was purified by distillation from calcium hydride. Infrared spectra were recorded on a Perkin-Elmer Model 710B infrared spectrometer. ^1H magnetic resonance spectra were determined on a Varian EM-360A, XL-300, or Bruker WH 90D spectrometer and are reported relative to tetramethylsilane. ^{13}C magnetic resonance spectra were determined on a Bruker WH 90D spectrometer and are reported relative to tetramethylsilane. ^{19}F magnetic resonance spectra were measured on a Varian XL-300 spectrometer and are reported relative to CCl_3F. Analytical samples were prepared by column chromatography on silical gel 200-425 (Davisil). Combustion analyses were performed by MicAnal (Tucson, AZ).

***N,N*-Dimethylfluoroacetamide.** To 30 mL of anhydrous diethyl ether at 0 °C containing 3.6 g (0.08 mol) of dimethylamine (Matheson) and 10.0 g of anhydrous potassium carbonate was dropwise added slowly 3.84 g (0.04 mol) of fluoroacetyl chloride (prepared by treatment of sodium fluoroacetate (Sigma) with phthaloyl chloride,[7] bp 65–71 °C) dissolved in 20 mL of anhydrous ether. After stirring at room temperature overnight, the product was filtered and concentrated in vacuo. The crude product, a colorless oil, isolated quantitatively, was used without further purification: ^1H NMR ($CDCl_3$) δ 4.72 (d, $J_{F,H}$ = 48 Hz, 2 H, CH_2F), 2.68 (d, $J_{F,H}$ = 2 Hz, 6 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 166.1 (d, $J_{F,C}$ = 19.53 Hz, C=O), 78.6 (d, $J_{F,C}$ = 176.3 Hz, CH_2F), 34.91 (d, $J_{C,F}$ = 4.1 Hz, CH_3), 34.64 (CH_3); ^{19}F NMR ($CDCl_3$) δ −227.54 (t, $J_{F,H}$ = 45.8 Hz).

***N*-(Fluoroacetyl)pyrrolidine** was prepared as above. Crude product was a yellow solid which was purified by recrystallization from hexanes: mp 43–44 °C; ^1H NMR ($CDCl_3$) δ 4.85 (d, $J_{F,H}$ = 47 Hz, 2 H, CH_2F), 3.47 (t, 6.8 Hz, 2 H), 3.37 (t, 6.8, 2 H), 1.93 (p, 6.4, 2 H), 1.81 (p, 6.4, 2 H); ^{13}C NMR ($CDCl_3$) δ 165.3 (d, $J_{F,C}$ = 19.1 Hz, C=O), 79.8 (d, $J_{F,C}$ = 179.3 Hz, CFH_2), 46.0, 45.1 (d, $J_{F,C}$ = 5.0 Hz), 26.0, 23.50; ^{19}F NMR ($CDCl_3$) δ −227.75 (t, $J_{F,H}$ = 45.8 Hz).

Anal. Calcd for $C_6H_{10}FNO$: C, 54.95; H, 7.69. Found: C, 54.54; H, 7.73.

***N,N*-Diisopropylfluoroacetamide** was prepared as described and purified by recrystallization from hexanes or pentane: mp 61–62 °C; ^1H NMR ($CDCl_3$) δ 4.8 (d, $J_{F,H}$ = 47.4 Hz, 2 H, CH_2F), 3.67 (m, 1 H, CH), 4.3 (m, 1 H, CH), 1.37 (d, 6 H, $J_{H,H}$ = 5.86 Hz, $(CH_3)_2$), 1.17 (d, 6 H, $J_{H,H}$ = 5.37 Hz, $(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 165.2 (d, $J_{F,C}$ = 18.1 Hz, C=O), 80.24 (d, $J_{F,C}$ = 177.3 Hz, CH_2F), 47.57 (CH), 45.85 (CH), 20.59 (CH_3), 20.11 (CH_3); ^{19}F NMR ($CDCl_3$) δ −224.67 (t, $J_{F,H}$ = 45.8).

Anal. Calcd for $C_8H_{16}FNO$: C, 59.60; H, 10.00. Found: C, 59.70; H, 10.08.

Typical Procedure for Enolate Formation and Aldol Reaction with *N,N*-Dimethylfluoroacetamide and *N*-(Fluoroacetyl)pyrrolidine. To a stirred round-bottomed flask containing 20 mL of anhydrous THF and 0.31 mL (0.0022 mol) of diisopropyl amine at 0 °C was added 1.4 mL (0.0022 mol) of a 1.5 M solution of methyllithium in diethyl ether. After 10 min of stirring at 0 °C and cooling to −85 °C, 0.002 mol of either *N,N*-dimethylfluoroacetamide or *N*-(fluoroacetyl)pyrrolidine dissolved in 2 mL of THF was added dropwise. After 5 additional min, 0.001 mol of the carbonyl compound dissolved in 2 mL of THF was rapidly added. The mixture was stirred for 5 min longer and then was quenched with 10 mL of saturated ammonium chloride. On warming to room temperature the mixture was diluted with 20 mL of distilled hexanes and was separated and the aqueous phase was extracted with three 10-mL portions of diethyl ether. The combined organic phases were washed twice with 20 mL of water, were dried over anhydrous magnesium sulfate, and were concentrated in vacuo to yield the crude product.

