Metal-Ion-Induced Self-Assembly of Functionalized 2,6-Oligopyridines. 1. Ligand Design, Synthesis, and Characterization[1]

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Abstract: Synthetic sequences utilizing α-oxoketene dithioacetal and enolate chemistry have been developed for the preparation of new functionalized bipyridines, terpyridines, quaterpyridines, quinquepyridines, sexipyridines, septipyridines, octipyridines, novipyridines, and decipyridines. Obtained in moderate to good yields, these oligopyridines were characterized by analytical and spectral data and, for sexipyridine, by X-ray crystallography.

Introduction

The principles of supramolecular chemistry[2] provide guidelines for the construction of quite complex molecules from relatively simple components. In this paper we report the synthesis and characterization of a designed group of oligopyridines. In later papers we will describe their metal-ion-induced self-assembly with transition metals to form polymetallic, double-stranded helical complexes of predetermined length and geometry, the spectral characterization of these polymetallic complexes, their redox properties, and their magnetic properties. These polymetallic complexes are of particular interest for the study of intramolecular electron transfer[3] and, ultimately, for the construction of molecular electronic and photonic devices.[4] The well-established coordination ability of 2,2′-bipyridine[5] (bipy) and 2,2′:6″-terpyridine[6] (terpy) suggested that ligands containing multiple pyridine rings joined through their 2,6-positions would be ideal for the self-assembly of mono-, double-, or triple-stranded helicates containing one or more transition-metal cations with a variety of coordination geometries. In such systems the metal centers will be organized in a well-defined array. The helical chirality inherent in these systems offers an opportunity for studying asymmetric electron transfer as well as for developing procedures for exploring the solution stability of these double-stranded helical complexes.

Our experience in the synthesis of several vinylterpyridines and their complexation with transition metals for chemically modified electrode studies[7] indicated that solubility in organic solvents is an important prerequisite for ligand design, enabling complexation to be carried out under mild conditions. These ligands should also contain substituents in a pyridine-ring 4-position to allow for organic functional group interconversions, as well as to have the potential of acting as ^{1}H NMR probes. The former requirement enables the incorporation of redox-active[8] (e.g., quinones, ferrocene, etc.) and photoactive[9] (e.g., metalloporphyrins, viologens, etc.) substituents in the periphery and external to the helical complex, as well as the inclusion of polymerizable groups for incorporation of the complexes into polymeric systems. Literature reports[10] indicated that, in general, terpyridine through sexipyridine along with their aryl-substituted derivatives had high melting points and were relatively insoluble in organic solvents. The unsubstituted systems have been available as mixtures obtained in poor yields from the pioneering high-temperature metal-mediated coupling procedures developed[11a] by Burstall and Morgan in 1932, whereas the 4-aryl-substituted systems were prepared in moderate to good yield by what is now known as the Kröhnke method.[11b] The limitations inherent in these syntheses emphasised the need for the development of a new, general approach that would result in good yields of 2,6-oligopyridines satisfying solubility and other requirements.

Our ligand synthesis was directed toward obtaining appropriately substituted quater-, quinque-, sexi-, septi-, octi-, novi-, and decipyridines, with 3- and 5-positions being devoid of substituents. Several factors entered into this choice: the ability of pyridine-containing ligands to accommodate bond and angle changes, as well as to be both good σ-donors and π-acceptors;[12a] the stabilizing of both high and low oxidation states of metal ions due to the pyridine's HOMO and LUMO being of suitable energy to interact with metal d-orbitals;[5a] and the stabilization due to

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(4) *Molecular Electronic Devices*; Carter, F. L., Siatkowski, R. G., Wohitjen, H., Eds.; Elsevier: Amsterdam, 1988, 303.

(5) For a review, see: Constable, E. C. *Adv. Inorg. Chem.* **1989**, *34*, 1.

(6) For a review, see: Constable, E. C. *Adv. Inorg. Electrochem.* **1986**, *30*, 69.

(7) Potts, K. T.; Usifer, D. A.; Guadalupe, A.; Abruna, H. D. *J. Am. Chem. Soc.* **1987**, *109*, 3961. Guadalupe, A. R.; Usifer, D. A.; Potts, K. T.; Hurrell, H. C.; Mogstad, A.-E.; Abruna, H. D. *J. Am. Chem. Soc.* **1988**, *110*, 3462. Hurrell, H. C.; Mogstad, A.-L.; Usifer, D. A.; Potts, K. T.; Abruna, H. D. *Inorg. Chem.* **1989**, *28*, 1080.

(8) See, e.g., Beer, P. D.; Kocian, O.; Mortiamer, R. J. *J. Chem. Soc., Dalton Trans.* **1990**, 3283.

(9) Lendzian, F.; Schlupmann, J.; von Gersdorf, J.; Mobium, K.; Kurreck, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1461. For a recent review of viologen chemistry, see: Sluva, W.; Bachowska, B.; Zelichowicz, N. *Heterocycles* **1991**, *32*, 2241.

(10) Kröhnke, F. *Synthesis* **1976**, 1.

(11) (a) Morgan, G. T.; Burstall, F. H. *J. Chem. Soc.* **1932**, 20. Burstall, F. H. *J. Chem. Soc.* **1938**, 1662. Morgan, G. T.; Burstall, F. H. *J. Chem. Soc.* **1937**, 1649. (b) The Kröhnke method has found numerous applications, e.g., Toner, J. L. *Tetrahedron Lett.* **1983**, 2707. Constable, E. C.; Lewis, J.; Schroder, M. *Polyhedron* **1982**, *1*, 311.

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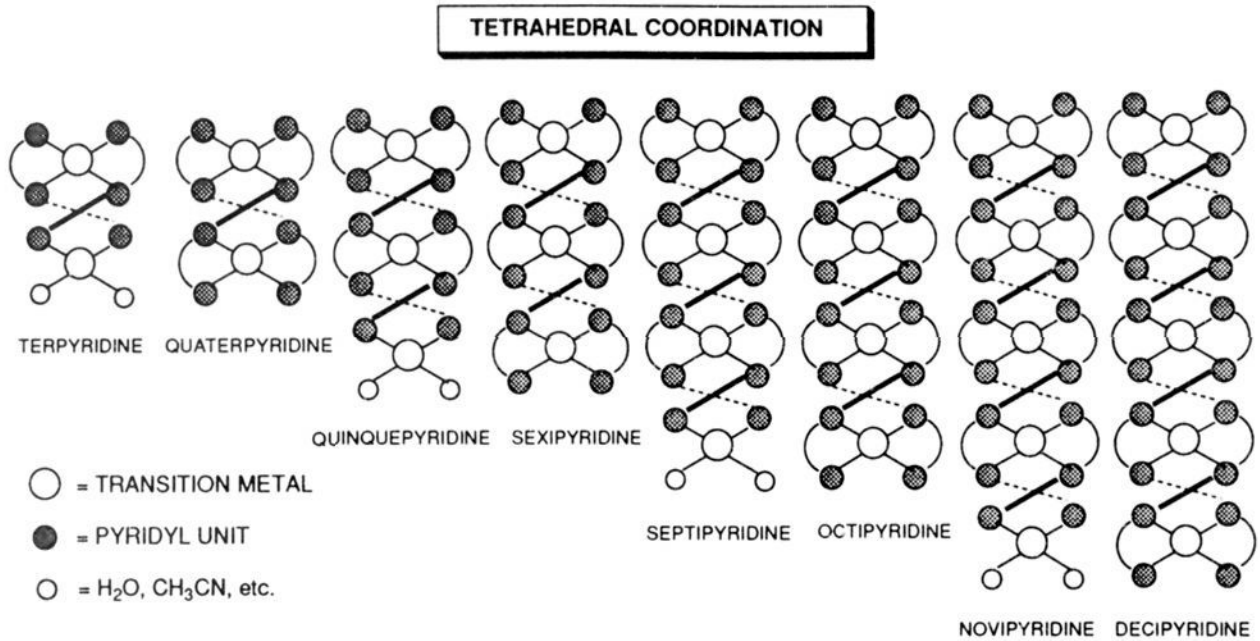
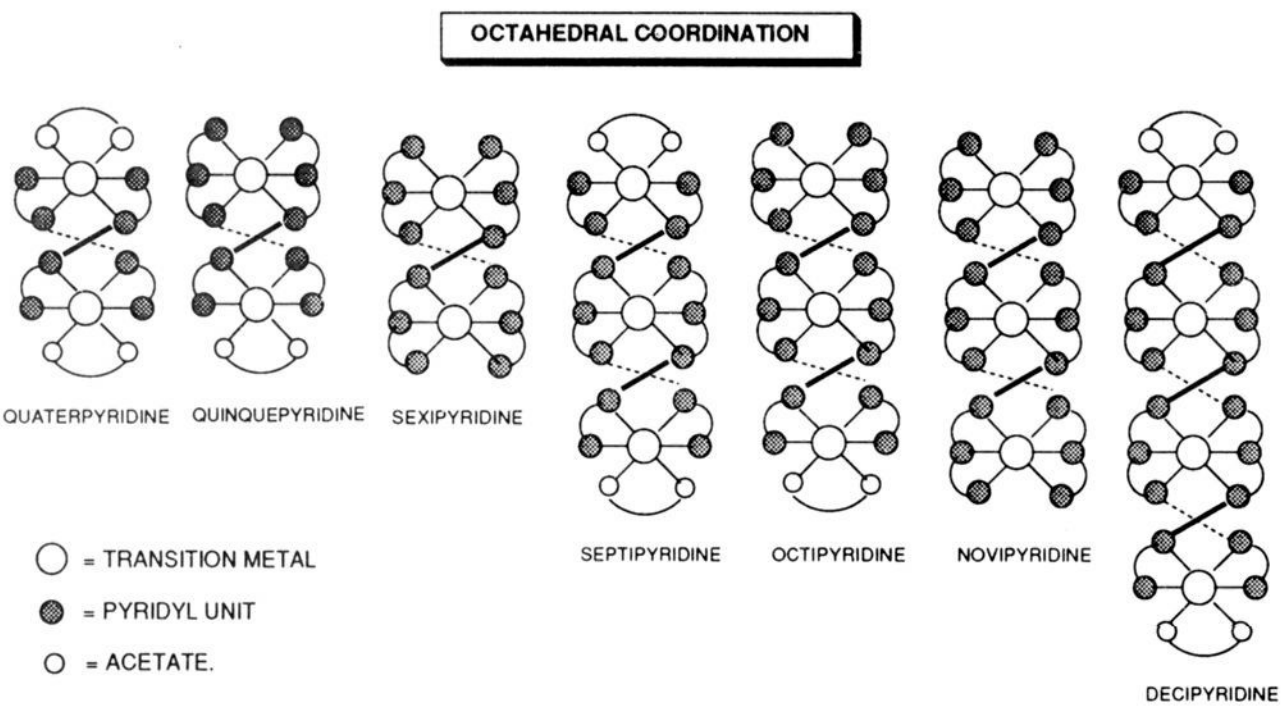
Scheme I. Possible Tetrahedral Coordination Patterns of Oligopyridines with Transition Metals



Scheme II. Possible Octahedral Coordination Patterns of Oligopyridines with Transition Metals



the chelate effect.[12b] In a double-stranded helical polymetallic complex derived from oligopyridines, the number of metal cations and their internuclear distances in a given complex can be varied depending on the oxidation state and the coordination geometry of the transition metal. Schemes I and II show a two-dimensional representation of the possible tetrahedral- and octahedral-like coordination geometries anticipated for a series of double-stranded helical structures derived from these oligopyridines. Other coordination geometries such as trigonal/linear and mixed coordination numbers are possible, and this aspect will be discussed in a later paper. Their formation depends on the number of ligating centers available in the pyridine strand (either an even or an odd number of pyridine rings) and also on the presence or absence of ligands available from external sources such as solvents, other ligands, or counterions. The well-known symmetric and asymmetric chelating ability of the carboxylate ion[13] is particularly attractive for filling two coordination sites on the metal and in certain cases allows for the use of metal carboxylates as the metal cation source.

The coordination patterns in Schemes I and II result from the oligopyridines having the potential to behave as discrete bipy or terpy subunits in a variety of combinations. In solution[14] and in

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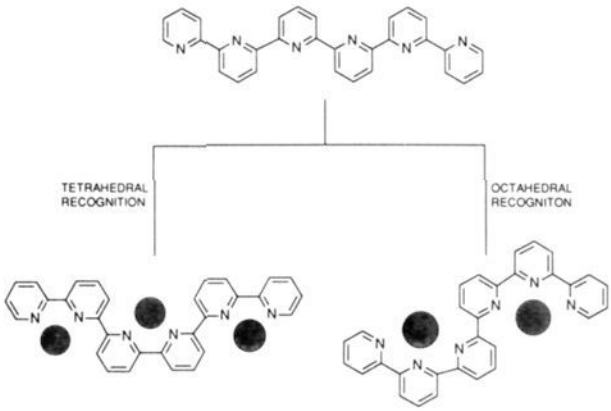
(13) Rardin, R. L.; Tolman, W. B.; Lippard, S. J. *New J. Chem.* **1991**, *15*, 417 and references listed therein.

Scheme III. Tetrahedral and Octahedral Recognition by Sexipyridine



the solid state, both bipyridine and terpyridine have conformations in which the nitrogen atom are trans to one another; in the presence of Lewis acids, particularly transition metals, recognition and a cis relationship results. This is illustrated in Scheme III for sexipyridine. In solution and in the solid state (see below), this ligand has the pyridine nitrogen atoms arranged in a transoid fashion. Sexipyridine may be considered to consist of three bipy units or two terpy units, and this stored information is recognized by the potential guest. There is no preorganization in these oligopyridines that would influence the coordination geometry. The freedom of choice in the ligand for a particular self-organization induced by the metal's tetrahedral or octahedral coordination number (or other preferred coordination number) is reflected in the assembly of a particular double-stranded helix. In highly preorganized systems, such as macrocyclic ligands, little conformational change occurs in the host on accepting the guest; in contrast, these acyclic oligopyridines belong to a class of hosts which undergo self-organization in the presence of the guest and which provide a unique opportunity for obtaining information of importance in developing a further understanding of biological order and the concepts underlying supramolecular chemistry.[2] In later papers the experimental realization of these concepts with terpyridines, quaterpyridines, quinquepyridines, sexipyridines, septipyridines, and octipyridines will be described, together with electrochemical and other data establishing that significant metal–metal interaction occurs in many of these polymetallic complexes.

Ligand Synthesis. α-Oxoketene dithioacetal chemistry, used in our earlier preparation[15] of 4′-(methylthio)-2,2′:6′-terpyridine, has, with appropriate variations revolving around the use of bifunctional pyridine derivatives, provided ready access to the desired oligopyridines. The retrosynthetic analysis of decipyridine (**1**) (Scheme IV) illustrates how the appropriate bis(α-oxoketene dithioacetal) of a 2,2′-bipyridine and 2 equiv of an appropriate ketone enolate of a terpyridine may be utilized to construct the 10 pyridine rings in a relatively few steps. Flexibility in the choice of the two reaction components exists (see below), and a considerable variety of functionalized oligoheteryl systems should be available by this general synthetic approach.

Scheme V shows these principles applied to the synthesis of septi-, octi-, novi-, and decipyridines by varying the two components of the reaction within narrow limits. These oligopyridines are now readily available. However, the practical success of these syntheses depended on the development of acceptable preparations of the appropriately functionalized bi- and terpyridine derivatives which, with the desired substitution patterns, were mostly unknown prior to our work.

Synthesis of Functionalized Bi- and Terpyridines. Homocoupling reactions, while excellent for relatively simple oligopyridines,[16] fall short of being a general procedure for more highly substituted derivatives. An added disadvantage is that the precursor bromo or iodo compounds are not readily available, often requiring their preparation from the corresponding amino compound via the diazonium reaction[17] or from the conversion of 2-pyridone carbonyl groups with phosphorus halides.[18] Although condensation procedures which lead to unsymmetrically substituted bipyridines and higher members have been developed,[10,19] these procedures restrict incorporation of substituents capable of further modification to functionally useful groups.

