~700 torr of F_2. The diaziridine (0.3 mmol) was then added to the evacuated flask and allowed to stand for 12 h. After this time, nearly complete isomerization was observed in each case. The Ni metal appeared to be the most reactive.

The possibility that the metal alone is responsible for the isomerization was then checked with the 200-mesh iron powder. Surprisingly, the rate of isomerization was qualitatively the same as with the fluorine-treated powder. This result clearly leaves the identity of the catalytic species open. It may be that small amounts of the Fe surface were first fluorinated by the N-F bond and that indeed metal fluorides are the catalytic species. However, the only conclusion that can be drawn at this time is that the isomerization is caused by Fe, Ni, and Cr and/or certain compounds of these elements.

In conclusion, fluoride-catalyzed reactions of CF_2=NF provide a facile route to a variety of *N*-fluoro compounds. Reactions of CF_3NF^- as a nucleophile can clearly by extended to other substrates which are at least as susceptible to nucleophilic attack as CF_2=NF. Finally, the isomerization sequence $CF_3NFCF{=}NF \rightarrow CF_3\overline{NCF_2}NF \rightarrow CF_3N{=}NCF_3$ is a fascinating example of the propensity of fluorocarbon nitrogen-fluoride derivatives to undergo fluorine shifts and skeletal rearrangements.

Acknowledgment. The financial support of this research by the U.S. Army Research Office (Grant No. DAAG29-80-C-0102) is gratefully acknowledged.

Registry No. CF_2=NF, 338-66-9; $CF_3C(O)F$, 354-34-7; $C_2F_5C(O)F$, 422-61-7; COF_2, 353-50-4; $CH_3C(O)F$, 557-99-3; KF, 7789-23-3; CsF, 13400-13-0; NaF, 7681-49-4; HgF_2, 7783-39-3; $CF_3NFCF{=}NF$, 41409-49-8; $CF_3C(O)NFCF_3$, 82241-74-5; $C_2F_5C(O)NFCF_3$, 84602-24-4; $CF_3NFC(O)F$, 68986-54-9; CF_3NF^-, 82241-77-8; $CF_3N{=}NCF_3$, 372-63-4; perfluoro-1-methyldiaziridine, 82241-73-4.

Versatile Syntheses of Quinolines by Annulation of Pyridines. Synthesis of Furo[2,3-*g*]- and -[3,2-*g*]quinolines

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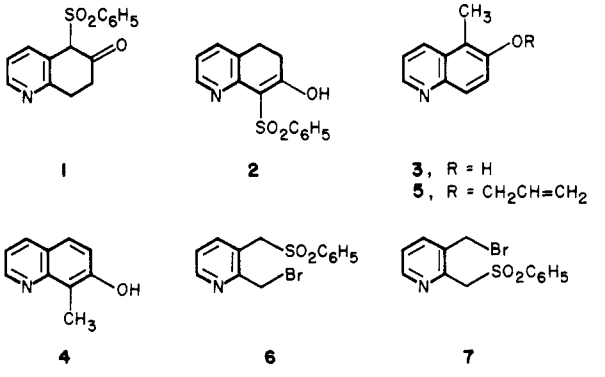
Received August 16, 1982

A new, versatile annulation route for the synthesis of substituted quinolines has been developed by using regioisomeric bifunctional pyridine derivatives with vicinal bromomethyl and (phenylsulfonyl)methyl groups. The sequence consists of (a) alkylation of substituted diethyl malonates with these (bromomethyl)pyridines and (b) intramolecular acylation with concomitant decarboxylation and leads to quinoline derivatives variously substituted in the carbocycle. A simultaneous desulfurization-aromatization of the carbocycle has been developed for these cyclized sulfones. 5-(Phenylsulfonyl)-7-allyl-6-quinolinol (**30**), obtained via this cyclization and dehydrogenation, was then used for the preparation of furo[2,3-*g*]quinoline derivatives. The novel parent systems furo[2,3-*g*]- and -[3,2-*g*]quinoline (**38** and **40**) were obtained in good yield in a one-operation acid-induced cyclization-elimination sequence from the bicyclic annulation products **22** and **28**, respectively.

Among the various methods available for synthesis of quinolines, the approach based on the annulation of pyridine derivatives has usually been ineffective and of minor synthetic importance or applicability, for reasons mentioned previously.[1] At the same time, the major routes leading to quinolines,[2] including newer methods,[3] impose limitations on the introduction of certain more complex substituents such as functionalized side chains at the various sites of the carbocycle. Development of new routes leading to quinolines via annulation of pyridines could possibly overcome these limitations and thus broaden the range of available quinoline derivatives, which are compounds of major biological and medicinal importance. Progress toward this goal has been recently reported by us[1] and subsequently by others.[4] The previously obtained bicyclic compounds **1** and **2** were, however, resistant to further substitution in the carbon ring (see below). Hence we have continued our efforts to develop a simple and more general annulation route which would extend the existing methodology by leading to variously substituted quinolines and providing new pathways to pyridine-fused polycyclic systems. We now describe the results of these efforts.

