yl)-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (2h). 2-Chloromethyl-5-(2,2-dicyanovinyl)-3,4-dimethylpyrrole (**1o,** 1.103 g, 0.005 mol = 1.0975 g) and 2-(2-cyano-2-methoxycarbonylvinyl)-3,4-dimethylpyrrole (**1b,** 1.022 g, 0.005 mol) were dissolved in dry methylene chloride (50 ml) with the exclusion of moisture. Anhydrous stannic chloride (1.3 g) was added, causing an immediate deepening of color to dark brown. After brief warming on the steam bath, the reaction mixture was quenched with concentrated hydrochloric acid, then water. The K_2CO_3-dried, filtered organic phase was boiled down and diluted with methanol, from which the product readily crystallized as yellow flakes, 1.37 g (70.8%).

An analytical sample was recrystallized from methylene chloride–methanol: mp 215–218 °C dec; ^{1}H NMR 2.01 (6 H, s), 2.14, 2.16 (6 H, two overlapping s), 3.82 (3 H, s), 4.03 (2 H, s), 7.33 (H, s), 7.91 (H, s), 9.45 ppm (2 H, bs); ir 3400 (NH), 2220 (C≡N), 1720 (C=O), 1590, 1535 cm^{-1} (C=C).

Anal. Calcd for $C_{22}H_{21}N_5O_2$: C, 68.20; H, 5.46; N, 18.08. Found: C, 67.68; H, 5.37; N, 18.33.

Acknowledgments. We wish to thank the National Institutes of Health (GM 04229 and AM 17989) and the Canadian National Research Council for financial assistance.

Registry No.—**1b,** 59434-99-0; **1d,** 59435-00-6; **1e,** 59435-01-7; **1f,** 59435-02-8; **1i,** 2199-46-4; **1j,** 27226-50-2; **1l,** 3855-78-5; **1m,** 59435-03-9; **1n,** 59435-04-0; **1o,** 59435-05-1; **2e,** 21211-62-1; **2g,** 59435-06-2; **2h,** 59435-07-3; **5a,** 4424-76-4; **5b,** 59435-08-4; **5c,** 59435-09-5; **5d,** 59435-10-8; **5e,** 59435-11-9; **5f,** 50634-31-6; **5g,** 59435-12-0; **5h,** 59435-13-1; **5i,** 59435-14-2; **5j,** 59435-15-3; **5k,** 34463-41-7; **5l,** 59435-16-4; **5n,** 59435-17-5; **5o,** 59435-18-6; **5p,** 59435-19-7; **5q,** 59435-20-0; **5r,** 59435-21-1; **5s,** 59435-22-2; **5t,** 59435-23-3; **6a,** 16200-50-3; **6b,** 34874-30-1; **6c,** 59435-24-4; **6d,** 41728-28-3; **6e,** 59435-25-5; **6f,** 59435-26-6; **6g,** 59435-27-7; **6h,** 59435-28-8; **6i,** 59435-29-9; **6k,** 59435-30-2 **6l,** 59435-31-3; **6m,** 59435-32-4; **7a,** 59435-33-5; **7b,** 59435-34-6; **7d,** 59435-35-7; **7e,** 59448-45-2; **7f,** 59435-36-8; methyl cyanoacetate, 105-34-0; benzyl oximinoacetoacetate, 27331-98-2; 3-methyl-2,4-pentanedione, 815-57-6; ethyl cyanoacetate, 105-56-6; *tert*-butyl acetoacetate, 540-88-5; *tert*-butyl oximinoacetoacetate, 14352-65-9; benzyl alcohol, 100-51-6; *p*-anisyl alcohol, 105-13-5; benzhydrol, 91-01-1; malononitrile, 109-77-3.

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Chemistry of 2-(Chloromethyl)furans. Reaction of 2-(Chloromethyl)furans with Aqueous Potassium Cyanide and Other Nucleophiles[1]

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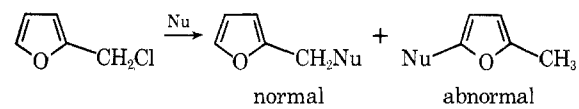
The reaction of 2-(chloromethyl)furan with aqueous cyanide solution was investigated. Experimental evidence is provided for the existence of 5-methylene-2,5-dihydro-2-furonitrile as a reaction intermediate. The effect of temperature, concentration, and solvent on the nature of the products was also examined. Analogous studies were carried out with 4-*tert*-butyl-2-(chloromethyl)furan. A number of 2-(chloromethyl)furans with substituents at various positions of the furan nucleus were synthesized and the reactions of these substituted furans with aqueous cyanide were investigated. The substituents were found to have a noticeable effect on the distribution of the isomeric nitriles obtained. The observed changes could be rationalized in terms of the electronic effects of the substituents. The reactions of 4-*tert*-butyl-2-(chloromethyl)furan with selected nucleophiles were also examined. A mechanism for the nucleophilic displacements of 2-(chloromethyl)furans is proposed.

The reactions of 2-(chloromethyl)furan (**1a**) with various nucleophiles in aqueous and nonaqueous media has generated considerable interest[1,3–20] since Kirner[3] reported the first practical synthesis of the compound more than 45 years ago. An intriguing feature of these reactions is that they often yield 2,5-disubstituted (abnormal) rather than 2-substituted furans (normal).



1a **2a** **3a**

As a result of previous studies, several facts have been established: (1) the so-called rearrangement takes place during

the reaction and only occurs in water or in protic solvents;[12-15] (2) the yield of abnormal product is controlled by an equilibrium established in the reaction mixture; (3) several nucleophiles (cyanide, alkoxide, phenoxide, benzenesulfinate, etc.) give rise to rearranged products[11,16,17] while others afford only the normal displacement products;[17] and (4) the alcoholysis of 2-(chloromethyl)furans is reported to follow first-order kinetics[12,16,19] while the reaction of **1a** with cyanide ion in aprotic solvents is believed to exhibit second-order kinetics.[13,14,15]

A few years ago, we demonstrated the existence of 5-methylene-2,5-dihydro-2-furonitrile (**4a**) as a primary product in the reaction of **1a** with aqueous cyanide,[1] and, more recently, other authors have shown that the rate-determining step in the formation of the abnormal product was proton removal from **4a**.[18] We have since investigated this reaction more thoroughly to establish the actual isomeric composition of the mixture and to examine the influence of conditions on the product distribution. Although the reactions of **1a** with various nucleophiles have been reported,[10,11,16,17,18] nucleophilic displacement reactions involving substituted 2-(chloromethyl)furans had not been investigated. It thus appeared of interest to compare the reactions of **1a** and various substituted 2-(chloromethyl)furans with aqueous potassium cyanide. In addition, a comparative study of the reactions of **1a** and 4-*tert*-butyl-2-(chloromethyl)furan (**1b**) with selected nucleophiles was also undertaken. On the basis of our findings and those of other investigators, a possible mechanism for the reactions of 2-(chloromethyl)furans is proposed.

Results

Although much work had been done by previous investigators, several aspects of the reaction of **1a** with aqueous cyanide still remained unexplored. The relative percentages of the principal products, **2a** and **3a**, had never been measured accurately or directly. Previous reports gave widely different values ranging from 0 to 100% for each of the products.[3,4,6,7,9] Similarly, in reactions involving other nucleophiles, different percentages of normal and abnormal compounds were reported.[10,20] These discrepancies may have arisen because **2a** and **3a** had never been isolated but were converted instead to derivatives whose yield was then established. The presence of possible by-products was never investigated and the optimum conditions for the reaction in an aqueous medium were never established. To clarify this situation, we first examined the composition of the reaction mixture. Unfortunately, early investigators did not describe the conditions under which they carried out their reactions, the first experimental details being given by Reichstein[5] in 1930. We adopted the Reichstein conditions in order to compare our results with those of previous workers although optimum yields are not obtained under this procedure. Mixture of the reagents produced an immediate exothermic reaction. After the exotherm subsided, all organic products were extracted with ether. The solvent was then removed under reduced pressure and the reaction mixture was analyzed by NMR. Both **2a** and **3a** were also prepared by independent routes. Several runs indicated that the yields of **2a** and **3a** were of comparable magnitude, averaging approximately 40 and 60%, respectively. In addition, a small amount of furfuryl alcohol (**5a**) was also formed. In runs at higher temperatures, another substance, a nitrile of unknown structure, was also observed. Although this product was never characterized, it was shown not to be the third possible isomer, 2-methyl-3-furonitrile (**6a**), which we synthesized via an alternative route. During our initial runs, no effort was made to control the temperature of the reaction. Depending upon the initial temperature of the reactants and the rate of stirring, the temperature of the mixture ranged between 60 and 90 °C. We did, however, examine the reaction at ambient temperature and at 0 °C. Analysis of the product mixture obtained from reactions carried out at low temperatures revealed the presence of two additional compounds, starting material and **4a**. The yield of **2a** did not change significantly as a function of temperature; the yield of **3a** was somewhat higher at lower temperatures. Although the observed difference was small (5%), it was real and reproducible in all reactions. A similar trend was also noticed in later investigations with substituted 2-(chloromethyl)furans.