The introduction of an acetyl group into a pyridine ring involves the initial formation of the lithiopyridine from the corresponding bromopyridine and *n*-butyllithium,[20] followed by reaction with *N*,*N*-dimethylacetamide (DMA) and hydrolytic workup. With the oligopyridines, this reaction is often unpredictable, and we have developed alternate routes to these important precursors. Scheme VI illustrates viable syntheses of 6-acetyl-2,2′-bipyridines **4a**,**b** and 6-acetyl-2,2′:6′,2″-terpyridines **4c**,**d**. From 6-methyl-4-(methylthio)-2,2′-bipyridine (**3a**), prepared in our earlier work,[21] oxidation of the methyl group to the carboxylic acid, esterification, and Claisen condensation make a convenient route to the substituted bipyridine **4a**. Use of 6-acetyl-2-picoline in the same reaction sequence gave the acetylterpyridines **4c**,**d**. A more direct route to **4a** (Scheme VI), which avoids the methyl oxidation step, is the reaction of the potassium enolate of the protected[22] biacetyl **5** with **2a**, followed by pyridine formation and then deprotection, a "one-pot" process, to give **4a** (43%). Use of the bis(α-oxoketene dithioacetal) **9b** (see Scheme VIII) and the enolate of the biacetyl **5** gave 4,4″-bis(*n*-propylthio)-6,6″-diacetyl-2,2′:6′,2″-terpyridine (**4e**) (30%).

An alternative approach to 6-acetylterpyridine **4d** (Scheme VII) is based on the known[16d,20] monolithiation of 2,6-dibromopyridine, which provides ready access to 2-acetyl-6-bromopyridine (**6**). Condensation of its potassium enolate with the 2-pyridyl-α-oxoketene dithioacetal **2b** gave 6-bromo-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (**7**). The usual *n*-butyllithium/DMA procedure failed to convert **7** into the corresponding methyl ketone, with insoluble lithium aggregates being formed. However, an attractive alternative was found in the acid-catalyzed hydration of the acetylene **8b**, obtained by deprotection of **8a** with NaOH, this protected acetylene being prepared by a Pd^0-mediated coupling of the bromo compound with 2-methyl-3-butyn-2-ol.[23]

An additional bipyridine required for oligopyridine construction was 6,6′-diacetyl-2,2′-bipyridine. This diketone was prepared via Holm's procedure[16d] in a two-step sequence from 2,6-dibromopyridine. The monolithium derivative, generated[20] with

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(16) For example see: (a) Newkome, G. R.; Pantaleo, D. C.; Puckett, W. E.; Ziefle, P. L.; Deutsch, W. A. *J. Inorg. Nucl. Chem.* **1981**, *43*, 1529. (b) Rode, T.; Breitmaier, E. *Synthesis* **1987**, 575. (c) Tecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Montanucci, M. S. *Synthesis* **1984**, 736. (d) Parks, J. E.; Wagner, B. E.; Holm, R. H. *J. Organomet. Chem.* **1973**, *56*, 53.

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(18) Lehn, J.-M.; Sauvage, J.-P.; Simon, J.; Ziessel, R.; Piccinni-Leopardi, C.; Germain, G.; Declereq, J.-P.; VanMeerssche, M. *Nouv. J. Chem.* **1983**, *7*, 413.

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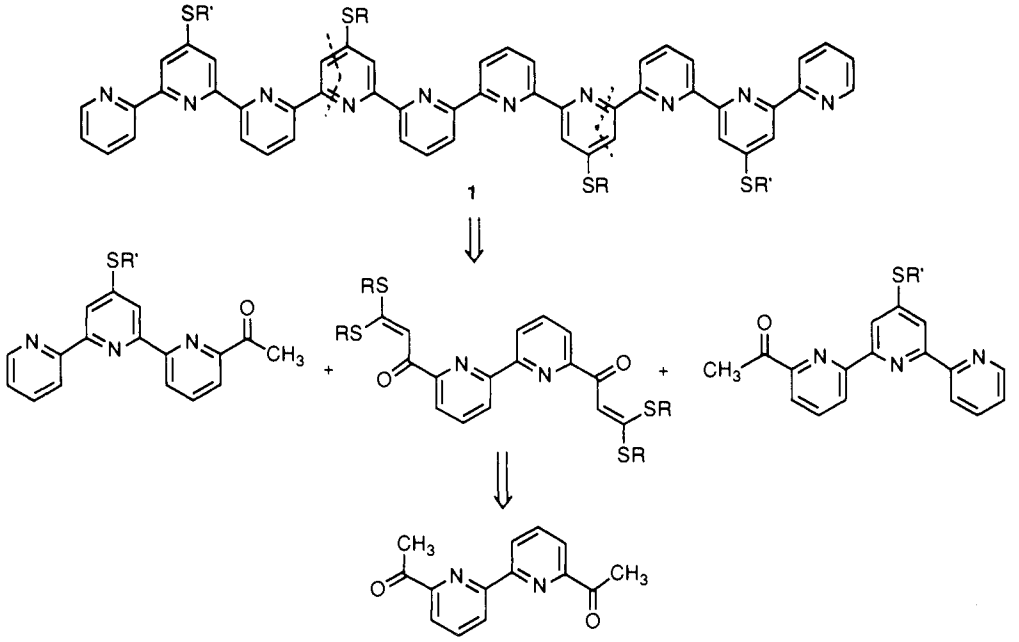
(20) Newkome, G. R.; Roper, J. M. *J. Organomet. Chem.* **1980**, *186*, 147, ref 15d.

(21) Potts, K. T.; Winslow, P. A. *J. Org. Chem.* **1985**, *50*, 5405.

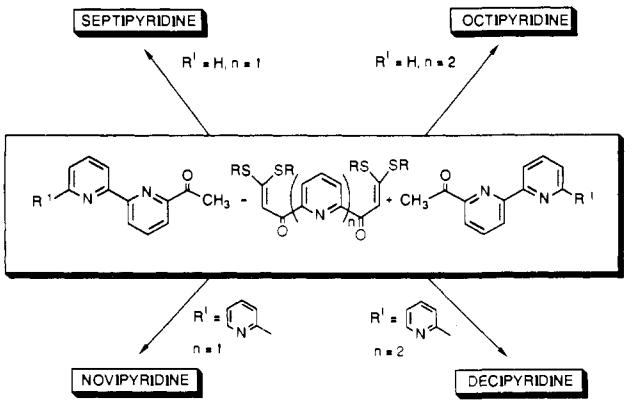
(22) Levine, S. G.; Mauney, C. U. *Synth. Commun.* **1988**, *18*, 689.

(23) Nye, S. A.; Potts, K. T. *Synthesis* **1988**, 375. See also: Sakamoto, T.; Kondo, Y.; Shiraiwa, M.; Yamanaka, H. *Synthesis* **1984**, 245; **1983**, 312.

Scheme IV. Retrosynthesis of Decipyridine **1**



Scheme V. General Synthetic Approach to the Synthesis of Oligopyridines



n-butyllithium in ether at −60 °C, underwent an oxidative coupling in the presence of copper(II) chloride or copper(I) and molecular oxygen, and the resultant dibromo compound (32%) was dilithiated with *n*-butyllithium at −80 °C (THF), followed by treatment with *N,N*-dimethylacetamide. This final conversion resulted in the diacetyl compound being obtained in 65% yield. Formation of the bis(α-oxoketene dithioacetal) **9c,d** from this diketone with both methylthio and *n*-propylthio substituents was according to the procedure developed earlier and is described in the Experimental Section. The various terpyridines prepared in the above transformations are reported in Table I.

4′,4″-Bis(methylthio)-2,2′:6′,2″:6″,2‴-quaterpyridine (10). Prior to the present work, only diaryl-substituted quaterpyridines were known. 6,6‴-Diaryl substituents (i.e., on the two terminal pyridine rings) have been synthesized[24] by α-oxoketene dithioacetal chemistry, and 4′,4″-diphenyl substituents have been introduced into quaterpyridine via the Kröhnke method.[10] Apart from quaterpyridine itself, prepared by a metal-mediated coupling,[11a,25] the only other quaterpyridine of note is the 5,5′,3″,5‴-tetramethyl-2,2′:6′,2″:6″,2‴-quaterpyridine prepared[17] by a more involved reaction sequence. The readily available 6-acetyl-4-(methylthio)-2,2′-bipyridine (**4a**) now provides a straightforward route to quaterpyridines by condensation of **4a** and the α-oxoketene dithioacetal **2a**, which resulted (71%) in 4′,4″-bis(methylthio)-2,2′:6′,2″:6″,2‴-quaterpyridine (**10**).

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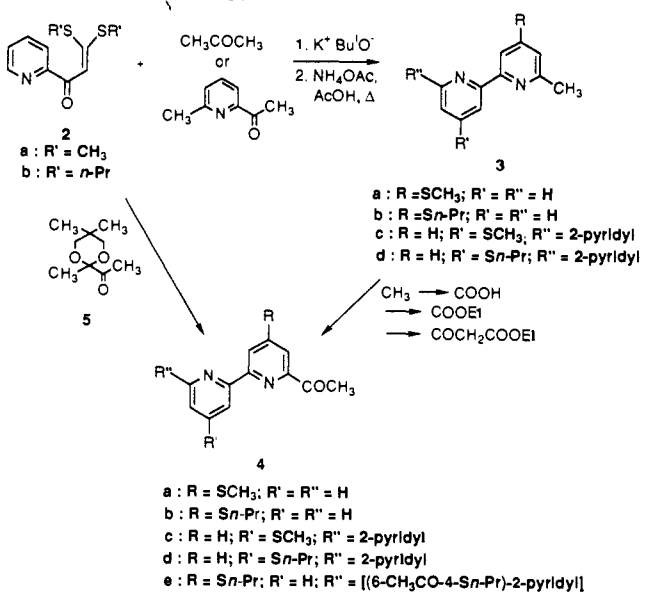
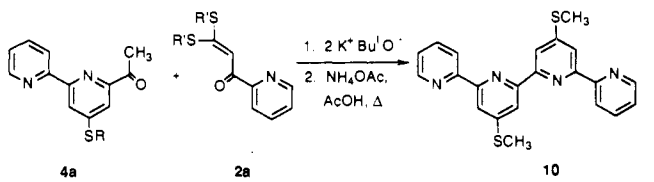
(25) Haginiwa, J.; Higuchi, Y. *Yakugaku Zasshi* **1973**, *93*, 144; *Chem. Abstr.* **1973**, *78*, 147751.

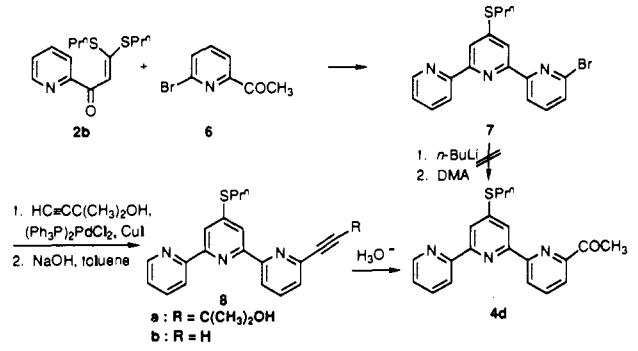
Scheme VI. Synthesis of 6-Acetyl-2,2′-bipyridines and 6-Acetyl-2,2′:6′,2″-terpyridines



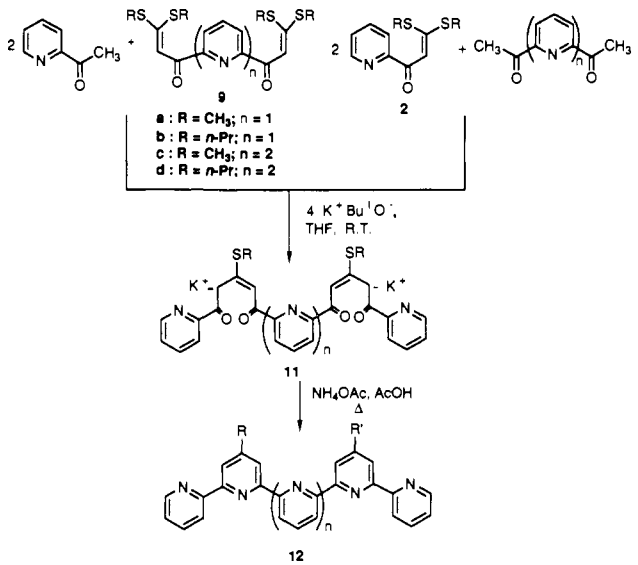


4′,4″-Bis(alkylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridines 12. Condensation of 2 equiv of 3,3-bis(methylthio)-1-(2-pyridinyl)propen-1-one (**2a**) and the bis(enolate) of 2,6-diacetylpyridine in THF together with an additional 2 equiv of potassium *tert*-butoxide needed to stabilize the dipotassium salt of the resultant bis(1,5-enedione) **11** (R = CH_3), followed by the addition of ammonium acetate in hot acetic acid, resulted in pure

Scheme VII. Synthesis of 6-Acetyl-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine from Acetylenes



Scheme VIII. Synthesis of Quinque- and Sexipyridines



crystalline 4′,4‴-bis(methylthio)quinquepyridine (**12a**) (55% yield) (Scheme VIII). The melting point (265–266 °C) and solubility of this bis(methylthio)quinquepyridine were only slightly different from those of the parent quinquepyridine (267–268 °C), the methylthio substituents being of insufficient length to affect these physical properties in a favorable manner. This problem was addressed by replacing the methylthio substituents with *n*-propylthio substituents. Using the same procedure, 4,4′-bis-(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (**12b**) (mp 158–159 °C) was isolated in low yield after Soxhlet extraction of the crude reaction product with *n*-hexane and final recrystallization from *n*-hexane and ethyl acetate. However, when the alternative approach to constructing the quinquepyridine nucleus from the 1,5-enedione involving the reaction of 2 equiv of the potassium enolate of 2-acetylpyridine with the bis(α-oxoketene dithioacetal) **9b** derived from 2,6-diacetylpyridine, followed by ammonium acetate ring closure, was used, a 69% yield of pure 4,4′-bis(*n*-propylthio)quinquepyridine (**12b**) resulted. This difference in yields of the final products, prepared by these two procedures, may be attributed in the former either to difficulty in generating sufficient amount of the bis anion of 2,6-diacetylpyridine or to its solubility in THF, an effect which we have also observed with other heteryl diketones. The physical constants of a variety of quinquepyridines obtained in this manner and also by 4′- and 4‴-alkylthio substituent conversions are listed in Table II.

These quinquepyridines were related to the known parent quinquepyridine by desulfurization with nickel boride. The 4′,4‴-bis(methylthio) compound **12a**, being only partly soluble in hot ethanol, underwent desulfurization poorly; in contrast, the 4,4′-bis(*n*-propylthio) compound **12b** was converted into the quinquepyridine in 40% yield.

4′,4‴-Dimethyl-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (12c). Part of our synthetic plan called for the replacement of the alkylthio groups with methyl and vinyl groups. A nickel-catalyzed cross-coupling reaction with Grignard reagents had been found successful earlier in the terpyridine series,[7] and application of these conditions to the quinquepyridines finally resulted in up to 65% yield of the dimethyl compound after considerable reaction development. Reaction of 4′,4‴-bis(methylthio)quinquepyridine (**12a**) in warm, anhydrous thiophene-free benzene with a mixture of bis(triphenylphosphine)nickel(II) dichloride and methylmagnesium bromide in benzene at 60 °C over 4 days gave **12c** without any formation of the monomethyl product. Traces of unreacted starting material were readily evident from the chemical shift of the SCH_3 protons (δ 2.71, s) in contrast to those of the CH_3 protons (δ 2.62 s). Adherence to the reaction conditions described in the Experimental Section results in reproducible yields of the dimethyl product. Although the corresponding 4′,4‴-bis(*n*-propylthio)quinquepyridine (**12b**) was more soluble in nonpolar solvents than **12a**, low yields of **12c** were obtained unless long reaction times and excess amounts of the catalyst and the Grignard reagent were used. Recent work in the terpyridine series in which a long-chain substituent was introduced[26] into the 4′-position found [1,3-bis(diphenylphosphine)propyl]nickel dichloride to be a more effective catalyst.

