1,2-*P,O*-Ferrocenes in Suzuki-Miyaura *C,C*-couplings

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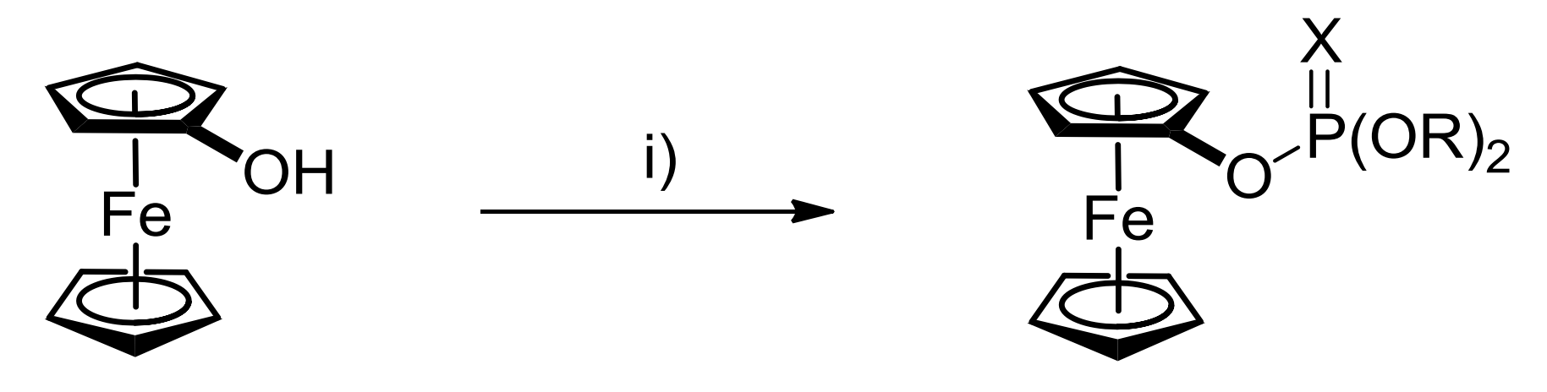
Introduction

Since its first synthesis, ferrocene has emerged as one of the most important organometallic structural motifs. Industrial and academic applications are well known and range from fuel additives to ferrocene-based highly-active and efficient ligands for homogeneous catalysis.[1] In particular, oxygen functionalized ferrocenes are rarely examined. Recent investigations already explored a pathway for the synthesis of ferrocenyl-aryl ethers and their suitability in *ortho*-directed metallations. However, unwanted side reactions result in the formation of 1,1'-substituted ferrocenes and require elaborate column chromatographic purification.[2] As an option, the intramolecular Phospho-Fries-rearrangement enhances the formation of *ortho*-substituted products, which is a well known synthesis strategy for phenyl-based compounds.[3]

Synthesis of Ferrocene–O–P Compounds

Suitable starting materials for anionic Fries rearrangements in general require electron withdrawing substituents to ensure *ortho*-lithiation and intramolecular attack. Starting from ferrocene, ferrocenol (**1**) can be synthesized in a four steps synthesis.[4] Treatment with chloro phosphorous compounds in the prescence of a base yields the Fc–O–P compounds **2a-c** (Schema 1). Electronically modified derivatives are easily accessible, starting from the P(III) compounds by adding either sulfur or borane-thf adduct. The obtained compounds are stable towards air and moisture.



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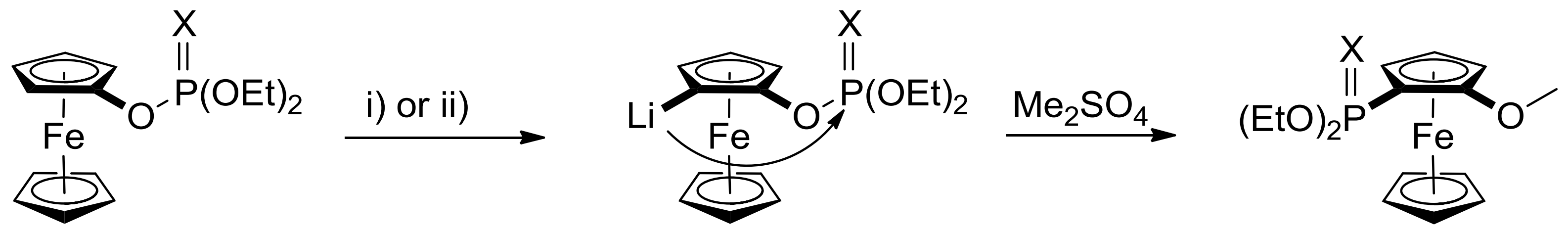
2a 90 % X = O, R = Et
2b 31 % X = S, R = Et
2c 76 % X = BH_3, R = Et