We also investigated the influence of cyanide concentration on the reaction products. Results obtained with 1, 2, and 4 N potassium cyanide solutions were compared with those obtained under our standard reaction conditions (6 N potassium cyanide). Compounds **2a, 3a, 5a,** and the unknown nitrile were each observed. As expected, at decreasing cyanide concentrations, the yield of **5a** increased. This is a result of the increasing probability of the reaction of **1a** with water rather than with cyanide. In more concentrated cyanide solutions the yields of **2a** and **3a** increased, but not equally. In dilute solution, the relative yield of **3a** was higher than that of **2a.**

Moldenhauer and co-workers[9] had attempted to change the relative distribution of **2a** and **3a** in the product mixture by using various metal cyanides. We examined the effect of mercuric, silver, cuprous, ammonium, and benzyltrimethylammonium cyanides on the ratio of **2a** and **3a.** Mercuric cyanide caused a violent reaction and, even at 0 °C afforded only an intractable black tar. Silver cyanide was too insoluble to allow use of our standard isolation procedure and we abandoned this reaction. Cuprous cyanide was also very insoluble, but a mixture of potassium cyanide and cuprous cyanide, which affords a water-soluble complex, was used. This reaction was examined at 0 °C, at ambient temperature, and without temperature control. The best yields were obtained at the lower temperature. Different proportions of potassium cyanide and cuprous cyanide were also employed, but again the standard isolation method could not be used. Ammonium and benzyltrimethylammonium cyanides were both prepared in situ and used in lower concentration than potassium cyanide. None of the various cations present in the reaction mixture changed the ratio of products significantly. Cuprous ions appeared to favor the formation of **2a** while a higher yield of **3a** was obtained with benzyltrimethylammonium cyanide.

Oshiro and co-workers[15] had thoroughly investigated the reaction of **1a** and metal cyanides in aprotic solvents. However, since the effect of mixed solvents had not been examined, we decided to examine the reaction of **1a** in aqueous 1,2-dimethoxyethane solutions of various composition (40, 60, 80, and 99% by volume of 1,2-dimethoxyethane). In 40% 1,2-dimethoxyethane, there was essentially no change in the product distribution. In 60% 1,2-dimethoxyethane, unreacted **1a** was observed. Based on the amount of starting material recovered, the reaction was approximately 10 times slower in 80% 1,2-dimethoxyethane and approximately 100 times slower in 99% 1,2-dimethoxyethane than in the 60% solvent mixture. In the presence of 40% 1,2-dimethoxyethane, the product distribution was the same as under standard conditions, and the relative yields of **2a** and **3a** did not change. The observed rate changes, therefore, appeared to be the result of the decreasing solubility of potassium cyanide in the organic medium as well as the decreasing polarity of the solvent. Oshiro's observation[15] that the reaction rate is directly proportional to the product of the dielectric constant of the solvent and the solubility of the inorganic reagent in that particular solvent is thus applicable to our conditions. Another expected effect of the decrease in water content was the decrease in the yield of **5a.**

The reaction between **1a** and potassium cyanide was also investigated in deuterium oxide at 0 °C. NMR analysis of the

mixture, after 3 h, indicated the presence of **1a, 2a, 3a, 4a,** and **5a.** The percentages of **1a** (10%) and **4a** (17%) were unexpectedly high as compared to the results in the undeuterated medium (1 and 14%, respectively). The relative proportions of **2a** and **3a** indicated that the formation of **2a** was slightly favored. The rate of the reaction was approximately 11% slower in deuterium oxide than in water. The difference may be due to the slower rate of hydrolysis of potassium cyanide in deuterium oxide or the slower ionization of **1a** in this medium. The rate of rearomatization of **4a** in deuterium oxide was also slower than in water. Incorporation of deuterium in the methylene group of **2a** and in the methyl group of **3a** was also observed.

All of the data thus obtained point to a unimolecular mechanism in which the rate is controlled by the heterolysis of **1a.** The product ratio is then determined by competition between the nucleophiles in the succeeding fast steps. In 1,2-dimethoxyethane, the reduced polarity of the medium decreased the rate of the reaction but did not change the product distribution significantly. If **2a** were formed by a bimolecular mechanism, a noticeable change should be seen in the relative ratios of **2a** and **3a.** The small increase of **3a** observed in the presence of cuprous cyanide also supports a unimolecular mechanism although it might be argued that a small amount of **2a** is formed by a competing bimolecular mechanism. The hydrolysis and alcoholysis of **1a** have been reported to be unimolecular processes[10-12] and it may be assumed that an analogous nucleophilic reaction would follow similar kinetics.

Since all experimental evidence seemed to support a unimolecular mechanism, the failure to detect even a small amount of the other possible isomer, **6a,** was disturbing. In order to evaluate qualitatively the distribution of the positive charge in the furfuryl cation, several Hückel type molecular orbital calculations were carried out.[21a,b] All calculations showed considerably less charge density at C_3 than at the methylene carbon or at C_5, thus supporting the observed reactivity at these positions.

Although **4a** had been postulated as an intermediate as early as 1932,[6] this compound had not been detected until recently. Yur'ev and co-workers[22] isolated 5-methylene-2-(chloromethyl)-2,5-dihydro-2-furonitrile from the reaction of 2,5-bis(chloromethyl)furan with potassium cyanide in aqueous benzene. A 2,5-dihydrofuran was also reported in the alcoholysis of **1a** under basic conditions.[10] A few years later, 5-methylene-2-methoxy-2,5-dihydrofuran was isolated by Hill.[16] In the present investigation, the presence of a transient species preceding the formation of **3a** was detected by a set of resonances in the NMR spectrum of the crude product mixture obtained from the reaction of **1a** and aqueous potassium cyanide at 0 °C.[1]

The reaction of 4-*tert*-butyl-2-(chloromethyl)furan (**1b**) with aqueous potassium cyanide was investigated next since, a priori, the bulk of a *tert*-butyl group in the 4 position could hinder the approach of an attacking nucleophile at the 5 position. While the reaction of **1a** with aqueous potassium cyanide went to completion in 0.5 h, at ambient temperature, the reaction of **1b** under the same conditions required over 24 h. The decrease in reactivity observed for **1b** relative to **1a** may partially be attributed to its lesser water solubility.

Several runs at 37.5 ± 0.5 °C afforded yields of normal (**2b**) and abnormal (**3b**) products averaging approximately 25 and 75%, respectively, as compared to 40% (**2a**) and 60% (**3a**) for **1a.** A time–concentration study showed that **3b** formed before **2b.** Intermediate **4b** was not observed during the first 6–7 h of the reaction. It did, however, appear toward the end of the reaction, indicating that the rate of aromatization must, at this stage, be decreasing.

The effect of temperature on the reaction of **1b** with aqueous cyanide was also investigated. The relative percentages of the isomeric products showed only a slight variation with increasing temperature. As in the case of **1a,** the yield of abnormal product appeared to decrease slightly with increasing temperature.

The influence of cyanide concentration on the reaction products was examined. A slight increase in the yield of **3b** was noted as the cyanide concentration was decreased, but again the total effect of this change on the isomer distribution was small.

The rate of the reaction of **1b** with aqueous potassium cyanide was much slower than that of **1a** with the same reagent. The yield of abnormal product was appreciably greater than that obtained from **1a,** indicating that substituents had a definite influence on the final isomeric composition.

Examination of a Courtauld model of **1b** showed considerable hydrogen–hydrogen repulsion between one of the protons on the *tert*-butyl group and the 5 proton of the furan ring, whereas a similar model of the intermediate methylene compound, 3-*tert*-butyl-5-methylene-2,5-dihydro-2-furonitrile (**4b**), showed less hydrogen–hydrogen interference. Relief of steric strain might therefore be invoked to explain the larger percentage of abnormal product. To test this hypothesis, 4-isopropyl-2-(chloromethyl)furan (**1c**) was synthesized (Scheme IV). Treatment of **1c** with aqueous potassium cyanide, however, afforded the highest observed yield of abnormal product (**3c**) among the 2-(chloromethyl)furans examined, 84%, thus eliminating steric strain as a determining factor in the reaction.

Since, in extended allylic systems susceptible to SN2′ mechanisms, a bulky group on the saturated carbon prevents formation of the normal product but does not affect the yield of abnormal product, the analogous furan system, 3-*tert*-butyl-2-(chloromethyl)furan (**1d**), was synthesized (Scheme V). When this halide was treated with aqueous potassium cyanide, at 70 °C, three products were obtained, the two expected isomeric products (**2d** and **3d**) and 4-*tert*-butyl-5-methyl-2(5*H*)-furanone (**7**). Lactone **7** could be eliminated, however, by carrying out the reaction at a lower temperature. The relative percentage of the two isomeric products was very similar (**2d,** 39% and **3d,** 61%) to that obtained for **1a.** Since the formation of the normal product was not suppressed, the operation of a SN2′ mechanism seems unlikely.

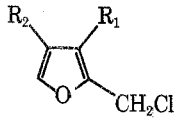
Halogen atoms have been known to act as electron-withdrawing or electron-donating groups depending on whether they primarily exert an inductive or resonance effect. It appeared of interest to examine the effect of a bromine substituent on the aforementioned product distribution. 4-Bromo-2-(chloromethyl)furan (**1e**) was thus synthesized (Scheme VI). Although the reaction of **1e** with aqueous potassium cyanide was slow, a yield of 83% of abnormal product (**3e**) was obtained.