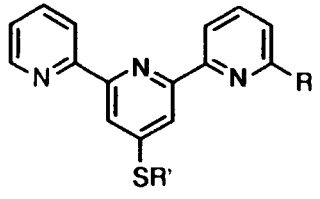
4′,4‴-Divinyl-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (12d). The procedure developed in the terpyridine series was applied successfully to this synthesis and also to that of the monovinylquinquepyridine **12e**. In initial efforts at carbanion generation from **12c** using lithium tetramethylpiperidide, followed by alkylation with chloromethyl methyl ether, despite visual indications of a successful reaction the isolated product was a mixture of starting material and mono- (**12g**) and bis(2-methoxyethyl) (**12f**) quinquepyridines. This mixture was separated into its components by alumina chromatography. The reaction conditions described in the Experimental Section reflect considerable reaction development, and when bromomethyl methyl ether was used as the alkylating agent greater yields of product resulted, up to 48% of analytically pure 4′,4‴-bis(methoxyethyl)quinquepyridine (**12f**). It should be emphasized that reaction times of up to 1 h were adequate for dianion generation; prolonged reaction times (2–3 h) often resulted in formation of a highly insoluble lithium-quinquepyridine aggregate.

These methoxyethyl ethers **12f,g** were readily converted into the corresponding mono- (**11e**) and divinylquinquepyridines (**11d**) by reaction with potassium *tert*-butoxide in anhydrous THF at room temperature. Yields of 72% and 68% of analytically pure mono- and divinylquinquepyridines, respectively, were obtained.

The variety of substituted quinquepyridines described in Table II enabled a complete ^1H NMR characterization to be made. Table III lists the chemical shifts and coupling constants for the pyridine ring protons and the 4′- and 4‴-substituents. Determined at 200 MHz in $CDCl_3$, extensive decoupling experiments were aided by the pyridine protons being in similar environments in these derivatives as well as by the effects exerted by the pyridine nitrogen atoms on protons in the 3- and 5-positions in adjacent rings. These data were extremely helpful in chemical shift assignments for the higher oligopyridines (Table IV) and for the oligopyridine-metal complexes which will be described in later

(26) Cuenoud, B.; Schepartz, A. *Tetrahedron Lett.* **1991**, *32*, 3325.

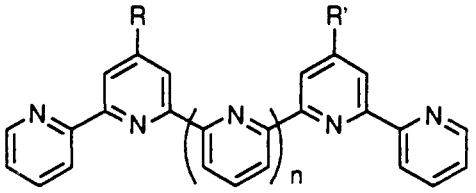
Table I. 6-Substituted 4′-(Alkylthio)-2,2′:6′,2″-terpyridines[a]



R	R′	yield, %	mp, °C	crystal form/solvent[b]	molecular formula	analytical data calcd/found C	H	N	$M^{\bullet+}$ (relative intensity) [fragment ion]	IR (KBr)[c]
COOH	CH_3	40	230–231 (CO_2)	prisms/A–B	$C_{12}H_{10}N_2O_2S \cdot {}^1/_4H_2O$	62.27	4.15	12.82	324 (100)	ν_{OH} 3580–3300
						62.44	4.16	12.84		ν_{CO} 1715
$CON(CH_3)_2$	CH_3	9	170–172	prisms/B	$C_{19}H_{18}N_4OS$	65.12	5.18	15.99	350 (30)[f]	ν_{CO} 1625
						64.95	5.25	15.92	279 (100)	$\nu_{C=N}$ 1500
									{[M + 1] − $CON(CH_3)_2$}	
CO_2Et	CH_3	62	135.5–136.5	needles/A	$C_{19}H_{17}N_3O_2S$	64.93	4.88	11.96	351 (100)	$\nu_{C=O}$ 1705
						64.99	4.92	11.94		
$COCH_2COOEt$	CH_3	79	134–136	prisms[d]/A	$C_{21}H_{19}N_3O_3S$	64.10	4.87	10.68	393 (100)	$\nu_{C=O}$ 1733, 1690
						64.16	4.90	10.67		
$COCH_3$	CH_3	68	128–130	needles/A	$C_{18}H_{15}N_3OS$	67.26	4.71	13.07	321 (100)	$\nu_{C=O}$ 1693
						67.18	4.73	13.04		
Br	*n*-Pr	54	81–83	prisms[e]/C	$C_{18}H_{16}N_3SBr$[g]	55.96	4.18	10.88	386 (39)[f]	ν_{CH} 2960–2865
						56.82[g]	4.38	11.10	344 (100)	
									{M − [CH_2=$CHCH_3$]}	
$C{\equiv}CC(CH_3)_2OH$	*n*-Pr	54	134–135.5	microprisms[d]/B–C	$C_{23}H_{23}N_3OS$	70.92	5.95	10.79	389 (66)[f]	ν_{OH} 3230 (b)
						70.83	5.99	10.76	347 (100)	
									{M − [CH_2=$CHCH_3$]}	
$C{\equiv}CH$	*n*-Pr	89	97–98	prisms[d]/B–C	$C_{20}H_{17}N_3S$	72.47	5.17	12.68	331 (41)[f]	$\nu_{\equiv CH}$ 3245
						72.39	5.21	12.65	289 (100)	$\nu_{C\equiv C}$ 2100
									{M − [CH_2=$CHCH_3$]}	
$COCH_3$	*n*-Pr	71	109–111	microprisms/C	$C_{20}H_{19}N_3OS \cdot {}^1/_4H_2O$	67.87	5.55	11.87	349 (42)[f]	$\nu_{C=O}$ 1692
						67.84	5.45	11.93	307 (100)	
									{M − [CH_2=$CHCH_3$]}	

[a] All colorless unless noted otherwise. [b] Crystallization solvents: A = EtOH; B = EtOAc; C = *n*-hexane. [c] All showed $\nu_{C=N,C=C}$ in the 1570–1450 region. [d] Yellow. [e] Tan. [f] CI, [M + 1]. [g] Compound tenaciously held traces of hydrocarbon solvent.

Table II. Substituted Quinquepyridines and Sexipyridines



compd no.	*n*	R/R′	yield, %	mp, °C	crystal form[a]/ solvent[b]	molecular formula[c]	analytical data calcd/found C	H	N	$M^{+\cdot}$ (El) (relative intensity) [fragment ion]
12a	1	SCH_3	55	271–272[d]	needles/B	$C_{27}H_{21}N_5S_2$	67.63 67.62	4.41 4.48	14.61 14.40	239 (34) [$C_{14}H_{11}N_2S$], 128 (25) [C_9H_6N], 77 (64) [$C_6H_5N^+$]
12b	1	S-*n*-Pr	64 (11)[f]	158–159	needles/B[e]	$C_{31}H_{29}N_5S_2$	69.50 69.54	5.46 5.50	13.07 13.07	535 (88), 451 (78) [$M^+ - 2C_3H_6$], 225 (68) [$C_{13}H_9N_2S^+$], 78 (58) [$C_5H_4N^+$]
12h	2	SCH_3	50	291–292	needles[g]/B	$C_{32}H_{24}N_6S_2$	69.04 65.80	4.35 4.69	15.10 15.10	556 (100) [M^+]
12i	2	S-*n*-Pr	38 (52)[f]	228–229	needles[g]/B	$C_{36}H_{32}N_6S_2$[h]	70.56 70.37	5.26 5.28	13.72 13.66	621 (31), 264 (100) [$C_{14}H_{10}N_3S$] 78 (51) [$C_5H_4N^+$]
12j	1	H	40	273–276[i]	prisms/A	$C_{25}H_{17}N_5$				387 (83) [M^+], 386 (100) [$M^+ - 1$], 78 (16) [$C_5H_4N^+$]
12c	1	CH_3	50	230–232	microneedles/E	$C_{27}H_{21}N_5$	78.05 77.89	5.09 5.16	16.86 16.79	416 (27) [$M^+ + 1$], 415 (100) [M^+]
12g	1	$CH_3/CH_2CH_2OCH_3$	48	141–144	microneedles/D	$C_{29}H_{25}N_5O$				
12f	1	$CH_2CH_2OCH_3$	17	177–179	microneedles/D	$C_{31}H_{29}N_5O_2$	73.93 73.93	5.80 5.95	13.91 13.68	503 (100) [M^+]
12e	1	$CH_3/CH{=}CH_2$	72	214–216	microprisms/D	$C_{28}H_{21}N_5$	78.66 78.51	4.95 5.13	16.39 16.11	427 (41), 78 (100) [$C_5H_4N^+$]
12d	1	$CH{=}CH_2$	68	237–239	microprisms/D	$C_{29}H_{21}N_5$	79.25 79.02	4.82 4.87	15.93 15.99	439 (19), 78 (100) [$C_5H_4N^+$]

[a] All colorless unless noted otherwise. [b] Solvents: A = hexane–$CHCl_3$; B = DMF; C = benzene; D = cyclohexane; E = EtOAc. [c] All showed $\nu_{C=N,C=C}$ in 1300–1605 region. [d] Lit.[15] mp 265–266 °C. [e] Pale green. [f] Refers to method of synthesis (see text, Experimental Section). [g] Beige. [h] Also crystallizes with benzene of crystallization. Anal Calcd: C, 73.01; H, 5.54; N, 12.17. Found: C, 72.74; H, 5.48; N, 12.30. [i] Lit.[11a] mp 267–268 °C.

papers. The preferred conformation in solution of these oligopyridines with the nitrogen atoms all trans to one another is consistent with that reported earlier for bipyridine and terpyridine,[14] and minimized energy calculations[27a] are also in agreement with this conformation. In the solid state the single crystal X-ray structure of the 4,4′′′′-bis(*n*-propylthio)sexipyridine (Figure 1) also shows[27b] this conformation, and it is anticipated that the higher oligopyridines exist in similar conformations in the solid state. Bipyridine[27c] and quaterpyridine[27d] have also been shown to have this solid-state conformation.

4′,4′′′′-Bis(alkylthio)-2,2′:6′,2′′:6′′,2′′′:6′′′,2′′′′:6′′′′,2′′′′′-sexipyridines 12h,i. As in the quinquepyridine case, two ways of assembling six pyridine rings are available (Scheme VIII). Using the bis(potassium enolate) of 6,6′-diacetyl-2,2′-bipyridine and **2a** resulted in a 38% yield of the sexipyridine **12h** which proved to be relatively insoluble in organic solvents. Via the alternative approach using the bis(α-oxoketene dithioacetal) **9d** and the enolate of 2-acetylpyridine, the yield of the sexipyridine **12i** was 52%. As the α-oxoketene dithioacetal **9d** was also prepared from the diketone in 52% yield, the sexipyridine **12i** with its favorable solubility characteristics is the one of choice.

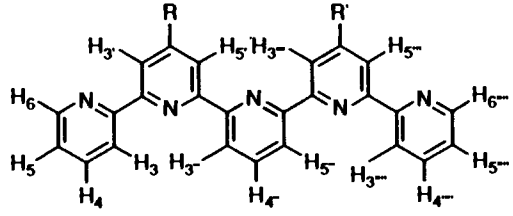
4′,4′′,4′′′′,4′′′′′-Tetrakis(alkylthio)-2,2′:6′,2′′:6′′,2′′′:6′′′,2′′′′:6′′′′,2′′′′′:6′′′′,2′′′′′:6′′′′′,2′′′′′′-septipyridines 13. The availability of the bipyridyl methyl ketone **4a** described above and the appropriate bis(α-oxoketene dithioacetal) allows us to construct alkylthio-substituted septipyridines (Table V). The tetrakis(methylthio) product **13a** was prepared from 2 equiv of the enolate of 6-acetyl-4-methyl-2,2′-bipyridine (**4a**) and 1 equiv of the α-oxoketene dithioacetal **9a** derived from 2,6-diacetylpyridine (Scheme V). The resultant bright red, heterogeneous mixture containing the bis(potassium salt) of the bis(1,5-enedione) was formed at room temperature over 26 h. Heating this mixture for 2 h with ammonium acetate and acetic acid completed the reaction. During the distillation of the THF from the reaction mixture, septipyridine began to precipitate from the hot acetic acid solution, and a 68% yield of crude product was obtained. Purification was effected by recrystallization from hot DMF, and **13a**, melting at 352–354 °C, had poor solubility in most common organic solvents.

This solubility problem in the septipyridine series was overcome by replacement of two methylthio groups with two *n*-propylthio groups. Thus, in the manner described above, 2 equiv of 6-acetyl-4-(methylthio)-2,2′-bipyridine (**4a**) and 1 equiv of 2,6-bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]pyridine (**9b**) resulted finally in 4′,4′′′′-bis(methylthio)-4′′,4′′′′-bis(*n*-propylthio)-2,2′:6′,2′′:6′′,2′′′:6′′′,2′′′′:6′′′′,5′′′′′:6′′′′′,2′′′′′′-septipyridine (**13b**) in 50% yield after recrystallization from $CHCl_3$. The melting point of this septipyridine derivative, 259–260 °C, was significantly lower, and the compound was appreciably soluble in organic solvents, e.g., $CHCl_3$, sufficiently so that a well-resolved ^1H NMR spectrum was obtained in $CDCl_3$ (Table IV).

4′,4′′′′′-Bis(methylthio)-4′′,4′′′′-bis(*n*-propylthio)-2,2′:6′,2′′:6′′,2′′′:6′′′,2′′′′:6′′′′,2′′′′′:6′′′′′,2′′′′′′:6′′′′′,2′′′′′′-octipyridine (14). This octipyridine derivative (Table V) was prepared via a similar double ring closure reaction (Scheme V) using 2 equiv of the above bipyridyl methyl ketone **4a** with the bis(α-oxoketene dithioacetal) of 6,6′-diacetyl-2,2′-bipyridine **9d** and potassium *tert*-butoxide in anhydrous THF. The immediate formation of the deep red dipotassium salt of the intermediate bis(1,5-enedione) was observed, followed by the precipitation of the salt over 24 h. In this instance, the ammonium acetate and hot glacial acetic acid reaction was quenched on ice, the crude product being

(27) (a) *PC Model*, Serena Software, Bloomington, IN, 1987. (b) The single crystal of **12i** was obtained from benzene solution. The molecule is planar with its six pyridine rings oriented in a transoid conformation. The sulfur and carbon atoms of the propylthio side chains lie in the plane of the pyridine rings, and pyridine C–N and C–C bond lengths were in the range of 1.327–1.352 and 1.356–1.394 Å, respectively. Typical C–N–C bond angles of the pyridine rings were in the range of 116.6–118.4°, and there is no detectable difference in the bond angles and bond lengths of the propylthio-substituted and the unsubstituted pyridine rings. The benzene solvent molecule that was found in both the ^1H NMR spectrum and analytical data was also present in the unit cell. (c) Chisholm, M. H.; Huffman, J. C.; Rothwell, I. P.; Bradley, P. G.; Kress, N.; Woodruff, W. H. *J. Am. Chem. Soc.* **1981**, *103*, 4945. (d) Constable, E. C.; Elder, S. M.; Healy, J.; Tocher, D. A. *J. Chem. Soc., Dalton Trans* **1990**, 1669.