Typical Procedure for Enolate Formation and Directed Aldol Reaction with *N,N*-Diisopropylfluoroacetamide. LDA (0.015 mol) was prepared as described above in 20 mL of THF. After cooling to −75 °C, 0.24 g (0.0015 mol) of *N,N*-diisopropylfluoroacetamide dissolved in 2 mL of THF was added. After an additional hour at −75 °C, the substrate carbonyl compound (0.001 mol) dissolved in 2 mL of THF was rapidly added and was allowed to stir for 30 min. The reaction mixture was quenched and the products were isolated as described above.

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Supplementary Material Available: Complete spectral and analytical data for all new compounds are available (11 pages). Ordering information is given on any current masthead page.

Synthesis of 4-, 5-, and 6-Methyl-2,2′-bipyridinyls[1]

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2,2′-Bipyridinyls continue to attract appreciable attention with practical applications ranging from effective herbicides[2a] to important ligands of great interest for chelation of transition metals, the ruthenium complexes being useful for photochemical generation of hydrogen from water and in chemically modified electrode studies.[2b] 2,2′-Bipyridinyls are prepared by four principal routes: (a) from the reaction of 2,2′-bipyridnyl with alkyllithium reagents[3] that leads to isomeric products; (b) from an α,β-unsaturated ketone and an appropriately substituted acylpyridinium salt in the presence of hot ammonium acetate/acetic acid[4] (the Kröhnke procedure); (c) by coupling reactions of pyridine *N*-oxides with pyridine,[5] or nickel–phosphine complex mediated homocoupling of halopyridines;[6] (d) by radical substitution of 2,2′-bipyridinyl complexes of iron(III), ruthenium(III), or osmium(III), the methyl radicals being generated[7] by thermolysis of acetyl peroxide or by oxidative cleavage of alkyl metals such as $(CH_3)_4Sn$, $(CH_3)_4Pb$, or $(CH_3)_2Hg$. These methods lead to symmetrically substituted 2,2′-bipyridinyls or result in complex mixtures of isomers and fail to provide a general method for the convenient synthesis of a monoalkyl-2,2′-bipyridinyl.

We now describe unambiguous syntheses of 4-, 5- and 6-methyl-2,2′-bipyridinyls from the appropriate α-oxoketene dithioacetals and the enolate of a suitable carbonyl compound. Two choices exist for the synthesis of a 2,2′-bipyridinyl by this route: the reaction of 2-acetylpyridine with an appropriately functionalized α-oxoketene dithioacetal or, conversely, the reaction of an α-oxoketene dithioacetal derived from 2-acetylpyridine with the enolate of an appropriate carbonyl compound.

The syntheses of 6- and 5-methyl-2,2′-bipyridinyls were the most straightforward of the isomeric series (Scheme I). Thus, reaction of equimolar quantities of 3,3-bis(methylthio)-1-(2-pyridinyl)-2-propen-1-one (1) with the

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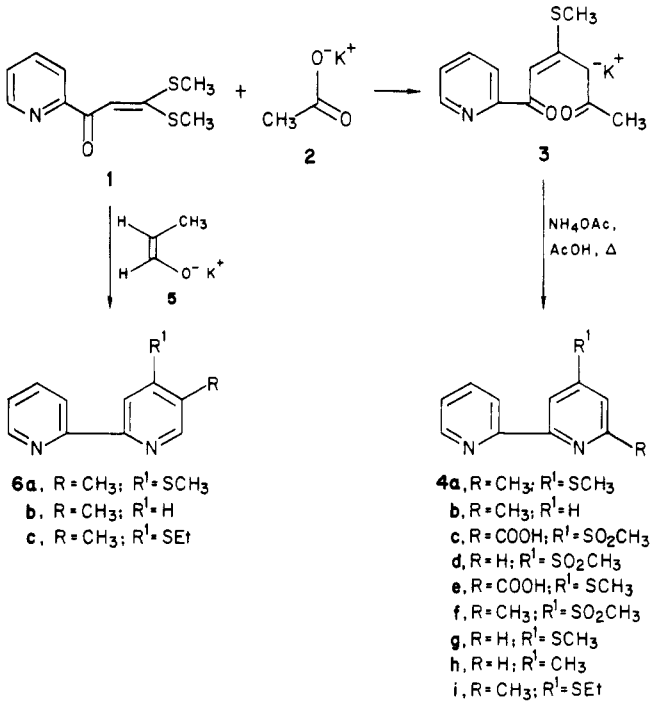
Table I. Unsymmetrically Substituted 2,2′-Bipyridinyls

