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Preface

Over the past century, synthetic organic chemists have relied more and more on the presence of heteroatoms to realize the ultimate end-goal of their synthetic quest. With the growing importance of metal centers in the supportive infrastructure, it became obvious that the family of *N*-heteraromatics has become an integral component of this arena. Thus, as our synthetic objectives rely increasingly on pyridine ingredients in these supra(macro)molecular puzzles, we decided that an overview of the syntheses of the parent and substituted 2,2′:6′,2″-terpyridines was in order to lay the foundation for future synthetic endeavors on this interesting group of heterocycles. The use of terpyridine to construct specific, stable, metal complexes will be demonstrated, and their unique properties and assemblies hopefully will inspire others to build on this interesting subunit and to incorporate it as a novel mode of structural connectivity. Although terpyridine was introduced to the synthetic world as early as 1931, it was only after its combination with supramolecular chemistry that its importance was duly realized. Then, its introduction into polymeric assemblies introduced important catalytic properties further emphasizing its importance, expanding new synthetic and nanoscale frontiers. We have attempted to compile the key examples to assist future researchers in this arena. However, although there are many excellent examples in the literature, space constraints have meant that only a limited number of these could be referred to, and we therefore apologize in advance to the authors of research papers that have not been cited.

The authors, as always, would be most grateful to be made aware of any errors which may have crept into the manuscript in spite of the proof-reading that was conducted by many of our acquaintances and colleagues. We also thank spouses, relatives, and friends for their patience and assistance during the completion of this work.

Eindhoven and Akron, January 2006

George R. Newkome
Harald Hofmeier
Ulrich S. Schubert

Contents

1
Introduction

Since 1987, when J.-M. Lehn, C. J. Pedersen, and D. J. Cram were honored with the Nobel prize for their results in selective host-guest chemistry [1–3], supramolecular chemistry has become a well-known concept and a major field in today's research community. This concept has been delineated [4] by Lehn: "Supramolecular chemistry may be defined as 'chemistry beyond the molecule', bearing on the organized entities of higher complexity that result from the association of two or more chemical species held together by intermolecular forces." Self-recognition and self-assembly processes represent the basic operational components underpinning supramolecular chemistry, in which interactions are mainly non-covalent in nature (e.g., van der Waals, hydrogen-bonding, ionic, or coordinative interactions); thus, these interactions are weaker and usually reversible when compared to traditional covalent bonds. Nature presents the ultimate benchmarks for the design of artificial supramolecular processes. Inter- and intramolecular non-covalent interactions are of major importance for most biological processes, such as highly selective catalytic reactions and information storage [5]; different non-covalent interactions are present in proteins, giving them their specific structures. DNA represents one of the most famous natural examples, where self-recognition of the complementary base pairs by hydrogen bonding leads to the self-assembly of the double helix. Starting with the development and design of crown ethers, spherands, and cryptands, modern supramolecular chemistry represents the creation of well-defined structures by self-assembly processes [6] (similar to Nature's well-known systems [7]).

One of the most important interactions used in supramolecular chemistry is metal-ligand coordination. In this arena, chelate complexes derived from *N*-heteroaromatic ligands, largely based on 2,2′-bipyridine and 2,2′:6′,2″-terpyridine (Figure 1.1), have become an ever-expanding synthetic and structural frontier.

Bipyridine has been known since 1888 when F. Blau first synthesized a bipyridine-iron complex [8]. One year later, it was again Blau who synthesized and analyzed bipyridine by dry distillation of copper picolinate [9]. Since this parent molecule consists of two identical parts, no directed coupling procedure is required for its construction. Therefore, unsubstituted and symmetrically substituted, in particular 4,4′-functionalized, bipyridines are readily accessible in good yields by simple coupling procedures. Apart from this, bipyridine metal complexes [10] (in

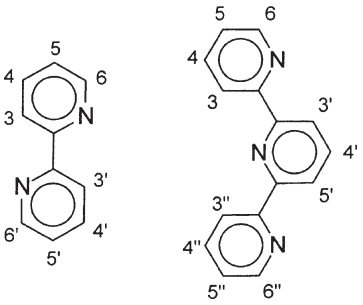


Figure 1.1 Structures of 2,2′-bipyridine and 2,2′:6′,2″-terpyridine.

particular ruthenium complexes) have very interesting photochemical properties making them ideal candidates for solar energy conversion [11].

The chemistry of 2,2′:6′,2″-terpyridines (designated as simply terpyridine or tpy; its other structural isomers are duly noted and will not be considered further here) is much younger than that of 2,2′-bipyridines. In the early 1930s, terpyridine was isolated for the first time by Morgan and Burstall [12, 13], who heated (340 °C) pyridine with anhydrous $FeCl_3$ in an autoclave (50 atm) for 36 h; the parent terpyridine was isolated along with a myriad of other *N*-containing products. It was subsequently discovered that the addition of Fe(II) ions to a solution of terpyridine compounds gave rise to a purple color giving the first indication of metal complex formation. Since this pioneering work was performed, the chemistry of terpyridine remained merely a curiosity for nearly 60 years, at which point its unique properties were incorporated into the construction of supramolecular assemblies. The number of publications dealing with terpyridine has risen sharply as shown in the histogram (Figure 1.2) – a trend that is predicted to continue, since it is a pivotal structural component in newly engineered constructs based on metallo-polymers and crystal engineering.