Table III. Chemical Shifts and Coupling Constants for Quinquepyridine Derivatives at 200 MHz in $CDCl_3$



substituents, compd no.	chemical shifts (δ) and coupling constants (J, Hz)							
	$H_6, H_{6''}$	$H_5, H_{5''}$	$H_4, H_{4''}$	$H_3, H_{3''}$	$H_{5'}, H_{3''}$	$H_{3'}, H_{5''}$	$H_{3''}, H_{5''}$	$H_{4''}$
R = R′ = H,[a] **12j**	8.73 (m, 2 H)	7.36 (m, 2 H) $J_{4,5}$ = 7.3 $J_{5,6}$ = 4.8 $J_{3,5}$ = 1.0	7.90 (td, 2 H) $J_{3,4} = J_{4,5}$ = 7.7 $J_{4,6}$ = 1.7	8.68 (bd, 2 H)	8.72 (bd, 2 H) $J_{4',5'}$ = 7.6	8.71 (bd, 2 H) $J_{3',4'}$ = 7.8	8.50 (dd, 2 H) $J_{3'',4''} = J_{4'',5''}$ = 7.8 $J_{3'',5''}$ = 0.8	8.05 (t, 1 H) $J_{3'',4''} = J_{4'',5''}$ = 7.7
R = R′ = SCH_3,[b] **12a**	8.72 (dt, 2 H) $J_{5,6}$ = 4.8 $J_{4,6}$ = 1.8	7.36 (m, 2 H) $J_{4,5}$ = 7.4 $J_{5,6}$ = 4.8 $J_{3,5}$ = 1.2	7.88 (td, 2 H) $J_{3,4} = J_{4,5}$ = 7.7 $J_{4,6}$ = 1.8	8.68 (bd, 2 H) $J_{3,4}$ = 8.0	8.53 (d, 2 H) $J_{3',5'}$ = 1.8	8.36 (d, 2 H) $J_{3',5'}$ = 1.8	8.65 (bd, 2 H) $J_{3'',4''} = J_{4'',5''}$ = 8.0	8.02 (t, 1 H) $J_{3'',4''} = J_{4'',5''}$ = 7.8
R = R′ = S-*n*-Pr,[c] **12b**	8.71 (dt, 2 H) $J_{5,6}$ = 4.7 $J_{4,6}$ = 1.7	7.35 (m, 2 H) $J_{4,5}$ = 7.4 $J_{5,6}$ = 4.7 $J_{3,5}$ = 1.2	7.87 (td, 2 H) $J_{3,4} = J_{4,5}$ = 7.8 $J_{4,6}$ = 1.9	8.64 (bd, 2 H) $J_{3,4}$ = 8.0	8.53 (d, 2 H) $J_{3',5'}$ = 1.8	8.36 (d, 2 H) $J_{3',5'}$ = 1.8	8.66 (bd, 2 H) $J_{3'',4''} = J_{4'',5''}$ = 7.8	8.01 (t, 1 H) $J_{3'',4''} = J_{4'',5''}$ = 7.8
R = R′ = CH_3,[d] **12c**	8.73 (m, 2 H)	7.35 (m, 2 H) $J_{4,5}$ = 7.5 $J_{5,6}$ = 4.8 $J_{3,5}$ = 1.2	7.89 (td, 2 H) $J_{3,4} = J_{4,5}$ = 7.7 $J_{4,6}$ = 1.7	8.69 (dd, 2 H) $J_{3,4}$ = 8.0 $J_{3,5}$ = 1.0	8.53 (s, 2 H)	8.34 (s, 2 H)	8.69 (bd, 2 H) $J_{3'',4''} = J_{4'',5''}$ = 8.0	8.03 (t, 1 H) $J_{3'',4''} = J_{4'',5''}$ = 7.9
R = CH_3, R′ = -$CH_2CH_2OCH_3$,[e] **12g**	8.73 (m, 2 H)	7.34 (m, 2 H)	7.88 (td, 2 H) $J_{3,4} = J_{4,5}$ = 7.8 $J_{4,6}$ = 1.6	8.66 (bd, 2 H) $J_{3,4}$ = 8.0	8.52 (s, 1 H, $H_{5'}$) 8.38 (d, 1 H) $J_{3'',5''}$ = 0.8 H, ($H_{3''}$)	8.34 (s, 1 H, $H_{3'}$) 8.58 (d, 1 H) $J_{3'',5''}$ = 1.2 H, ($H_{5''}$)	8.68 (bd, 2 H) $J_{3'',4''} = J_{4'',5''}$ = 8.0	8.02 (t, 1 H) $J_{3'',4''} = J_{4'',5''}$ = 7.8
R = R′ = -$CH_2CH_2OCH_3$,[f] **12f**	8.73 (m, 2 H)	7.35 (m, 2 H)	7.89 (td, 2 H) $J_{3,4} = J_{4,5}$ = 7.8 $J_{4,6}$ = 1.7	8.67 (bd, 2 H) $J_{3,4}$ = 8.0	8.38 (s, 2 H)	8.58 (s, 2 H)	8.69 (bd, 2 H) $J_{3'',4''} = J_{4'',5''}$ = 8.0	8.02 (t, 1 H) $J_{3'',4''} = J_{4'',5''}$ = 7.8

[a] 8.03 (t, 2 H, $J_{3',4'} = J_{4',5'}$ = 7.7 Hz, $H_{4'}$). [b] 2.71 (s, 6 H, SCH_3). [c] 3.21 (t, 4 H, $SCH_2CH_2CH_3$), 1.89 (sextet, 4 H, $SCH_2CH_2CH_3$), 1.17 (t, 6 H, $SCH_2CH_2CH_3$). [d] 2.62 (s, 6 H, CH_3). [e] 3.83 (t, 2 H, $CH_2CH_2OCH_3$), 3.44 (s, 3 H, OCH_3), 3.16 (t, 2 H, $CH_2CH_2OCH_3$), 2.61 (s, 3 H, py-CH_3). [f] 3.83 (t, 4 H, $CH_2CH_2OCH_3$), 3.44 (s, 6 H, $CH_2CH_2OCH_3$), 3.16 (t, 4 H, $CH_2CH_2OCH_3$).

Table IV. Chemical Shifts (δ) and Coupling Constants (J, Hz) (200 MHz, $CDCl_3$) for (Alkylthio)-Substituted Sexipyridine, Septipyridine, Octipyridine, Novipyridine, and Decipyridine

sexipyridine **12i**	septipyridine **13b**	octipyridine **14**
8.69 (dd, 2 H, $J_{6,5}$ = 4.9 $J_{4,6}$ = 1.2, H_6)	8.72 (m, 2 H, H_6)	8.73 (d, 2 H, H_6)
8.65 (bd, 2 H, $J_{4,3}$ = 8.0, H_3)	8.67 (d, 2 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 8.0, $H_{3''}$)	8.72, 8.70 (2d, 4 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8, $H_{3''}$, $H_{4''}$)
8.63 (bd, 2 H, $J_{4',3'}$ = 7.4, $H_{3'}$)	8.62 (d, 2 H, $J_{3,4}$ = 8.0 H_3)	8.64 (d, 2 H, $J_{3,4}$ = 8.0, H_3)
8.62 (bd, 2 H, $J_{4'',3''}$ = 7.4, $H_{3''}$)	8.53 (d, 4 H, $J_{3',4'}$ = 2.2, $H_{3'}$ & $H_{4'}$)	8.60 (d, 2 H, $J_{3',4'}$ = 1.8, $H_{3'}$)
8.53 (d, 2 H, $J_{3',4'}$ = 1.9, $H_{4'}$)	8.52 (d, 2 H, $J_{3',4'}$ = 1.8, $H_{3'}$)	8.55 (d, 2 H, $J_{3'',4''}$ = 1.6, $H_{4''}$)
8.34 (d, 2 H, $J_{3'',4''}$ = 1.9, $H_{3''}$)	8.34 (d, 2 H, $J_{3'',4''}$ = 1.6, $H_{3''}$)	8.54 (d, 2 H, $J_{3'',4''}$ = 1.4, $H_{3''}$)
8.00 (t, 2 H, $J_{4'',4'''}$ = $J_{3'',4'''}$ = 7.6, $H_{4''}$)	8.07 (t, 1 H, $J_{3'',4''}$ = $J_{4'',4'''}$ = 7.8, $H_{4''}$)	8.35 (d, 2 H, $J_{3,4}$ = 1.8, H_3)
7.85 (td, 2 H, $J_{4,3}$ = $J_{3,4}$ = 8.0, $J_{4,6}$ = 1.2, H_4)	7.88 (dt, 2 H, $J_{3,4}$ = $J_{4,5}$ = 7.7, $J_{4,6}$ = 1.7, H_4)	8.09 (t, 2 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8, $H_{4''}$)
7.32 (m, 2 H, $J_{4,5}$ = 7.1, $J_{6,5}$ = 4.9, H_5)	7.35 (m, 2 H, H_5)	7.90 (td, 2 H, $J_{3,4}$ = $J_{4,5}$ = 7.8, $J_{4,6}$ = 1.7, H_4)
3.20 (t, 4 H, $SCH_2CH_2CH_3$)	3.24 (t, 4 H, $SCH_2CH_2CH_3$)	7.37 (m, 2 H, $J_{4,5}$ = 7.6, $J_{5,6}$ = 4.9, $J_{3,4}$ = 1.2, H_5)
1.19 (sextet, 4 H, $SCH_2CH_2CH_3$)	2.72 (s, 6 H, SCH_3)	3.25 (t, 4 H, $SCH_2CH_2CH_3$)
1.16 (t, 6 H, $SCH_2CH_2CH_3$)	1.95 (sextet, 4 H, $SCH_2CH_2CH_3$)	2.73 (s, 6 H, SCH_3)
	1.21 (t, 6 H, $SCH_2CH_2CH_3$)	1.97 (sextet, 4 H, $SCH_2CH_2CH_3$)
		1.22 (t, 6 H, $SCH_2CH_2CH_3$)

novipyridine **15b**	decipyridine **16b**
8.76–8.55 (m, 16 H, 2 × H_3, H_6, $H_{5'}$, $H_{3''}$, $H_{5''}$, $H_{3'''}$, $H_{5'''}$, $H_{3''''}$)	8.76–8.58 (m, 18 H, 2 × H_3, H_6, $H_{5'}$, $H_{3''}$, $H_{5''}$, $H_{3'''}$, $H_{5'''}$, $H_{3''''}$, $H_{5''''}$)
8.37 (d, 2 H, $J_{3',5'}$ = 1.8, $H_{3'}$)	8.37 (d, 2 H, $J_{3',5'}$ = 2.0, $H_{3'}$)
8.07 (m, 3 H, $H_{4''''}$, 2 × $H_{4''}$)	8.05 (t, 2 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.6, $H_{4''}$)
7.88 (td, 2 H, $J_{3,4}$ = $J_{4,5}$ = 7.6, $J_{4,6}$ = 1.6, H_4)	7.89 (td, 2 H, $J_{3,4}$ = $J_{4,5}$ = 7.8, $J_{4,6}$ = 1.8, H_4)
7.37 (m, 2 H, H_5)	7.35 (m, 2 H, H_5)
3.22 (m, 8 H, $SCH_2CH_2CH_3$)	3.28 (t, 4 H, $SCH_2CH_2CH_3$)
1.94 (m, 8 H, $SCH_2CH_2CH_3$)	3.23 (t, 4 H, $SCH_2CH_2CH_3$)
1.24 (t, 6 H, $SCH_2CH_2CH_3$)	1.95 (sextet, 8 H, $SCH_2CH_2CH_3$)
	1.24 (t, 6 H, $SCH_2CH_2CH_3$)
	1.18 (t, 6 H, $SCH_2CH_2CH_3$)

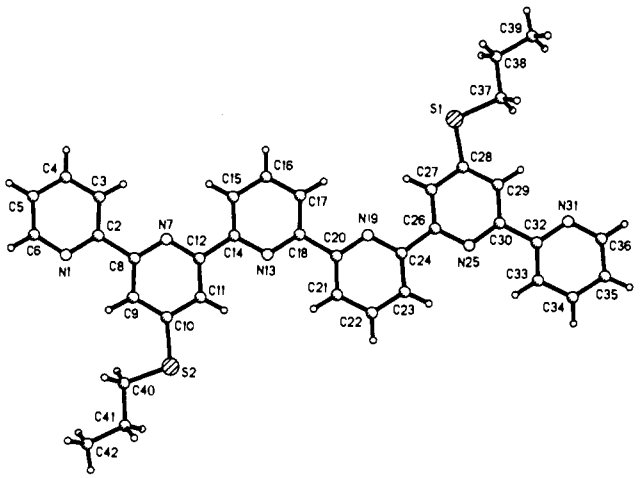


Figure 1. X-ray structure of 4′,4‴″-bis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″-sexipyridine (**12i**).

obtained in 78% yield. Recrystallization from hot $CHCl_3$ afforded the octipyridine derivative as colorless, irregular prisms in 49% yield. Its ^1H NMR data are listed in Table IV.

4′,4‴,4⁗″,4⁗‴′-Tetrakis(alkylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″:6⁗″,2⁗‴:6⁗‴,2⁗⁗′:6⁗⁗′,2⁗⁗″-novipyridines 15. The synthesis of these oligopyridines (Table VI) was accomplished by reacting 2 equiv of the potassium enolate of 6-acetyl-4′-(methylthio)-2,2′:6′,2″-terpyridine (**4c**) with the bis(α-oxoketene dithioacetal) of 2,6-diacetylpyridine (**9b**) in anhydrous THF, the final disposition of alkylthio groups in **15** depending on those present in **4** and **9**. Double ring closure of the resultant bis-(1,5-enedione) with ammonium acetate and hot glacial acetic acid afforded the novipyridine **15a** in a crude yield of 81%. The novipyridine containing four *n*-propylthio groups, **15b**, was prepared in 97% crude yield in an analogous manner from **4d** and **9b**. The ^1H NMR data for **15b** are listed in Table IV.

4′,4‴,4⁗″,4⁗‴′-Tetrakis(alkylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″:6⁗″,2⁗‴:6⁗‴,2⁗⁗′:6⁗⁗′,2⁗⁗″:6⁗⁗″,2⁗⁗‴-decipyridines 16. To accommodate the additional pyridine ring in the decipyridine derivative, only one component in the reaction leading to **15** need be changed. Two equivalents of the appropriate 6-acetyl-4′-(alkylthio)-2,2′:6′,2″-terpyridine **4c** or **4d** and the bis-(α-oxoketene dithioacetal) of 6,6′-diacetyl-2,2′-bipyridine **9c** or **9d** condensed as above resulted in the decipyridines (Table VI). Thus, the decipyridine **16a** was obtained in 83% crude yield from **4c** and **9d**, and, similarly, the tetrakis(*n*-propylthio)-substituted decipyridine **16b** was obtained in 81% crude yield by the condensation of **4d** and **9d**. The ^1H NMR data for **16b** are also listed in Table IV.

Experimental Section

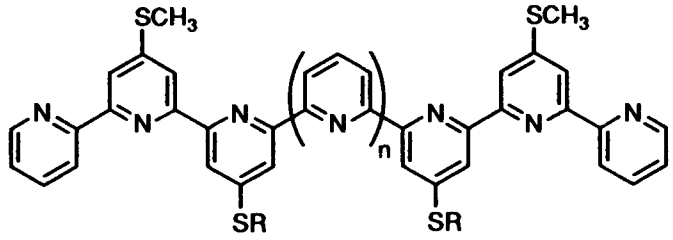
All reactions sensitive to air and moisture were carried out in a flame-dried apparatus, usually a 3-neck, round-bottom flask, under a dry nitrogen atmosphere using either magnetic or mechanical stirring. The following instruments were used for spectral characterizations: infrared spectra, Perkin-Elmer Model 298 grating infrared spectrophotometer and Perkin-Elmer Model 1850 Fourier transform infrared spectrometer; ^1H NMR spectra, Varian XL-200 or Hitachi Perkin-Elmer R-600 Fourier transform spectrometer in $CDCl_3$, except where noted, with TMS as an internal standard; mass spectra, Hewlett-Packard GC-MS system Model 5987A spectrometer; UV/vis spectra, Varian Cary 219 spectrophotometer. Single crystal X-ray data were collected on a Nicolet R3m 4-circle single crystal X-ray diffractometer, the structures being solved using the Patterson Method and the Direct Method.