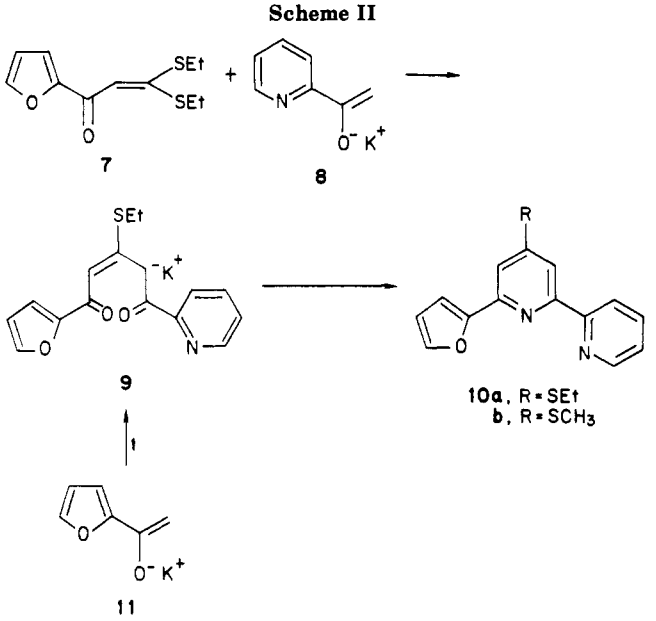
compd	yield, %	mp/bp, °C/mm	phys char	mol formula[a]	M^+:m/e (% rel intens)
4a	94	42–44	colorless irreg prisms[b]	$C_{12}H_{12}N_2S$	216 (100)
4i	37	45–47	colorless irreg prisms[b]	$C_{13}H_{14}N_2S$	230 (96)
4b	73	73/0.02	pale yellow oil[c,d]	$C_{11}H_{10}N_2$	170 (100)
6a	44	86–87	colorless irreg prisms[b]	$C_{12}H_{12}N_2S$	216 (94)
6c	47	59–60	tan irreg prisms[b]	$C_{13}H_{14}N_2S$	230 (95)
6b	77	92/0.05	colorless liquid[c]	$C_{17}H_{13}N_5O_7$[e]	170 (100)
10a	25	74–76	light yellow irreg prisms[b]	$C_{16}H_{14}N_2OS$	283 (100)[e]
10b	87	80–82	colorless needles[g]	$C_{15}H_{12}N_2OS$	268 (64)
4c	66	222–224 dec	tan irreg prisms[h]	$C_{12}H_{10}N_2O_4S$	278 (55)
4d	67	108–110	yellow irreg prisms[g]	$C_{11}H_{10}N_2O_2S$	235 (100)[f]
4f	55	120–122	colorless needles[g]	$C_{12}H_{12}N_2O_2S$	248 (50)
4e	84	206–208 dec	gold irreg prisms[g]	$C_{12}H_{10}N_2O_2S$	247 (14)[f]
4g	84	40–42	colorless irreg prisms[b]	$C_{11}H_{10}N_2S$	203 (100)[f]
4h	86	62–64	colorless needles[b]	$C_{17}H_{13}N_5O_7$[e]	170 (100)
13	52	59–61	colorless needles[i]	$C_{15}H_{18}N_2S$	258 (90)

[a] All compounds reported gave satisfactory analytical data (±0.4%; C, H, N). [b] Recrystallized from *n*-hexane. [c] Purified by high-vacuum distillation. [d] Compound previously reported[16] and characterized as picrate, mp 163–164 °C lit.[3] mp 163–165.5 °C). [e] Analyzed as the monopicrate, mp 151–153 °C. [f] Data correspond to the (M^+ + 1) from chemical ionization spectrum. [g] Recrystallized from ethanol. [h] Recrystallized from 1,2-dimethoxyethane/hexane. [i] Recrystallized from ethanol/water. ^1H NMR data (200 MHz) ($CDCl_3$ except **4c**, Me_2SO-d_6) showed following ranges: aromatic protons δ 6.30–8.90; SCH_3 δ 2.56–2.84; 4-CH_3 δ 2.45; 5-CH_3 δ 2.32–2.49; 6-CH_3 δ 2.55–2.58; SCH_2CH_3 δ_{CH_2} 3.10–3.22, δ_{CH_3} 1.37–1.50; SO_2CH_3 δ 3.08–3.40.

Scheme I



Scheme II



potassium enolate (**2**) of acetone gave the bright green potassium salt **3** of the 1,5-enedione which, without attempted isolation, was treated in situ with ammonium acetate (2 equiv) in hot acetic acid. High-vacuum distillation (10^{-6} mm) of the above resultant oil afforded a 72% yield of 6-methyl-4-(methylthio)-2,2′-bipyridinyl (**4a**) as a pale yellow liquid that soon solidified. The optimum yield of **4a** resulted when formation of **3** was carried out in concentrated solution, e.g., 44 mmol of **1** in 250 mL of THF, and the crude **4a** was purified by column chromatography. Desulfurization of **4a** and **4b** was most satisfactorily carried out with nickel boride[8] and afforded 6-methyl-2,2′-bipyridinyl (**4b**) as a light yellow oil in 72% yield. Other alkyl groups attached to the sulfur atoms in **1** may also be used, the *S*-ethyl derivative **4i** affording **4b** in 73% overall yield.

5-Methyl-2,2′-bipyridinyl (**6b**) was synthesized in an analogous reaction sequence using the potassium enolate of propionaldehyde. The bipyridinyl **6b** was obtained[9] previously as a degradation product of Streptonigrin, and our characterization data provide confirmation of this initial assignment (Experimental Section).