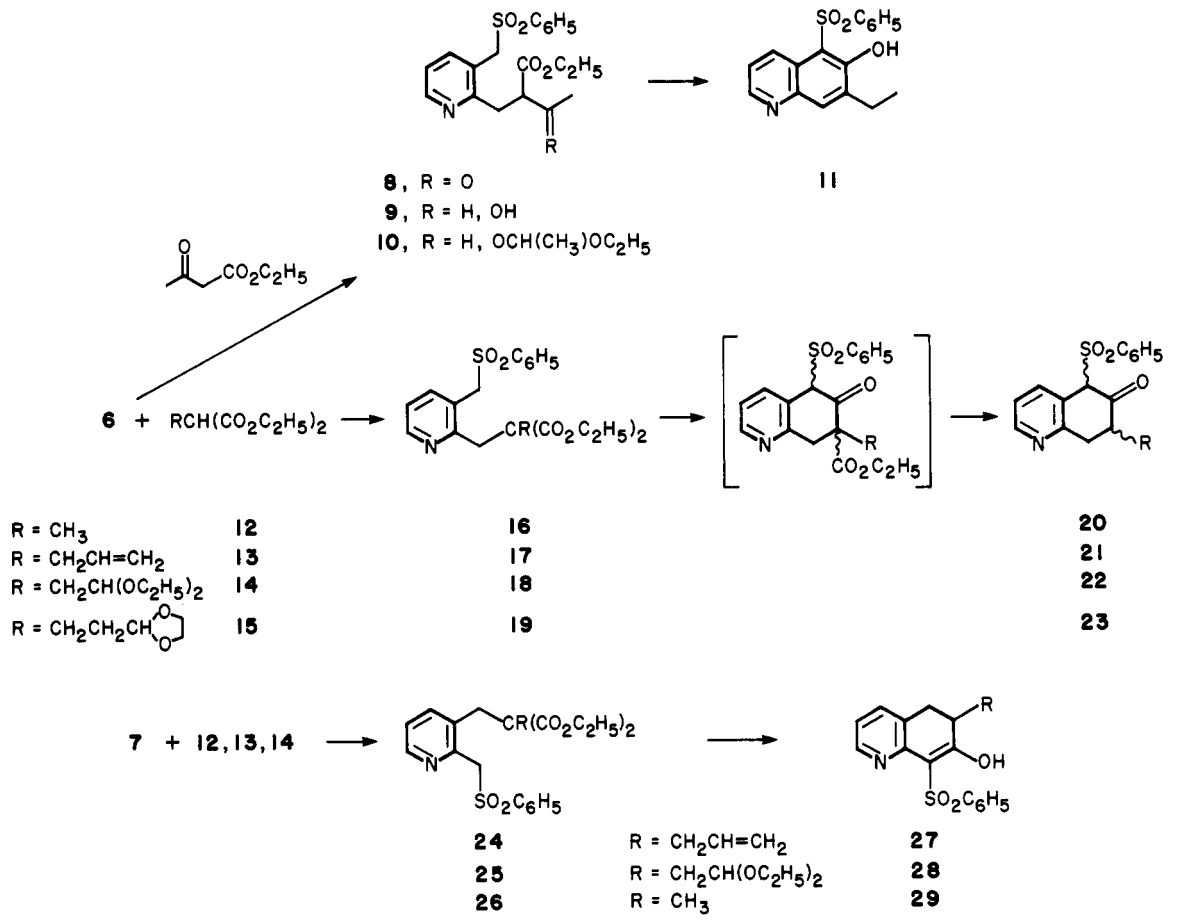
Chart I



(1) Ghera, E.; Ben-David, Y.; Rapoport, H. *J. Org. Chem.* **1981**, *46*, 2059.
(2) Jones, G. *Chem. Heterocycl. Compd.* **1977**, *32*, 93.
(3) Meth-Cohn, O.; Rhouati, S.; Tarnowski, B.; Robinson, A. *J. Chem. Soc.* **1981**, 1537 and preceding papers.
(4) van Leusen, A. M.; Terpstra, J. W. *Tetrahedron Lett.* **1981**, 5097. The reported annulations are, however, of limited scope and low overall yields.

0022-3263/83/1948-0774$01.50/0

Scheme I



First, possibilities were explored for further substitution in **1** and **2** as well as in **3** and **4** (Chart I), which were derived from them.[1] The allyl ether **5** could not be induced to undergo Claisen rearrangement even at high temperature, in various solvents, with and without acidic catalysts.[5,6] Moreover, direct alkylation of **1** and **2** at C-7 and C-6, respectively, by kinetic deprotonation using strong, hindered bases like lithium diisopropylamide, was unsuccessful, as was alkylation of the unstable 6-oxo-5,6,7,8-tetrahydroquinoline, obtained by reductive desulfurization of **1**.

A broader annulation scheme was required, and the previously prepared bifunctional pyridine derivatives, bromo sulfones **6** and **7**,[7] were used for the elaboration of such a route. Compounds with sufficiently activated methylene or methine groups, even with bulky substitution, could be alkylated with these bromo sulfones. Thus ethyl acetoacetate, initially deprotonated by sodium hydride, reacted with **6** to give the alkylated pyridine sulfone **8**. Successful outcome of the reaction depended on the presence of a slight excess of keto ester over base, in order to avoid the presence of any free hard base, which catalyzes the polymerization of bromo sulfone **6** (and **7**). Such a base-induced polymerization of a structurally similar aromatic chloro sulfone has been recently observed.[8]

Acylation of α-sulfonyl carbanions by carboxylic esters is well documented,[9] and we have reported[1] a cyclization via an intramolecular acylation of this type. Before attempting such a cyclization of **8**, we effected selective reduction of the keto group to alcohol **9** and blocking of the resulting hydroxyl as acetal **10**. This avoided preferential deprotonation at the more acidic methine group in **8**. Cyclization of **10** was then achieved with NaH in THF/Me_2SO. An acidic quench following the cyclization reaction resulted in cleavage of the acetal and gave a crude mixture of stereoisomeric alcohols. Heating (120 °C/10 mm) this mixture led to dehydration and migration of the double bond into the ring, the single product being quinoline **11** in 71% yield.

Following this initial cyclization process, a more versatile and simpler route to substituted quinolinol derivatives was developed by alkylating various monosubstituted malonates with bromo sulfones **6** and **7**. The illustrative malonates **12–15** underwent alkylation with **6** (Scheme I) in yields consistently above 90%, and the products **16–19** were obtained under conditions analogous to those used with acetoacetic ester. Similarly, pyridine derivatives **24–26** were obtained by the alkylation of initially deprotonated malonates with the regioisomeric bromo sulfone **7**.

Cyclization of the above compounds was effected either directly, by treating the reaction mixture from the alkylation with excess NaH in THF/Me_2SO, or, preferably,[10] by isolating the alkylated products before this treatment.

(5) While there are numerous examples of Claisen rearrangements involving (allyloxy)pyridines and hetero ring (allyloxy)quinolines, we find no examples of such rearrangements when the allyloxy residue is in the benzene ring of quinolines.[6]

(6) Bennett, G. B. *Synthesis* **1977**, 589 and the referenced related reviews.

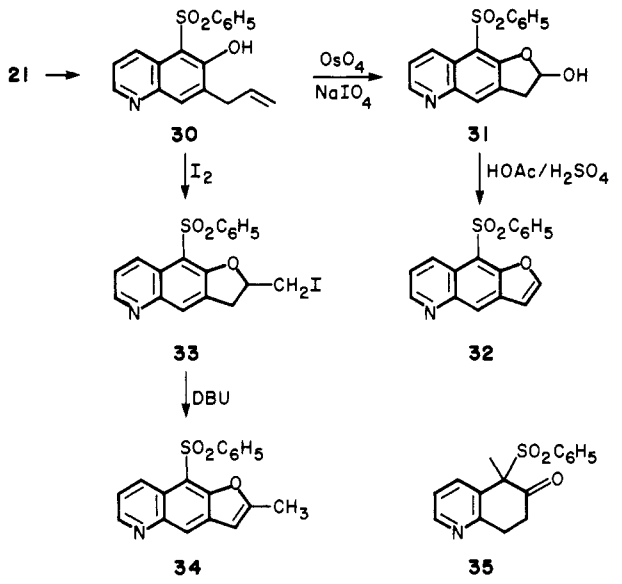
(7) Originally prepared in ref 1; an improved preparation of **7** is given in the Experimental Section.