Since bromine appeared to function as an electron-donating group, it was decided to study the effect of an electron-withdrawing substituent, such as a carbethoxy or cyano group, in the 4 position. The reaction of ethyl 2-(chloromethyl)-4-furoate (**1f**) with aqueous potassium cyanide gave 53% of normal product (**2f**) and only 47% of the abnormal product (**3f**). When 5-(chloromethyl)-3-furonitrile (**1g**) was treated with the same reagent, a quantitative yield of the normal product (**2g**) was obtained.

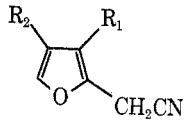
The results of the reactions of the various substituted 2-(chloromethyl)furans with aqueous potassium cyanide are summarized in Table I.

It may be seen from Table I that electron-donating groups favor the formation of the abnormal product and that this effect is most pronounced when the substituent is in the 4 position. Electron-withdrawing groups retard the reaction considerably and may completely inhibit the formation of

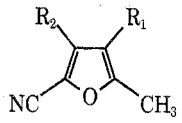
Table I. Relative Percentages of the Isomeric Nitriles Formed from the Reactions of Substituted 2-(Chloromethyl)furans with Aqueous Potassium Cyanide



1a-f



2a-f



3a-f

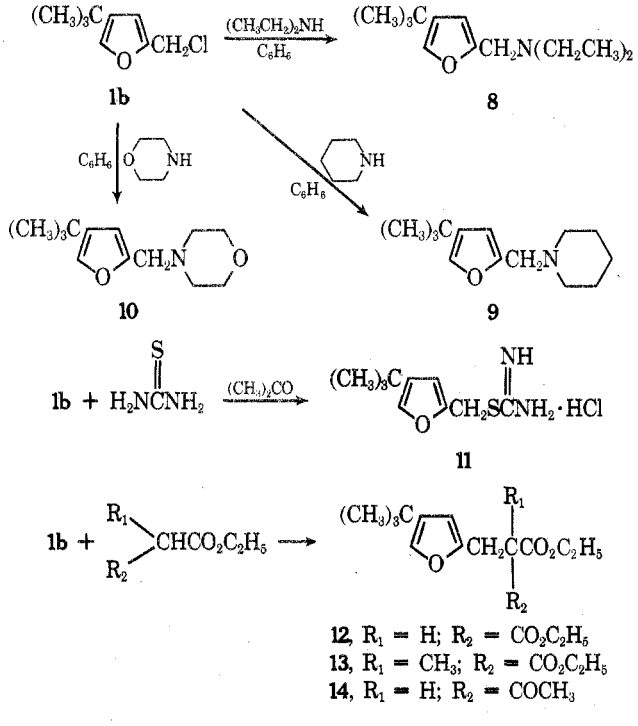
	Substituents		Time, h at 37.5 ± 0.5°C	Normal product, %	Abnormal product, %
	R_1	R_2			
a	H	H	0.5	40	60
b	H	$C(CH_3)_3$	15	25	75
c	H	$CH(CH_3)_2$	28	16	84
d	$C(CH_3)_3$	H	48	39	61
e	H	Br	96	17	83
f	H	$CO_2C_2H_5$	168	53	47
g	H	CN	168	100	0

abnormal product. The effects of these substituents are consistent with the stabilization of an electron-deficient center and lend support to the postulation of 2-methylenefuryllium ions as the first intermediates formed in the ionization of the corresponding 2-(chloromethyl)furans.

Since nucleophilic displacements with ions other than cyanide had all been performed on 2-(chloromethyl)furan (**1a**), a comparative study of the reactions of **1a** and 4-*tert*-butyl-2-(chloromethyl)furan (**1b**) with selected nucleophiles appeared of interest.

The reactions of **1b** with amines in benzene, with thiourea in acetone, and with esters in sodium ethoxide all yielded normal products (8–14) (Scheme I).

Scheme I



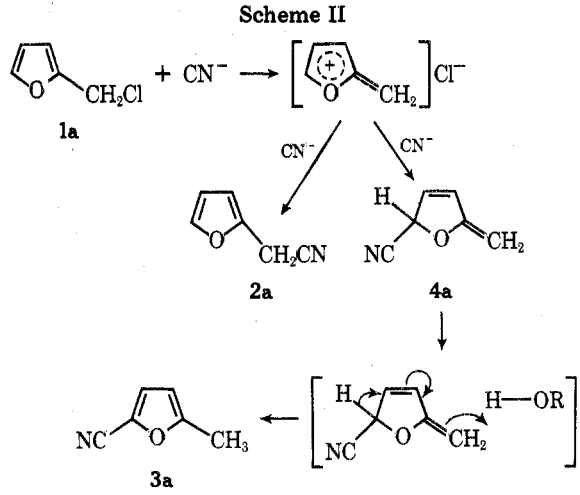
These results confirmed the fact that no rearranged products have ever been observed in nonaqueous media.[12-15]

Although the reaction of **1a** with sodium azide was reported to give only the normal product,[11] NMR analysis of the reaction of **1b** with this nucleophile clearly showed resonances for both a normal and abnormal product. The reaction of **1a** with potassium thiocyanate was previously reported to give the normal thiocyanate.[17] Again the NMR spectrum of the reaction mixture clearly shows resonances for two distinct compounds, a normal and abnormal product. In the case of the normal product, both the isothiocyanate and thiocyanate could be observed. We could not, however, determine whether the abnormal product was a thiocyanate, isothiocyanate, or a mixture of both. Since the cited nucleophiles do not give abnormal products with **1a**, these reactions further illustrate the importance of substituents in the 2-(chloromethyl)furan. Although we did not conduct a rigorous investigation, preliminary NMR studies indicate that the percentage of abnormal product is greater at lower temperatures.

Discussion

On the basis of our findings and those of other investigators,[3-18] a possible mechanism for the reactions of 2-(chloromethyl)furans is proposed in Scheme II.

Scheme II



The reaction is initiated by heterolysis of 2-(chloromethyl)furan to give a furyllium ion as an intimate ion pair with an appropriate anion. After the solvolytic cage of this ion pair collapses, the more nucleophilic ion attacks either at the methylene carbon or at the 5 position. The less nucleophilic hydroxide ion may compete for the cation to a small extent. When hydroxide ion adds to the 5 position, the product is unstable and results in the opening of the furan ring to give products that polymerize. The last step consists of aromatization of 5-methylene-2,5-dihydro-2-furonitrile (**4a**).

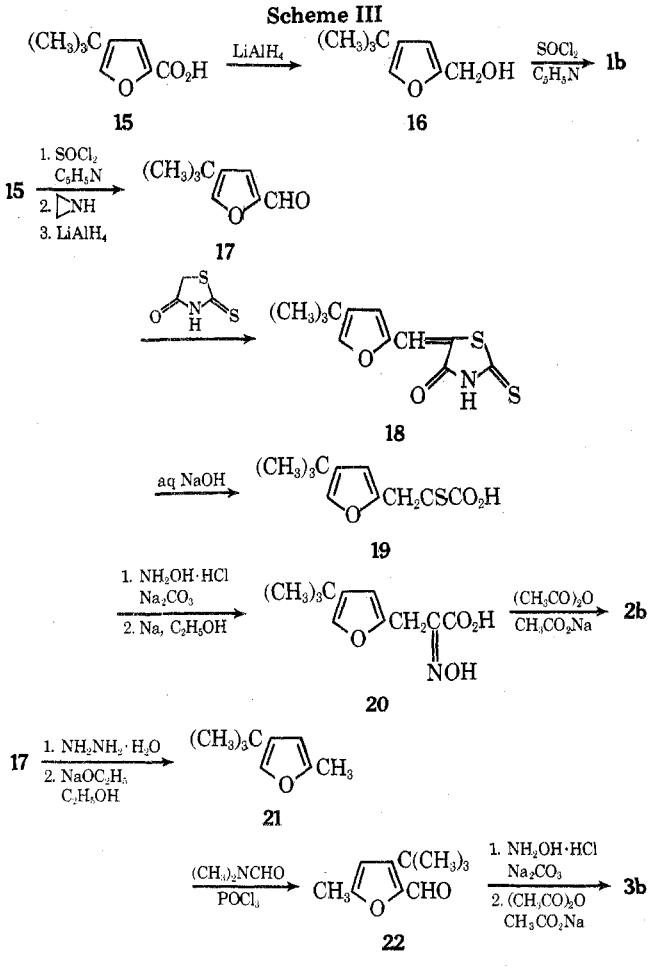
The ease of heterolysis of **1a** is supported by the cleavage products of **1a** in the mass spectrum. Elimination of a chloride ion is the favored process in the decomposition of this compound. The stability of the resulting cation is indicated by the fact that the *m/e* 81 peak is the base peak in the fragmentation of **1a**. Stable furyllium salts have been prepared and are

known to react readily with nucleophiles.[23] Furthermore, the stability of such a cation should be very much dependent on substituents. As we have demonstrated, substituent effects in this system are consistent with stabilization of an electron-deficient center. The effect is most noticeable with substituents in the 4 position, i.e., the position closest to the most electron-deficient site in the ion, the 5 position. Destabilization of the furyllium ion by an electron-withdrawing substituent such as a cyano group results in the exclusive formation of the normal product. The importance of this stabilization is also evident in the reactions of **1a** and **1b** with azide and thiocyanate ions; abnormal product formed only from **1b**, which gives rise to the better stabilized furyllium ion. Therefore, it appears likely that attack at the methylene group and at the 5 position could be competitive processes with many nucleophiles if a sufficiently stabilized furyllium ion is involved in the intimate ion pair. It is well to remember, however, that certain nucleophiles such as hydroxide ion can lead to ring opening when introduced at the 5 position. The large amount of polymeric material observed in these reactions is no doubt the result of such a sequence.