4-(Methylthio)-2,2′-bipyridinyl (**4g**) was obtained in only 2% yield from **1** with the enolate of acetaldehyde. A more satisfactory method was condensation of the enolate **8** with 3,3-bis(ethylthio)-1-(2-furyl)-2-propen-1-one (**7**) to give **10a** in 25% yield or, better, the enolate **11** with **1** (87%) (Scheme II). For conversion of **4g** into 4-methyl-2,2′-bipyridinyl (**4h**), the oxidative removal of the furan substituent was effected with molecular oxygen in the presence of potassium *tert*-butoxide in DMF,[11] the carboxylic acid **4e** being obtained in 84% yield (Table I) from **4a** under these conditions. Thermal decarboxylation of the acid **4e**

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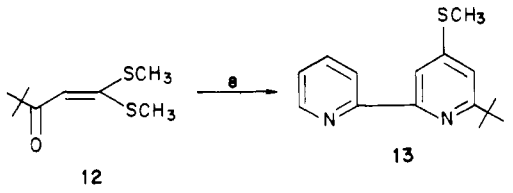
Scheme III



in diphenyl ether at 240 °C occurred readily, giving **4g** in 84% yield. Introduction of the desired methyl substituent involves a nickel-mediated coupling reaction of methylmagnesium bromide with **4g**. This reaction type has been utilized[12] to couple a variety of Grignard reagents with several aliphatic, aromatic, and heteroaromatic thiols and sulfides, and in this instance, bis(triphenylphosphine)-nickel(II) chloride in refluxing diethyl ether gave 4-methyl-2,2′-bipyridinyl (**4h**) in 86% yield (Table I). It is interesting to note that oxidation of **4a** with $KMnO_4$ only resulted in sulfone formation without any oxidation of the methyl group (compound **4f**) and with *m*-chloroperbenzoic acid compound **4a** also gave **4f** (73%) with no *N*-oxide formation being observed.

Oxidation of **10b** with excess $KMnO_4$ in acetone resulted in cleavage of the furan ring to a carboxyl group, but also conversion of the methylthio group into a sulfone group, giving **4c** whose spectral characteristics are listed in Table I. Decarboxylation of **4c** occurred on heating in diphenyl ether to give **4d** whose structure was confirmed by oxidation of 4-(methylthio)-2,2′-bipyridinyl with ether *m*-chloroperbenzoic acid or with potassium permanganate using standard procedures.

The above synthetic routes now make readily available a variety of alkyl-substituted 2,2′-bipyridinyls from readily accessible starting materials. For example, introduction of a 2-*tert*-butyl substituent as in **13** results from the reaction of 4,4-dimethyl-1,1-bis(methylthio)-1-pentene-3-one (**12**) with the potassium enolate 8 of 2-acetylpyridine by using the above reaction procedure (Scheme III). The yield of **13** was 52% (Table I). The potential for displacement of the methylthio group with a variety of Grignard reagents further extends the utility of this approach.

As the success of these and related transformations depends on a reliable route to α-oxoketene dithioacetals, we have developed two general procedures suitable for the majority of potential applications. The use of potassium *tert*-butoxide in THF provides a much simplified experimental procedure for the direct generation of a vareity of ketene dithioacetals. By varying the order of addition of the reagents, this method has been successfully employed to convert aromatic and heteryl methyl ketones, aliphatic ketones, esters, and aldehydes into the corresponding ketene dithioacetals in moderate to good yields. These variations are described to two procedures (Experimental Section). With an active methylene compound containing only one enolizable site, the best results were obtained when the ketone was added to a stirred solution of 2 equiv of potassium *tert*-butoxide in THF, followed by sequential addition of carbon disulfide and methyl iodide (method A). With compounds likely to undergo self-condensation, e.g. esters, a procedure using slow addition of an equimolar solution of carbon disulfide and the methylene compounds to a stirred solution of 2 equiv of potassium *tert*-butoxide in THF, followed by addition of methyl iodide, gave satisfactory results (method B).

The generation of monoketene dithioacetals from compounds containing two enolizable sites, e.g. acetone, 2-butanone, and 3-pentanone, has been complicated by competing reactions involving bis(ketene dithioacetal) formation and ring closure to a thiapyran-4-one. Acetone and 2-butanone readily formed the corresponding ketene dithioacetal by using method B, but 3-pentanone gave the thiapyranone exclusively with method B. When the enolate of acetone was generated in the presence of CS_2 and methyl iodide, 1,1,5,5-tetrakis(methylthio)-1,4-pentadien-3-one was obtained exclusively. Under related conditions both 2-butanone and 3-pentanone gave exclusively the thiapyran-4-ones. However, in addition to these limitations, aliphatic nitriles and nitro compounds and cyclic ketones gave only poor yields of the desired ketene dithioacetals. Ethyl acetate was converted into its ketene dithioacetal only in modest yield by using method B and was associated with its transesterification product *tert*-butyl 3,3-bis(methylthio)propenoate whose structure was verified by its synthesis from *tert*-butyl acetate under analogous conditions.