The terpyridine molecule contains three nitrogen atoms and can therefore act as a tridentate ligand [14, 15]. It has been extensively studied as an outstanding complexing ligand for a wide range of transition metal ions. The ever-expanding potential applications are the result of advances in the design and synthesis of tailored terpyridine derivatives. The well-known characteristics of terpyridine metal complexes are their special redox and photophysical properties, which greatly depend on the electronic influence of the substituents. Therefore, terpyridine complexes may be used in photochemistry for the design of luminescent devices [16] or as sensitizers for light-to-electricity conversion [17, 18]. Ditopic terpyridinyl units may form polymetallic species that can be used to prepare luminescent or electrochemical sensors [19, 20]. In clinical chemistry and biochemistry, functionalized terpyridines have found a wide range of potential applications [21], from colorimetric metal determination [22, 23] to DNA binding agents [24–26] and anti-tumor research [27–29].

Terpyridines have also been utilized for catalytic purposes [30, 31] and in asymmetric catalysis [32]. Another interesting application regarding novel

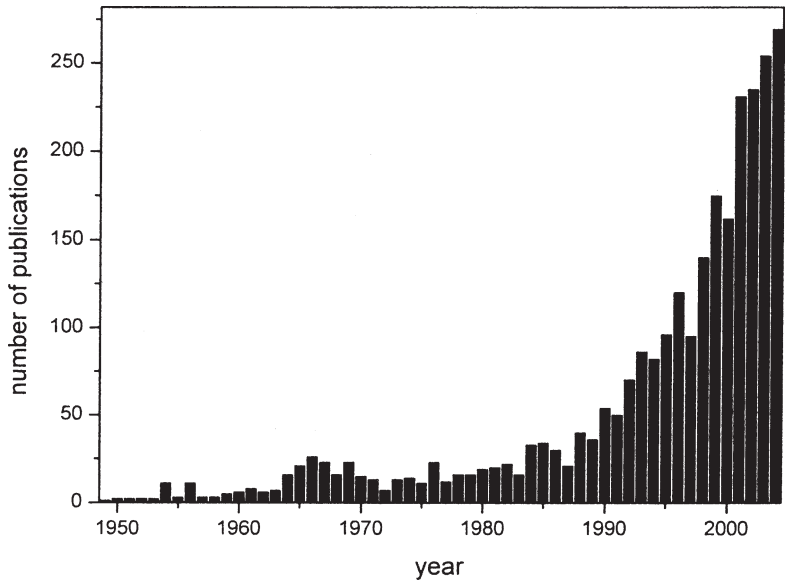


Figure 1.2 Histogram of the number of publications containing the term "terpyridine" using SciFinder (search performed 10.05.2005).

supramolecular architectures is the formation of "mixed complexes", where two differently functionalized terpyridine ligands are coordinated to a single transition metal ion [33–35]. One of the most promising fields for new terpyridine compounds is their unique application in supramolecular chemistry [36]. In this context, the formation of supramolecular terpyridine containing dendrimers [4, 37–41] can be pointed out. Layer-by-layer self-assembly of extended terpyridine complexes on graphite surfaces forms grid-like supramolecular structures [42–45]. Self-assembly of terpyridine compounds on gold [46], CdS [47] or TiO_2 [48], as well as surface functionalization with specially functionalized terpyridine ligands [49], should also be mentioned in this context. Terpyridines, incorporated in macromolecules, enable well-defined supramolecular polymer architectures to be formed, opening up the opportunity of "switching" within physical and chemical properties of materials [34, 35, 50–55].

In view of the notable importance of 2,2′:6′,2″-terpyridine ligands and their metal complexes in the current research, we herein focus on architectures containing this ligand and the corresponding metal complexes. Therefore, this book is divided into topics featuring different architectures and concepts containing terpyridine metal complexes.

Chapter 2 summarizes the known synthetic strategies leading to different terpyridines. Since 4′-substituted terpyridine currently represents the most valuable family of derivatives, emphasis is directed toward the routes to its synthesis.

Chapter 3 describes the preparation and properties of terpyridine metal complexes. Emphasis will be on *bis*terpyridine-Ru(II) complexes and their optical

properties as well as related dyads and triads. Other metal(II) complexes could potentially act as "molecular switches", thus opening up avenues to the construction of nano-devices.

Chapter 4 features various supramolecular aggregates composed of terpyridine-metal subunits, ranging from grids to cyclic structures; moreover, special complexes, where terpyridine complexes are combined with fullerenes or biochemical groups, are described.

Chapter 5 presents polymeric architectures containing terpyridine systems with various architectures, ranging from side-chain-functionalized polymers via main-chain metallopolymers to biopolymers.

Chapter 6 addresses metallodendrimers, micelles, and resins, representing approaches to nanoreactors and immobilized novel catalysts.

Chapter 7 describes catalysis using surface-modified terpyridine metal complexes, opening up potential utilitarian applications, such as assemblies and layers capable of behaving as photoactive materials for use in organic solar cells and LEDs.