Scheme 1. i) (R = Et, X = O) NEt_3, CH_2Cl_2, –30 °C, $ClP(O)(OEt)_2$; (R = Et, X= S, BH_3) NEt_3, CH_2Cl_2, $ClP(OEt)_2$, –30 °C, S_8/BH_3-thf.

Anionic Phospho-Fries-Rearrangement

The anionic Phospho-Fries rearrangement is induced by lithiation in *ortho*-position of the ferrocenyl oxygen. The *ortho*-Directing effect of the O–P substituents enables selective deprotonation in the desired position. The usage of non-nucleophilic bases is essential to avoid nucleophilic attack at the phosphorous atom. Esters **2a-c** rearrange at –30 °C to the appropriate Phospho-Fries products **3a-c** within a strict temperature regime. The addition of an electrophile protects the OH-functionality, which is sensitive to oxidation.



2a E = O
2b E = S
2c E = BH_3

3a 94 % E = O
3b 50 **%** E = S
3c 37 % E = BH_3

Scheme 2. i) **2a,c**: LDA, –30 °C, 4 h, thf. ii) **2b**: ^{s}BuLi, –30 °C, thf, 4 h.

Conversion of a Phosphonate to Phosphane 5

Phosphonate **3a** could converted to phosphine **4** by reduction using $LiAlH_4$/Me_3SiCl [5a] in the abscence of oxygen. The sbsequent Stelzer reaction[5b] allows the C–P-bond formation and produces **5** in moderate yields. Compound **5** was tested as a supporting ligand in *C,C* cross-coupling reactions for the synthesis of hindered biaryls bearing three *ortho*-substitutents. The obtained activated and de-activated biaryls are racemic mixtures of the axial chiral compounds.