The aromatization process is first order in 5-methylene-2,5-dihydro-2-furonitrile. However, cyanide is essential in this process since the presence of **4a** could only be observed when the cyanide concentration was decreased. Finally, the role of the solvent is all important. A polar solvent is needed for heterolysis of the halide and stabilization of the furyllium ion formed. Furthermore, the solvent must also be protic; the formation of abnormal product has only been observed in water or alcohol. Solvent is apparently needed as a proton source at the methylene carbon in order for aromatization of **4a** to occur.

Synthetic Schemes. The synthetic routes leading to **1b**, **2b**, and **3b** are shown in Scheme III.

Scheme III

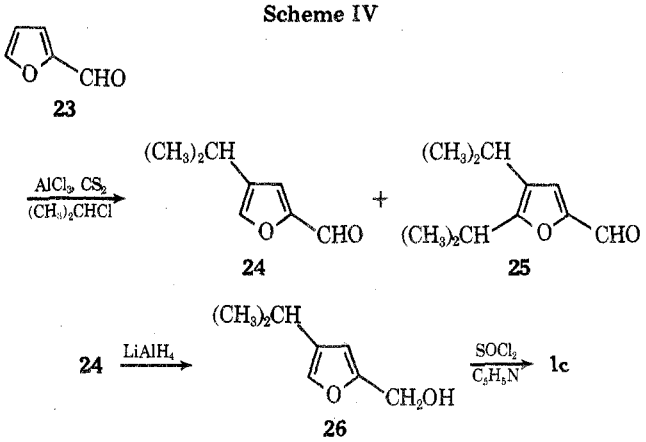


4-*tert*-Butyl-2-(chloromethyl)furan (**1b**) was prepared via the reaction of 4-*tert*-butylfurfuryl alcohol (**16**) with thionyl chloride in pyridine. The alcohol, in turn was obtained by the reduction of 4-*tert*-butyl-2-furoic acid (**15**) with lithium aluminum hydride.

4-*tert*-Butyl-2-furanacetonitrile (**2b**) was synthesized by the rhodanine method[24a,b] from 4-*tert*-butyl-2-furaldehyde (**17**). The aldehyde in turn was obtained by treating the corresponding acid halide with aziridine and reducing the intermediate acyl aziridine with lithium aluminum hydride.[25] The rhodanine derivative of **17** (**18**) was cleaved with aqueous sodium hydroxide to give 4-*tert*-butyl-α-thio-2-furanpyruvic acid (**19**) which was then converted to 4-*tert*-butyl-2-furanpyruvic acid oxime (**20**) with hydroxylamine hydrochloride and sodium ethoxide. Decarboxylation and dehydration of the oximino acid using sodium acetate and acetic anhydride gave **2b**.

4-*tert*-Butyl-5-methyl-2-furonitrile (**3b**) was synthesized in four steps from 4-*tert*-butyl-2-furaldehyde hydrazone. Reduction of the hydrazone with sodium ethoxide in absolute ethanol[26] afforded 4-*tert*-butyl-2-methylfuran (**21**) which, in turn, was formylated with *N,N*-dimethylformamide and phosphorus oxychloride[27] at low temperature to give 3-*tert*-butyl-5-methyl-2-furaldehyde (**22**). Treatment of the aldehyde with hydroxylamine and dehydration of the resulting oxime with acetic anhydride produced **3b**. 4-Isopropyl-2-(chloromethyl)furan (**1c**) was synthesized as shown in Scheme IV.

Scheme IV

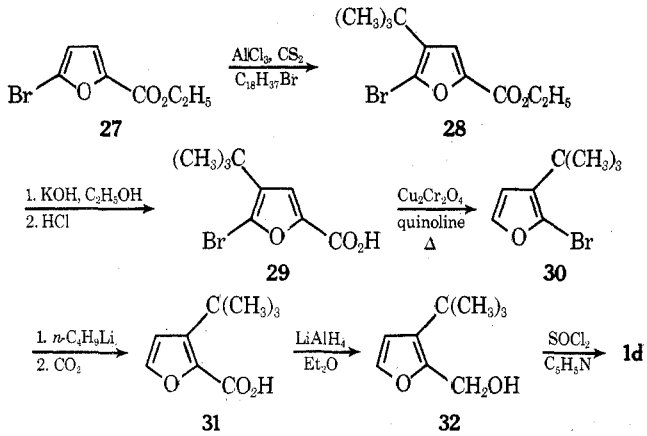


Furaldehyde (**23**) was alkylated with isopropyl chloride and aluminum chloride, in carbon disulfide, to afford 4-isopropyl-2-furaldehyde (**24**). Compound **24** was reduced with lithium aluminum hydride in ether to the corresponding alcohol (**26**) which, in turn, was converted to **1c** on treatment with thionyl chloride in ether–pyridine solution.

The alkylation of **23** with isopropyl chloride was previously described by Gilman[28a,b] and reported to give only 4-isopropyl-2-furaldehyde (**24**). We, however, isolated two products, the desired aldehyde, **24**, and 4,5-diisopropyl-2-furaldehyde (**25**). Furans substituted with electron-withdrawing groups at the 2 position normally undergo electrophilic substitution at the 5 position.[29] Under the conditions of this reaction (excess aluminum chloride), however, **23** undoubtedly complexes with the Lewis acid with resulting reduction of electron density within the furan ring. This effect would be manifested at the 3 and 5 positions, but not at the 4 position. The approximate charge distributions at the 4 and 5 positions of some 2-furyl ketones have been calculated as 0.4 and 0.5, respectively.[30] These values are relatively similar and it is conceivable that deactivation of the 5 position by complexation sufficiently perturbs the electron densities at the 4 and 5 positions to account for the observed substituent orientation in **24** and **25**.

3-*tert*-Butyl-2-(chloromethyl)furan (**1d**) was prepared as illustrated in Scheme V.

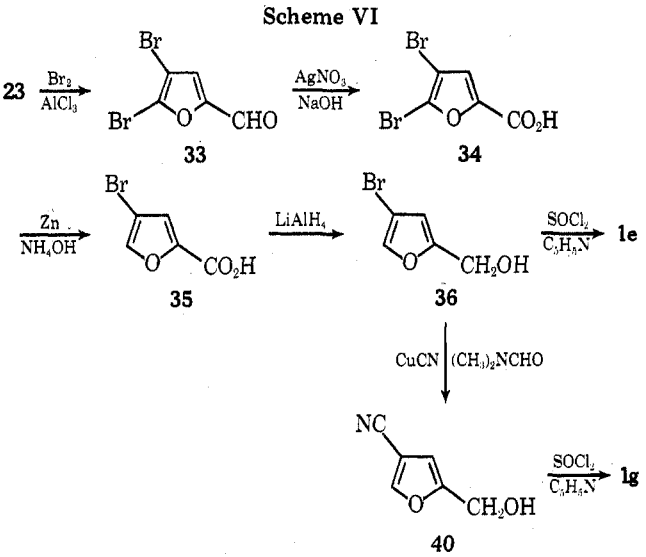
Scheme V



Esterification of 5-bromo-2-furoic acid with ethanol and sulfuric acid,[31] followed by alkylation of the resultant ester (**27**) with *n*-octadecyl bromide and aluminum chloride,[32] afforded ethyl 5-bromo-4-*tert*-butyl-2-furoate (**28**). Hydrolysis of compound **28** with alcoholic potassium hydroxide and decarboxylation of the intermediate acid (**29**) with copper chromite and quinoline[33] then gave 2-bromo-3-*tert*-butylfuran (**30**). Treatment of **30** with *n*-butyllithium and dry ice afforded 3-*tert*-butyl-2-furoic acid (**31**) which, in turn, was converted to **1d** via the corresponding alcohol (**32**).

4-Bromo-2-(chloromethyl)furan (**1e**) was prepared as shown in Scheme VI.

Scheme VI

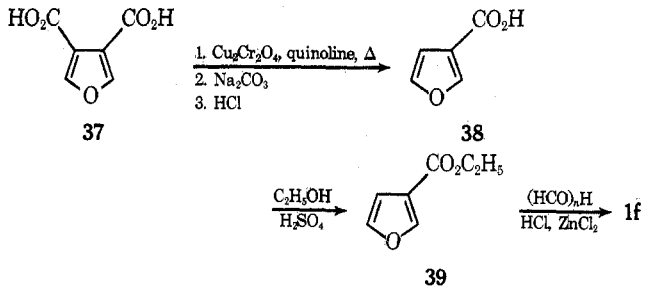


2-Furaldehyde (**23**) was brominated in the presence of excess aluminum chloride[34] to give 4,5-dibromo-2-furaldehyde (**33**) in almost quantitative yield. Oxidation of compound **33** with silver nitrate and sodium hydroxide produced 4,5-dibromofuroic acid[35] (**34**) which was then reduced to 4-bromo-2-furoic acid (**35**) with zinc and ammonium hydroxide.[36] Direct reduction of **35** afforded 4-bromofurfuryl alcohol (**36**). Treatment of compound **36** with thionyl chloride in ether–pyridine solution then gave **1e**.