References

1 D. J. Cram, *Angew. Chem. Int. Ed. Engl.* **1988**, *28*, 1009–1020.
2 C. J. Pedersen, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1021–1027.
3 J.-M. Lehn, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89–112.
4 G. R. Newkome, R. Güther, C. N. Moorefield, F. Cardullo, L. Echegoyen, E. Pérez-Cordero, H. Luftmann, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2023–2026.
5 J. Darnell, H. Lodish, B. Baltimore, *Molecular Cell Biology*, Scientific American Books, New York, **1990**.
6 J.-M. Lehn, *Supramolecular Chemistry, Concepts and Perspectives*, VCH, Weinheim, **1995**.
7 D. Philp, F. J. Stoddart, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1154–1196.
8 F. Blau, *Ber. D. Chem. Ges.* **1888**, *21*, 1077–1078.
9 F. Blau, *Monatsh. Chem.* **1889**, *10*, 375–380.
10 P. Tomasik, Z. Ratajewicz, *Pyridine Metal Complexes* (Eds.: G. R. Newkome, L. Strekowski), John Wiley & Sons, New York, **1985**.
11 K. Kalyanasundaram, *Coord. Chem. Rev.* **1982**, *46*, 159–244.
12 S. G. Morgan, F. H. Burstall, *J. Chem. Soc.* **1931**, 20–30.
13 S. G. Morgan, F. H. Burstall, *J. Chem. Soc.* **1937**, 1649–1655.
14 W. R. McWhinnie, J. D. Miller, *Adv. Inorg. Chem. Radiochem.* **1969**, *12*, 135–215.
15 E. C. Constable, *Adv. Inorg. Chem. Radiochem.* **1986**, *30*, 69–121.
16 A. Harriman, R. Ziessel, *Coord. Chem. Rev.* **1998**, *171*, 331.
17 B. O'Regan, M. Grätzel, *Nature* **1991**, *353*, 737–740.
18 O. Kohle, S. Ruike, M. Grätzel, *Inorg. Chem.* **1996**, *35*, 4779–4787.
19 M. Schmittel, H. Ammon, *Chem. Commun.* **1995**, 687–688.

20 M. T. Indelli, C. A. Bignozzi, F. Scandola, J.-P. Collin, *Inorg. Chem.* **1998**, *37*, 6084–6089.
21 B. N. Trawick, A. T. Daniher, J. K. Bashkin, *Chem. Rev.* **1998**, *98*, 939–960.
22 B. Zak, E. S. Baginsky, E. Epstein, L. M. Weiner, *Clin. Chim. Acta* **1970**, *29*, 77–82.
23 B. Zak, E. S. Baginsky, E. Epstein, L. M. Weiner, *Clin. Toxicol.* **1971**, *4*, 621–629.
24 H. Q. Liu, T. C. Cheung, S. M. Peng, C. M. Che, *Chem. Commun.* **1995**, 1787–1788.
25 P. M. V. Vliet, M. S. Toekimin, J. G. Haasnoot, J. Reedijk, O. Novakova, O. Vrana, V. Brabec, *Inorg. Chim. Act.* **1995**, *231*, 57–64.
26 P. J. Carter, C. C. Cheng, H. H. J. Thorp, *J. Am. Chem. Soc.* **1998**, *120*, 632–642.
27 W. C. Xu, Q. Zhou, C. L. Ashendel, C. T. Chang, C. J. Chang, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2279–2282.
28 D. S. H. L. Kim, C. L. Ashendel, Q. Zhou, C. T. Chang, E. S. Lee, C. J. Chang, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2695–2698.
29 Y. Zhang, C. B. Murphy, W. E. Jones, *Macromolecules* **2002**, *35*, 630–636.
30 K. Umeda, A. Nakamura, F. Toda, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2260–2267.
31 A. Vavasori, L. Toniolo, *J. Mol. Cat. A: Chemical* **2000**, *151*, 37–45.
32 G. Chelucci, A. Saba, F. Soccolini, D. Vignola, *J. Mol. Cat. A: Chemical.* **2002**, *178*, 27–33.
33 E. C. Constable, C. E. Housecroft, T. Kulke, C. Lazzarini, E. R. Schofield, Y. Zimmermann, *J. Chem. Soc., Dalton Trans.* **2001**, 2864–2871.
34 U. S. Schubert, P. R. Andres, H. Hofmeier, *Polym. Mater.: Sci. Eng.* **2001**, *85*, 510–511.
35 M. Heller, U. S. Schubert, *Macromol. Rapid Commun.* **2002**, *23*, 411–415.
36 J. P. Sauvage, J. P. Collin, J. C. Chambron, C. S. Guillerez, Coudret, V. Balzani, F. Barigelletti, L. D. Cola, L. Flamigni, *Chem. Rev.* **1994**, *94*, 993–1019.
37 U. S. Schubert, C. H. Weidl, C. N. Moorefield, G. R. Baker, G. R. Newkome, *Polym. Prepr.* **1999**, *40*, 940–941.
38 H.-F. Chow, I. Y.-K. Chan, P.-S. Fung, T. K.-K. Mong, M. F. Nongrum, *Tetrahedron* **2001**, *57*, 1565–1572.
39 D. J. Diaz, S. Bernhard, G. D. Storrier, H. D. Abruña, *J. Phys. Chem. B* **2001**, *105*, 8746–8757.
40 G. R. Newkome, F. Cardullo, E. C. Constable, C. N. Moorefield, A. M. W. C. Thompson, *Chem. Commun.* **1993**, 925–927.
41 G. R. Newkome, E. He, *J. Mater. Chem.* **1997**, *7*, 1237–1244.
42 G. S. Hanan, D. Volkmer, U. S. Schubert, J.-M. Lehn, G. Baum, D. Fenske, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1842–1844.
43 A. Semenov, J. P. Spatz, M. Möller, J.-M. Lehn, B. Sell, D. Schubert, C. H. Weidl, U. S. Schubert, *Angew. Chem. Int. Ed.* **1999**, *38*, 1021–1027.
44 U. Ziener, J.-M. Lehn, A. Mourran, M. Möller, *Chem. Eur. J.* **2002**, *8*, 951–957.