(8) Gowland, B.; Durst, T. *Can. J. Chem.* **1979**, 1462.

(9) Bartlett, P. A.; Green, F. R.; Rose, E. H. *J. Am. Chem. Soc.* **1978**, *100*, 4852 and references therein.

(10) Decarboxylation was eventually found to be more effective with purified alkylated products.

Scheme II



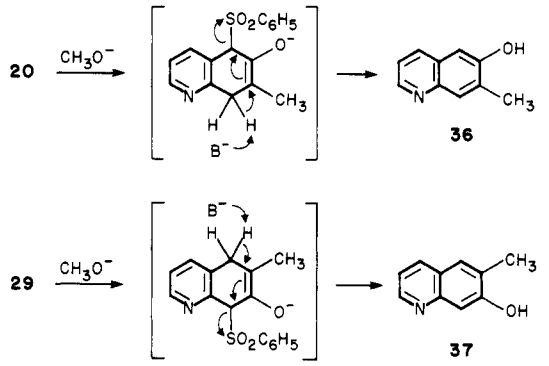
While cyclization occurred at room temperature, warming the reaction mixture to 60 °C also resulted in smooth decarboxylation of the bicyclic product without any additional proton source. Formation of ethanol during cyclization may facilitate decarboxylation, and compounds **20–23** (Scheme I) were thus obtained, usually as a crystalline mixture of two diastereomers.

The combined cyclization–decarboxylation was analogously effective with the regioisomeric series originating from **7** and afforded excellent yields of compounds **27–29** (Scheme I). These compounds, in contrast to their 6-oxo regioisomers, are stable in the enolic form, as evidenced by their IR and ^1H NMR spectra, probably due to the greater acidity of the C-8 proton; therefore, no diastereomers were present. This tautomeric change may also explain the observed difference in the rate of hydrolysis of the acetal group in **22** as compared to that in **28**. In **28** the acetal group is hydrolyzed readily by traces of acid whereas prolonged acid treatment ($HCl/MeOH/CH_2Cl_2$) of **22** did not afford the aldehyde, probably due to the stabilizing effect of the neighboring keto group. Although the cyclization and decarboxylation conditions were identical in both regioisomeric series, it was necessary to omit aqueous treatment in the isolation of the 7-hydroxy compounds (**27–29**) in order to avoid hydrolytic loss of products.

The synthetic potential of the developed route was next explored by investigating the conversion of the quinoline derivatives thus obtained to compounds and systems of more general interest. This investigaton comprised aromatization and desulfurization reactions as well as the synthesis of the linear furo[2,3-*g*]- and -[3,2-*g*]quinolines.

Aromatization by dehydrogenation of the carbon ring in **21** was first effected with 2,3-dichloro-5,6-dicyanoquinone (DDQ) in refluxing benzene, but the yield of the 7-allylquinolinol **30** was in the range 45–50%. Better results for this transformation (82% yield) were achieved by a one-operation bromination–dehydrobromination sequence, using phenyltrimethylammonium perbromide (PTAB) in tetrahydrofuran, followed by treatment with 1,5-diazobicyclo[5.4.0]undecene (DBU). This procedure is applicable also to other bicyclic compounds in the 6-oxo series. Allylquinolinol **30** could be further converted into furo[2,3-*g*]quinolines **32** and **34** in high yields, as shown in Scheme II. Thus, cleavage of the allylic side chain in **30** gave the lactol **31** which on treatment with HOAc/H_2SO_4 (1:1) afforded furoquinoline **32**. The 2-methyl-substituted analogue was prepared by starting from **30** in a transformation via the (iodomethyl)dihydrofuran **33**, which was dehydroiodinated directly by addition of DBU to the reaction mixture.

Scheme III



Formation of the furan in **32** and **34** as well as of a dihydrofuran in **33** resulted in an unusually strong deshielding effect for an aromatic proton which shifted to δ 9.74 in **32**, δ 9.59 in **33**, and δ 9.71 in **34**. This signal was identified by decoupling of the 270-MHz NMR spectrum as the C-4 proton of the quinoline (or C-8 proton in furoquinoline numbering) which should normally appear at δ 7.90–8.0. We assume therefore that the formation of an additional ring (or conversion of the C-6 hydroxyl into a bulkier group[11]) forces the sulfone substituent into a conformation which produces deshielding of the C-4 proton.

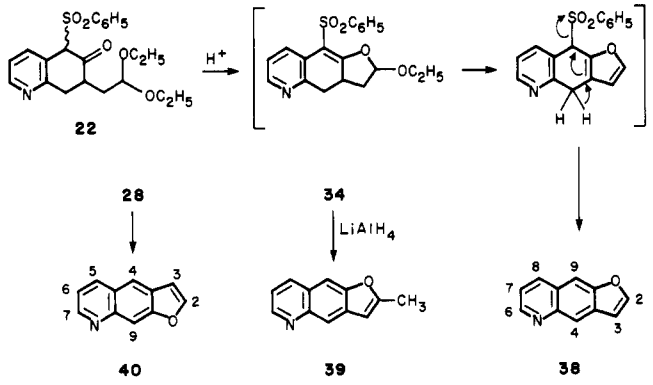
Desulfurization with Raney nickel, which was successful in less substituted bicyclic analogues,[1] resulted in polymerization when applied to **20–23**, probably due to the instability of the resulting air-sensitive tetrahydroquinolones. Thus it seemed more practical to achieve desulfonylation with concomitant aromatization instead of attempting initial reductive desulfurization with other reagents. Base-induced elimination of a tertiary phenylsulfonyl group was previously achieved in **35**[1] by use of potassium *tert*-butoxide at room temperature. With **20**, however, containing a phenylsulfonyl group at a less substituted carbon, no reaction was observed under the above conditions. A change to prolonged reflux with methoxide in methanol (20 h) resulted in a clean conversion of **20** into 7-methyl-6-quinolinol (**36**) by the probable pathway shown in Scheme III, although dominant enolization under the above conditions might have been expected to occur toward C-5.

The base-induced elimination of a β-keto sulfinate group is unusual and may be considered as a case of "umpolung"[12] which is triggered by the drive for aromatization. Interestingly, an analogous eliminative desulfurization occurred under the same conditions in **29** to give **37**. The elimination in this regioisomer would be expected to occur less readily in view of the vinylic character of the phenylsulfonyl group and the requirement for deprotonation at the less acidic β-pyridyl C-5 site (compared with deprotonation at the α-pyridyl C-8 site in **20**) in order to effect elimination (Scheme III).