All melting points were determined in capillaries using a Thomas-Hoover capillary melting point apparatus or a mel-temp apparatus and are uncorrected. All solvent evaporations were carried out under reduced pressure using a Buchi Rotovap apparatus. Microanalyses were performed by Atlantic Microlab, Inc., Atlanta, GA or Quantitative Technologies, Inc. Whitehouse, NJ.

Anhydrous solvents and reagents were prepared and stored as follows: tetrahydrofuran (THF) and diethyl ether (Et_2O), distilled over sodium/benzophenone; *N*,*N*-dimethylformamide (DMF), distilled over CaH_2 and stored over 4-Å molecular sieves; ethyl acetate, acetonitrile, and methylene chloride, distilled over P_2O_5 and stored over 4-Å molecular sieves; *N*,*N*-dimethylacetamide (DMA), fractionally distilled over BaO_2 or CaH_2 and stored under an inert atmosphere; thiophene-free benzene, washed with H_2SO_4, H_2O, aqueous NaOH, and H_2O, stirred over $CaCl_2$, and distilled over sodium/benzophenone. Solutions of organolithium reagents were standardized by titration with a 1.0 M xylene solution of 2-butanol using 1,10-phenanthroline as the indicator. Chromatographic separations were performed with alumina gravity or flash columns, preparative thin-layer plates, or a Chromatron rotary thin-layer chromatograph. Ion exchanges were performed using Dowex 1X8-50 ion-exchange resin (Cl form or regenerated with $NaClO_4$).

α-Oxoketene dithioacetals were prepared according to procedures described earlier.[15]

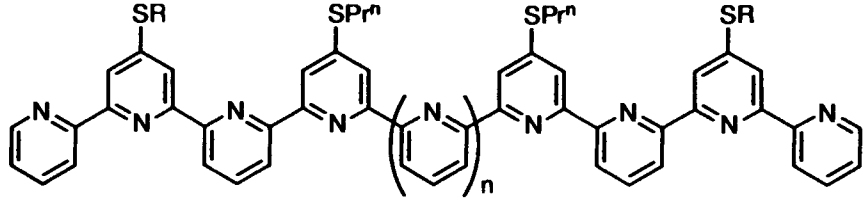
Table V. (Alkylthio)-Substituted Septipyridines and Octipyridine[a]



compd no.	n	R	yield,[b] %	mp, °C	crystal form[c]	molecular formula	analytical data calcd/found C	H	N	M$^{+\cdot}$ (relative intensity) [Fragment ion] EI/FAB[d]	IR (KBr)
13a	1	CH_3	83 (28)	352–354 dec	tan microneedles	$C_{39}H_{31}N_7S_4$	64.52 64.44	4.30 4.34	13.51 13.45	EI: 725 (37), 207 (100) [$C_{13}H_9N_3^+$] FAB: 726 (86)[a] 27 (100) [HCN]$^+$	$\nu_{C=N,C=C}$ 1550, 1536, 1369
13b	1	Pr^n	95 (45)	259–260 dec	tan microneedles	$C_{43}H_{39}N_7S_4$	66.03 66.18	5.03 5.06	12.54 12.61	EI: 781 (12), 391 (100) [$C_{22}H_{21}N_3S_2^+$] FAB: 782 (100)	ν_{CH} 2960–2865, $\nu_{C=N,C=C}$ 1560, 1543, 1374
14	2	Pr^n	78 (49)	310–312 dec	colorless prisms	$C_{48}H_{42}N_8S_4$	67.10 67.12	4.93 4.94	13.04 13.00	FAB: 859 (100)	ν_{CH} 2960–2870, $\nu_{C=N,C=C}$ 1559, 1546, 1380

[a] See Table IV for ^{1}H NMR data. [b] Crude yield (purified yield). [c] All crystallized from DMF. [d] Positive ion FAB mass spectrum, $[M + H]^+$.

Table VI. (Alkylthio)-substituted Novipyridines and Decipyridines



compd no.	n	R	yield,[a] %	mp, °C	crystal form[b]	molecular formula	Analytical Data Calcd/Found C	H	N	FAB (M + H)$^+$ (relative intensity)	IR (KBr)
15a	1	CH_3	81 (51)	333–335 dec	tan micropsisms	$C_{53}H_{45}N_9S_4 \cdot {}^1/_2H_2O$	67.34 67.36	4.90 4.98	13.34 13.43		$\nu_{C=N,C=C}$ 1572, 1560, 1541, 1388 ν_{CH} 2960–2865
15b	1	Pr^n	97 (35)	307–309 dec	colorless microprisms	$C_{57}H_{53}N_9S_4 \cdot H_2O$	67.76 67.84	5.49 5.13	12.48 12.68	992 (100)	ν_{CH} 2960–2865 $\nu_{C=N,C=C}$ 1572, 1560, 1541, 1390
16a	2	CH_3	85 (53)	345–348 dec	tan microprisms	$C_{58}H_{48}N_{10}S_4 \cdot H_2O$	67.54 67.58	4.89 4.86	13.58 13.54		ν_{CH} 2960–2870 $\nu_{C=N,C=C}$ 1560, 1542, 1390
16b	2	Pr^n	81 (33)	311–312 dec	colorless microprisms	$C_{62}H_{56}N_{10}S_4$	69.63 69.44	5.28 5.01	13.10 12.94	1069 (100)	ν_{CH} 2980–2870 $\nu_{C=N,C=C}$ 1561, 1542, 1390

[a] Crude yield (purified yield). [b] All crystallized from DMF.

Ethyl 4-(Methylthio)-2,2′-bipyridine-6-carboxylate. 4-(Methylthio)-2-(2-pyridinyl)pyridine-6-carboxylic acid[21] (2.5 g, 10.0 mmol), absolute EtOH (25 mL), and concentrated sulfuric acid (2.6 g, 25.0 mmol) were refluxed for 3 h, and the reaction mixture was cooled to 0 °C and diluted with ice–water (25 g), followed by neutralization with saturated, aqueous K_2CO_3. The resultant solid ester which separated was collected and air dried. The filtrate was extracted with ether (3 × 10 mL), the extracts were combined and dried (Na_2SO_4), and the ether was removed, producing additional product. The ester was purified by recrystallization from EtOH, giving colorless needles: 2.7 g (84%); mp 89–91 °C; IR (KBr) 1550 (C=N, C=C), 1720 (CO) cm^{-1}; ^{1}H NMR (200 MHz) δ 8.68 (dt, 1 H, $J_{5',6'}$ = 4.8 Hz, $J_{4',6'}$ = 1.8 Hz, $H_{6'}$), 8.55 (dd, 1 H, $J_{3',4'}$ = 7.8 Hz, $J_{3',5'}$ = 1.0 Hz, $H_{3'}$), 8.44 (d, 1 H, $J_{3,5}$ = 2.0 Hz, H_3), 7.94 (d, 1 H, $J_{3,5}$ = 1.8 Hz, H_5), 7.85 (td, 1 H, $J_{3',4'} = J_{4',5'}$ = 7.6 Hz, $J_{4',6'}$ = 1.6 Hz, $H_{4'}$), 7.35 (m, 1 H, $J_{4',5'}$ = 7.4 Hz, $J_{5',6'}$ = 4.8 Hz, $J_{3',5'}$ = 1.1 Hz, $H_{5'}$), 4.49 (q, 2 H, OCH_2CH_3), 2.63 (s, 3 H, SCH_3), 1.48 (t, 3 H, OCH_2CH_3); mass spectrum m/z (relative intensity) (El) $M^{\bullet+}$ 274 (9), 202 (100) [$M^{\bullet+}$ – COOEt].

Anal. Calcd for $C_{14}H_{14}N_2O_2S$: C, 61.29; H, 5.14; N, 10.21. Found: C, 61.22; H, 5.16; N, 10.19.

6-(Ethoxymalonyl)-4-(methylthio)-2,2′-bipyridine. Absolute EtOH (6.3 mL, 108.0 mmol) was treated slowly with sodium shavings (400 mg, 18.0 mmol), and the mixture was heated until complete reaction of the sodium had occurred. The excess EtOH was then distilled. The resultant solid NaOEt was heated at 140 °C for 1 h and then diluted with anhydrous benzene (20 mL). The distillation apparatus was replaced with a pressure-equalizing dropping funnel and a N_2(g) inlet tube, and a solution of ethyl 4-(methylthio)-2,2′-bipyridine-6-carboxylate (3.2 g, 12.0 mmol) and EtOAc (2.3 mL, 2.1 g, 21.0 mmol) in benzene (30 mL) was added dropwise with stirring. The resultant mixture was heated slightly for 30 min to dissolve the NaOEt, and, as the golden-yellow sodium salt began to precipitate from the solution, the oil bath was removed and the mixture was then stirred vigorously for 20 h. The reaction was quenched with ice–water (50 mL) and filtered, the collected yellow solid was suspended in cold water (400 mL), and the resultant suspension was basified with dilute NH_4OH and finally neutralized with 10% aqueous HCl. The precipitated yellow β-keto ester was collected and air dried. The filtrate layers were separated; the organic layer was extracted with water (1 × 20 mL), and the aqueous layer was extracted with benzene (1 × 20 mL). The aqueous layers were combined, cooled to 0 °C and neutralized with 10% aqueous HCl, and the resultant pale yellow solid which precipitated was collected and combined with the first crop. Recrystallization of the crude product from *n*-hexane produced colorless needles: 3.0 g (75%); mp 95–96 °C; IR (KBr) 1555, 1410 (C=N, C=C), 1700, 1720 (CO) cm^{-1}; ^{1}H NMR (200 MHz) δ 8.69 (dt, 1 H, $J_{5',6'}$ = 4.8 Hz, $J_{4',6'}$ = 1.6 Hz, $H_{6'}$), 8.51 (d, 1 H, $J_{3,5}$ = 2.0 Hz, H_3), 8.47 (bd, 1 H, $J_{3',4'}$ = 8.0 Hz, $H_{3'}$), 7.88 (d, 1 H, $J_{3,5}$ = 2.0 Hz, H_5), 7.87 (td, 1 H, $J_{3',4'} = J_{4',5'}$ = 7.8 Hz, $J_{4',6'}$ = 1.7 Hz, $H_{4'}$), 7.36 (m, 1 H, $J_{4',5'}$ = 7.5 Hz, $J_{5',6'}$ = 4.8 Hz, $J_{3',5'}$ = 1.1 Hz, $H_{5'}$), 4.20 (s, 2 H, $COCH_2CO$), 4.17 (q, 2 H, OCH_2CH_3), 2.62 (s, 3 H, SCH_3), 1.18 (t, 3 H, OCH_2CH_3); mass spectrum m/z (relative intensity) (El) $M^{\bullet+}$ 316 (23), 244 (100) [$M^{\bullet+}$ – COOEt].

Anal. Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.74; H, 5.10; N, 8.85. Found: C, 60.83; H, 5.12; N, 8.85.

6-Acetyl-4-(methylthio)-2,2′-bipyridine (4a). Anhydrous NaOEt was prepared as above from anhydrous EtOH (5 mL) and sodium shavings (200 mg, 7.5 mmol). The cake of NaOEt was heated at 140 °C for 1 h and then diluted with anhydrous benzene (3 mL). The distillation apparatus was replaced with a Claisen-head adapter fitted with a reflux condenser, a N_2(g) inlet tube, and a pressure-equalizing dropping funnel. A solution of ethyl 4-(methylthio)-2,2′-bipyridine-6-carboxylate (1.4 g, 5.0 mmol), freshly distilled EtOAc (1.0 mL, 0.9 g, 10.0 mmol), and benzene (12 mL) was added dropwise to the stirred suspension, and the resultant mixture was heated to dissolve the sodium ethoxide. When the yellow sodium salt of the intermediate β-keto ester began to precipitate, the oil bath was removed and the heterogeneous mixture was stirred at 25 °C for 24 h. The reaction was then quenched with a cold, 10% aqueous NaOH solution (10 mL), precipitating a yellow solid which was collected and air dried. The filtrate layers were separated, the aqueous layer was extracted with benzene (2 × 10 mL), and the organic layer was extracted with water (2 × 10 mL). The respective layers were combined, and the benzene fractions were discarded. The above solid was suspended in the aqueous layer, which was diluted to 75 mL with cold water and acidified with concentrated HCl (13 mL) while being cooled in an ice-water bath. The resultant reaction mixture was refluxed for 2 h and then cooled to 0 °C and neutralized with saturated, aqueous K_2CO_3. The resultant tan solid was collected, air dried, and then recrystallized from *n*-hexane, producing colorless needles: 1.1 g (87%); mp 104–106 °C; IR (KBr) 1550, 1400 (C=N, C=C), 1680 (CO) cm^{-1}; ^{1}H NMR (200 MHz) δ 8.70 (dt, 1 H, $J_{5',6'}$ = 4.8 Hz, $J_{4',6'}$ = 1.8 Hz, $H_{6'}$), 8.52 (bd, 1 H, $J_{3',4'}$ = 8.0 Hz, $H_{3'}$), 8.47 (d, 1 H, $J_{3,5}$ = 2.0 Hz, H_3), 7.87 (td, 1 H, $J_{3',4'} = J_{4',5'}$ = 7.7 Hz, $J_{4',6'}$ = 1.6 Hz, $H_{4'}$), 7.86 (d, 1 H, $J_{3,5}$ = 2.0 Hz, H_5), 7.36 (m, 1 H, $J_{4',5'}$ = 7.4 Hz, $J_{5',6'}$ = 4.8 Hz, $J_{3',5'}$ = 1.2 Hz, $H_{5'}$), 2.82 (s, 3 H, $COCH_3$), 2.61 (s, 3 H, SCH_3); mass spectrum m/z (relative intensity) (El) $M^{\bullet+}$ 244 (59), 78 (100) [$C_5H_4N^+$].

Anal. Calcd for $C_{13}H_{12}N_2OS$: C, 63.90; H, 4.95; N, 11.47. Found: C, 63.92; H, 4.96; N, 11.41.

Alternative Preparation of 6-Acetyl-4-(methylthio)-2,2′-bipyridine (4a). Freshly distilled butane-2,3-dione monoketal[22] (**5**) (10.0 g, 58 mmol), 3,3-bis(methylthio)-1-(2-pyridinyl)propen-1-one (**2a**) (13.1 g, 58 mmol), and anhydrous THF (260 mL) were mixed in a previously flame-dried apparatus, and KBu^{t}O (13.1 g, 116 mmol) was added in one portion with stirring. The resultant green heterogeneous mixture was then stirred at 25 °C for 42 h. NH_4OAc (45 g, 58 mmol) and glacial AcOH (175 mL) were added, and the solution was refluxed for 3 h, the THF being removed during this 3-h period. The dark green residue was cooled to 25 °C and poured into ice-cold dilute HCl (70 mL, 6N). After this mixture was stirred for 12 h, it was diluted with water (200 mL) and neutralized with saturated $NaHCO_3$ solution. A crude product separated as an off-white powder (6.1 g, 43%), which crystallized from hexane (charcoal) as colorless needles: 5.5 g (39%); mp 104–106 °C; identical in all respects with the product prepared by the Claisen route.

6,6′-Diacetyl-2,2′-bipyridine. The following procedure was found to give reproducible results. Anhydrous THF (200 mL) and *n*-BuLi (17.6 mL of 2.5 M solution in hexane, 44.0 mmol, 10% excess) were added to a flame-dried apparatus, and this mixture was cooled to –80 °C in a liquid N_2/pentane bath. A solution of 6,6′-dibromo-2,2′-bipyridine[16d,20] (6.3 g, 20.0 mmol) in THF (360 mL) was added dropwise while the reaction temperature was maintained below –70 °C. The resultant red solution was stirred at –75 °C for an additional 45 min and then cooled below –80 °C. A solution of DMA (4.5 mL, 4.2 g, 48.0 mmol, 20% excess) in anhydrous Et_2O (100 mL) was then added dropwise to the mixture over 55 min. After the resultant mixture was stirred for 2 h at –80 °C, it was warmed slowly to –10 °C and then hydrolyzed with 6 N HCl (40 mL). The solvent was removed, and the resultant acidic residue was cooled in an ice bath and treated with 20% aqueous NaOH (pH 8–9). The solid which separated was collected, air dried, and recrystallized from EtOH (charcoal), giving colorless needles: 3.1 g (65%); mp 182–184 °C (lit.[16d] mp 182–184 °C). Spectral characteristics were identical in all respects with those reported[16d] earlier.