45 D. G. Kurth, M. Schütte, J. Wen, *Colloids and Surfaces A: Physicochem. Eng.* **2002**, *198–200*, 633–643.
46 L. S. Pinheiro, M. L. A. Temperini, *Surface Sci.* **2000**, *464*, 176–182.
47 G. Billancia, D. Wouters, A. A. Precup, U. S. Schubert, *Polym. Mater.: Sci. Eng.* **2001**, *85*, 508–509.
48 C. R. Rice, M. D. Ward, M. K. Nazeeruddin, M. Grätzel, *New J. Chem.* **2000**, *24*, 651–652.
49 M. Maskus, H. D. Abruña, *Langmuir* **1996**, *12*, 4455–4462.
50 U. S. Schubert, C. Eschbaumer, *Angew. Chem. Int. Ed.* **2002**, *41*, 2892–2926.
51 M. Heller, U. S. Schubert, *Macromol. Rapid Commun.* **2001**, *22*, 1358–1363.
52 J.-F. Gohy, B. G. G. Lohmeijer, U. S. Schubert, *Macromolecules* **2002**, *35*, 7427–7435.
53 J.-F. Gohy, B. G. G. Lohmeijer, U. S. Schubert, *Macromol. Rapid Commun.* **2002**, *23*, 555–560.
54 U. S. Schubert, H. Hofmeier, *Macromol. Rapid Commun.* **2002**, *23*, 561–566.
55 J.-F. Gohy, B. G. G. Lohmeijer, S. K. Varshney, U. S. Schubert, *Macromolecules* **2002**, *35*, 4560–4563.

2
Syntheses of Functionalized 2,2′:6′,2″-Terpyridines

2.1
Introduction

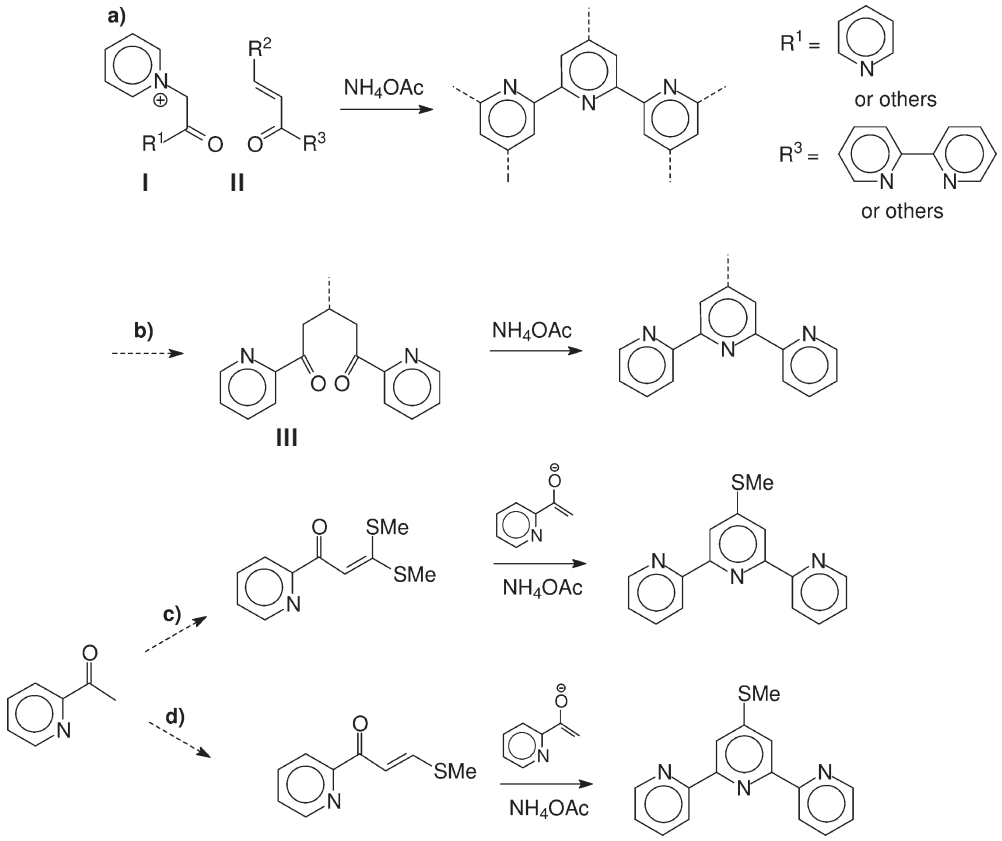
In view of the wide range of research and potential utilitarian applications of 2,2′:6′,2″-terpyridines, an easily accessible "pool" of different functionalized building blocks is mandated. Therefore, highly efficient routes to these ligands are as essential as their well-defined derivatization at every ring position. Functional groups may be introduced directly during their construction or by various substitution interconversions. While publications concerning the chemistry of terpyridine complexes continued to increase, comparatively few preparations of functionalized 2,2′:6′,2″-terpyridine ligand derivatives have been reported as yet. In 1997, Cargill-Thompson [1] reviewed the historical syntheses of the simple terpyridine ligands, and in 2003 Fallahpour [2] reviewed the 4′-substituted terpyridines. In this chapter, both innovative new synthetic strategies and an up-to-date overview of the classical approaches leading to new 2,2′:6′,2″-terpyridine derivatives will be presented. The new developments in the preparation of chiral terpyridines [3–6] and ditopic terpyridine containing ligands [7–14] can be found elsewhere.

