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Directed Synthesis of Monofunctionalized 5,5'-Disubstituted 2,2'-Bipyridines and their first Application as Metallo-Supramolecular Initiators[#]

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[#] *Dedicated to Professor Dr. George R. Newkome on the occasion of his 60th birthday.*

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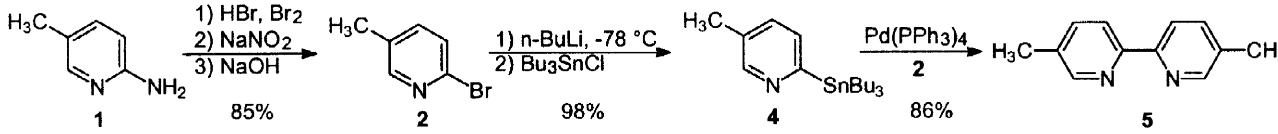
Abstract

Monofunctionalized 5,5'-disubstitued 2,2'-bipyridines were synthesized in very high yields and used in a first application for the construction of a metal centered star-like AB block copolymer.

Keywords: bipyridines; Stille coupling; bromination; living polymerization

In the last decades, many well-defined supramolecular architectures were achieved by the self-assembly of organic components with metal ions [1]. However, only a few organic systems fulfill the requirements for practical applications such as recognition-directed self-assembly features, availability in usable quantities, and functionalized end groups. Most prominent examples are the *oligo*(2,2'-bipyridine) Cu(I), Ni(II) or Fe(II) complexes due to their ability to form defined double, triple or circular helical architectures ("helicates") [1,2]. The preparation of monofunctionalized or unsymmetrical *bis*functionalized 6,6'- and 5,5'-disubstituted 2,2'-bipyridines has always been the major drawback in the synthetic strategies towards such supramolecular building units. We describe here a new approach towards monofunctionalized 5,5'-disubstituted bipyridine building blocks made during our research to new metallo-supramolecular initiators for living polymerizations [3].

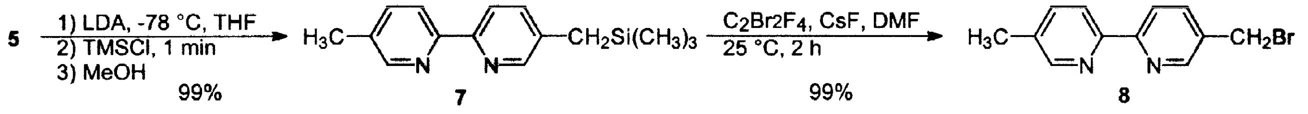
The synthesis of 5,5'-dimethyl-2,2'-bipyridine has been reported previously using classical coupling procedures in rather low yields (0.5-36%) [4]. We developed a new directed strategy using organotin intermediates and Stille coupling procedures [5]. The well-described 2-bromo-5-methyl-pyridine **2** (synthesized from **1** in a 140 gram scale with 85% yield using a modified literature procedure [6] in a special glass reactor) was reacted with butyllithium at −78 °C to obtain the corresponding lithio compound **3** and directly treated with tributyltin chloride to yield 98% of **4** in a 70 gram scale using Kugelrohr distillation (for earlier preparations of **4** see [5,7]). Stille-type coupling of **4** with **2** yielded 86% of the 5,5'-dimethyl-2,2'-bipyridine **5** [8] (Scheme 1).



Scheme 1

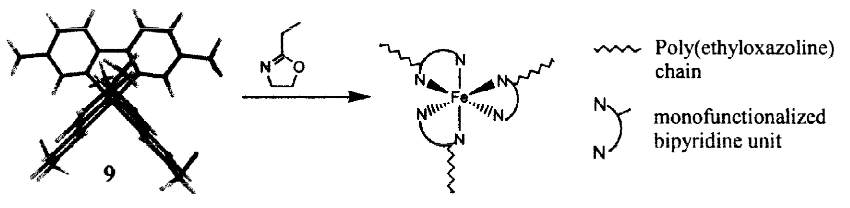
PII: S0040-4039(98)02041-3

In contrast to the 5,5'-*bis*(bromomethyl)-2,2'-bipyridine, which can be easily obtained using NBS [9], the corresponding monofunctionalized ligand is very difficult to synthesize via radical bromination. However, there are two examples of a directed monofunctionalization of other bipyridines described, taking advantage of the different solubility characteristics of intermediates versus starting materials [10]. We discovered a similar effect: Reaction of **5** with 2.2 equivalents of LDA in THF at –78 °C yielded in a precipitate (obviously an unsymmetrical lithium complex). Addition of trimethylsilyl chloride (TMSCl) and quenching after 1 minute with MeOH yielded 99% of the 5-trimethylsilylmethyl-5'-methyl-2,2'-bipyridine **7** [11]. Reaction of **7** with $C_2Br_2F_4$ and CsF [12] gave 99% of the 5-bromomethyl-5'-methyl-2,2'-bipyridine **8** [13] (Scheme 2).