6,6′-Bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]-2,2′-bipyridinyl[28] (9d). KBu^{t}O (1.8 g, 16.0 mmol, 5% excess) and anhydrous THF (15 mL) were mixed, and a solution of 6,6′-diacetyl-2,2′-bipyridine (920 mg, 3.8 mmol) in anhydrous THF (50 mL) was added dropwise over 10 min. The resultant mixture was then stirred for an additional 5 min. A solution of CS_2 (0.46 mL, 580 mg, 7.6 mmol) in THF (5 mL) was added dropwise over 30 min, and the resultant bright orange heterogeneous mixture was then treated dropwise with 1-bromopropane (1.5 mL, 16.5 mmol, 8% excess) dissolved in THF (5 mL). After 1 h the addition was completed. The resultant orange heterogeneous mixture was stirred at 25 °C for 24 h, and then the reaction was quenched on ice (100 g) and set aside for a further 24 h. The solid product that separated was collected, air dried, taken up in hot hexane, and filtered, and the hexane-insoluble orange needles were air dried: 1.10 g (52%); mp 200–202 °C; IR (KBr) ν_{CO} 1618; ^{1}H NMR δ 8.64 (dd, 2 H, H_5, $H_{5'}$, $J_{4,5}$ = 6.0 Hz), 8.30 (dd, 2 H, H_3, $H_{3'}$, $J_{3,4}$ = 6.0 Hz), 8.03 (t, 2 H, H_4, $H_{4'}$), 7.98 (s, 2 H, vinylic), 3.24–3.12 (2t, 8 H, $SCH_2CH_2CH_3$), 2.07–1.75 (2 sextets, 8 H, $SCH_2CH_2CH_3$), 1.24–1.07 (2t, 12 H, $SCH_2CH_2CH_3$); mass spectrum m/z (relative intensity) $M^{\bullet+}$ 560 (4).

Anal. Calcd for $C_{28}H_{36}N_2O_2S_4$: C, 59.96; H, 6.47; N, 5.00. Found: C, 59.97; H, 6.48; N, 4.99.

The corresponding bis(ethylthio) compound crystallized as pale yellow prisms from DMF, mp 245–247 °C, in 48% yield: IR (KBr) ν_{CO} 1618; ^{1}H NMR δ 8.60 (dd, 2 H, H_5, $H_{5'}$, $J_{4,5}$ = 6.0 Hz), 8.27 (dd, 2 H, H_3, $H_{3'}$, $J_{3,4}$ = 6.0 Hz), 8.02 (t, 2 H, H_4, $H_{4'}$), 7.92 (s, 2 H, vinylic), 3.29–3.11 (2qt, 8 H, SCH_2CH_3), 1.54 (t, 6 H, SCH_2CH_3), 1.41 (t, 6 H, SCH_2CH_3); mass spectrum m/z (relative intensity) $M^{\bullet+}$ 504 (3).

Anal. Calcd for $C_{24}H_{28}N_2O_2S_4$: C, 57.11; H, 5.59; N, 5.55. Found: C, 57.11; H, 5.59; N, 5.52.

Similarly, the bis(methylthio) compound **9c** crystallized from DMF as irregular orange prisms, mp 276–279 °C, in 32% yield: IR (KBr) ν_{CO}

1610; ^{1}H NMR δ 8.70–8.0 (m, 6 H, pyridine), 7.89 (s, 2 H, vinylic), 2.69 (s, 6 H, SCH_3), 2.57 (s, 6 H, SCH_3); mass spectrum m/z (relative intensity) $M^{\bullet+}$ 448 (3).

Anal. Calcd for $C_{20}H_{10}N_2O_2S_4$: C, 53.54; H, 4.49; N, 6.24. Found: C, 53.53; H, 4.50; N, 6.24.

4′-(Methylthio)-2,2′:6′,2″-terpyridine-6-carboxylic Acid and 6-(*N*,*N*-Dimethylamido)-4′-(methylthio)-2,2′:6′,2″-terpyridine. Using the above KBu^{t}O, DMF, and air procedure, 6-methyl-4′-(methylthio)-2,2′:6′,2″-terpyridine (**3c**) (14.7 g, 0.05 mol) gave a reaction mixture which was filtered (see below), and the DMF/H_2O filtrate was concentrated in vacuo. The resultant solid residue was suspended in cold H_2O, filtered, air dried, and then recrystallized from EtOH/EtOAc, yielding colorless prisms of the acid: 6.5 g (40%); mp 230–231 °C (CO_2↑) (Table 1); ^{1}H NMR (200 MHz) δ 8.90 (dd, 1 H, $J_{3,4}$ = 7.8 Hz, $J_{3,5}$ = 1.1 Hz, H_3), 8.73 (d, 1 H, $J_{5'',6''}$ = 4.8 Hz, $H_{6''}$), 8.59 (bd, 1 H, $J_{3'',4''}$ = 8.0 Hz, $H_{3''}$), 8.39 (d, 1 H, $J_{3',5'}$ = 1.8 Hz, $H_{3'}$), 8.31 (dd, 1 H, $J_{4,5}$ = 7.6 Hz, $J_{3,5}$ = 1.0 Hz, H_5), 8.20 (d, 1 H, $J_{3',5'}$ = 1.8 Hz, $H_{5'}$), 8.14 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.7 Hz, H_4), 7.89 (td, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8 Hz, $J_{4'',6''}$ = 1.8 Hz, $H_{4''}$), 7.38 (m, 1 H, $J_{4'',5''}$ = 7.8 Hz, $J_{3'',5''}$ = 1.0 Hz, $H_{5''}$), 2.69 (s, 3 H, SCH_3).

The original filtercake was dissolved in $CHCl_3$, the resultant suspension was filtered, and the $CHCl_3$ was evaporated, leaving a pale yellow solid. The dimethylamide crystallized from EtOAc as colorless prisms: 1.6 g (9%); mp 170–172 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.72–7.32 (m, 9 H, pyridine), 3.22 [s, 6 H, CON(CH_3)$_2$], 2.66 (s, 3 H, SCH_3). Hydrolysis of this amide with KBu^{t}O in aqueous THF gave colorless prisms (52%) of the above acid.

Ethyl 4′-(Methylthio)-2,2′:6′,2″-terpyridine-6-carboxylate was prepared by esterification of 4′-(methylthio)-2,2′:6′,2″-terpyridine-6-carboxylic acid (6.5 g, 0.02 mol) with absolute EtOH (35 mL) and concentrated sulfuric acid (5.1 mL, 4.9 g, 0.05 mol) as in the bipyridine series. The ester crystallized from EtOH as colorless needles: 4.3 g (62%); mp 135.5–136.5 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.78 (dd, 1 H, $J_{3,4}$ = 7.8 Hz, $J_{3,5}$ = 1.2 Hz, H_3), 8.68 (m, 1 H, $J_{5'',6''}$ = 4.8 Hz, $J_{4'',6''}$ = 1.8 Hz, $J_{3'',6''}$ = 0.9 Hz, $H_{6''}$), 8.58 (dd, 1 H, $J_{3'',4''}$ = 8.0 Hz, $J_{3'',5''}$ = 1.0 Hz, $H_{3''}$), 8.43 (d, 1 H, $H_{3'}$), 8.32 (d, 1 H, $H_{5'}$), 8.14 (dd, 1 H, $J_{4,5}$ = 7.8 Hz, $J_{3,5}$ = 1.2 Hz, H_5), 7.97 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.8 Hz, H_4), 7.84 (dt, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8 Hz, $J_{4'',6''}$ = 2.0 Hz, $H_{4''}$), 7.33 (m, 1 H, $J_{4'',5''}$ = 7.4 Hz, $J_{5'',6''}$ = 4.8 Hz, $J_{3'',5''}$ = 1.2 Hz, $H_{5''}$), 4.52 (q, 2 H, OCH_2CH$_3$), 2.68 (s, 3 H, SCH_3), 1.49 (t, 3 H, OCH$_2$CH_3).

6-(Ethoxymalonyl)-4′-(methylthio)-2,2′:6′,2″-terpyridine. This β-keto ester was prepared from ethyl 4′-(methylthio)-2,2′:6′,2″-terpyridine-6-carboxylate (1.1 g, 3.0 mmol) and freshly distilled EtOAc (0.6 mL, 500 mg, 6.0 mmol) as in the bipyridine series. It was obtained as a yellow solid which crystallized from EtOH as yellow prisms: 2.2 g (79% based on reacted starting material); mp 134–136 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.86 (dd, 1 H, $J_{3,4}$ = 7.6 Hz, $J_{3,5}$ = 1.5 Hz, H_3), 8.70 (dd, 1 H, $J_{5'',6''}$ = 4.8 Hz, $H_{6''}$), 8.60 (dd, 1 H, $J_{3'',4''}$ = 7.8 Hz, $H_{3''}$), 8.36 (d, 2 H, $H_{3'}$, $H_{5'}$), 8.12 (dd, 1 H, $J_{4,5}$ = 7.6, $J_{3,5}$ = 1.5 Hz, H_5), 8.02 (t, 1 H, H_4), 7.87 (dt, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.7 Hz, $J_{4'',6''}$ = 1.6 Hz, $H_{4''}$), 7.36 (m, 1 H, $J_{4'',5''}$ = 7.6 Hz, $J_{5'',6''}$ = 4.8 Hz, $J_{3'',5''}$ = 1.3 Hz, $H_{5''}$), 4.21 (s, 2 H, COCH_2CO), 4.19 (q, 2 H, OCH_2CH$_3$), 2.72 (s, 3 H, SCH_3), 1.17 (t, 3 H, OCH$_2$CH_3).

6-Acetyl-4′-(methylthio)-2,2′:6′,2″-terpyridine (4c). Hydrolysis of 6-(ethoxymalonyl)-4′-(methylthio)-2,2′:6′,2″-terpyridine (1.5 g, 3.8 mmol) with 20% aqueous HCl (25 mL) as in the bipyridine series gave **4c**, which was recrystallized from CH_3OH, forming colorless needles: 0.8 g (68%); mp 128–130 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.82 (dd, 1 H, $J_{3,4}$ = 7.6 Hz, $J_{3,5}$ = 1.2 Hz, H_3), 8.71 (d, 1 H, $J_{5'',6''}$ = 4.8 Hz, $H_{6''}$), 8.61 (dd, 1 H, $J_{3'',4''}$ = 8.0 Hz, $J_{3'',5''}$ = 1.1 Hz, $H_{3''}$), 8.42 (d, 1 H, $J_{3',5'}$ = 1.0 Hz, $H_{3'}$), 8.36 (d, 1, H, $J_{3',5'}$ = 1.2 Hz, $H_{5'}$), 8.09 (dd, 1 H, $J_{4,5}$ = 7.6 Hz, $J_{3,5}$ = 1.3 Hz, H_5), 7.99 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.6 Hz, H_4), 7.88 (dt, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8 Hz, $J_{4'',6''}$ = 1.7 Hz, $H_{4''}$), 7.36 (m, 1 H, $J_{4'',5''}$ = 8.0 Hz, $J_{5'',6''}$ = 4.8 Hz, $H_{5''}$), 2.87 (s, 3 H, COCH_3), 2.69 (s, 3 H, SCH_3).

6-Bromo-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (7). A mixture of 2-acetyl-6-bromopyridine[20b] (**6**) (2.0 g, 10.0 mmol), 3,3-bis(*n*-propylthio)-1-(2-pyridinyl)propen-1-one (**2b**) (2.8 g, 10.0 mmol), and anhydrous THF (30 mL) was stirred for 10 min, and then a solution of KBu^{t}O (2.5 g, 22.0 mmol, 10% excess) in THF (30 mL) was added dropwise over 30 min. The resultant deep red heterogeneous mixture was stirred at 25 °C for 17 h. NH_4OAc (7.7 g, 100.0 mmol) and glacial AcOH (40 mL) were added, and the mixture was refluxed for 2 h with continuous removal of the THF. After the resultant acidic residue was cooled to 25 °C, it was poured onto ice (100 g) and set aside for 4 h in an ice-water bath. The dark oil that separated was extracted from the aqueous solution with $CHCl_3$, and the $CHCl_3$ extracts were combined, washed with water until the aqueous wash was neutral, and then dried over Na_2SO_4. Removal of the $CHCl_3$ yielded a dark oil which was passed through an alumina flash column and eluted with hexane/acetone (20:1). The solvent was evaporated, and the resultant yellow oil solidified on trituration with *n*-hexane. Recrystallization of this solid from hot hexane produced tan prisms: 2.1 g (54%); mp 81–83 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.69 (m, 1 H, $J_{5'',6''}$ = 4.8 Hz, $J_{4'',6''}$ = 2.0 Hz, $H_{6''}$), 8.54 and 8.53 (2d, 2 H, $J_{3,4}$ = 7.6 Hz, H_3, $H_{3''}$), 8.32 (d, 1 H, $J_{3',5'}$ = 1.8 Hz, $H_{3'}$), 8.27 (d, 1 H, $J_{3',5'}$ = 1.8 Hz, $H_{5'}$), 7.83 (dt, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.7 Hz, $J_{4'',6''}$ = 1.8 Hz, $H_{4''}$), 7.67 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.7 Hz, H_4), 7.49 (d, 1 H, $J_{4,5}$ = 7.8 Hz, H_5), 7.33 (m, 1 H, $J_{4'',5''}$ = 7.2 Hz, $J_{5'',6''}$ = 4.9 Hz, $J_{3'',5''}$ = 1.1 Hz, $H_{5''}$), 3.14 (t, 2 H, SCH_2CH$_2$CH$_3$), 1.82 (sextet, 2 H, SCH$_2$CH_2-CH$_3$), 1.12 (t, 3 H, SCH$_2$CH$_2$CH_3).

2-Methyl-4-[4′-(*n*-propylthio)-2,2′:6′,2″-terpyridin-6-yl]-3-butyn-2-ol (8a). A mixture of 2-bromo-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (**7**) (3.9 g, 10.0 mmol), 2-methyl-3-butyn-2-ol (1.1 mL, 1.0 g, 11.4 mmol) $(PPh_3)_2PdCl_2$ (7.0 mg, 0.01 mmol), copper(I) iodide (3.8 mg, 0.02 mmol), and Et_3N (38 mL) was refluxed for 24 h, during which time the mixture first became homogeneous and then a tan-colored inorganic salt began to precipitate. The resultant suspension was cooled to 25 °C, diluted with Et_2O (40 mL), and filtered, and the filtercake was washed with Et_2O. The organic filtrate was concentrated, yielding a viscous brown oil which solidified on trituration with *n*-hexane.

(It is possible to cleave the protecting group at this point by treating the crude product with NaOH in refluxing toluene, thus eliminating the isolation and purification steps and producing the desired terminal acetylene in higher yield.) The crude product was dissolved in a small volume of $CHCl_3$, applied to an alumina flash column and eluted with *n*-hexane/EtOAc (9:1). Removal of the solvent produced a colorless solid residue that crystallized from *n*-hexane/EtOAc as colorless microprisms: 2.1 g (54%); mp 134–135.5 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.70 (dt, 1 H, $J_{5'',6''}$ = 4.8 Hz, $J_{4'',6''}$ = 1.8 Hz, $J_{3'',6''}$ = 0.9 Hz, $H_{6''}$), 8.60–8.52 (2d, 2 H, H_3, $H_{3''}$), 8.35 (d, 2 H, $J_{3',5'}$ = 1.4 Hz, $H_{3'}$, $H_{5'}$), 7.85 (td, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8 Hz, $J_{4'',6''}$ = 1.8 Hz, $H_{4''}$), 7.81 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.8 Hz, H_4), 7.46 (dd, 1 H, $J_{4,5}$ = 7.6 Hz, $J_{3,5}$ = 1.0 Hz, H_5), 7.34 (m, 1 H, $J_{4'',5''}$ = 7.4 Hz, $J_{5'',6''}$ = 4.9 Hz, $J_{3'',5''}$ = 1.1 Hz, $H_{5''}$), 3.17 (t, 2 H, SCH_2CH$_2$CH$_3$), 2.24 (bs, 1 H, OH), 1.83 (sextet, 2 H, SCH$_2$CH_2CH$_3$), 1.12 (t, 3 H, SCH$_2$CH$_2$CH_3).