Ethyl 5-(chloromethyl)-3-furoate (**1f**) was synthesized as shown in Scheme VII.

Decarboxylation of 3,4-furandicarboxylic acid (**37**) was accomplished by heating this compound with copper chromite and quinoline.[37] The resultant acid[37] (**38**) was esterified and its ester (**39**) immediately chloroformylated[38] with paraformaldehyde, hydrogen chloride, and zinc chloride to give **1f**.

Scheme VII



5-(Chloromethyl)-3-furonitrile (**1g**) was prepared via the corresponding alcohol (**40**) which, in turn, was synthesized by heating **36** with cuprous cyanide in *N,N*-dimethylformamide[39] as shown in Scheme VI.

Experimental Section

General. Melting points were determined with a Thomas-Hoover apparatus and are uncorrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn., Alfred Bernhardt Microanalytisches Laboratorium, West Germany; and Microanalysis, Inc., Wilmington, Del. NMR spectra were recorded in carbon tetrachloride solutions (Me_4Si standard) with a Varian A-60A or HA-100D spectrometer. Ir spectra, both neat and in 10% carbon tetrachloride, were obtained on a Perkin-Elmer 521 grating infrared spectrophotometer. Mass spectra were determined on a Consolidated Electrodynamic Corp. CEC-110 double-focusing mass spectrometer. A Nester-Faust NF-190 spinning band column (6 × 450 mm, 23 theoretical plates) was employed for fractional distillations. Analytical gas chromatography was carried out on a F & M 700 chromatograph with a thermal conductivity detector using 12 ft × 0.5 in. o.d. columns packed with 20% silicone oil or 10% Carbowax. Helium was employed as a carrier gas at a flow rate of 60 ml/min. The oven temperature was programmed at 10 °C/min from 80 to 120 °C. For preparative gas chromatography, an Aerograph Autoprep A-700 instrument was employed. Time–concentration studies at 37.5 ± 0.5 °C were carried out in an Elberbach water bath shaker.

2-(Chloromethyl)furan (1a). This compound was synthesized according to the procedure of Kirner[3] using freshly distilled furfuryl alcohol (bp 54–56 °C at 8 mm), thionyl chloride, and pyridine in anhydrous ether. After the removal of pyridinium hydrochloride, the product was obtained as an orange solution in ether and was stored in this form at −20 °C over anhydrous potassium carbonate. Immediately before use, the solvent was removed on a rotary evaporator and the crude product was distilled through a micro-Vigreux column: bp 19–19.5 °C (1.25 mm) [lit.[3] bp 37 °C (15 mm)]; ir (CCl_4) 3150, 3120, 2970, 2920, 1730, 1605, 1496, 1379, 1220, 1150, 1008, 936, 882, 742, and 738 cm^{-1}; NMR (neat) δ 7.30 (m, 1 H, H-5), 6.22 (m, 2 H, H-4 and H-3), and 4.48 (m, 2 H, CH_2); mass spectrum *m/e* (rel intensity) 116 (M^+, 20), 81 ($C_5H_5O^+$, 100), 52 ($C_4H_4^+$, 16), 51 ($C_4H_3^+$, 22), 50 ($C_4H_2^+$, 13), and 39 ($C_3H_3^+$, 7). *Caution: This compound should always be stored in solution because neat samples decompose slowly, even at −20 °C, to give hydrogen chloride which catalyzes polymerization of the furan ring with explosive violence.*

2-Furylacetonitrile (2a). An authentic sample of **2a** was synthesized in 41% yield from 2-furfural according to the procedure of Plucker and Amstutz:[24a] bp 56–58 °C (5 mm) [lit.[23] bp 78–80 °C (20 mm)]; ir (CCl_4) 3158, 3122, 2962, 2920, 2258, 1740, 1600, 1505, 1410, 1218, 1148, 1015, 950, 886, 818, 750, and 740 cm^{-1}; NMR (neat) δ 7.37 (m, 1 H, H-5), 6.28 (m, 2 H, H-4 and H-3), and 3.68 (m, 2 H, CH_2); mass spectrum *m/e* (rel intensity) 107 (M^+, 72), 81 ($C_5H_5O^+$, 7), 79 ($C_5H_5N^+$, 37), 78 ($C_5H_4N^+$, 19), 52 ($C_4H_4^+$ and/or $C_3H_2N^+$, 100), 51 ($C_4H_3^+$, 32), 50 ($C_4H_2^+$, 14), 39 ($C_3H_3^+$, 33). 2-Furylacetonitrile should be stored as a neat liquid at −20 °C because it is heat sensitive and discolors at room temperature within 24 h. Samples refluxed in toluene, xylene, or pyridine for 3 h undergo strong discoloration and, although approximately 60% of **2a** can be recovered, afford intractable tars. The instability of this compound may account for the small amounts of normal product observed by some authors.

To ascertain whether **2a** could rearrange to **3a** under the conditions of our experiment, **2a** was stirred in a saturated potassium cyanide solution at 80 °C for 3 h. Although the solution darkened considerably, only unreacted starting material could be isolated. Other experiments carried out in the presence of potassium chloride or a catalytic amount of furfuryl alcohol were also negative. No trace of an isomeric nitrile could be detected in any of the reaction mixtures.

5-Methyl-2-furonitrile (3a). An authentic sample of **3a** was prepared in 48% yield from 5-methyl-2-furfural via the procedure described by Scott and Johnson:[7] bp 50–51 °C (7 mm) [lit.[7] bp 74–75 °C (27 mm)]; ir (CCl_4) 3180, 3130, 2960, 2928, 2224, 1720, 1595, 1522, 1220, 950, and 796 cm^{-1}; NMR (neat) δ 7.02 (d, 1 H, H-4), 6.17 (m, 1 H, H-3), and 2.34 (m, 3 H, $-CH_3$); mass spectrum *m/e* (rel intensity) 107 (M^+, 100), 106 ($C_6H_4NO^+$, 57), 81 ($C_5H_5O^+$, 3), 79 ($C_5H_5N^+$, 25), 78 ($C_5H_4N^+$, 20), 53 ($C_4H_5^+$, 53), 52 ($C_4H_4^+$ or $C_3H_2N^+$, 67), 51 ($C_4H_3^+$, 32), 50 ($C_4H_2^+$, 22), 43 ($C_2H_3O^+$, 27), and 39 ($C_3H_3^+$, 10).

5-Methyl-2-furonitrile is considerably more stable than the isomeric 2-furylacetonitrile. Attempts to isomerize compound **3a** at 80 °C, in potassium cyanide solution, in the presence of potassium chloride, or with a catalytic amount of furfuryl alcohol, were unsuccessful. Therefore, **3a**, once formed, does not rearrange to **2a** under the conditions of our experiments.

2-Methyl-3-furonitrile (6a). This compound was prepared from ethyl 2-methyl-3-furancarboxylate. The ester was hydrolyzed to the corresponding acid which was then converted to the acid chloride with thionyl chloride and pyridine. Treatment of the acid chloride with ethyleneimine and subsequent reduction of the intermediate acylaziridinium compound with lithium aluminum hydride[25] gave 2-methyl-3-furancarboxaldehyde. This compound reacted with hydroxylamine hydrochloride to yield the corresponding oxime (89.1% yield, mp 74–77 °C) which, in turn, was converted to **6a** without further purification.

2-Methyl-3-furancarboxaldoxime (9.8 g, 0.08 mol) was heated for 10 min in 15 ml of acetic anhydride. The solution was poured into 200 ml of ice-cold water and neutralized with sodium carbonate, whereupon the product was isolated by steam distillation. The distillate was extracted with ether and the organic layer was then separated and dried over anhydrous magnesium sulfate. Solvent was removed on a rotary evaporator, and the residue was distilled, first through a micro-Vigreux column and then through a spinning band column. The yield of pure **6a** was 2.3 g (27%): bp 42–44 °C (2.5 mm); ir (CCl_4) 3160, 2960, 2920, 1680, 1600, 1517, 1240, 950, and 742 cm^{-1}; NMR (neat) δ 7.37 (d, 1 H, H-4), 6.51 (d, 1 H, H-5), and 2.42 (s, 3 H, $-CH_3$); $J_{H_4H_5}$ = ±2.29 Hz. Compound **6a** had approximately the same stability as **3a**.

4-*tert*-Butylfurfuryl Alcohol (16). A solution of 4-*tert*-butyl-2-furoic acid (**15**, 20.0 g, 0.12 mol) in 180 ml of anhydrous ether was added dropwise to a solution of lithium aluminum hydride (6.0 g, 0.16 mol) in 600 ml of anhydrous ether at such a rate as to produce gentle reflux. After the addition was completed, the reaction mixture was refluxed for 2 h longer with continuous stirring. The solution was cooled and water was added dropwise to destroy the excess hydride. The resulting inorganic salts were removed by filtration. The ether filtrate was washed with 5% aqueous sodium carbonate and then dried with anhydrous sodium sulfate. Solvent was removed under reduced pressure and the residue was distilled in vacuo to yield 10.0 g (64.9%) of product: bp 73–74 °C (6 mm); NMR (CCl_4) δ 7.07 (s, 1 H, H-5), 6.21 (s, 1 H, H-3), 4.83 (s, 1 H, –OH), 4.48 (s, 2 H, CH_2), and 1.18 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_9H_{14}O_2$: C, 70.13; H, 9.09. Found: C, 70.32; H, 9.25.