Scheme 2

As first application we used the corresponding iron(II) metal complex **9** (prepared from **8** [14]) as initiator for the living polymerization of 2-oxazolines resulting in star-like AB block copolymers (see also [3]) [15].



Scheme 3. Living polymerization of 2-ethyl-2-oxazoline with **9** (Molecular Modeling, MacSpartan, level MM2).

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References and Notes

[1] Lehn, J.-M. *Supramolecular Chemistry - Concepts and Perspectives*, VCH, Weinheim, Germany, **1995**.

[2] See e.g. Piguet, C.; Bernardinelli, G.; Hopfgarten, G. *Chem. Rev.* **1997**, *97*, 2005-2062.

[3] Hochwimmer, G.; Nuyken, O.; Schubert, U. S. *Macromol. Rapid Commun.* **1998**, *19*, 309-313.

[4] Sasse, W. H. F. *Org. Synth.* **1966**, *46*, 5-10; Polin, J.; Schmohel, E.; Balzani, V. *Synthesis* **1998**, 321-324.

[5] For a recent example see e.g.: Hanan, G. S.; Schubert, U. S.; Volkmer, D.; Riviere, E.; Lehn, J.-M.; Kyritsakas, N.; Fischer, J. *Can. J. Chem.* **1997**, *75*, 169-182.

[6] Windscheif, P. M.; Vögtle, F. *Synthesis* **1994**, 87-92.

[7] Bolm, C.; Erhard, M.; Felder, M.; Schlingloff, G. *Chem. Ber.* **1992**, *125*, 1169-1190.

[8] White solid, mp 114–115 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): 2.37 (s, 6 H, 7,7'-H), 7.60 (dd, 2 H, *J* = 8.0, 2.1, 4,4'-H), 8.24 (d, 2 H, *J* = 8.0, 3,3'-H), 8.48 (s, 2 H, 6,6'-H).

[9] E.g.: Ebmayer, F.; Vögtle, F. *Chem. Ber.* **1989**, *122*, 1725-1727.

[10] Eisenbach, C. D.; Schubert, U. S.; Baker, G. R.; Newkome, G. R. *J. Chem. Soc., Chem. Commun.* **1995**, 69-70; Newkome, G. R.; Groß, J.; Patri, A. K. *J. Org. Chem.* **1997**, *62*, 3013-3014.

[11] White solid, mp 79–80 °C. Selected spectroscopic data: ^{1}H NMR ($CDCl_3$): 7.44 (d, 1 H, *J* = 8.0, 4'-H), 7.61 (d, 1 H, *J* = 8.0, 4-H), 8.21 (d, 1 H, *J* = 5.3, 3'-H), 8.23 (d, 1 H, *J* = 5.3, 3-H), 8.34 (s, 1 H, 6'-H), 8.48 (s, 1 H, 6-H).

[12] See also: Fraser, C. L.; Anastasi, N. R.; Lamba, J. J. S. *J. Org. Chem.* **1997**, *62*, 9314-9317.

[13] White solid, mp 153–154 °C. ^{1}H NMR ($CDCl_3$): 2.41 (s, 3 H, 7'-H), 4.53 (s, 2 H, 7-H), 7.67 (d, 1 H, *J* = 8.3, 4'-H), 7.85 (dd, 1 H, *J* = 8.3, 2.3, 4-H), 8.32 (d, 1 H, *J* = 7.9, 3'-H), 8.41 (d, 1 H, *J* = 8.3, 3-H), 8.53 (s, 1 H, 6'-H), 8.67 (s, 1 H, 6-H). Further purification on silica resulting 75% of very pure product (partially destruction on the column).

[14] Prepared using $FeSO_4 \times 7\ H_2O$ and MeOH (anion exchange with NH_4PF_6) in 37% yield. MALDI-TOF-MS: 1006 [$M^+ - PF_6 + H_2O$], 879 [$M^+ - 2\ PF_6 + 2\ H_2O$]; λ_{max} (CH_3CN)/nm (ε): 257 (31 768), 304 (68 293), 525 (3 776).

[15] E.g.: 15 mg **9**, 3 d, 80 °C, CH_3CN, 58 mg polymer. λ_{max} (CH_3CN, $\overline{M}_n$ = 1474 g/mol)/nm (ε): (8 869), 304 (16 203), 519 (1 398); MALDI-TOF-MS: 1474 [M^+]; GPC ($CHCl_3$, PS standard): $\overline{M}_n$ = 1 540 g/mol, $\overline{M}_n/\overline{M}_w$ = 1.32.