2.2
Basic Synthetic Strategies

The two basic synthetic approaches to terpyridines are by either central ring-assembly or coupling methodologies. Ring assembly is still the most prevalent strategy, but because of their multiplicity and efficiency, modern Pd-catalyzed, cross-coupling procedures have recently become seriously competitive and may surpass the traditional ring-closure processes.

2.2.1
Ring Assembly

Over the last couple of decades, various new terpyridine ring-assembly strategies have been developed; Scheme 2.1 displays these frequently used routes. The most

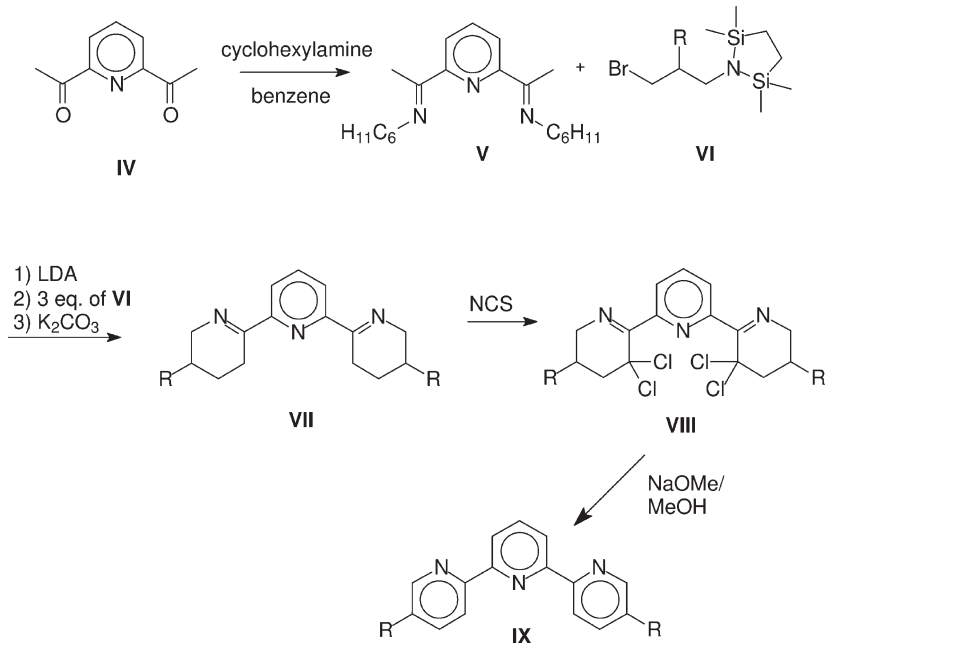


Scheme 2.1 Ring-assembly methods to terpyridines:
(a) and (b) Kröhnke reaction, (c) Potts methodology, (d) Jameson methodology.

common ring assembly of terpyridines is still the well-known Kröhnke condensation (Route a), which initially involves synthesis of *N*-heteropyridinium salts, e.g., **I**, then subsequent ammonia condensation with an enone **II** [15, 16]. Other important methods are the initial construction of 1,5-diketones **III** and subsequent ring closure with an appropriate *N*-source (Route b) [17-19], α-oxoketene dithioacetal methodology (Route c) [16], and the Jameson method by condensation of an *N*,*N*-dimethylaminoenone with 2-acetylpyridinenolate (Route d) [20].

The major disadvantage of these methods is that the final condensation step usually yields tarry crude by-products that require special efforts to isolate and purify the desired terpyridine.

High yield conversions with good product purities were obtained by a four-step procedure starting from the commercially available 2,6-diacetylpyridine (**IV**), which was subsequently converted to the 2,6-*bis*(*N*-cyclohexylacetimidoyl)pyridine (**V**), derived from a multistep procedure, by reaction with cyclohexylamine (Scheme 2.2) [21]. Cyclization of **V** with *Si*-protected 3-bromopropylamines **VI** afforded the

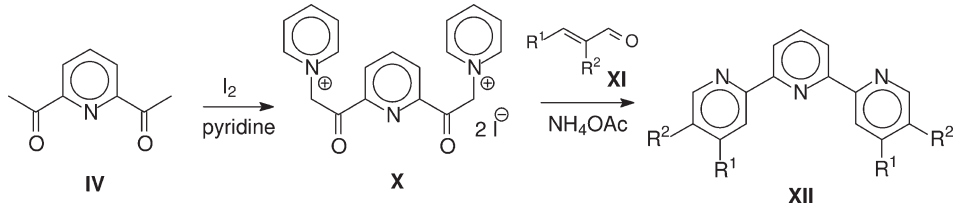


Scheme 2.2 Terpyridine synthesis from 2,6-diacetylpyridine.