Experimental Section[13]

General Procedure for α-Oxoketene Dithioacetal Formation. Method A. Synthesis of 3,3-Bis(methylthio)-1-(2-pyridinyl)-2-propen-1-one (1). Potassium *tert*-butoxide (96.5 g, 0.86 mol) in freshly distilled THF (1000 mL) in a 3-L three-necked flask fitted with an efficient mechanical stirrer, a pressure-equalizing dropping funnel, and a reflux condenser attached to a nitrogen gas inlet was treated dropwise with freshly distilled 2-acetylpyridine (50.0 g, 0.41 mol) over a period of 5–10 min. After the mixture was stirred for 10 min carbon disulfide (32.7 g, 0.43 mol) was added followed by methyl iodide (122.1 g, 0.86 mol). The resultant tan mixture was stirred at room temperature for 12 h and poured into ice water (2000 mL), and the mixture diluted to 3000 mL with water and allowed to stand for 4 h. A light brown solid separated and was collected and recrystallized from ethanol from which yellow needles separated: 87.0 g (94%); mp 108 °C (lit.[14] mp 108 °C).

Ethyl 3,3-Bis(methylthio)-2-phenylpropenoate. Method B. After the apparatus above was purged with nitrogen, potassium *tert*-butoxide (6.5 g, 60.9 mmol) and anhydrous THF (150 mL) were added. An equimolar solution of ethyl phenylacetate (5.0 g, 30.5 mmol) and carbon disulfide (2.3 g, 30.5 mmol) was added dropwise followed by a similar addition of methyl iodide (8.6 g, 60.9 mmol). The cream-colored mixture was stirred at room temperature for 10 h, poured onto ice, diluted to 1000 mL with water, and allowed to stand. Chloroform extraction followed by drying the $CHCl_3$ extract over Na_2SO_4 and evaporation of the

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(13) Spectral characterizations were carried out on the following instruments: infrared spectra, Perkin-Elmer Model 298 or 337 grating infrared spectrophotometer; ^1H NMR spectra, Varian XL-200 or Hitachi Perkin-Elmer R-600 Fourier transform spectrometer with Me_4Si as an internal standard; mass spectra, Hitachi Perkin-Elmer RMU-6E (low-resolution spectrometer) utilizing the direct-insertion probe for solid samples with a variable gas/liquid inlet for perfluorokerosene standard and the Hewlett-Packard GC–MS system Model 5987A spectrometer. All melting points were determined in capillaries using a Thomas-Hoover capillary melting point apparatus or a Mel-temp apparatus and are unconnected. Evaporations were carried out under reduced pressure by using a Buchi Rotovap apparatus. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN, or Atlantic Microlab, Inc., Atlanta, GA. Anhydrous solvents were prepared and stored as follows: tetrahydrofuran (THF), stored over potassium hydroxide, refluxed and distilled over either metallic potassium or sodium/benzophenone; dimethyl sulfoxide (Me_2SO), stirred in the presence of calcium hydride, refluxed and distilled under reduced pressure; *N,N*-dimethylformamide (DMF), dried over calcium hydride, refluxed and distilled under reduced pressure and stored over 4-Å molecular sieves.

(14) Potts, K. T.; Cipullo, M. J.; Ralli, P.; Theodoridis, G. *J. Org. Chem.* **1982**, *47*, 3027.

$CHCl_3$ resulted in an orange oil. Purification by column chromatography (silica gel, hexane/5% acetone, v/v) afforded the desired product in a pure state; 7.0 g (85%).

General Procedure for Pyridine Ring Formation. Synthesis of 4-(Methylthio)-6-methyl-2,2′-bipyridinyl (4a). A 500-mL three-necked flask fitted with a mechanical stirrer, efficient reflux condenser, and nitrogen gas inlet was charged with anhydrous THF (250 mL) and 3,3-bis(methylthio)-1-(2-pyridinyl)-2-propen-1-one (1; 10.0 g, 0.04 mol). Acetone (2.8 g, 0.04 mol) was then added followed by potassium *tert*-butoxide (10.0 g, 0.08 mol). The mixture was stirred at room temperature for 10 h. During this period the reaction mixture assumed a green color, and the green potassium salt of the enedione separated. Ammonium acetate (14.0 g, 0.18 mol) and glacial acetic acid (300 mL) were added, and the nitrogen inlet was replaced with a distillation head fitted with a thermometer. THF was distilled off over a 3-h period, and the residual green solution after cooling was poured over ice and set aside for 3 h. The resultant green tar was extracted with chloroform, washed with water, and then dried over anhydrous sodium sulfate. After removal of the solvent the green oil was chromatographed on alumina and eluted with hexane/acetone (20:1). On distillation (bp 116–120 °C/(0.001 mm)) the distillate solidifed and was recrystallized from *n*-hexane from whence colorless irregular prisms separated: 9.1 g (94%); mp 42–44 °C (Table I).