6-Ethynyl-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (8b). A solution of 2-methyl-4-[4′-(*n*-propylthio)-2,2′:6′,2″-terpyridin-6-yl]-3-butyn-2-ol (**8a**) (2.0 g, 5.1 mmol), NaOH (400 mg, 100 mmol), and toluene (30 mL) was refluxed for 2 h. The resultant golden-brown solution was poured into a large evaporating dish, and the solvent was evaporated, leaving a viscous oil. Trituration of this oil with *n*-hexane produced a gold-colored solid which was taken up in hot anhydrous Et_2O (100 mL) and filtered, and the Et_2O was allowed to evaporate. The residue was dissolved in a small amount of $CHCl_3$, passed through an alumina flash column, and eluted with *n*-hexane/EtOAc (9:1). Removal of solvent and recrystallization of the solid residue from *n*-hexane/EtOAc produced yellow prisms of the ethyne: 1.5 g (89%); mp 97–98 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.70 (dt, 1 H, $J_{5'',6''}$ = 4.8 Hz, $J_{4'',6''}$ = 1.6 Hz, $H_{6''}$), 8.60 (bd, 1 H, $J_{3,4}$ = 8.0 Hz, H_3), 8.58 (dd, 1 H, $J_{3'',4''}$ = 8.0 Hz, $J_{3'',5''}$ = 1.0 Hz, $H_{3''}$), 8.37 (d, 1 H, $J_{3',5'}$ = 1.7 Hz, $H_{5'}$), 8.34 (d, 1 H, $J_{3',5'}$ = 1.7 Hz, $H_{3'}$), 7.85 (td, 1 H, $H_{4''}$, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8 Hz, $J_{4'',6''}$ = 1.7 Hz, $H_{4''}$), 7.83 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.8 Hz, H_4), 7.53 (dd, 1 H, $J_{4,5}$ = 7.6 Hz, $J_{3,5}$ = 1.0 Hz, H_5), 7.33 (m, 1 H, $H_{5''}$), 3.21 (s, 1 H, C≡CH), 3.15 (t, 2 H, SCH_2-CH$_2$CH$_3$), 1.82 (sextet, 2 H, SCH$_2$CH_2CH$_3$), 1.11 (t, 3 H, SCH$_2$-CH$_2$CH_3).

6-Acetyl-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (4d). A mixture of concentrated H_2SO_4 (600 mg, 6.0 mmol), $HgSO_4$ (900 mg, 3.0 mmol), and 80% aqueous acetone (25 mL) was treated with a warm solution of 6-ethynyl-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (1.0 g, 3.0 mmol) in 80% aqueous acetone (30 mL) added in one portion, and the resultant orange mixture was refluxed for 2 h. The mixture was cooled to 25 °C, and the acetone was removed. The resultant aqueous residue was basified with saturated, aqueous K_2CO_3 and diluted with H_2O, and the tan-colored solid which separated was collected and air dried. The filtrate was then extracted with $CHCl_3$ (3 × 25 mL), the extracts were dried (Na_2SO_4), and the $CHCl_3$ was removed, yielding a second crop. The crude product was dissolved in a small amount of $CHCl_3$, applied to an alumina flash column, and eluted with *n*-hexane/EtOAc (9:1). After the solvent was removed, the resultant product was recrystallized from hexane, affording colorless microprisms: 700 mg (71%); mp 109–111 °C (Table 1); ^{1}H NMR (200 MHz) δ 8.79 (dd, 1 H, $J_{3,4}$ = 7.8 Hz, $J_{3,5}$ = 1.4 Hz, H_3), 8.72 (m, 1 H, $J_{5'',6''}$ = 4.8 Hz, $J_{4'',6''}$ = 1.8 Hz, $H_{6''}$), 8.60 (dd, 1 H, $J_{3'',4''}$

= 8.0 Hz, $J_{3'',5''}$ = 1.0 Hz, $H_{3''}$), 8.42 (d, 1 H, $J_{3',5'}$ = 1.8 Hz, $H_{5'}$), 8.36 (d, 1 H, $J_{3',5'}$ = 1.8 Hz, $H_{3'}$), 8.09 (dd, 1 H, $J_{4,5}$ = 7.8 Hz, $J_{3,5}$ = 1.4 Hz, H_5), 7.99 (t, 1 H, $J_{4,5}$ = $J_{3,4}$ = 7.7 Hz, H_4), 7.87 (td, 1 H, $J_{3'',4''}$ = $J_{4'',5''}$ = 7.8 Hz, $J_{4'',6''}$ = 1.9 Hz, $H_{4''}$), 7.37 (m, 1 H, $J_{4'',5''}$ = 7.6 Hz, $J_{5'',6''}$ = 4.8 Hz, $J_{3'',5''}$ = 1.2 Hz, $H_{5''}$), 3.17 (t, 2 H, $SCH_2CH_2CH_3$), 2.86 (s, 3 H, $COCH_3$), 1.87 (sextet, 2 H, $SCH_2CH_2CH_3$), 1.14 (t, 3 H, $SCH_2CH_2CH_3$).

4,4''-Bis(*n*-propylthio)-6,6''-diacetyl-2,2':6',2''-terpyridine (4e). The bis(ketene dithioacetal) **9b** (7.3 g, 1.5 mmol) in dry THF (200 mL) was treated with biacetyl monoketal **5** (5.2 g, 3.0 mmol) and KBu^tO (7.4 g, 6.6 mmol). After being stirred at 25 °C for 24 h, the green heterogeneous reaction mixture was treated with NH_4OAc (23.1 g) and glacial AcOH (180 mL), and the resultant mixture was heated for 4 h with continuous distillation of the THF. The resultant dark colored mixture was poured into ice-cold 6 N HCl (140 mL), and the acidic solution was stirred at room temperature for 8 h. Neutralization with aqueous NaOH (20%) gave a dark brown residue which was extracted with CH_2Cl_2 (3 × 30 mL), and the extract was concentrated. Trituration of the resultant brown oil with CH_3OH yielded an off-white product (2.1 g, 30%) which crystallized from cyclohexane as colorless microneedles: 1.5 g (22%); mp 164–166 °C; IR (KBr) 1695 cm^{-1} (CO); ^1H NMR (200 MHz) δ 8.6 (d, 2 H, $J_{5,3}$ = 1.9 Hz, H_3), 8.57 (d, 2 H, $J_{4',3'}$ = 7.9 Hz, $H_{3'}$), 8.01 (t, 1 H, $J_{3',4'}$ = 7.9 Hz, $H_{4'}$), 7.89 (d, 2 H, $J_{3,5}$ = 1.9 Hz, H_5), 3.13 (t, 4 H, $SCH_2CH_2CH_3$), 2.83 (s, 6 H, $COCH_3$), 1.84 (sextet, 4 H, $SCH_2CH_2CH_3$), 1.14 (t, 6 H, $SCH_2CH_2CH_3$); mass spectrum *m/z* (relative intensity) M^+ 465 (10).

Anal. Calcd for $C_{25}H_{27}N_3O_2S_2$: C, 64.36; H, 5.85; N, 9.03. Found: C, 64.34; H, 5.76; N, 8.94.

4',4''-Bis(methylthio)-2,2':6',2'':6'',2'''-quaterpyridine (10). 6-Acetyl-4-(methylthio)-2,2'-bipyridine (**4a**) (2.75 g, 11.2 mmol), KBu^tO (2.51 g, 22.4 mmol), and anhydrous THF (125 mL) were mixed, and 3,3-bis(methylthio)-1-(2-pyridinyl)propen-1-one (**2a**) (2.53 g, 11.2 mmol) was then added. The resultant red heterogeneous mixture was stirred at 25 °C for 24 h. NH_4OAc (8.6 g, 112.0 mmol) and glacial AcOH (56 mL) were added, and the resultant mixture was refluxed for 5 h, during which time the THF was distilled. After the reaction mixture was cooled to 25 °C, ice-water (500 mL) was added, and the mixture was allowed to stand overnight. The brown solid product was collected, washed with H_2O, and then air dried. This crude product was then dissolved in CH_2Cl_2, passed through an alumina flash column, and eluted with CH_2Cl_2. After the solvent was removed, the solid residue (3.4 g, 76%) was recrystallized from cyclohexane, producing colorless needles of the quaterpyridine: 3.2 g (71%); mp 245–246.5 °C; IR (KBr) 1570–1540, 1372 (C=N, C=C) cm^{-1}; ^1H NMR (200 MHz) δ 8.71 (m, 2 H, $J_{5,6}$ = 4.8 Hz, $J_{4,6}$ = 1.8 Hz, $J_{3,6}$ = 0.8 Hz, H_6), 8.64 (dd, 2 H, $J_{3,4}$ = 8.0 Hz, $J_{3,5}$ = 1.0 Hz, H_3), 8.50 (d, 2 H, $J_{3',5'}$ = 1.8 Hz, $H_{5'}$), 8.34 (d, 2 H, $J_{3',5'}$ = 1.8 Hz, $H_{3'}$), 7.89 (td, 2 H, $J_{3,4}$ = $J_{4,5}$ = 7.8 Hz, $J_{4,6}$ = 1.8 Hz, H_4), 7.36 (m, 2 H, $J_{4,5}$ = 7.5 Hz, $J_{5,6}$ = 4.8 Hz, $J_{3,5}$ = 1.2 Hz, H_5), 2.70 (s, 6 H, SCH_3); mass spectrum *m/z* (relative intensity) (EI) $M^{+\cdot}$ 402 (84), 78 (100) [$C_5H_4N^+$].

Anal. Calcd for $C_{22}H_{18}N_4S_2$: C, 65.64; H, 4.51; N, 13.92. Found: C, 65.85; H, 4.67; N, 13.88.

4',4'''-Bis(methylthio)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (12a). Method A. A mixture of KBu^tO (13.9 g, 0.124 mol), anhydrous THF (500 mL), and 2,6-diacetylpyridine (5.0 g, 0.031 mol) was stirred for 10 min. 3,3-Bis(methylthio)-1-(2-pyridinyl)propen-1-one (**2a**) (14.0 g, 0.062 mol) was added, and stirring was continued for 24 h at 25 °C. The resultant bright red heterogeneous mixture was treated with NH_4OAc (47.8 g, 0.62 mol) and glacial AcOH (400 mL), and the mixture was refluxed for 4 h with continuous removal of THF. After being cooled to 25 °C, the mixture was poured onto ice (300 g), diluted with cold H_2O (200 mL), and set aside for 6 h. The resultant green solid was collected, washed with cold H_2O, and air dried. The crude product separated as grey needles from hot DMF and was then recrystallized from $CHCl_3$: 8.1 g (55%); mp 267–268 °C (Table II).

Method B. 2,6-Bis[(3,3-bis(methylthio)-1-oxopropen-1-yl]pyridine (**9a**) (10.0 g, 26.9 mmol), anhydrous THF (200 mL), and 2-acetylpyridine (6.5 g, 6.1 mL, 54 mmol) were added to a previously flame-dried apparatus. On the addition of KBu^tO (12.3 g, 110 mmol), a deep red heterogeneous mixture resulted which was stirred at 25 °C for 24 h. NH_4OAc (31.0 g, 390 mmol) and glacial AcOH (160 mL) were then added, and the resultant mixture was refluxed for 4 h with continuous removal of THF. The dark green residue was cooled to 25 °C, poured onto ice (200 g), and diluted with cold H_2O (100 mL). After the mixture warmed to 25 °C, the solid product was collected, washed with cold water, and then air dried. Recrystallization from DMF, followed by $CHCl_3$, afforded colorless needles: 5.1 g (41%); mp 267–268 °C.

4',4'''-Bis(*n*-propylthio)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (12b). Method A. Anhydrous THF (300 mL), KBu^tO (15.3 g, 0.136 mol, 10% excess), and 2,6-diacetylpyridine (5.0 g, 0.031 mol) were added to a previously flame-dried apparatus. After the mixture was stirred for 10 min, a solution of 3,3-bis(*n*-propylthio)-1-(2-pyridinyl)propen-1-one (**2b**) (17.5 g, 0.062 mol) in THF (50 mL) was added dropwise, and the stirring was continued at 25 °C for 24 h. NH_4OAc (46.6 g, 0.604 mol) and glacial AcOH (230 mL) were added, and the brown solution was refluxed for 3 h, during which time the THF was removed by distillation. After the resultant mixture was cooled to 25 °C, the acidic residue was poured onto ice (300 g), diluted to 600 mL with cold H_2O, and allowed to stand for 12 h. The dark gray solid product that separated was collected, washed with cold H_2O, dried, and purified by Soxhlet extraction with *n*-hexane. After evaporation of the hexane, the light brown solid (8.4 g, 51%) crystallized from *n*-hexane/EtOAc as tan prisms: 1.9 g (11%); mp 158–160 °C (Table II).

Method B. 2,6-Bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]pyridine (**9b**) (5.0 g, 10.0 mmol), anhydrous THF (100 mL), and 2-acetylpyridine (2.5 g, 2.4 mL, 21.0 mmol) were added to a previously flame-dried apparatus. On the addition of KBu^tO (5.1 g, 45.0 mmol), a deep red heterogeneous mixture resulted which was stirred for 24 h. NH_4OAc (15.0 g, 195.0 mmol) and glacial AcOH (75 mL) were then added, and the resultant mixture was refluxed for 4 h with continuous removal of THF. The dark green residue was cooled to 25 °C, poured onto ice (100 g), and diluted with cold H_2O (50 mL). After the mixture was warmed to 25 °C, the solid product was collected, washed with cold H_2O, and air-dried. Recrystallization from DMF, followed by $CHCl_3$, afforded colorless needles: 3.5 g (69%); mp 155–158 °C (Table II).

2,2':6',2'':6'',2''':6''',2''''-Quinquepyridine (12j). 4',4'''-Bis(*n*-propylthio)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (**12b**) (0.54 g, 1.0 mmol), absolute EtOH (35 mL) and $NiCl_2 \cdot 6H_2O$ (4.75 g, 20.0 mmol) were added to a previously flame-dried apparatus, and after being stirred for 20 min, the mixture was cooled in an ice-water bath. A suspension of $NaBH_4$ (2.27 g, 60.0 mmol) in 40% aqueous NaOH solution (14.2 mL) was added dropwise over 2 h while the temperature was maintained at 0–5 °C. After the addition funnel was replaced with a reflux condenser, the thick black heterogeneous mixture was refluxed for 24 h. The hot mixture was then filtered through a sintered glass funnel, and the solid black residue was collected, dried, and placed in a continuous extraction thimble and extracted with hot $CHCl_3$. After removal of the $CHCl_3$, the crude solid product was recrystallized from hexane/$CHCl_3$, yielding colorless, irregular prisms: 160 mg (40%); mp 273–276 °C (lit.[11a] mp 267–268 °C) (Table II).

