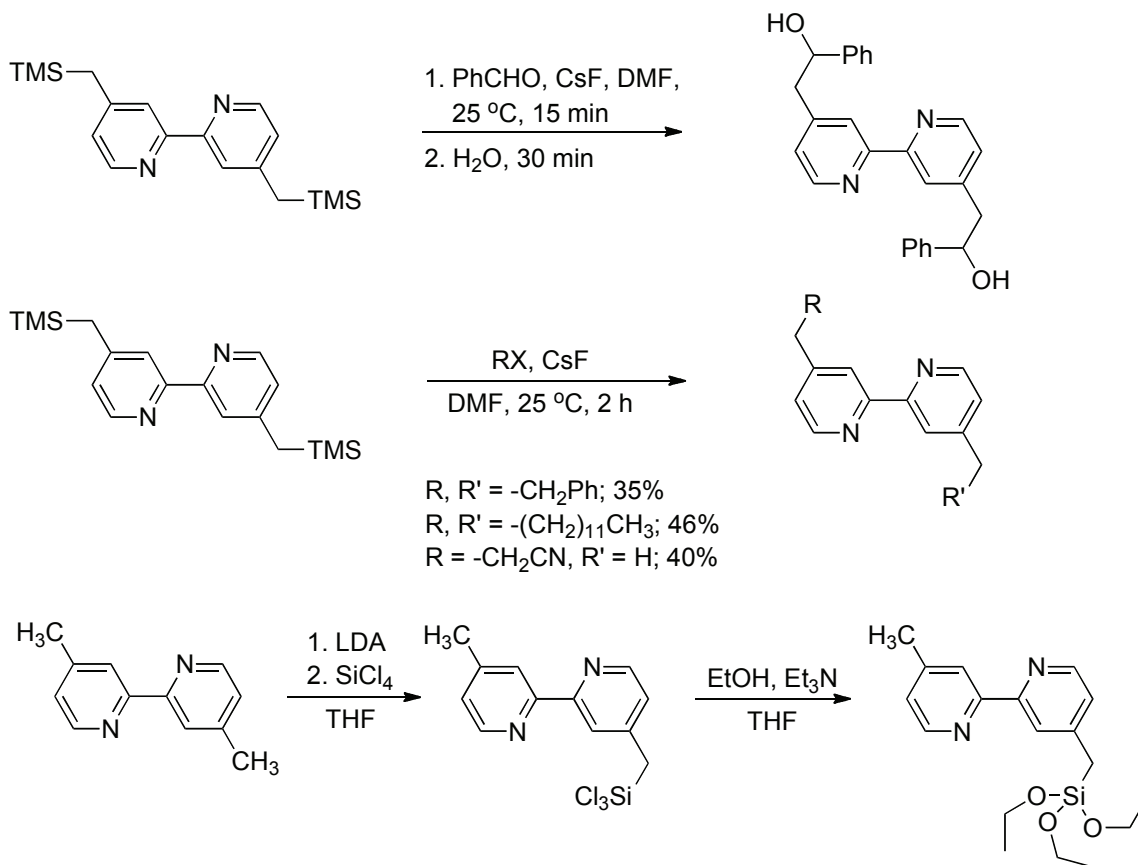


Figure 2. Compounds derived from trimethylsilylmethyl bipyridine.

Polymers Containing Bipyridines

Bipyridyl units appear frequently in functionalized polymeric materials as ligands for metal atoms or to modify electronic or optical properties.¹⁰⁻¹⁴ The bis(halomethyl)-bipyridine complexes and their corresponding compounds with ruthenium or iron were utilized as initiators to generate metallopolymers, including block polymers.¹⁵⁻²¹