General Procedure for Desulfurization Using Nickel Boride. Formation of 6-Methyl-2,2′-bipyridinyl (4b). A 1-L three-neck flask was fitted with an efficient mechanical stirrer, a pressure-equalizing dropping funnel, and a reflux condenser attached to a nitrogen inlet. The apparatus was charged with ethanol (300 mL of absolute), 4-(methylthio)-6-methyl-2,2′-bipyridinyl (**4a**; 5.0 g, 0.02 mol), and finely ground nickel chloride hexahydrate (55.0 g, 0.23 mol). The resultant green heterogeneous mixture was purged with nitrogen and cooled in an ice bath for ~15 min. Cautious dropwise addition of sodium borohydride (0.157 mL, 0.69 mol, 12% in 40% aqueous sodium hydroxide) initiated a vigorous exothermic reaction accompanied by hydrogen evolution. After completion of addition and the evolution of hydrogen had subsided, the dark heterogeneous mixture was warmed to room temerature and then refluxed for an additional 12 h. Hot filtration through a Celite pad followed by copious washings with hot ethanol and evaporation to dryness yielded a tan residue. Subsequent dilution with water (300 mL) followed by neutralization (AcOH), chloroform extraction, and reduction afforded a dark oil that was distilled under reduced pressure to yield a light yellow oil: 2.82 g (72%); bp 73 °C (0.02 mm) (lit.[15] bp 117–119 (0.1 mm)); monopicrate mp 163–164 °C (lit.[3] mp 163–165.5 °C).

4-(Methylsulfonyl)-2,2′-bipyridinyl-6-carboxylic Acid (4c). 2-(2-Pyridinyl)-4-(methylthio)-6-(2-furanyl)pyridine (2.0 g, 7.45×10^{-3} mol) and potassium permanganate (2.3 g, 0.01 mol) in dry acetone (400 mL) were stirred at room temperature until the purple color disappeared. An additional portion of potassium permanganate (3.5 g, 0.02 mol) was added and the mixture stirred until the purple color was again lost. This procedure was repeated three additional times over a 3-day period. The resultant purple–brown mixture was poured into water (750 mL) and stirred for 24 h and filtered twice to yield a light yellow solution (pH 8). Removal of the acetone by evaporation followed by acidification with H_2SO_4 (concentrated) (pH 4) and continuous chloroform extraction yielded a tan residue. Recrystallization from 1,2-dimethoxyethane/hexane afforded a tan powder: 1.37 g (66%); mp 222–224 °C dec.

4-(Methylsulfonyl)-2,2′-bipyridinyl (4d). 2-(2-Pyridinyl)-4-(methylsulfonyl)pyridine-6-carboxylic acid (1.0 g, 3.59×10^{-3} mol) and diphenyl ether (10 mL) were heated together slowly to 240 °C until the carbon dioxide evolution subsided. A black residue formed and was removed by filtration. The filtrate was diluted with diethyl ether (25 mL) and extracted with HCl (10%). Adjustment of the pH with ammonium hydroxide (concentrated) (pH 8) resulted in a tan precipitate that separated from ethanol as yellow irregular prisms: 0.56 g (67%); mp 108–110 °C.

4-(Methylthio)-2,2′-bipyridinyl-6-carboxylic Acid (4e). A 500-mL three-necked flask fitted with a magnetic stir bar, pressure-equalizing dropping funnel, and an oxygen gas inlet was charged with potassium *tert*-butoxide (5.2 g, 0.05 mol) and anhydrous DMF (200 mL). A solution of 4-(methylthio)-6-methyl-2,2′-bipyridinyl (**4a**) (5.0 g, 0.02 mol) in DMF (60 mL) was added dropwise. After stirring at room temperature for 30 min, the mixture began to thicken. Oxygen was then bubbled in for 45 min and the resultant mixture poured onto ice, diluted to 500 mL with water, neutralized with HCl (pH 6–7), extracted with chloroform, dried over anhydrous sodium sulfate, and evaporated to dryness to yield a tan residue. Recrystallization from ethanol afforded gold irregular prisms: 4.77 g (84%); mp 206–208 °C dec.

Decarboxylation of 4-(Methylthio)-2,2′-bipyridinyl-6-carboxylic Acid (4e). Formation of 4-(Methylthio)-2,2′-bipyridinyl (4g). The carboxylic acid **4e** (4.8 g, 0.02 mol) and diphenyl ether (50 mL) were heated together slowly to 240 °C until the carbon dioxide evolution subsided. After cooling to room temperature, the solution was diluted with Et_2O and extracted with hydrochloric acid (3 N) (5 × 25 mL). The hydrochloric acid phase was then cooled in an ice/water bath as the pH was adjusted with ammonium hydroxide (concentrated) (pH 8). Chloroform extraction followed by drying over anhydrous sodium sulfate and evaporation under reduced pressure yielded a brown oil that ws purified via column chromatography using neutral alumina with *n*-hexane/acetone (20:1) as eluent. Recrystallization from cold *n*-hexane afforded colorless irregular prisms: 3.29 g (84%); mp 40–42 °C.