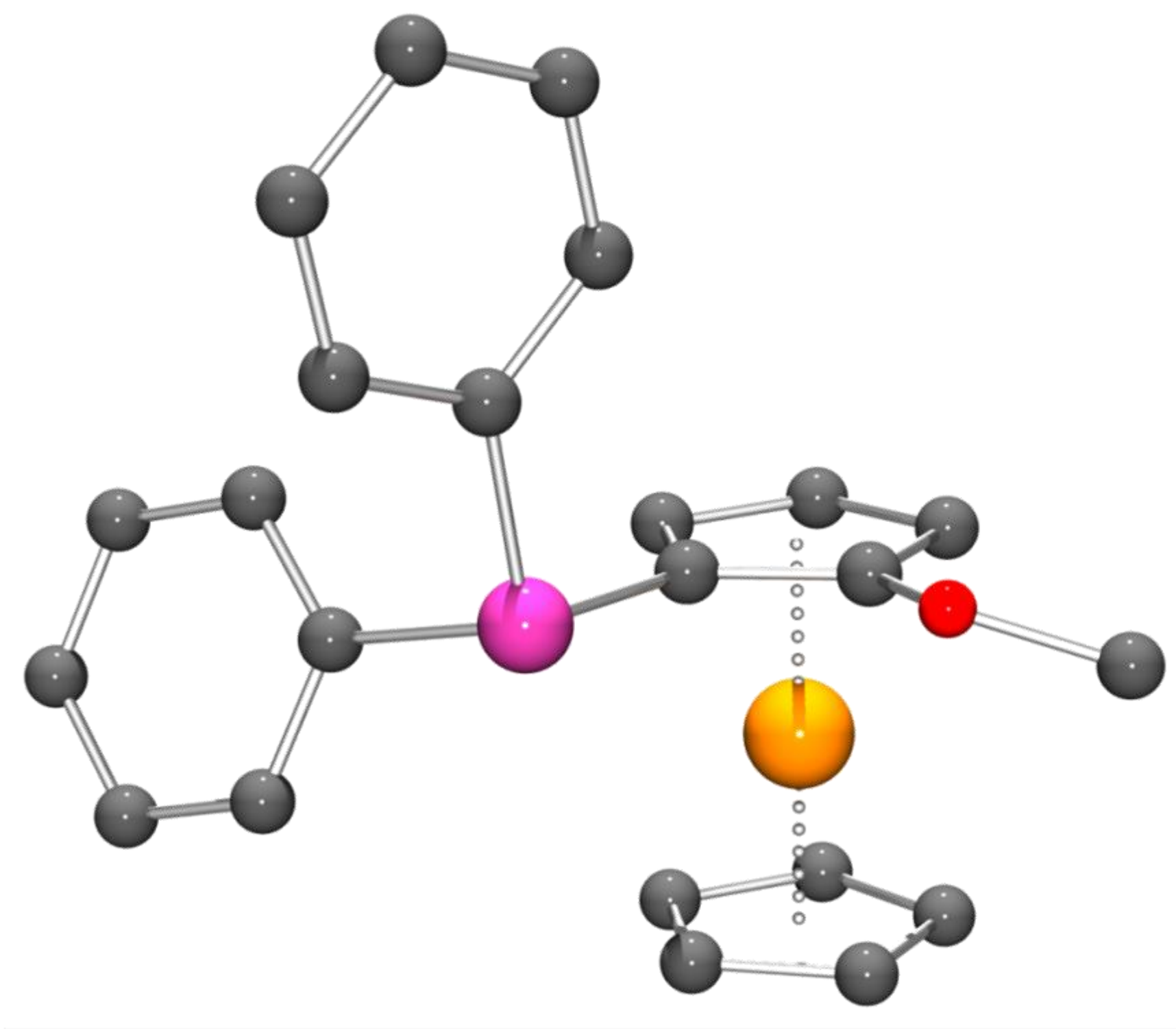
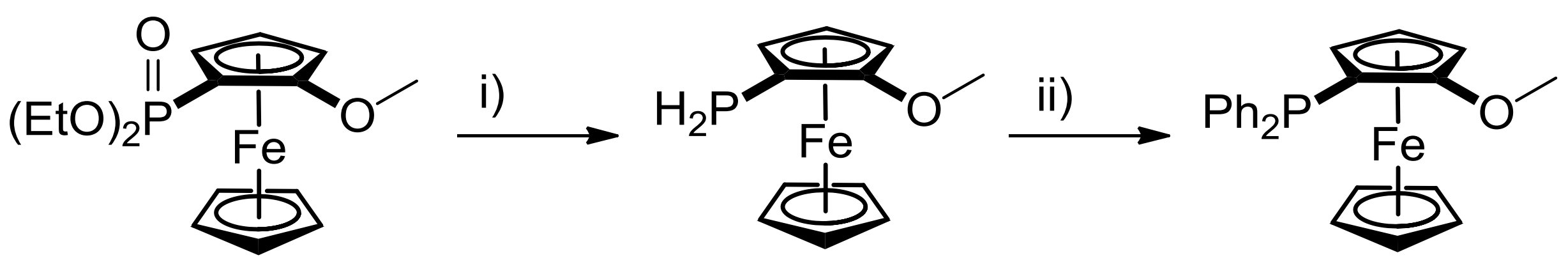