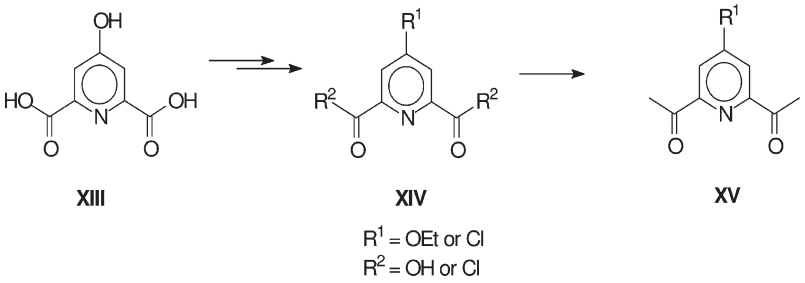
tetrahydropyridines **VII**, which, after chlorination, gave the tetrachloro adducts **VIII**, then onto the desired terpyridines **IX** with a respectable (73–93%) overall yield from **V**.

An effective and simple two-step Kröhnke-type [15] synthesis of polysubstituted symmetric terpyridines from 2,6-diacetylpyridine (**IV**) has been described by Sasaki et al. [22] (Scheme 2.3), in which *bis*pyridinium iodide **X**, obtained (85%) from **IV**, was subsequently reacted with various α,β-unsaturated aldehydes **XI** at 80 °C for 4 h in formamide in the presence of ammonium acetate to give in variable yields the different symmetric terpyridines **XII**.

A novel 4-functionalized 2,6-diacetylpyridine **XV**, the key intermediate for the Kröhnke methodology [15], was prepared from 4′-hydroxy-2,6-pyridinedicarboxylic acid **XIII** (Scheme 2.4) [23], by initial esterification to give diethyl 4-chloropyridine-2,6-dicarboxylate, which yielded the corresponding diacid; subsequent conversion to the 2,6-*bis*(chlorocarbonyl)-4-ethoxypyridine (**XIV**) was accomplished. The



Scheme 2.3 Sasaki-type Kröhnke reaction on 2,6-diacetylpyridine.



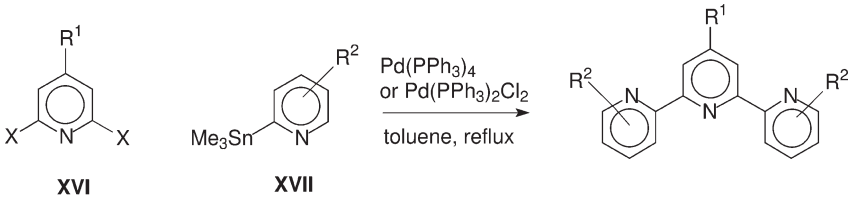
Scheme 2.4 Synthetic approach to functionalized 2,6-diacetylpyridines, as intermediates for the preparation of terpyridines.

reaction with 2,2-dimethyl-1,3-dioxan-4,6-dione followed by hydrolysis with aqueous acetic acid resulted in the formation (36%) of 4-ethoxy-2,6-diacetylpyridine (**XV**). Subsequent Kröhnke-type procedures afforded the desired 4′-substituted terpyridine derivatives.

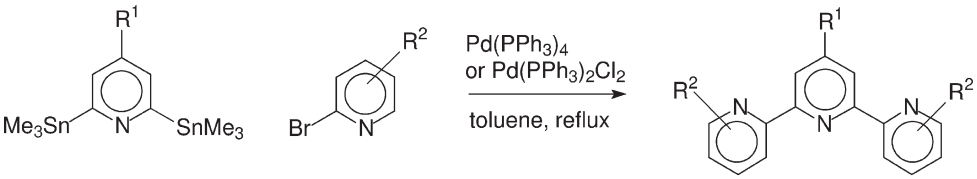
Recently, the Kröhnke method has also been modified to yield terpyridines under solventless conditions; thus, grinding the starting materials with solid NaOH leads to the quantitative formation of the diketone within 20 min [24–26]. Besides the fast and facile reaction procedures, the environmental friendliness (no solvents are used) is a main advantage of this useful modification.

2.2.2
Cross-Coupling Procedures

In the last few years, appropriate methodologies for the construction of functionalized terpyridines were based on directed cross-coupling procedures. Traditional examples, such as the cross-coupling of organosulfur compounds [27] or lithiopyridines with $CuCl_2$ [28], have the disadvantage that they generally result in overall poor conversions. Modern Pd(0)-catalyzed coupling reactions combine the desired efficiency and simplicity with controllable substitution possibilities. Suzuki [29], Negishi [30], and Stille couplings [31] are all based on a Pd(0)/Pd(II) catalytic cycle. Particularly, the Stille cross-coupling has become a popular route to terpyridines, because of its (a) universal building block principle, (b) multi-gram product accessibility, and (c) well-directed functionalization at almost every desired position (Scheme 2.5) [32–35]. 2,2′:6′,2″-Terpyridines, functionalized at the central



Scheme 2.5 Stille-coupling 2-trimethylstannylpyridines and 2,6-dihalopyridines.