4-*tert*-Butyl-2-(chloromethyl)furan (1b). This compound was synthesized from 4-*tert*-butylfurfuryl alcohol (**16**), thionyl chloride, and pyridine in anhydrous ether, by the procedure described for **1a**. The crude product was distilled in vacuo to yield 7.35 g (42.70%) of **1a**: bp 42–42.5 °C (2.1 mm); NMR (CCl_4) δ 7.13 (s, 1 H, H-5), 6.30 (s, 1 H, H-3), 4.47 (s, 2 H, CH_2), and 1.20 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_9H_{13}ClO$: C, 62.61; H, 7.32; Cl, 20.28. Found: C, 62.38; H, 7.54; Cl, 20.53.

4-*tert*-Butyl-2-furaldehyde (17). This compound was synthesized from 1-(4-*tert*-butyl-2-furoyl)aziridine and lithium aluminum hydride.[25] The yield of aldehyde was 47.9%: bp 55–56 °C (2.5 mm) [lit.[32] bp 93–95 °C (13 mm)]; ir (CCl_4) 3150, 2980, 2850, 2700, 1680, 1580, 1500, 1460, 1365, 1250, 1210, 1145, 943, 760, and 755 cm^{-1}; NMR (CCl_4) δ 9.45 (s, 1 H, –CHO), 7.36 (s, 1 H, H-5), 7.02 (s, 1 H, H-3), and 1.30 [s, 9 H, $-C(CH_3)_3$].

The aziridine derivative was prepared in situ from 4-*tert*-butyl-2-furoyl chloride and ethyleneimine. 4-*tert*-Butyl-2-furoyl chloride was obtained by heating 4-*tert*-butyl-2-furoic acid (12.0 g, 0.072 mol) and thionyl chloride (16.0 g, 0.15 mol) in 30 ml of benzene for 6 h. The excess thionyl chloride and benzene were removed by distillation under reduced pressure. The residue was then distilled in vacuo to give 4-*tert*-butyl-2-furoyl chloride (9.22 g, 69.0% yield): bp 69–71 °C (1.5 mm); ir (CCl_4) 2960, 1750, 1735, 1430, 1150, 1090, 965, and 945 cm^{-1}; NMR (CCl_4) δ 7.46 (s, 1 H, H-5, $J_{3,5}$ = ±1.5 Hz), 7.31 (s, 1 H, H-3, $J_{5,3}$ = +1.5 Hz), and 1.30 [s, 9 H, $-C(CH_3)_3$]. Because of the instability of the halide, an elemental analysis could not be obtained for this compound. The halide was, however, converted to the corresponding anhydride in 57.7% yield to provide additional proof of structure: mp 120–121 °C; ir (CCl_4) 2960, 1795, 1735, 1500, 1460, 1365, 1310, 1245, 1215, 1145, 1095, and 945 cm^{-1}; NMR (CCl_4) δ 7.46 (s, 1 H, H-5), 7.26 (s, 1 H, H-3), and 1.30 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.74; H, 6.83.

5-(4-*tert*-Butylfurfurylidene)rhodanine (18). A solution of 4-*tert*-butyl-2-furaldehyde (3.58 g, 0.024 mol) and rhodanine (3.0 g, 0.023 mol) in 15 ml of glacial acetic acid was heated with anhydrous sodium acetate (5.55 g, 0.068 mol) for 1.5 h and then poured into 100 ml of cold water. The yellow solid that formed was washed with water and recrystallized from 50% aqueous ethanol to yield 5.60 g (89.0%) of product: mp 187–188 °C; ir (CCl_4) 3440, 2980, 1690, 1610, 1565, 1435, 1220, 1190, and 965 cm^{-1}; NMR (CCl_4) δ 7.53 (s, 1 H, =CH), 7.41 (s, 1 H, H-5), 6.83 (s, 1 H, H-3), and 1.20 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{12}H_{13}O_2NS_2$: C, 53.89; H, 4.87; N, 5.26; S, 23.91. Found: C, 53.74; H, 4.96; N, 5.25; S, 23.93.

4-*tert*-Butyl-α-thio-2-furanpyruvic Acid (19). A suspension of 5-(4-*tert*-butylfurfurylidene)rhodanine (5.60 g, 0.021 mol) in 40 ml of 10% aqueous sodium hydroxide (4.0 g, 0.10 mol) was heated on a steam bath for 0.5 h. The solution was cooled and treated with 40 ml of 10% hydrochloric acid to precipitate the acid. The resulting solid was washed with water and recrystallized from 45% aqueous ethanol to yield 4.15 g (88.0%) of yellow product: mp 96–98 °C; ir (CCl_4) 2960, 2900, 2870, 1700, 1600, 1500, 1410, 1260, and 950 cm^{-1}; NMR (CCl_4) δ 7.80 (s, 1 H, $-CO_2H$), 7.40 (s, 1 H, H-5), 6.90 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2), and 1.40 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.41; H, 6.19; S, 14.16. Found: C, 58.26; H, 6.20; S, 14.28.

4-*tert*-Butyl-2-furanpyruvic Acid Oxime (20). This compound was synthesized by heating 4-*tert*-butyl-α-thio-2-furanpyruvic acid (4.15 g, 0.019 mol), hydroxylamine hydrochloride (4.15 g, 0.059 mol), and an ethanolic sodium ethoxide solution [prepared from 1.35 g of sodium (0.059 g-atom) and 90 ml of absolute ethanol] for 1.5 h. The ethanol was removed under reduced pressure and the residue was dissolved in 10 ml of 5% aqueous sodium hydroxide. The sulfur that formed was removed by filtration and the filtrate was acidified with 9 ml of 10% hydrochloric acid. Recrystallization of the resulting brown solid from petroleum ether (bp 60–110 °C) gave 2.90 g of product, 71.4% yield: mp 122–123 °C; ir (CCl_4) 3230, 2960, 2900, 2870, 1700, 1600, 1470, 1460, 1420, 1360, 1205, 1180, 1130, 1120, 1095, 1030, 900, and 700 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}NO_4$: C, 58.67; H, 6.67; N, 6.67. Found: C, 58.59; H, 6.43; N, 6.73.

4-*tert*-Butyl-2-furanacetonitrile (2b). Compound **20** (1.50 g, 0.007 mol) was heated in acetic anhydride (5.50 g, 0.008 mol) for 1.5 h. The mixture was then treated with 125 ml of water and steam distilled. The distillate was extracted with ether, and the ether extracts were then neutralized with a saturated aqueous sodium carbonate solution and dried over anhydrous magnesium sulfate. Evaporation of the solvent and distillation of the residue in vacuo afforded 0.98 g (85.6%) of **2b**: bp 72–72.5 °C (3.5 mm); ir (CCl_4) 2960, 2900, 2870, 2250, 1610, 1540, 1470, 1460, 1420, 1360, 1210, 1120, 1110, 970, 950, and 665 cm^{-1}; NMR (CCl_4) δ 7.08 (s, 1 H, H-5), 6.25 (s, 1 H, H-3), 3.63 (s, 2 H, CH_2), and 1.20 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.62; H, 7.97; N, 8.59. Found: C, 73.50; H, 8.00; N, 8.74.

4-*tert*-Butyl-2-methylfuran (21). This compound was prepared by the reduction of 4-*tert*-butyl-2-furaldehyde hydrazone which, in turn, was synthesized from compound **17** (2.32 g, 0.015 mol) and 99% hydrazine hydrate (3.0 g, 0.06 mol) in 5 ml of ether. The mixture was treated with calcium chloride (1.65 g, 0.015 mol) and stirred for 1.5 h. The ether layer was decanted and dried over magnesium sulfate. Removal of the solvent under reduced pressure afforded 1.87 g (78.2% yield) of crude 4-*tert*-butyl-2-furaldehyde hydrazone. This compound was next added dropwise to a warm ethanolic solution of sodium ethoxide prepared from 0.23 g (0.01 g-atom) of sodium and 6 ml of absolute ethanol. The mixture was heated at reflux for 4 h and the resulting solution was then distilled at atmospheric pressure to yield **21** and ethanol. A saturated aqueous sodium chloride solution was added to the distillate. The oily layer that formed was separated, dried over anhydrous potassium carbonate, and distilled at atmospheric pressure to yield 1.20 g (72.9%) of compound **21** as a clear liquid: bp 151–152 °C; ir (CCl_4) 2960, 2900, 2860, 1610, 1540, 1465, 1455, 1390, 1380, 1360, 1350, 1290, 1220, 1200, 1115, 1110, 960, 920, and 795 cm^{-1}; NMR (CCl_4) δ 7.10 (s, 1 H, H-4), 6.03 (s, 1 H, H-3), 2.23 (s, 3 H, $-CH_3$), and 1.22 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_9H_{14}O$: C, 78.27; H, 10.14. Found: C, 78.09; H, 10.24.