Among various furoquinoline systems, distinguished by ring sequence and geometry, the natural furoquinolines, in which the pyridine ring is fused to the furan, have been investigated the most. Contrastingly, reports on the syn-

(11) A similar deshielding effect at the C-4 proton of **11** (δ 9.37) was observed when its hydroxy group was converted to an acetoxy group.
(12) Seebach, D. *Angew. Chem.* **1979**, *91*, 259.

Scheme IV



thesis of furo[2,3-*g*]- and -[3,2-*g*]quinolines have been very limited. The closest known derivatives of the parent systems are the 2,3-dimethyl-substituted compounds, obtained previously in very low yields (~5%) along with their tricyclic angular isomers.[13] Simple, good yield, one-operation preparations of both parent systems by starting from **22** and **28**, respectively, have now been developed.

Furoquinoline **38** (mp 114–115 °C) was formed in 70% yield by heating the acetal **22** in $HOAc/H_2SO_4$ (1:1), and its structure was confirmed by spectral and analytical data. Its ultraviolet spectrum showed very similar absorption maxima to those of the phenylsulfonyl derivative **32**; hence, the sulfone group does not provide an additional conjugative effect.[14] The presumed pathway for the transformation, as shown in Scheme IV, implies migration of the double bond in the central ring followed by elimination of phenylsulfinic acid which is probably triggered by the drive to achieve aromatization. We are not aware of previous examples of sulfinic acid eliminations under acidic conditions. The 2-methylfuroquinolines **39** and **38** were obtained by reductive desulfonylation when **34** and **32**, respectively, were refluxed with $LiAlH_4$ in THF solution. Attempted desulfurization of the above compounds by using aluminum amalgam, the reagent of choice for the reductive cleavage of vinylic sulfones,[15] gave poor results. Thus $LiAlH_4$ appears to be a more effective reagent for desulfurization of aromatic sulfones.

Furo[3,2-*g*]quinoline (**40**, mp 85 °C) was obtained under conditions identical with those used to prepare the [2,3-*g*] isomer **38**. Optimal yields were achieved by direct use of crude **28** as it was obtained from the cyclization of the pyridine derivative **25**, because of the tendency of the acetal group in **28** to undergo rapid hydrolysis and thus lower the yield. The overall yield from **25** was 76%, and the UV absorption maxima were almost identical with those of furo[2,3-*g*]quinoline (**38**).

Experimental Section

Melting points were determined on a hot-stage microscope and are uncorrected. ^1H NMR spectra were recorded in $CDCl_3$ (unless stated otherwise) with Varian T-80 or T-270 (80 and 270 MHz, respectively) spectrometers. IR spectra were recorded on a Perkin-Elmer 462 spectrometer, and UV spectra were taken on a Cary 118 instrument. Flash chromatography with silica gel (234–400 mesh) was used for the purification of compounds, and precoated Merck Kieselgel 60 F_{254} plates were used for thin-layer chromatography (TLC) tests. All air-sensitive reactions were carried out in flame-dried, argon-flushed, two-necked flasks sealed with rubber septa, and the reagents were introduced with a syringe. Monosubstituted malonic esters used for alkylation reactions were prepared from malonic ester and the corresponding bromides by known procedures with sodium hydride as the base and dimethylformamide as the solvent.[16]

2-[(Phenylthio)methyl]-3-methylpyridine. The reported[1] preparation of the above compound, used to obtain **7**, was improved in order to avoid sporadic contamination with the 2-bis(phenylthio)methyl derivative. 2,3-Lutidine (3.65 g, 34 mmol) was added to an ice-cooled solution of 1.5 M butyllithium/hexane (26 mL, 39 mmol) diluted with dry ether (40 mL), and the reaction mixture was stirred for 1 h at 0 °C, a yellow precipitate being formed. The mixture was then transferred dropwise, with a syringe, into another flask containing a stirred solution of Ph_2S_2 (7.4 g, 34 mmol) in dry THF (50 mL) at −60 °C. After 1 h the product was isolated as reported to afford 5.86 g (80%) of pure product. Oxidation to **7** was done as described.[1]

General Alkylation Procedure Using Bromo Sulfones 6 and 7. Sodium hydride (80% dispersion in mineral oil, net weight 0.067 g, 2.8 mmol) was washed twice with dry pentane under argon with the help of a syringe. A solution of the corresponding diethyl malonate or acetoacetic ester (3 mmol) in dry THF (8 mL) was added and the mixture stirred at room temperature for 30 min as it became gradually clear. The bromo sulfone (**6** or **7**, 0.652 g, 2 mmol) in THF (8 mL) was then added and the mixture stirred for an additional 30 min when TLC indicated the conversion to a single new compound. It was then poured into cold aqueous NH_4Cl and extracted (three times) with ether/$CHCl_3$ (4:1). The combined organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and evaporated. Flash chromatography (ether/pentane, 2:1) was used to remove the remaining malonate.

The products formed were also used directly for cyclization, without prior isolation, by transferring the reaction mixture into another flask containing excess of NaH in THF/Me_2SO (for conditions see the cyclization procedure below). Cyclization occurred readily, but decarboxylation sometimes did not proceed to completion; therefore, initial isolation of alkylated products was prefered.

2-[2-(Ethoxycarbonyl)-3-oxo-1-butyl]-3-[(phenylsulfonyl)methyl]pyridine (8): 87%; mp 56–58 °C (from hexane/ether); IR ($CHCl_3$) 1700, 1702 cm^{-1}; NMR δ 1.23 (t, 3), 2.32 (s, 3), 3.07 (m, 2), 4.15 (q, 2), 4.25 (t, J = 7 Hz, 1), 4.47 (s, 2), 7.06–7.80 (m, 7), 8.42 (dd, J = 3 Hz, 1.5 Hz, 1). Anal. Calcd for $C_{19}H_{21}NO_5S$: C, 60.8; H, 5.6. Found: C, 60.7; H, 5.7.

2-[2,2-Bis(ethoxycarbonyl)-1-propyl]-3-[(phenylsulfonyl)methyl]pyridine (16): 95%; mp 77–78 °C (hexane/ether); NMR δ 1.19 (t, 6), 1.35 (s, 3), 3.08 (s, 2), 4.14 (q, 4), 4.45 (s, 2), 7.10–7.72 (m, 7), 8.41 (dd, J = 4, 1.5 Hz, 1). Anal. Calcd for $C_{21}H_{25}NO_6S$: C, 60.1; H, 6.0. Found: C, 60.0; H, 6.1.