4-Methyl-2,2′-bipyridinyl (4h). A 250-mL three-necked flask was fitted with an efficient reflux condenser, rubber septum, magnetic stir bar, and nitrogen gas inlet. The apparatus was purged with nitrogen and while under a positive pressure, was charged with bis(triphenylphosphine)nickel(II) chloride (0.5 g, 7.50×10^{-4} mol), anhydrous diethyl ether (50 mL), and methylmagnesium bromide (2.88 mL, 7.50×10^{-3} mol, 2.6 M in *n*-hexane), and was stirred at room temperature for 10 min. The resultant red–brown solution was then treated with a solution of 4-(methylthio)-2,2′-bipyridinyl (**4g**; 1.0 g, 4.94×10^{-3} mol) in anhydrous diethyl ether (50 mL). The brown solution was refluxed for 48 h, cooled to room temperature, poured into a saturated ammonium chloride solution (400 mL), stirred for 15 min, and filtered and the filtrate extracted with chloroform. The extract was then dried over anhydrous sodium sulfate and evaporated under reduced pressure to yield a brown oil. This material was extracted with boiling *n*-hexane, reduction of which afforded a tan residue that separated from *n*-hexane as colorless needles: 0.74 g (86%) (Table I); monopicrate mp 144–146 °C.

Ethyl 3,3-Bis(methylthio)propenoate. Method B. Apparatus of the type above was purged with nitrogen, and while under positive pressure potassium *tert*-butoxide (12.7 g, 113.5 mmol) and anhydrous THF (200 mL) were added. An equimolar solution of ethyl acetate (5.0 g, 56.7 mmol) and carbon disulfide (4.3 g, 56.74 mmol) was added dropwise, followed by the similar addition of methyl iodide (16.1 g, 113.5 mmol). The cream-colored mixture was stirred at room temperature for 10 h, poured onto ice, diluted to 1000 mL with water, and set aside. Chloroform extraction followed by drying the $CHCl_3$ extract over Na_2SO_4 and evaporation resulted in a red-orange oil that on preparative HPLC (hexane) produced two major fractions. The first fraction gave the desired product that separated from *n*-hexane as colorless needles, mp 44–45 °C; IR (KBr) ν_{CO} 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.53 (s, 1, vinyl), 4.15 (q, 2, OCH_2CH_3, J = 7.2 Hz), 2.47 (s, 3, SCH_3), 2.39 (s, 3, SCH_3), 1.24 (t, 3, OCH_2CH_3, J = 7.2 Hz); mass spectrum $M^{+\cdot}$ m/e 192 (85). Anal. Calcd for $C_7H_{12}O_2S_2$: C, 43.72; H, 6.30. Found: C, 43.65; H, 6.31.

The second fraction yielded the transesterification product that separated from *n*-hexane as colorless needles: mp 88–89 °C; IR (KBr) ν_{CO} 1678 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.48 (s, 1, vinyl), 2.44 (s, 3, SCH_3), 2.37 (s, 3, SCH_3), 1.45 (s, 9, CH_3); mass spectrum $M^{+\cdot}$ m/e 220 (79). Anal. Calcd for $C_9H_{16}O_2S_2$: C, 49.05; H, 7.33. Found: C, 49.15; H, 7.36.

Registry No. 1, 78570-34-0; 2, 25088-58-8; 3, 99112-36-4; 4a, 99112-37-5; 4b, 56100-22-2; 4b·picrate, 56100-23-3; 4c, 99112-38-6; 4d, 99112-39-7; 4e, 99112-40-0; 4f, 99112-41-1; 4g, 99112-42-2; 4h, 56100-19-7; 4h·Picrate, 99112-43-3; 4i, 99112-44-4; 5, 99112-45-5;

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6a, 99112-46-6; **6b**, 56100-20-0; **6b**·picrate, 56100-21-1; **6c**, 99127-91-0; **7**, 99112-47-7; **8**, 99112-48-8; **10a**, 99112-49-9; **10b**, 99112-50-2; **11**, 99112-51-3; **12**, 51507-09-6; **13**, 99112-52-4; CS_2, 75-15-0; H_3CI, 74-88-4; $EtOCOC(C_6H_5)=C(SCH_3)_2$, 5841-53-2; $C_6H_5CH_2CO_2Et$, 101-97-3; H_3CBr, 74-83-9; $EtOCOCH=C(SCH)_2$, 19606-92-9; H_3CCO_2Et, 141-78-6; $(H_3C)_3COCOCH=C(SCH_3)_2$, 99112-53-5; 2-acetylpyridine, 1122-62-9.

Observations Regarding δ- and ε-Cyano Radical Cyclizations

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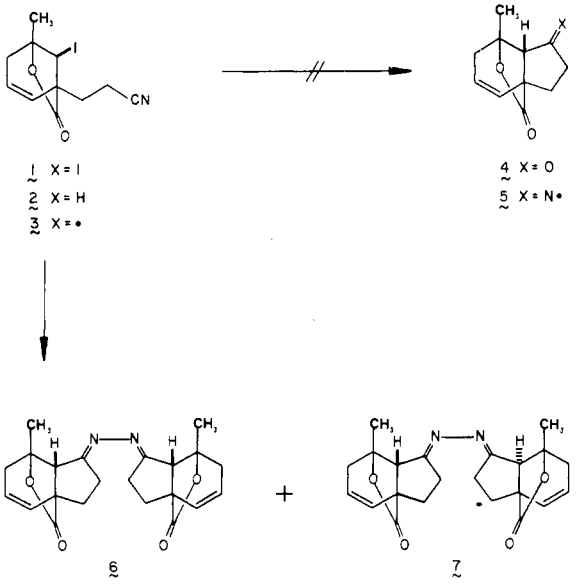
A number of intramolecular free radical additions to nitriles have been reported.[2-4] For example, such reactions have seen limited use in cyclopentanone[3] and cyclohexanone[4] synthesis. This note presents several observations which further define the scope and limitations of this free-radical-cyclization approach to cycloalkanones.