3-*tert*-Butyl-5-methyl-2-furaldehyde (22). To a stirred mixture of *N,N*-dimethylformamide (1.27 g, 0.017 mol) and phosphorus oxychloride (2.66 g, 0.018 mol), prepared at 10 °C, was carefully added freshly distilled **21** (2.40 g, 0.018 mol) at such a rate as to maintain the temperature of the system at 10 °C. The resulting mixture was stirred for 0.5 h at ambient temperature. It was then poured into 20 ml of ice water, and recrystallized from absolute ethanol to yield 1.54 g (51.5%) of 3-*tert*-butyl-5-methyl-2-furaldehyde (**22**) as pale yellow crystals: mp 40–41 °C; ir (CCl_4) 2965, 2925, 2905, 2870, 1680, 1590, 1505, 1475, 1390, 1370, 1360, 1275, 1235, 1231, and 1060 cm^{-1}; NMR (CCl_4) δ 9.73 (s, 1 H, –CHO), 6.13 (s, 1 H, H-4), 2.35 (s, 3 H, $-CH_3$), and 1.33 [s, 9 H, $-C(CH_3)_3$].

Compound **22** (1.24 g, 0.0075 mol), hydroxylamine hydrochloride (0.84 g, 0.072 mol), and a solution of sodium carbonate (0.64 g, 0.006 mol) in 25 ml of water were heated on a steam bath for 4 h. The resulting solution was allowed to stand overnight, whereupon it was treated with distilled water (10 ml) and then extracted with three 10-ml portions of ether. The ether was removed on a rotary evaporator and the crude oxime (1.09 g, 85.1% yield) used directly in the next step.

3-*tert*-Butyl-5-methyl-2-furonitrile (3b). A solution of crude 3-*tert*-butyl-5-methyl-2-furaldehyde oxime (1.09 g, 0.006 mol) in acetic anhydride (4.40 g, 0.047 mol) was heated at reflux for 0.5 h. The solution was cooled, treated with distilled water (60 ml), and then steam distilled. The distillate was extracted three times with 15-ml portions of ether. After the ether extracts were neutralized with a saturated aqueous sodium carbonate solution and dried over anhydrous magnesium sulfate, the solvent was removed on a rotary evaporator and the residue was distilled in vacuo to give 0.84 g (84.9% yield) of **3b**: bp 50.5–51 °C (1.5 mm); ir (CCl_4) 2980, 2885, 2210, 1670, 1660, 1595, 1530, 1475, 1360, 1235, 1200, 1060, 965, and 810 cm^{-1}; NMR (CCl_4) δ 6.08 (s, 1 H, H-4), 2.30 (s, 3 H, $-CH_3$), and 1.33 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.62; H, 7.97; N, 8.59. Found: C, 73.60; H, 7.76; N, 8.38.

Reaction of 2-(Chloromethyl)furans (1a and 1b) with Potassium Cyanide. This reaction was carried out under the conditions described by Reichstein.[5] To a vigorously stirred solution of potassium cyanide (8.0 g, 0.123 mol) in 15 ml of water was added freshly distilled 2-(chloromethyl)furan (10.0 g, 0.085 mol). The reaction was exothermic. Within 30 min, the exotherm subsided and a heavy precipitate of potassium chloride formed. Stirring was continued for 2 h to assure completion of the reaction. The mixture was extracted with ether and the extracts were then treated with charcoal, dried, and evaporated under reduced pressure. The crude mixture was analyzed directly by NMR or first diluted with carbon tetrachloride and then analyzed. The following product distribution was obtained: furfuryl alcohol, 3%; **2a**, 38%; **3a**, 57%; and a compound of unknown structure, 2%. The relative proportion of **2a** and **3a** observed under these conditions was 40:60, respectively.

Although we utilized Reichstein's conditions[5] in our rate studies, we found that the highest yields of product were obtained when **1a** (10.0 g, 0.085 mol) was treated with a large excess of potassium cyanide (13.0 g, 0.2 mol, 15 ml of water). At lower cyanide levels (6.5 g, 0.1 mol), yields were comparable to those observed with the Reichstein procedure.[5]

The reaction of **1b** with potassium cyanide required 16 h at 37.5 ± 0.5 °C to reach completion. Erlenmeyer flasks containing **1b** (0.30 g, 0.018 mol) and a solution of potassium cyanide (0.18 g, 0.027 mol) in 0.5 ml of water were placed in an Elberbach water bath shaker at the cited temperature. At various time intervals, samples were withdrawn and analyzed as described.

Temperature Studies. Temperature studies were conducted at 0 and 37.5 °C for **1a**, and at 60, 80, 90, and 100 °C for **1b**. The freshly distilled 2-chloromethyl compound (0.018 mol) was added to solutions of potassium cyanide (0.03 mol) in 0.5 ml of water. The resulting mixtures were then stirred in an appropriate constant temperature bath. With compound **1a** at 0 °C, after 3 h, the average product distribution was as follows: furfuryl alcohol, 2%; **1a**, 1%; **2a**, 37%; **3a**, 46%; and **4a**, 14%. At 37.5 °C, the values follow: furfuryl alcohol, 4%; **1a**, trace; **2a**, 37%; and **3a**, 59%.

Concentration Studies. Compound **1a** (10.0 g, 0.085 mol) was treated with 1, 2, and 4 N cyanide solutions prepared from 8.0 g (0.123 mol) of potassium cyanide and appropriate amounts of water. The temperature of the reaction was not controlled and the products were analyzed after 3 h.

Compound **1b** (0.6 g, 0.003 mol) was treated with solutions of potassium cyanide (0.36 g, 0.006 mol) in 0.6, 1, 1.5, and 2 ml of distilled water. The samples were placed in an Elberbach water bath shaker and kept at 37.5 ± 0.5 °C for 96 h. The products were analyzed in the usual manner.

The absolute yields of **2a** and **3a** increased with cyanide concentration. However, when the relative yields of the two nitriles were compared, dilution appeared to favor the formation of **3a**; in more concentrated solutions, larger amounts of **2a** formed. The same trend was observed in the reactions of **1b** with aqueous cyanide.

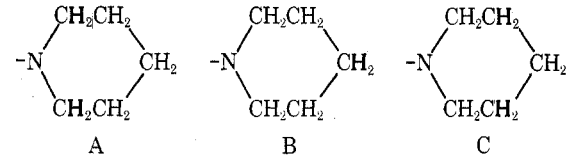
Studies of the Effect of Cations. Various metallic and organic cyanides were used as a source of cyanide ions. Silver cyanide (16.4 g, 0.123 mol) was extremely insoluble in the reaction medium and made it impossible to isolate the products in the usual manner. Mercuric cyanide (31.0 g, 0.123 mol) caused the polymerization of **1a**, even at 0 °C. Cuprous cyanide was used as a complex prepared from 8.3 g (0.128 mol) of potassium cyanide and 1.2 g (0.013 mol) of cuprous cyanide in 15 ml of water. The reactions of this complex with **1a** were performed both with and without temperature control. Ammonium cyanide was prepared in situ by the reaction of 6.5 g (0.122 mol) of ammonium chloride with 8.0 g (0.123 mol) of potassium cyanide in 45 ml of water. Benzyltrimethylammonium cyanide was also generated in situ using 37.2 g (0.123 mol) of benzyltrimethylammonium chloride and 8.0 g (0.123 mol) of potassium cyanide in 67 ml of water. The reactions of ammonium and benzyltrimethylammonium cyanides with **1a** were carried out without temperature control.

Solvent Studies. A gradual change in the polarity of the medium was achieved by the use of mixed solvents; 40, 60, 80, and 99% aqueous 1,2-dimethoxyethane solutions (20 ml), respectively. With the exception of the reaction time, which was increased to 3 h to ensure completion of the reaction, all other conditions remained the same.

Reactions of 1b with Amines, Scheme I. The general procedure used will be described for the preparation of 4-*tert*-butyl-*N,N*-diethylfurfurylamine (**8**). A solution of diethylamine (2.20 g, 0.03 mol) in 4.5 ml of benzene was added dropwise, with vigorous stirring, to a solution of 4-*tert*-butyl-2-(chloromethyl)furan (2.50 g, 0.015 mol) in 7.5 ml of benzene. The mixture was heated at reflux for 4 h, cooled, and acidified (Congo red) with 10% aqueous hydrochloric acid. The acid layer was separated and the benzene layer was washed with 20 ml of distilled water. The acid layer and aqueous washings were combined and neutralized with saturated aqueous sodium carbonate. Ether and 1 ml of 10% aqueous sodium hydroxide were then added. The ether layer was separated and the aqueous layer was extracted with three 15-ml portions of ether. After the extracts were dried over anhydrous sodium sulfate, the ether was removed under reduced pressure and the residue was distilled in vacuo to give 2.50 g (79.8% yield) of **8** as a clear liquid: bp 57–57.5 °C (1.5 mm); ir (neat) 2960, 2860, 2800, 1380, 1360, 1060, 965, and 925 cm^{-1}; NMR (CCl_4) δ 7.00 (s, 1 H, H-5), 6.04 (s, 1 H, H-3), 3.53 (d, 2 H, CH_2), 2.43 (q, 2 H, $-CH_2CH_3$, J = 7 Hz), 1.20 [s, 9 H, $-C(CH_3)_3$], and 1.02 (t, 6 H, $-CH_2CH_3$, J = 7 Hz).

Anal. Calcd for $C_{13}H_{23}NO$; C, 74.64; H, 11.01; N, 6.70. Found: C, 74,80; H, 11.11; N, 6.88.