2-[2,2-Bis(ethoxycarbonyl)-4-penten-1-yl]-3-[(phenylsulfonyl)methyl]pyridine (17): 96%; oil; NMR δ 1.18 (t, 6), 2.65 (d, J = 7 Hz, 2), 3.0 (s, 2), 4.23 (q, 4), 4.44 (s, 2), 4.95–5.07 (br d, 2), 5.42–5.86 (m, 1), 7.02–7.73 (m, 7), 8.39 (dd, J = 4, 1.5 Hz, 1). Anal. Calcd for $C_{23}H_{27}NO_6S$: C, 62.0; H, 6.1. Found: C, 62.1; H, 6.1.

2-[2,2-Bis(ethoxycarbonyl)-4,4-diethoxy-1-butyl]-3-[(phenylsulfonyl)methyl]pyridine (18): 91%; mp 128 °C (MeOH/Et_2O); NMR δ 1.05–1.26 (m, 12), 2.33 (d, J = 6 Hz, 2), 3.21 (s, 2), 3.4–3.59 (m, 4), 4.11 (q, 4), 4.49 (s, 2), 4.52 (t, J = 6 Hz, 1), 7.10–7.72 (m, 7), 8.42 (dd, J = 4, 1.5 Hz, 1). Anal. Calcd for $C_{26}H_{35}NO_8S$: C, 59.9; H, 6.7. Found: C, 59.8; H, 6.8.

2-[2,2-Bis(ethoxycarbonyl)-5,5-(ethylenedioxy)-1-pentyl]-3-[(phenylsulfonyl)methyl]pyridine (19): 98%, mp 79–80 °C (hexane/ether); NMR δ 1.17 (t, 6), 1.56–2.09 (m, 4), 3.06 (s, 2), 3.78–3.98 (m, 4), 4.13 (q, 4), 4.46 (s, 2), 4.77 (t, J = 5 Hz, 1), 7.07–7.75 (m, 7), 8.39 (dd, J = 4, 1.5 Hz, 1). Anal. Calcd for $C_{25}H_{31}NO_8S$: C, 59.4; H, 6.1. Found: C, 59.6; H, 6.1.

2-[(Phenylsulfonyl)methyl]-3-[2,2-bis(ethoxycarbonyl)-4-penten-1-yl]pyridine (24): 98%; mp 54–55 °C (hexane/ether);

(13) Pene, C.; Demerseman, P.; Cheutin, A.; Royer, R. *Bull. Soc. Chim. Fr.* **1966**, 586. Demerseman, P.; Gene, C.; Colin, G.; Royer, R. *Ibid.* **1972**, 1366. For some related compounds see also: Royer, R.; Demerseman, P.; Pene, C.; Colin, G. *Ibid.* **1967**, 915. Albrecht, R. *Justus Liebigs Ann. Chem.* **1973**, *762*, 55. Cruickshand, P. A.; Lee, F. T.; Lupichuk, A. *J. Med. Chem.* **1970**, *13*, 1110.

(14) True, W. E.; Klinger, T. C.; Brand, D. W. In "Organic Chemistry of Sulfur"; Oae, S.; Ed.; Plenum Press: New York, 1977; p 528.

(15) Pascali, V.; Umani-Ronchi, A. *J. Chem. Soc., Chem. Commun.* **1973**, 351. Metcalf, B. W.; Bonilavri, E. *Ibid.* **1978**, 914.

(16) Bien, S.; Ovadia, D. *J. Org. Chem.* **1974**, *39*, 2258.

NMR δ 1.06 (t, 6), 2.54 (d, J = 7 Hz, 2), 3.26 (s, 2), 4.01 (q, 4), 4.60 (s, 2), 4.80–5.02 (br d, 2), 5.32–5.76 (m, 1), 6.74–7.50 (m, 7), 8.22 (d, J = 4 Hz, 1). Anal. Calcd for $C_{23}H_{27}NO_6S$: C, 62.0; H, 6.1. Found: C, 62.0; H, 6.1.

2-[(Phenylsulfonyl)methyl]-3-[2,2-bis(ethoxycarbonyl)-4,4-diethoxy-1-butyl]pyridine (25): 92%; mp 99–100 °C (hexane/$CHCl_3$); NMR δ 1.11 (t, 6), 1.21 (t, 6), 2.28 (d, J = 6 Hz, 2), 3.46 (s, 2), 3.41–3.70 (m, 4), 4.12 (q, 4), 4.61 (t, J = 4.5 Hz, 1), 4.84 (s, 2), 7.09–7.74 (m, 7), 8.26 (d, J = 4 Hz, 1). Anal. Calcd for $C_{26}H_{35}NO_8S$: C, 59.9; H, 6.7. Found: C, 60.0; H, 6.7.

2-[(Phenylsulfonyl)methyl]-3-[(2,2-bis(ethoxycarbonyl)-1-propyl]pyridine (26): 97%; mp 91–92 °C (from ether/pentene); NMR δ 1.16 (t, 6), 1.36 (s, 3), 3.24 (s, 2), 4.02 (q, 4), 4.61 (s, 2), 6.92–7.68 (m, 7), 8.16 (d, J = 4 Hz, 1). Anal. Calcd for $C_{21}H_{25}NO_6S$: C, 60.1; H, 6.0. Found: C, 60.3; H, 6.0.

General Procedure for Cyclization and Decarboxylation. To an excess of NaH (0.36 g, 15 mmol, 80% dispersion in oil, washed as described above) was added a solution of the alkylated pyridine derivative (3 mmol) in THF (35 mL) and Me_2SO (1.75 mL). After 30–60 min, TLC showed complete conversion of the pyridine derivative into two more polar compounds. The stirred reaction mixture was then heated (60 °C) by using an oil bath (1–2 h) until TLC showed the presence of a single product (identical with the more polar product detected initially). For products derived from **6**, the reaction mixture was poured slowly into cold aqueous NH_4Cl, acidified with a 5% HCl solution, and made alkaline (pH 8) again by addition of aqueous $NaHCO_3$. Extraction with $CHCl_3$ (three times) followed by evaporation of the dried (Na_2SO_4) and filtered organic layers gave a residue which was flash chromatographed (ether/5% MeOH).

The isolation of products derived from bromo sulfone **7** was modified as follows: excess NaH was decomposed by dropwise addition of a 1:1:1 mixture of AcOH/H_2O/MeOH, dry $NaHCO_3$ was added, and the mixture was diluted with $CHCl_3$, dried (Na_2SO_4), and filtered with multiple washings of the precipitate with warm $CHCl_3$. The combined organic layers were evaporated under reduced pressure, and the residue was heated in vacuo (80 °C, 0.1 mm) to eliminate Me_2SO and then chromatographed (ether/5–10% MeOH).