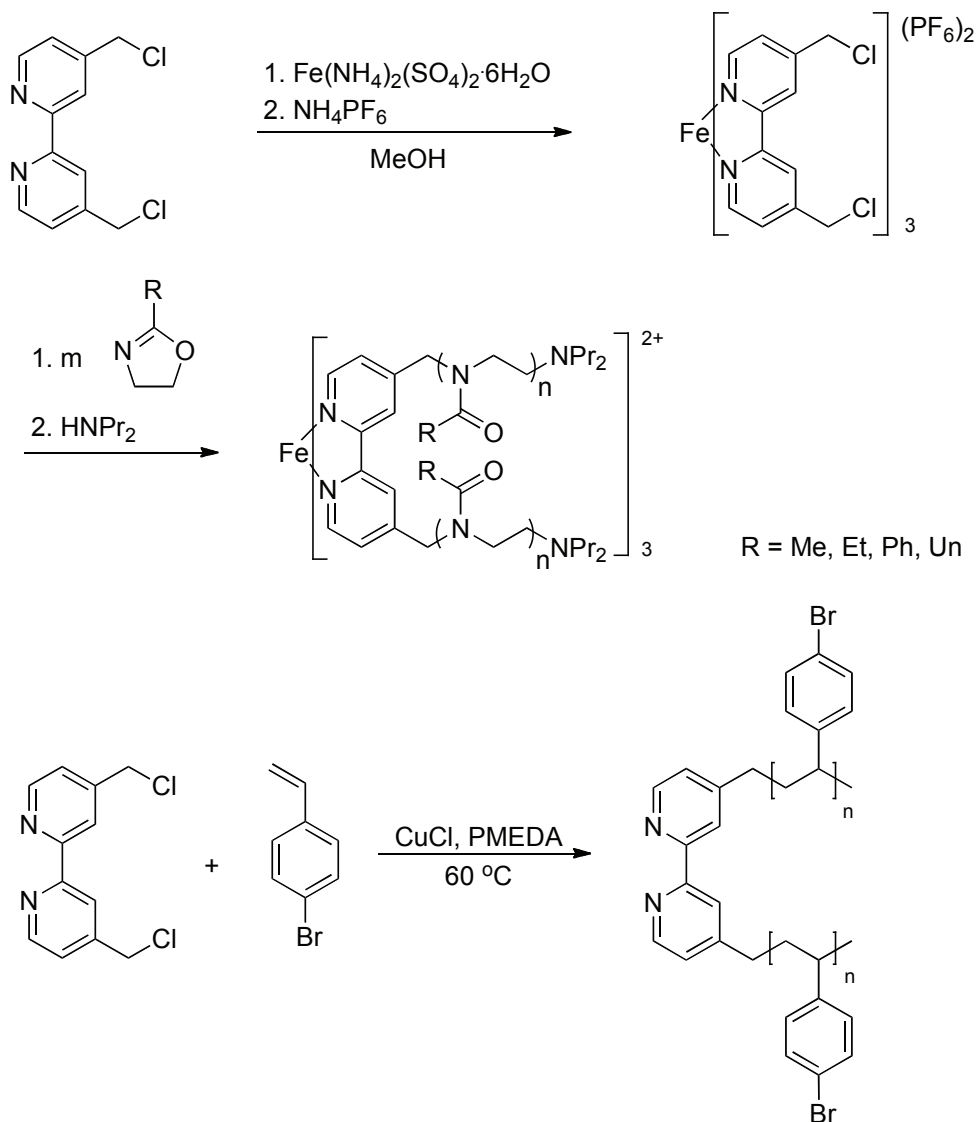


Figure 3. Bis(halomethyl) bipyridine in polymerization.

Bisphosphonate Bipyridine Complexes

Le Bozec, et al. used 4,4'-bis(bromomethyl)-2,2'-bipyridine to prepare 4,4'-bis(phosphonate)-2,2'-bipyridine, which can be used to produce many new derivatives via Wadsworth-Emmons reactions with aldehydes.^{22,23} A similar approach was adopted by Grätzel and coworkers to generate bipyridines with extended π conjugation for solar cell applications.²⁴

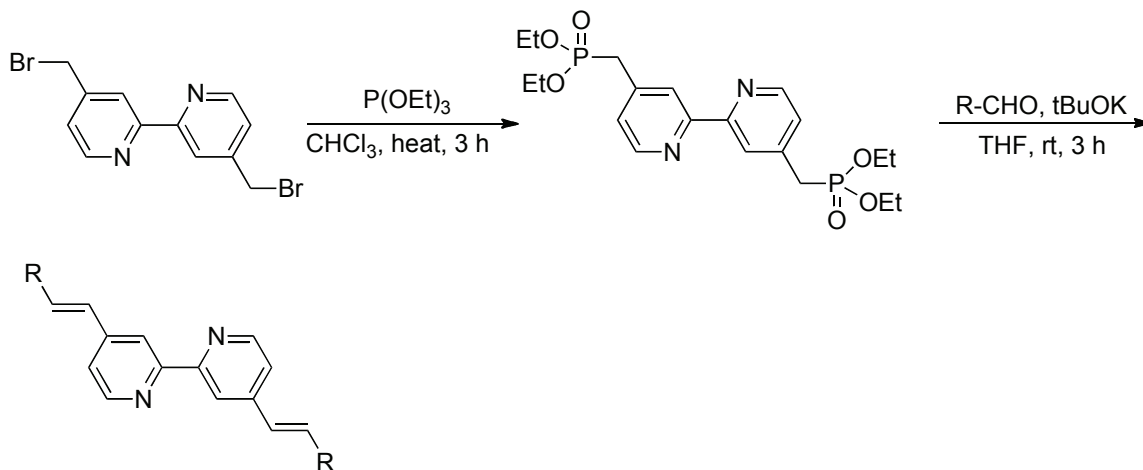


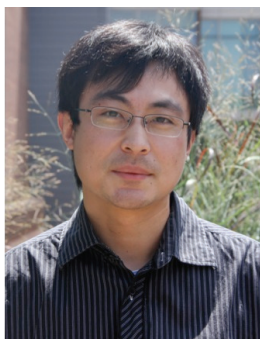
Figure 4. Preparation of bis(phosphonate) bipyridine compounds.

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