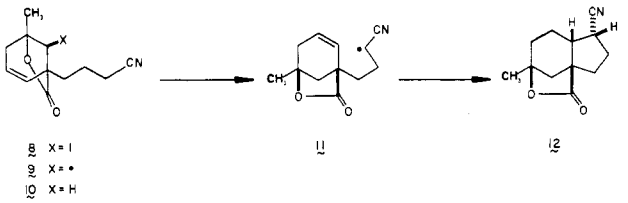
During the course of a synthetic project, we had reason to attempt the free-radical cyclization of δ-iodo nitrile **1**. Treatment of a benzene solution of **1**[5] with tri-*n*-butyltin hydride[6] and a catalytic amount of AIBN under high-dilution conditions at reflux gave none of the desired cyclopentanone **4**. Only nitrile **2**, derived from reduction



of radical **3**, was isolated in 95% yield. In an attempt to generate **3** in the absence of hydrogen atom donors, we turned to hexaalkyldistannanes as a source of trialkylstannyl radicals. Such a ploy has previously been used to generate free radicals for use in fragmentation[7] and intermolecular coupling[8] reactions. Thus, a benzene solution of **1** and hexamethyldistannane[9] was irradiated through Pyrex with a 450 W Hanovia medium-pressure lamp for 52 h to afford two isomeric products along with 42% of recovered **1**. The products gave spectral data which were consistent with structures **6** (16%) and **7** (10%), resulting from dimerization of iminyl radical **5**. The structure of **7** was ultimately established by X-ray crystallography.[10]

This result indicates that the strategy for generating **3** under conditions where cyclization can compete with intermolecular processes is successful, although not outstanding from an operational standpoint.

Cyclization of iodo nitrile **8** was also examined. Treatment of a benzene solution of **8** with tri-*n*-butyltin hydride and AIBN under reflux gave lactone **10** (71%) and perhydroindan **12** (13%). The gross structures of **10** and



12 were consistent with spectral data, and the stereochemistry of **12** was established by X-ray crystallography.[10] It is clear that reduction (**9** → **10**) and rearrangement (**9** → **11**) of the initially formed radical compete with cyclization and ultimate cycloalkanone formation.[11] The rearrangement is noteworthy and perhaps explains the paucity of examples of cyclohexanone synthesis via ε-cyano

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(5) Iodo lactones **1** and **8** were prepared via reductive alkylation of *m*-toluic acid with the appropriate bromo nitriles followed by iodo lactonization of the resulting dihydrobenzoic acids. The overall yields of **1** and **8** were 78% and 76%, respectively. For similar sequences see: Chuang, C.-P.; Hart, D. J. *J. Org. Chem.* **1983**, *49*, 1782.

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(9) Hexamethyldistannane was prepared using the procedure of Smith, G. F.; Kuivila, H. G.; Simon, R.; Sultan, L. *J. Am. Chem. Soc.* **1981**, *103*, 833. For other uses of hexamethyldistannane see: Krusic, P. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 846. Irradiation of **1** in the absence of hexamethyldistannane gave no reaction.

(10) Both diffraction data of compounds **7** and **12** were collected on an Enraf-Nonius CAD4 diffractometer at room temperature. Both data were corrected for Lorenz and polarization effects. All crystallographic computations were carried out on a PDP 11/44 computer using SDP (Structure Determination Package) of B. A. Frenz and Associates, Inc., which was obtained from Enraf-Nonius. Structures were solved by a combination of direct methods and difference Fourier syntheses. Colorless crystals of compound **7** crystallize in space group $p2_1/C$ with $Z = 4$ in a cell dimensions $a = 10.965$ (3) Å, $b = 11.556$ (2) Å, $c = 15.221$ (3) Å, $\beta = 95.80$ (2)°, $V = 1917.96$ Å^3: $R_F = 0.037$ and $R_{wF} = 0.046$ with 350 variable parameters for 1352 reflections [$I > 3.0\sigma(I)$ of 2500 symmetry-independent reflections collected in the range of $4° < 2\theta < 50°$]. Colorless crystals of compound **12** crystallize in space group $P\bar{1}$ with $Z = 4$ in a cell dimensions $a = 7.760$ (1) Å, $b = 19.993$ (2) Å, $c = 7.125$ (2) Å, $\alpha = 91.18$ (1)°, $\beta = 98.17$ (3)°, $\gamma = 83.45$ (1)° and $V = 1087.04$ Å^3. $R_F = 0.030$ and $R_{wF} = 0.036$ with 392 variable parameters for 2245 reflections [$I > 3.0\sigma(I)$ of 3078 unique reflections collected in the range of $4° < 2\theta < 48°$]. Complete crystallographic data appear in the supplementary material.

(11) Reduction of **8** with tri-*n*-butyltin deuteride showed that **10** was derived predominantly, if not exclusively, from reduction of radical **9** rather than **11** based on 500-MHz ^{1}H NMR analysis.

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