Conversion of the Keto Ester 8 into 10 and Preparation of 5-(Phenylsulfonyl)-6-hydroxy-7-ethylquinoline (11). To an ice-cooled solution of keto ester **8** (1.12 g, 3 mmol) in 20 mL of methanol was added excess $NaBH_4$ (0.2 g), and the mixture was stirred for 2 h at 0 °C. After being quenched with a few drops of aqueous AcOH, the reaction mixture was poured into aqueous $NaHCO_3$ and extracted with ether/20% $CHCl_3$. The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was evaporated. Crude **9**, homogeneous by TLC, was dissolved in CH_2Cl_2 (30 mL) to which ethyl vinyl ether (1 mL) and *p*-toluenesulfonic acid (20 mg) were added. The yellow solution was stirred for 1 h at room temperature, poured into aqueous $NaHCO_3$, and then extracted with ether. Flash chromatography (ether/pentane, 2:1) of the residue from the usual isolation gave **10** as an oil, homogeneous on TLC, 1.08 g (81% overall yield). The complex NMR spectrum of **10** showed the presence of a diastereomeric mixture [δ 0.99–1.33 (m, 12 H), 2.60–3.65 (m, 5), 3.84–4.82 (m, 6), 6.98–7.74 (m, 7), 8.46 (d, J = 4 Hz, 1)] which was used directly for cyclization under conditions described in the general procedure. After 30 min at 25 °C two more polar compounds were formed (TLC). The reaction mixture was poured into cold aqueous 5% HCl, brought to pH 8 with aqueous $NaHCO_3$, and extracted with chloroform. The residue obtained from the usual isolation was heated under reduced pressure (120 °C, 10 mm) for 30 min and was converted to the single, less polar product **11** which crystallized from chloroform/hexane: 0.53 g (71%); mp 149–151 °C; NMR δ 1.37 (t, 3), 2.91 (q, 2), 7.22–7.64 (m, 4), 7.84–7.99 (m, 2), 8.07 (s, 1), 8.62–8.72 (m, 2). Anal. Calcd for $C_{17}H_{15}NO_3S$: C, 65.2; H, 4.8. Found: C, 65.3; H, 4.6.

5-(Phenylsulfonyl)-6-oxo-7-methyl-5,6,7,8-tetrahydroquinoline (20): 60%; crystalline mixture of diastereomers; mp 138–140 °C; IR ($CHCl_3$) 1700 cm^{-1}; NMR δ 1.23 and 1.31 (2 d, 3), 2.89–3.58 (m, 3), 4.85 and 5.03 (2 s, 1), 7.14–7.86 (m, 7), 8.58 (d, J = 5 Hz, 1). Anal. Calcd for $C_{16}H_{15}NO_3S$: C, 63.8; H, 5.0. Found: C, 63.9; H, 5.1.

5-(Phenylsulfonyl)-6-oxo-7-(2-propen-1-yl)-5,6,7,8-tetrahydroquinoline (21): 87%; crystalline diastereomeric mixture; mp 135–137 °C (MeOH/benzene); IR ($CHCl_3$) 1700 cm^{-1}; NMR δ 2.34–3.24 (m, 5), 4.86 (s, 1), 4.85–5.24 (m, 2), 5.52–6.23 (m, 1), 7.07–7.91 (m, 7), 8.57–8.64 (d, J = 5 Hz, 1). Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.0; H, 5.2. Found: C, 65.8; H, 5.3.

5-(Phenylsulfonyl)-6-oxo-7-(2,2-diethoxyeth-1-yl)-5,6,7,8-tetrahydroquinoline (22): 88%; oil; mixture of diastereomers; IR ($CHCl_3$) 1700 cm^{-1}; NMR δ 1.18 (t, 6 H), 1.33–2.89 (m, 3), 3.16–3.74 (m, 6), 4.45–4.84 (2 t, 1), 4.89 (s, 1), 7.06–7.79 (m, 7), 8.58 (d, J = 4 Hz, 1). Anal. Calcd for $C_{21}H_{25}NO_5S$: C, 62.5; H, 6.2. Found: C, 62.4; H, 6.2.

5-(Phenylsulfonyl)-6-oxo-7-[3,3-(ethylenedioxy)-1-propyl]-5,6,7,8-tetrahydroquinoline (23): 78%; crystalline diastereomeric mixture; mp 105–107 °C; IR 1698 cm^{-1}; NMR δ 1.60–3.55 (m, 7), 3.82–3.97 (m, 4), 4.84–4.95 (m, 2), 7.14–7.87 (m, 7), 8.54–8.64 (d, J = 4 Hz, 1). Anal. Calcd for $C_{20}H_{21}NO_5S$: C, 62.0; H, 5.4. Found: C, 62.2; H, 5.6.

5-(Phenylsulfonyl)-6-hydroxy-7-(2-propen-1-yl)quinoline (30). To a stirred solution containing 0.18 g (0.55 mmol) of **21** in dry THF (6 mL) at 25 °C was added portionwise phenyltrimethylammonium perbromide (0.208 g, 0.55 mmol). After 15 min the initially formed sticky precipitate turned into a powder, and TLC showed the reaction to be complete. The mixture was then diluted with CH_2Cl_2 (4 mL), and DBU (0.2 mL) was added. After 30 min the mixture was poured into cold aqueous NaCl and extracted with chloroform, and the organic layer was dried (Na_2SO_4), filtered, and concentrated to a residue which on chromatography (pentane/ether, 1:1) gave **30**: 0.15 g (84%); mp 130–131 °C (MeOH/hexane); NMR δ 3.62 (d, J = 6 Hz, 2), 5.07–5.37 (br d, 2), 5.87–6.29 (m, 1), 7.23–7.69 (m, 4), 7.87–8.22 (m, 3), 8.60–8.77 (m, 2). Anal. Calcd for $C_{18}H_{15}NO_3S$: C, 66.5; H, 4.6. Found: C, 66.3; H, 4.7.