4,4'''-Dimethyl-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (12c). Anhydrous, thiophene-free benzene (200 mL) and $(PPh_3)_2NiCl_2$ (4.9 g, 7.5 mmol) were added to a previously flame-dried apparatus, followed by CH_3MgBr (30 mL of a 3.0 M solution in Et_2O, 90.0 mmol), which was injected into the flask via needle and syringe. The dark mixture was stirred for 15 min and then heated to 40 °C. A warm solution of 4',4'''-bis(methylthio)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (**12a**) (6.0 g, 12.5 mmol) and benzene (800 mL) was transferred under N_2 pressure to the reaction mixture from a round-bottom flask through a double-ended needle. The resultant dark green mixture was then heated at 60 °C for 4 days. After the reaction was quenched with CH_3OH (25 mL) and a saturated, aqueous NH_4Cl solution (300 mL), the resultant mixture was filtered through a sintered glass funnel, and the filtrate layers were separated. The organic layer was washed with water (1 × 100 mL), dried over Na_2SO_4, and evaporated to give a brown solid. The aqueous layer was extracted with $CHCl_3$ (3 × 50 mL), and the extracts were reserved. The brown residue that was collected above was washed with copious volumes of $CHCl_3$, and all the $CHCl_3$ fractions were combined, dried over Na_2SO_4, and evaporated to dryness, yielding additional product. Purification of the crude product was best accomplished by first washing with hot CH_3OH and then dissolving the semipure product containing some starting material in a small amount of $CHCl_3$ and applying it to a $^3/_4$-in. × 12-in. alumina column. Elution with hexane/EtOAc (9:1) effected separation of the product and starting material, with the dimethyl compound being eluted first. After removal of the solvent, the product crystallized as colorless microneedles from EtOAc: 2.6 g (50%); mp 230–232 °C (Table II).

4'-Methyl-4'''-(2-methoxyethyl)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (12g) and 4',4'''-Bis(2-methoxyethyl)-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (12f). In a flame-dried apparatus, 4',4'''-dimethyl-2,2':6',2'':6'',2''':6''',2''''-quinquepyridine (**12c**) (200 mg, 0.50 mmol) dissolved

in anhydrous THF (25 mL) was cooled to −20 °C. The addition funnel was filled via needle and syringe with anhydrous THF (5 mL), 2,2,6,6-tetramethylpiperidine (0.25 mL, 210 mg, 1.50 mmol), and CH_3Li (1.06 mL of a 1.41 M solution in ether, 1.50 mmol). The contents of the addition funnel were agitated to facilitate reaction of the base and the organolithium reagent. When gas (CH_4) evolution had subsided, the lithiotetramethylpiperidide solution was added dropwise to the original reaction mixture over 35 min at −20 °C. The resultant deep purple mixture was stirred for an additional 30 min at −20 °C, and bromomethyl methyl ether (0.15 mL, 0.23 g, 1.8 mmol) was injected into the mixture all at once. After being stirred at −20 °C for 4 h, the yellow mixture was then slowly warmed to 25 °C over a 12-h period, and finally the reaction was quenched with distilled H_2O (15 mL). Removal of the THF produced a brown oil which was extracted from the aqueous layer with CH_2Cl_2 (3 × 10 mL). The extracts were combined and dried (Na_2SO_4); and the solvent was removed, giving a yellow oil which solidified upon standing. The product was a mixture of monoalkylated and dialkylated quinquepyridinyl derivatives **12g** and **12f** which were separated by column chromatography. The above crude mixture was dissolved in a small amount of CH_2Cl_2, applied to an alumina column, and eluted with hexane:EtOAc (10:1). The monoalkylated product **12g** was eluted first, and, after removal of solvent, a colorless solid (40 mg, 17%) was isolated. Recrystallization of this solid from cyclohexane produced colorless microneedles: mp 141–144 °C (Table II).

The dialkylated product **12f** was eluted second, and, after removal of solvent, a colorless solid resulted. Recrystallization from cyclohexane produced colorless microneedles: 100 mg (48%); mp 177–179 °C (Table II).

4′-Methyl-4‴-vinyl-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (12e). KBu^{t}O (200 mg, 1.8 mmol) and anhydrous THF (25 mL) were added to a flame-dried apparatus, and a solution of 4′-methyl-4‴-(2-methoxyethyl)-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (**12g**) (300 mg, 0.65 mmol) in anhydrous THF (25 mL) was then added dropwise over 1 h. After the mixture was stirred for an additional 2 h, the reaction was quenched with H_2O (100 mL), and a pale yellow solid precipitated. After removal of the THF, the product was collected and air dried. The filtrate was extracted with $CHCl_3$ (3 × 25 mL), the extracts were combined and dried (Na_2SO_4), and the $CHCl_3$ was removed, yielding a small amount of product which was combined with that above. Recrystallization from cyclohexane produced colorless microprisms: 0.2 g (72%); mp 214–216 °C (Table II).

4′,4‴-Divinyl-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (12d). KBu^{t}O (250 mg, 2.2 mmol) and anhydrous THF (25 mL) were added to a flame-dried apparatus, and a solution of 4′,4‴-bis(methoxyethyl)-2,2′:6′,2″:6″,2‴:6‴,2⁗-quinquepyridine (**12f**) (200 mg, 400 μmol) dissolved in THF (25 mL) was added dropwise over 1 h. After the mixture was stirred for an additional 2 h, it was poured into cold H_2O (100 mL), and the colorless solid which precipitated was collected and air dried. The filtrate was extracted with $CHCl_3$ (3 × 20 mL), the extracts were combined and dried (Na_2SO_4), and the $CHCl_3$ was removed, yielding a small amount of additional product. Recrystallization from cyclohexane produced colorless microneedles: 120 mg (68%); mp 237–239 °C (Table II).

4′,4⁗-Bis(methylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′-sexipyridine[28] (12h). KBu^{t}O (2.00 g, 8.96 mmol) and anhydrous THF (100 mL) were added to a flame-dried apparatus, and after the resultant suspension was stirred for 15 min, 6,6′-diaetyl-2,2′-bipyridine[20b] (960 mg, 4.00 mmol) dissolved in THF (15 mL) was added all at once. The resultant yellow solution was stirred for an additional 15 min, and a solution of 3,3-bis(methylthio)-1-(2-pyridinyl)propen-1-one (**2a**) (1.83 g, 8 mmol) in THF (5 mL) was then added, and the resultant red mixture was stirred for 24 h. NH_4OAc (11 g, 148 mmol) and glacial AcOH (56 mL) were then added, and the resultant mixture was refluxed for 4 h with continuous removal of the THF. After the remaining dark residue was cooled to 25 °C, it was poured onto ice (800 g) and allowed to stand for 12 h. The crude product which separated was collected, washed with cold H_2O, air dried, and recrystallized first from DMF and then from $CHCl_3$, affording beige needles: 1.10 g (50%): mp 291–292 °C (Table II).

4′,4⁗-Bis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′-sexipyridine[28] (12i). Using the above procedure, 6,6′-diacetyl-2,2′-bipyridine[20b] (480 mg, 2.00 mmol) and 3,3-bis(*n*-propylthio)-1-(2-pyridinyl)propen-1-one (**2b**) (1.17 g, 4.17 mmol) were combined to give a crude product which was recrystallized first from DMF and then from benzene, affording beige needles of **12i**: 460 mg (38%); mp 224–226 °C (Table II).

4′,4″,4⁗,4⁗′-Tetrakis(methylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″-septipyridine (13a). KBu^{t}O (500 mg, 4.4 mmol, 10% excess), 6-acetyl-4-(methylthio)-2,2′-bipyridine (**4a**) (500 mg, 2.0 mmol), and anhydrous THF (10 mL) were mixed in a flame-dried apparatus, and a solution of 2,6-bis[3,3-bis(methylthio)-1-oxopropen-1-yl]pyridine (**9a**) (380 mg, 1.0 mmol) in warm THF (30 mL) was added dropwise over 2 h. The resultant red heterogeneous mixture was stirred at 25 °C for 26 h. NH_4OAc (1.55 g, 20.0 mmol) and glacial AcOH (10 mL) were then added, and the resultant solution was refluxed for 2 h with continuous removal of the THF. (Note: The poorly soluble septipyridine began precipitating shortly after the reaction reached reflux temperature.) After the remaining acidic residue was cooled to 25 °C, it was poured onto ice (50 g), diluted to 75 mL with cold H_2O, and allowed to stand for 3 h. The orange-colored product which separated was collected, washed with H_2O, and air dried (0.60 g, 83%). Recrystallization from DMF afforded tan microneedles: 0.20 g (28%), mp 352–354 °C dec (Table V).

4′,4⁗′-Bis(methylthio)-4″,4⁗″-bis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″:6⁗″,2⁗‴-septipyridine (13b). KBu^{t}O (2.0 g, 17.8 mmol), 6-acetyl-4-(methylthio)-2,2′-bipyridine (**4a**) (2.0 g, 8.2 mmol), and anhydrous THF (70 mL) were mixed in a flame-dried apparatus, and, after this yellow solution was stirred for 10 min, 2,6-bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]pyridine (**9b**) (2.0 g, 4.0 mmol) in THF (70 mL) was added dropwise over 2 h. The resultant deep red mixture was then stirred at 25 °C for 23 h, NH_4OAc (6.2 g, 80.2 mmol) and glacial AcOH (40 mL) were added, and the mixture was refluxed for 2 h with continuous distillation of the THF. The resultant orange heterogeneous mixture was cooled to 25 °C, poured onto ice (400 g), diluted to 300 mL with cold H_2O, and set aside for 5 h. The crude product which separated was collected, washed with H_2O, and air dried (3.52 g, 95%). Recrystallization from $CHCl_3$ produced tan microneedles: 1.50 g (50%), mp 259–260 °C dec (Table V). The ^1H NMR data are described in Table IV.

4′,4⁗′-Bis(methylthio)-4″,4⁗″-bis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″:6⁗″,2⁗‴-octipyridine (14). KBu^{t}O (500 mg, 4.4 mmol, 10% excess), 6-acetyl-4-(methylthio)-2,2′-bipyridine (**4a**) (500 mg, 2.0 mmol), and anhydrous THF (25 mL) were mixed in a flame-dried apparatus, and 6,6′-bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]-2,2′-bipyridine (**9d**) (570 mg, 1.0 mmol) in THF (5 mL) was then added dropwise. The resultant bright red mixture was stirred at 25 °C for 24 h, followed by the addition of NH_4OAc (1.54 g, 20.0 mmol) and glacial AcOH (10 mL). The condenser was replaced with a distillation head, and the reaction mixture was then refluxed for 2 h with continuous removal of the THF. The resultant acidic residue was cooled to 25 °C, poured onto ice, diluted with cold water to 50 mL, and allowed to stand for 3 h. The crude product which separated was collected, washed with H_2O, air dried (670 mg, 78%), and recrystallized from $CHCl_3$, separating as colorless, irregular prisms: 420 mg (49%); mp 310–312 °C dec (Table V). The ^1H NMR data are listed in Table IV.

4′,4⁗′′-Bis(methylthio)-4‴,4⁗′′-bis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″:6⁗″,2⁗‴:6⁗‴,2⁗′′-novipyridine (15a). KBu^{t}O (250 mg, 2.2 mmol, 10% excess) and anhydrous THF (25 mL) were mixed in a flame-dried apparatus, and 6-acetyl-4′-(methylthio)-2,2′:6′,2″-terpyridine (**4c**) (320 mg, 1.0 mmol) was then added to the mixture with stirring, followed by 2,6-bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]pyridine (**9b**) (240 mg, 500 μmol). The resultant red heterogeneous mixture was stirred at 25 °C for 21 h. NH_4OAc (770 mg, 10.0 mmol) and glacial AcOH (5 mL) were then added, and the resultant mixture was refluxed for 2 h with continuous removal of the THF. The remaining acidic residue was cooled to 25 °C, poured over ice (25 g), diluted with cold H_2O to 50 mL, and allowed to stand for 3 h. The pale orange product which separated was collected, washed with H_2O, and air dried, giving a crude yield of 380 mg (81%). Recrystallization from $CHCl_3$ afforded tan microprisms: 240 mg (51%); mp 333–335 °C dec (Table VI).

4′,4‴,4⁗′,4⁗′′-Tetrakis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗,2⁗′:6⁗′,2⁗″:6⁗″,2⁗‴:6⁗‴,2⁗′′-novipyridine (15b). Anhydrous THF (20 mL), KBu^{t}O (300 mg, 2.7 mmol, 10% excess), and a solution of 2-acetyl-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (**4d**) (420 mg, 1.2 mmol) in THF (5 mL) were mixed in a flame-dried apparatus, and a suspension of 2,6-bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]pyridine (**9b**) (290 mg, 600 μmol) in THF (5 mL) was then added. The resultant bright red heterogeneous mixture was stirred at 25 °C for 24 h. NH_4OAc (0.92 g, 12.0 mmol) and glacial AcOH (10 mL) were added, and the mixture was refluxed for 2 h. During the last hour of reflux, the THF was distilled off. After the mixture was cooled to 25 °C, it was poured into ice–water (50 g) and allowed to stand for 3 h. The orange-brown solid that separated was collected, washed well with H_2O, and air dried to give the crude novipyridinyl **15b**: 580 mg (97%). Recrystallization

(28) We thank Dr. P. Ralli for the initial preparation of these compounds.

from $CHCl_3$ afforded colorless microprisms: 210 mg (35%); mp 307–309 °C dec (Table VI). ^1H NMR data are listed in Table IV.

4′,4‴″,4⁗″,4⁗′″-Bis(methylthio)-4‴,4⁗″-bis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗′,2⁗″:6⁗″,2⁗‴:6⁗‴,2⁗⁗:6⁗⁗,2⁗⁗′:6⁗⁗′,2⁗⁗″:6⁗⁗″,2⁗⁗‴-decipyridine (16a). KBu^{t}O (250 mg, 2.2 mmol, 10% excess), 6-acetyl-4′-(methylthio)-2,2′:6′,2″-terpyridine (**4c**) (320 mg, 1.0 mmol), and anhydrous THF (25 mL) were mixed in a flame-dried apparatus. 6,6′-Bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]-2,2′-bipyridine (**9d**) (280 mg, 500 μmol) was then added to the stirred solution, and the stirring of the resultant red heterogeneous mixture was continued at 25 °C for 21 h. NH_4OAc (770 mg, 10.0 mmol) and glacial AcOH were added, and the mixture was refluxed for 2 h, during which time the THF was removed and a pale orange solid precipitated. After being cooled to 25 °C, the acidic residue was poured onto ice (50 g) and allowed to stand for 12 h. The crude solid which separated was collected, washed with H_2O, and air dried, yielding 430 mg (85%). Recrystallization from DMF afforded tan microprisms: 270 mg (53%); mp 345–348 °C dec (Table VI).

4′,4‴,4⁗″,4⁗′″-Tetrakis(*n*-propylthio)-2,2′:6′,2″:6″,2‴:6‴,2⁗:6⁗′,2⁗″:6⁗″,2⁗‴:6⁗‴,2⁗⁗:6⁗⁗,2⁗⁗′:6⁗⁗′,2⁗⁗″:6⁗⁗″,2⁗⁗‴-decipyridine (16b). KBu^{t}O (300 mg, 2.7 mmol, 10% excess), 6-acetyl-4′-(*n*-propylthio)-2,2′:6′,2″-terpyridine (**4d**) (420 mg, 1.2 mmol), and anhydrous THF (20 mL) were mixed in a flame-dried apparatus, and a suspension of 6,6′-bis[3,3-bis(*n*-propylthio)-1-oxopropen-1-yl]-2,2′-bipyridine (**9d**) (0.34 g, 0.6 mmol) in THF (20 mL) was added. The resultant red heterogeneous mixture was stirred at 25 °C for 24 h. NH_4OAc (920 mg, 12.0 mmol) and glacial AcOH (10 mL) were added, and the mixture was refluxed for 2 h with continuous removal of the THF. The acidic residue was poured into ice–water (50 g) and set aside for 3 h. The orange solid which precipitated was collected, washed with H_2O, and air dried, giving a crude yield of 520 mg (81%). The desired product crystallized from DMF as colorless, irregular prisms: 60 mg (9%); mp 314–315 °C dec. The DMF was diluted with water, and the solid which precipitated was collected, air dried, and recrystallized from DMF to give a second crop: 150 mg (24%); mp 311–312 °C (Table VI).

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Supplementary Material Available: Full details of the X-ray structural determination including crystal data, atomic coordinates, isotropic thermal parameters, bond lengths, bond angles, anisotropic thermal parameters, H-atom coordinates, and isotropic thermal parameters (6 pages). Ordering information is given on any current masthead page.