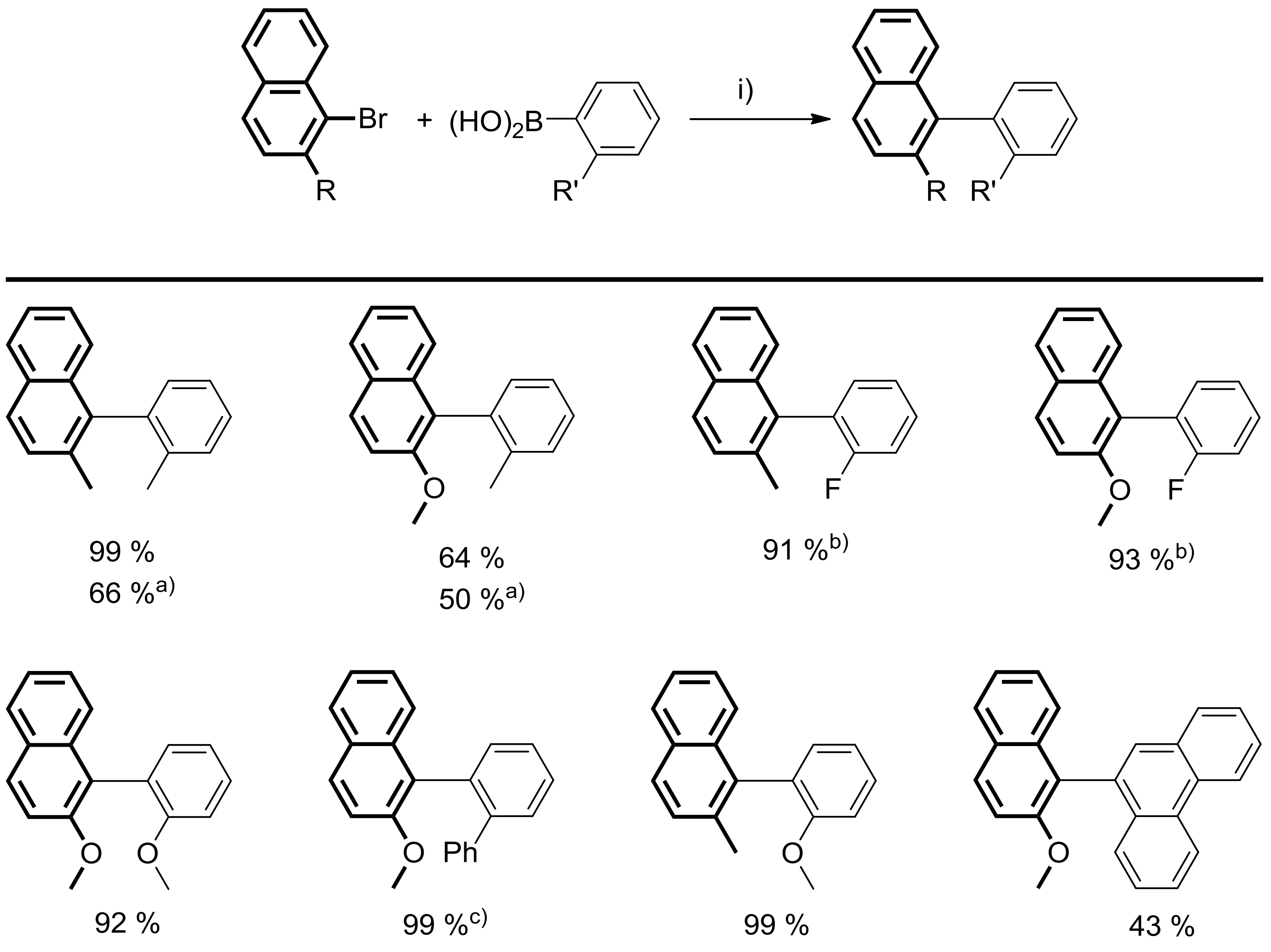
Figure 1. *Ball-and-Stick m*odell of the structure of *rac*-**5** in the solid state. Space group: $P2_1/c$.



3a **4** **5**

Scheme 3. i) $LiAlH_4$, Me_3SiCl, thf, 45 °C, quant. ii) 2 eq K_3PO_4, 2 eq PhI, 2-mol% $[Pd(dppf)Cl_2]$, toluene, 110 °C, 14 h, 50 % (re **4**).

P,O-Ferrocenyl-Phosphane 5 in Suzuki-Miyaura Reactions



a) 50 °C, b) K_3PO_4 x 3 H_2O, c) 100 °C

Scheme 4. $[Pd_2(dba)_3]$ (0.25-mol%), **1** (1 mol%), K_3PO_4 x H_2O, toluene, 70 °C, 24 h.

Summary

The successfull synthesis of 1,2-*P,O*-substituted ferrocenes via the anionic Phospho-Fries rearrangement enables a new synthesis pathway starting from easily accessible ferrocenylphosphates. The rearrangement products can be converted to phosphane **5**, which is suitable as a supporting ligand in *C,C* cross-coupling reactions for the synthesis of hindered biaryls under mild conditions. Running the anionic Phospho-Fries rearrangement stereoselectively should result in a planar chiral phosphane **5** and thus, should result in the formation of enantio-enriched biaryls, which is currently in progress. A further functionalization at the oxygen moiety is planned to increase the catalytic activity.

References and Acknowledgement

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