Preparation of Lactol 31 and Its Conversion to 9-(Phenylsulfonyl)furo[2,3-*g*]quinoline (32). The quinolinol **30** (98 mg, 0.3 mmol) was dissolved in 9 mL of THF/H_2O (5:4), and an ether solution of OsO_4 (5 mg in 0.5 mL) was added at room temperature. After 10 min of stirring, $NaIO_4$ in excess (0.33 g) was added, and the mixture was stirred for an additional 30 min, poured into aqueous NaCl, and extracted (5 × 20 mL) with chloroform. The combined organic layers were dried (Na_2SO_4), filtered, and evaporated, and the resulting residue was chromatographed ($CHCl_3$/5% MeOH) to give **31**: 80 mg (82%); mp 203–205 °C (from $CHCl_3$); NMR δ 3.98 (br, 2), 6.75 (br, 1), 7.34–7.55 (m, 3), 7.89–8.12 (m, 3), 8.65–8.77 (m, 2), 9.90 (br, 1). Anal. Calcd for $C_{17}H_{13}NO_4S$: C, 62.4; H, 4.0. Found: C, 62.4; H, 3.9.

Lactol **31** (80 mg, 0.24 mmol) was dissolved in a 1:1 mixture of H_2SO_4/AcOH (2 mL), and the solution was heated (60 °C) in a stoppered vial, with occasional stirring. After 1.5 h the mixture was poured into ice-cold water and adjusted to pH 6 with 10% NaOH and then with aqueous $NaHCO_3$ to pH 8. After extraction with $CHCl_3$ (three times) the combined organic layers were washed once with aqueous NaCl and dried (Na_2SO_4). Filtration, evaporation of the solvent, and chromatographic purification of the residue (ether) gave **32**: 64 mg (84%); mp 186–188 °C (MeOH); UV (EtOH) λ_{max} 237 nm (ε 72 000), 325–328 (21 000); 270-MHz NMR δ 7.01 (d, J = 2 Hz, 1), 7.45–7.56 (m, 3), 7.57 (dd, J = 91, 4 Hz, 1), 7.91 (d, J = 2 Hz, 1), 8.13 (br s, 1), 8.16 (br s, 1), 8.59 (s, 1), 8.96 (dd, J = 4, 1 Hz, 1), 9.74 (dd, J = 9, 1 Hz, 1), pyridine protons (identified by decoupling) 7.57 (C-3), 8.96 (C-2), 9.74 (C-4). Anal. Calcd for $C_{17}H_{11}NO_3S$: C, 66.0; H, 3.6. Found: C, 65.9; H, 3.6.

Preparation of 2-Methyl-9-(phenylsulfonyl)furo[2,3-*g*]quinoline (34) via the Iodo Ether 33. To **30** (70 mg, 0.22 mmol), dissolved in acetonitrile (3 mL), was added iodine (90 mg, 0.35 mmol), and the reaction mixture was kept in the dark for 30 h (TLC). The mixture was then diluted with CH_2Cl_2 (3 mL), and DBU (0.2 mL) was added. After being stirred for 6 h at room temperature, the red solution was poured into aqueous NaCl and extracted with $CHCl_3$. The organic layers were washed with aqueous $Na_2S_2O_3$ and aqueous NaCl, dried (Na_2SO_4), filtered. Evaporation of the filtrate under reduced pressure gave 57 mg (82%) of **34** (after hexane washing of the crystalline residue): mp 219 °C (from $CHCl_3$/hexane); UV (EtOH) λ_{max} 242 nm (ε 66 000), 332–334 (20 000); 270-MHz NMR δ 2.56 (s, 3), 6.59 (s, 1), 7.45–7.56 (m, 4), 8.12–8.15 (m, 2), 8.39 (s, 1), 8.92 (dd, J = 4, 1 Hz, 1), 9.71 (d, J = 8 Hz, 1), pyridine protons (identified by decoupling) 7.52

(C-3), 8.92 (C-2), 9.71 (C-4). Anal. Calcd for $C_{18}H_{13}NO_3S$: C, 66.9; H, 4.0. Found: C, 66.7; H, 4.1. In a separate reaction the intermediate iodo ether **33** was isolated by pouring the reaction mixture into cold aqueous $NaHCO_3$ and extracting with $CHCl_3$. The organic layer was washed (aqueous $Na_2S_2O_3$ and NaCl) and dried (Na_2SO_4), and the filtrate was evaporated to a crystalline residue: 89 mg (92%); mp 175–157 °C; NMR δ 3.16–3.63 (m, 4), 5.05–5.16 (br, 1), 7.46–7.57 (m, 4), 8.03–8.09 (m, 3), 8.78 (d, J = 4 Hz, 1), 9.59 (d, J = 9 Hz, 1). Anal. Calcd for $C_{18}H_{14}NO_3SI$: C, 47.9; H, 3.1. Found: C, 47.9; H, 3.2.

8-(Phenylsulfonyl)-7-hydroxy-6-(2-propen-1-yl)-5,6-dihydroquinoline (27): 92%; mp 170–171 °C ($CHCl_3$/hexane); NMR δ 2.32–2.86 (m, 5), 4.68–4.92 (m, 2), 5.22–5.71 (m, 1), 6.64 (t, J = 7 Hz, 1), 7.38–7.65 (m, 5), 7.99–8.11 (m, 2). Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.1; H, 5.2. Found: C, 66.2; H, 5.2.

8-(Phenylsulfonyl)-7-hydroxy-6-(2,2-diethoxy-1-ethyl)-5,6-dihydroquinoline (28): 83%, mp 108–109 °C (Et_2O); NMR δ 1.12 (t, 6), 2.22–3.22 (m, 5), 3.31–3.76 (m, 4), 4.52 (dd, J = 3, 2 Hz, 1), 6.64 (t, J = 6 Hz, 1), 7.38–7.81 (m, 5), 7.97–8.10 (m, 2). Anal. Calcd for $C_{21}H_{25}NO_5S$: C, 62.5; H, 6.2. Found: C, 62.7; H, 6.3.

8-(Phenylsulfonyl)-7-hydroxy-6-methyl-5,6-dihydroquinoline (29): 80%; mp 180–181 °C ($MeOH/Et_2O$); NMR δ 1.05 (d, J = 7 Hz, 3), 2.39–2.86 (m, 3), 6.62 (t, J = 6 Hz, 1), 7.37–7.66 (m, 5), 7.99–8.11 (m, 2). Anal. Calcd for $C_{16}H_{15}NO_3S$: C, 63.8; H, 5.0. Found: C, 63.6; H, 5.0.

7-Methyl-6-quinolinol (36). To 0.28 g (0.93 mmol) of **20**, dissolved in anhydrous MeOH (30 mL), was added 0.251 g of NaOMe (500 mol %), and the resulting solution was refluxed for 20 h and then concentrated under reduced pressure. The residue was dispersed on silica and chromatography by using a dry silica column and eluting with pentane/ether (5:1) to give **36**: 0.104 g (70%); mp 230–232 °C ($MeOH/Et_2O$); NMR (methanol-d_4) δ 2.48 (s, 3), 7.12 (s, 1, C-5 proton), 7.41 (dd, J = 8, 4.5 Hz, 1, C-3 proton), 7.77 (s, 1, C-8 proton), 8.18 (d, J = 8 Hz, 1, C-4 proton), 8.60 (d, J = 4.5 Hz, C-2 proton). Anal. Calcd for $C_{10}H_9NO$: C, 75.5; H, 5.7. Found: C, 75.5; H, 5.7.