XVIII **XIX**

Scheme 2.6 Stille-coupling of *bis*(trimethylstannyl)pyridines and 2-bromopyridines.

and/or terminal pyridine rings, can be obtained utilizing appropriate 2,6-dihalopyridines **XVI** as central building blocks, which can be reacted with 2-trialkylstannylpyridines **XVII** and Pd(0) catalysts in toluene for at least 24 h.

Terpyridine synthesis via the Stille procedure can be conducted by utilizing 2,6-*bis*(trimethylstannyl)pyridines **XVIII** as a central ring, and coupling them with the corresponding 2-bromopyridines **XIX** (Scheme 2.6) [36, 37].

Other Pd-catalyzed cross-coupling procedures have not yet been used for the synthesis of terpyridines themselves, but seem to be appropriate methods; for instance, Negishi cross-coupling was used for the synthesis of terpyridine-related compounds [38] and related 2,2′-bipyridines [39] in excellent yields.

2.3
Synthesis of 2,2′:6′,2″-Terpyridine Derivatives

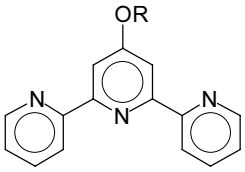
Terpyridines may be functionalized at both the central and the terminal rings; therefore, the desired groups must be incorporated into the initial substituted starting compounds via ring-assembly or coupling procedures. In this overview, the terpyridine derivatives are organized by their ring-substitution positions.

2.3.1
4′-Substituted-2,2′:6′,2″-Terpyridinoxy Derivatives

4′-Terpyridinoxy derivatives represent a dominant substitution pattern because of their convenient accessibility via (a) nucleophilic aromatic substitution of 4′-haloterpyridines by any primary alcohols and analogs or (b) S_N2-type nucleophilic substitution of the alcoholates of 4′-hydroxyterpyridines (the "enol" tautomer of the 4-terpyridone). An overview of the routes is presented in Scheme 2.7. A large variety of functional terpyridinoxy derivatives have been originated from these methods (Table 2.1).

Sampath et al. [40] and Schubert et al. [41, 42] reported a number of linear 4′-terpyridinyl-ethers with terminal hydroxy- (**1a–e**), carboxy- (**1f–g**) (see also [43]), *tert*-butoxy- (**1h**), thio- (**1i**) and amino-groups (**1j–k**). These ethers were prepared in high (~60–90%) yields from 4′-chloroterpyridine with an alcohol and a suspension of base (KOH or NaH) in polar non-protic solvent (DMSO or DMF). The same route was utilized to synthesize 4′-(3-phenylpropoxy)terpyridine (**1l**) [44].

Table 2.1 4′-Terpyridinoxy derivatives.



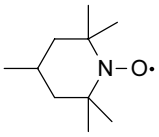
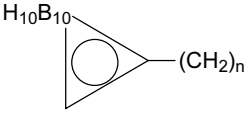
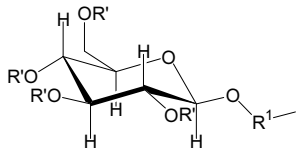
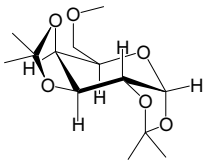
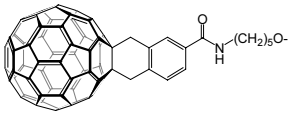
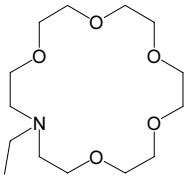
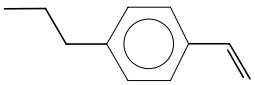
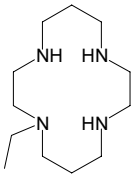
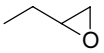
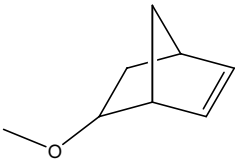
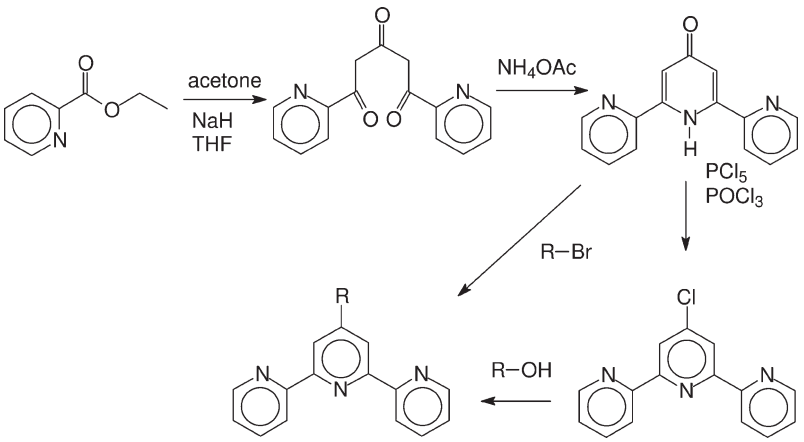
No./Lit.	*R*	*No./Lit.*	*R*
1a [40]	$(CH_2)_3OH$	**1j** [40]	$(CH_2)_3NH_2$
1b [40, 41]	$(CH_2)_4OH$	**1k** [41, 42]	$(CH_2)_5NH_2$
1c [40, 41]	$(CH_2)_6OH$	**1l** [44]	$(CH_2)_3Ph$
1d [40]	$(CH_2)_8OH$	**1m** [45]	
1e [40]	$(CH_2)_{10}OH$	**1n** [46, 47]	
1f [40, 43]	$(CH_2)_3CO_2H$	**1o** [47]	 n = 1, 3
1g [41, 42]	$(CH_2)_5CO_2H$	**1p** [14]	 R′ = H, CH_3CO; R^1 = nothing or $(CH_2)_2O$.
1h [41]	$(CH_2)_4O^tBu$	**1q** [14]	
1i [41, 42]	$(CH_2)_6SH$	**1r** [41, 49]	