6-Methyl-7-quinolinol (37). To 86 mg (0.28 mmol) of **29**, dissolved in 10 mL of anhydrous MeOH, was added NaOMe (77 mg, 500 mol %), and the resulting solution was refluxed for 24 h. Isolation as described for **36** and chromatographic purification (ether/MeOH, 98:2) gave **37**: 37 mg (82%); mp 253–255 °C (ether/MeOH) (lit.[17] mp 244 °C); NMR (methanol-d_4) δ 2.37 (s, 3), 7.24 (dd, J = 4.5, 8 Hz, 1), 7.25 (s, 1), 7.59 (s, 1), 8.11 (d, J = 8 Hz, 1), 8.59 (d, J = 4.5 Hz, 1). Anal. Calcd for $C_{10}H_9NO$: C, 75.5; H, 5.7. Found: C, 75.6; H, 5.6.

Furo[2,3-*g*]quinoline (38). Sulfone **22** (0.253 g, 0.63 mmol) was dissolved in 2 mL of AcOH with warming. To this solution, cooled at 0 °C, was slowly added 2 mL of H_2SO_4, and the resulting mixture was heated at 60 °C with occasional stirring for 1.5 h. Isolation as described for **32** gave a homogeneous residue (TLC) which on chromatography (ether/pentane, 3:1) yielded crystalline **38**: 74 mg (70%); mp 115 °C [sublimed, 90 °C (0.5 mm)]; UV (EtOH) λ_{max} 243 nm (ε 60000), 321 (13200), 332 (14900); 270-MHz NMR δ 6.94 (dd, J = 2, 1 Hz, C-3 proton), 7.33 (dd, J = 9, 4 Hz, C-7 proton), 7.76 (d, J = 2 Hz, C-2 proton), 7.83 (s, C-4 or C-9 proton), 8.21 (d, J = 9 Hz, C-8 proton), 8.34 (s, C-4 or C-9 proton), 8.89 (dd, J = 4, 2 Hz, C-6 proton); mass spectrum, m/e 169, 140, 114. Anal. Calcd for $C_{11}H_7NO$: C, 78.1; H, 4.1. Found: C, 78.2; H, 4.2.

Furo[3,2-*g*]quinoline (40). Sulfone **25** (0.892 g, 1.71 mmol) was submitted to cyclization conditions as described above. Nonaqueous isolation as described previously gave a residue which was dried (80 °C, 0.1 mm) and treated with 5 mL of AcOH and 5 mL of H_2SO_4 as in the preparation of **38**. Analogous isolation gave a residue which was purified by chromatography (pentane/ether, 1:1) to give 0.220 g of crystals, 76% overall yield. An analytical sample was obtained by sublimation (90 °C, 0.5 mm): mp 85 °C; UV (EtOH) λ_{max} 244 nm (ε 59000), 321 (12300), 333 (13400); 270-MHz NMR δ 6.91 (sp d, J = 2 Hz, C-3 proton), 7.36 (dd, J = 9, 4 Hz, C-6 proton), 7.79 (d, J = 2 Hz, C-2 proton), 8.02 (s, C-4 or C-9 proton), 8.21 (s, J = 2 Hz, C-4 or C-9 proton) 8.26 (d, J = 9 Hz, C-5 proton), 8.92 (dd, J = 4, 2 Hz, C-7 proton); mass spectrum, m/e 169, 140, 114. Anal. Calcd for $C_{11}H_7NO$: C, 78.1; H, 4.1. Found: C, 78.0; H, 4.2.

2-Methylfuro[2,3-*g*]quinoline (39). To a suspension of $LiAlH_4$ (0.18 g) in THF (10 mL) was added a solution of furoquinoline **34** (0.17 g, 0.526 mmol) in 10 mL of THF, and the stirred mixture was refluxed for 2 h, when TLC showed the conversion to a less polar product to be complete. After the mixture cooled, the excess reagent was decomposed with aqueous Na_2SO_4, and the mixture was dried (Na_2SO_4), diluted with $CHCl_3$, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by chromatography (pentane/ether, 1:1) to give **39**, 78 mg (81%). An analytical sample was obtained by sublimation: mp 116–118 °C; NMR δ 2.52 (s, 3), 6.57 (s, 1), 7.33 (dd, J = 8, 4 Hz, 1), 7.74 (s, 1), 8.17 (s, 1), 8.22 (d, J = 8 Hz, 1), 8.87 (d, J = 4 Hz, 1); mass spectrum, m/e 183, 154. Anal. Calcd for $C_{12}H_9NO$: C, 78.7; H, 4.9 Found: C, 78.8; H, 4.9.

Acknowledgment. We are grateful to Mr. M. Greenberg for his assistance with the ^1H NMR.

Registry No. **6**, 76915-69-0; **7**, 76915-70-3; **8**, 84583-30-2; **9**, 84583-38-0; **10**, 84583-39-1; **11**, 84583-55-1; **12**, 609-08-5; **13**, 2049-80-1; **14**, 21339-47-9; **15**, 23985-06-0; **16**, 84583-31-3; **17**, 84583-32-4; **18**, 84583-33-5; **19**, 84583-34-6; *cis*-**20**, 84583-40-4; *trans*-**20**, 84583-56-2; *cis*-**21**, 84583-57-3; *trans*-**21**, 84583-41-5; *cis*-**22**, 84583-58-4; *trans*-**22**, 84583-42-6; *cis*-**23**, 84583-59-5; *trans*-**23**, 84583-43-7; **24**, 84583-35-7; **25**, 84583-36-8; **26**, 84583-37-9; **27**, 84583-49-3; **28**, 84583-50-6; **29**, 84583-51-7; **30**, 84583-44-8; **31**, 84583-45-9; **32**, 84583-46-0; **33**, 84583-48-2; **34**, 84583-47-1; **36**, 84583-52-8; **37**, 84583-53-9; **38**, 7260-69-7; **39**, 84583-54-0; **40**, 268-71-3; Ph_2S_2, 882-33-7; 2-[(phenylthio)methyl]-3-methylpyridine, 76915-52-1; 2,3-lutidine, 583-61-9; ethyl acetoacetate, 141-97-9; ethyl vinyl ether, 109-92-2.

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