Table 2.1 (continued)

No./Lit.	*R*	*No./Lit.*	*R*
1s [8]		**1w** [48]	
1t [9]		**1x** [48]	
1u [50]		**1y**	$(CH_2)_4NCO$
1v [48]			



Scheme 2.7 Synthetic approach to terpyridinoxy derivatives via the chloroterpyridine and pyridine routes.

The reaction of 4-hydroxy-2,2,6,6-tetramethylpiperidin-1-oxyl (HO-TEMPO) with 4′-chloroterpyridine afforded the 4′-O-TEMPO-derivative **1m**, which represents a convenient spin-labeled terpyridine [45].

By treatment of 4-terpyridone with K_2CO_3 in DMF, followed by the addition of functionalized bromides and tosylates, various 4′-terpyridinoxy derivatives were obtained in high yields [48]. Among the examples are 10-bromodecyloxy, allyloxy, oxiranylmethoxy, 1-cyanopropyloxy, 4-vinylbenzyloxy, 2-[1-methoxyethoxy]ethoxy, and 2,7-*bis*[2-(2-oxyethoxy)ethoxy]naphthalene [51] groups.

Constable et al. [46, 47] reported the reaction of terpyridin-4′(1′-*H*)-one with 3-bromoprop-1-yne to give (56%) the alkyne-functionalized terpyridine ligand **1n**, which was subsequently treated with $B_{10}H_{14}$ in acetonitrile; however, only poor yields of the desired carbaborane-derivative **1o** (n = 1) were reported [47]. An analogous carbaborane **1o** (n = 3) was, however, prepared by treatment of 4′-hydroxyterpyridine with 1-(3-iodopropyl)-*closo*-1,2-carbaborane in the presence of potassium carbonate. Lithiated carbaborane cages (protection of the second CH group with $SiMe_2{}^tBu$ to prevent *bis*-lithiation) could also be reacted with chloroterpyridine, resulting in a directly linked carbaborane in an improved yield (36% over 2 reaction steps). In order to probe molecular recognition events by functionalization of biomolecules with metal-binding sites, Constable and Mundwiler [14] have also presented a new class of terpyridines possessing a sugar moiety. Glucosides have been attached directly or with a spacer-linkage (ethylene glycol) to 4′-hydroxyterpyridine by the use of α-bromo- or α-bromoethyl-glucose and their tetraacetyl-protected derivatives. The sugar-functionalized terpyridines **1p** were isolated in 27% (directly linked) and 68% yield (linked via ethylene glycol spacer), respectively [14]. Furthermore, a protected galactose derivative attached to the terpyridine unit at the 6-position of the sugar afforded (52%) **1q**.

Schubert et al. [49] investigated the special electronic properties associated with the novel ether-coupled examples, such as the fullerene-functionalized 4′-terpyridine **1r**, which was prepared (47%) by the reaction of **1k** with a chlorocarbonylfullerene. Fullerenes play an important role in the development of organic photophysical devices; thus, complex ligands such as **1r** could find applications as novel donor-acceptor arrays in organic solar cells.

Attachment of aza-crown macrocycles to the 4′-position of terpyridines was postulated to have important uses as luminescent or electrochemical sensors [52] and as di- or multi-topic terpyridine ligands [8, 9]. Thus, Ward et al. [8] described the preparation of 4′-substituted and 4′-(phenyl)-substituted terpyridines (see Section 2.2) with aza-18-crown-6-groups (**1s**) that were prepared (55%) by treatment of 4′-bromoterpyridine with aza-18-crown-6. Also, Martínez-Máñez et al. [9] reported a similar system by the reaction of 4′-(bromomethyl)terpyridine (see Section 2.3.3, **3bb**) with cyclam, which generated (50%) the functionalized 1,4,8,11-tetraazacyclotetradecane derivative **1t**.

The 4′-terpyridinoxynorbornene (**1u**) was prepared (61%) from 4′-chloroterpyridine and 5-norbornene-2-methanol via the Williamson ether synthesis [50]. Utilizing the nucleophilic substitution of the alcoholate of 4′-hydroxyterpyridine and functionalized bromides/tosylates ("pyridone-route"), other polymerizable