1-(4-*tert*-Butylfurfuryl)piperidine (9), Scheme I. A solution of **1b** (1.50 g, 0.009 mol) in 5 ml of benzene was treated with a solution of piperidine (1.54 g, 0.0018 mol) in 7.5 ml of benzene as described in the preparation of **8**. The residual liquid was distilled in vacuo to yield 1.64 g (82.3% yield) of **9** as a clear liquid: bp 72–72.5 °C (1.0 mm); ir (CCl_4) 2960, 2940, 2860, 2875, 2800, 1470, 1440, 1360, 1340, 1300, 1205, 1160, 1150, 1125, 1095, 1100, 1040, 995, 965, 900, and 860 cm^{-1}; NMR

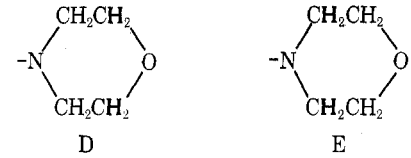


A B C

(CCl_4) δ 6.98 (s, 1 H, H-5), 6.02 (s, 1 H, H-3), 3.35 (s, 2 H, CH_2), 2.30 (m, 4 H, see A), 1.66 (s, 2 H, see B), 1.43 (m, 4 H, see C), and 1.20 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{14}H_{23}NO$: C, 76.02; H, 10.86; N, 6.33. Found: C, 75.95; H, 10.72; N, 6.30.

4-(4-*tert*-Butylfurfuryl)morpholine (10), Scheme I. A solution of **1b** (1.50 g, 0.009 mol) in 5 ml of benzene was treated with a solution of morpholine (1.57 g, 0.018 mol) in 7.5 ml of benzene as described in the preparation of **8**. The residue was distilled in vacuo to yield 1.55 g (77%) of **10** as a clear liquid: bp 78–79 °C (0.75 mm); ir (CCl_4) 2960, 2860, 1605, 1470, 1460, 1450, 1360, 1345, 1330, 1240, 1200, 1125, 1110,



D E

1105, 1090, 1070, 1005, 980, 960, 950, 925, 900, and 865 cm^{-1}; NMR (CCl_4) δ 7.03 (s, 1 H, H-5), 6.09 (s, 1 H, H-3), 3.38 (s, 2 H, CH_2), 3.58 (m, 4 H, see D), 2.36 (m, 4 H, see E), and 1.20 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.90; H, 9.41; N, 6.27. Found: C, 69.77; H, 9.33; N, 6.12.

2-(4-*tert*-Butylfurfuryl)-2-thiopseudourea Monohydrochloride (11), Scheme I. A mixture of **1b** (2.00 g, 0.012 mol) and thiourea (10.92 g, 0.012 mol) in 6 ml of acetone was heated at reflux on a steam bath for 5 h. The solid that formed was collected and recrystallized from ethanol–acetone to give 2.33 g (78.3% yield) of **11**: mp 184–185 °C; ir (KBr) 3240, 3050, 2950, 2860, 2770, 2730, 1660, 1645, 1420, 1140, 1120, 1090, 950, 755, and 700 cm^{-1}; NMR (EtOH) δ 6.98 (s, 1 H, H-5), 6.15 (s, 1 H, H-3), 4.98 (s, 2 H, CH_2), and 1.23 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{10}H_{17}ClN_2OS$: C, 48.30; H, 6.84; S, 13.28; Cl, 14.27; N, 11.27. Found: C, 48.50; H, 6.71; S, 12.98; Cl, 14.42; N, 11.12.

Diethyl (4-*tert*-Butylfurfuryl)malonate (12), Scheme I. Diethyl malonate (4.80 g, 0.031 mol) was stirred for 2 h with an ethanolic solution of sodium ethoxide [prepared from 0.69 g of sodium (0.030 g-atom), and 12 ml of absolute ethanol] and then treated with compound **1b** (2.00 g, 0.012 mol). The mixture was heated at reflux for 4 h. Ethanol was removed under reduced pressure and water was added to the residue. The oily layer that formed was separated and the aqueous layer was extracted with three 10-ml portions of ether. The oily layer and ether extracts were combined, washed with water, and dried over magnesium sulfate. Removal of the ether under reduced pressure and distillation of the residue in vacuo gave 3.0 g (84.8% yield) of **12** as a yellow liquid: bp 112–113 °C (0.9 mm); ir (CCl_4) 2960, 2900, 2860, 1750, 1730, 1470, 1460, 1440, 1365, 1335, 1295, 1145, 1120, 1095, 1030, 960, 925, and 885 cm^{-1}; NMR (CCl_4) δ 7.02 (s, 1 H, H-5), 6.00 (s, 1 H, H-3), 3.61 [t, 1 H, $-CH(CO_2C_2H_5)_2$], 3.13 (d, 2 H, CH_2), 4.14 (q, 4 H, $-CO_2CH_2CH_3$, J = 7 Hz), 1.25 (t, 6 H, $-CO_2CH_2CH_3$, J = 7 Hz), and 1.25 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.86; H, 8.14. Found: C, 64.70; H, 8.02.

Diethyl (4-*tert*-Butylfurfuryl)methyl Malonate (13), Scheme I. Compound **1b** (1.50 g, 0.009 mol) was treated with diethyl methyl malonate (4.30 g, 0.025 mol) and an ethanolic solution of sodium ethoxide [prepared from 0.53 g of sodium (0.023 g-atom) and 9 ml of absolute ethanol] as described for the preparation of **12**. The residue was distilled in vacuo to yield 2.21 g (79.2%) of **13** as a yellow liquid: bp 107–108 °C (2 mm); ir (CCl_4) 2960, 2930, 2900, 2860, 1770, 1730, 1460, 1375, 1360, 1240, 1100, 1020, 980, 925, and 855 cm^{-1}; NMR (CCl_4) 6.96 (d, 1 H, H-5), 5.97 (s, 1 H, H-3), 4.05 (q, 4 H, $-CO_2CH_2CH_3$, J = 7 Hz), 3.08 (s, 2 H, CH_2), and 1.18, 1.20 [m, 18 H, $-CH_3$ and $-C(CH_3)_3$].

Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.81; H, 8.39. Found: C, 65.94; H, 8.55.

Ethyl α-Acetyl-4-*tert*-butyl-2-furanpropionate (14), Scheme I. Compound **1b** (1.50 g, 0.009 mol) was treated with ethyl acetoacetate (3.70 g, 0.023 mol) and an ethanolic solution of sodium ethoxide [prepared from 0.53 g of sodium (0.023 g-atom) and 9 ml of absolute ethanol] as described in the preparation of **12**. The residue was distilled in vacuo to yield 2.06 g (81.6%) of **14** as a yellow liquid: bp 110–111 °C (3 mm); ir (CCl_4) 2960, 2860, 1770, 1742, 1740, 1720, 1425, 1360, 1235, 1198, 1120, 1060, 1025, 960, 940, and 860 cm^{-1}; NMR (CCl_4) δ 6.96 (s, 1 H, H-3), 5.93 [m, 1 H, $-CH(CO_2C_2H_5)COCH_3$], 3.05 (d, 2 H, CH_2), 4.18 (q, 2 H, $-CH_2CH_3$, J = 7 Hz), 2.13 (s, 3 H, $-COCH_3$), 1.20 (t, 3 H, $-CH_2CH_3$, J = 7 Hz), and 1.21 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.77; H, 8.28. Found: C, 67.75; H, 8.45.

Reaction of 1b with Sodium Azide. A mixture of compound **1b** (1.80 g, 0.011 mol) and sodium azide (0.98 g, 0.015 mol) in 3.5 ml of water was stirred and heated on a steam bath for 24 h. Ether (10 ml) was added to the cooled mixture. The layers that formed were separated and the aqueous layer was extracted with two 10-ml portions of ether. The combined ether extracts were dried over anhydrous magnesium sulfate. Removal of the ether under reduced pressure and distillation of the residue in vacuo afforded 1.21 g (62.2% yield) of a clear liquid, bp 45–47 °C (1.3 mm), which was diluted with carbon tetrachloride and analyzed by NMR spectroscopy. The following resonances were characteristic of 2-(azidomethyl)-4-*tert*-butylfuran: δ 7.08 (s, 1 H, H-5), 6.23 (s, 1 H, H-3), 4.13 (s, 2 H, CH_2), and 1.21 [s, 9 H, $C(CH_3)_3$]. 2-Azido-4-*tert*-butyl-5-methylfuran was responsible for resonances at δ 6.44 (s, 1 H, H-3), 2.33 (s, 3 H, $-CH_3$), and 1.21 [s, 9 H, $-C(CH_3)_3$]. The ir (CCl_4) spectrum of the mixture exhibited different absorptions for the two azide groups. The following absorptions were noted: 2960, 2920, 2900, 2860, 2055, 2045, 1465, 1455, 1360, 1330, 1260, 1230, 1200, 1125, 1090, 960, 925, 910, 865, 815, and 770 cm^{-1}. When the reaction was performed at 80 °C, the ratio of the isomeric azides was 92% (normal) and 8% (abnormal). At 40 °C, the ratio was 81%:19%.

Reaction of 1b with Potassium Thiocyanate. Compound **1b** (1.50 g, 0.009 mol) was added dropwise to a solution of aqueous potassium thiocyanate (1.20 g, 0.012 mol) and the resulting mixture was heated for 24 h. Runs were carried out at 37, 40, and 80 °C. Ether (15 ml) was added to the cooled mixture and the resulting layers were separated. The aqueous layer was extracted with two 10-ml portions of ether. The combined ether extracts were then dried with anhydrous magnesium sulfate. Removal of the ether under reduced pressure and distillation of the residue in vacuo gave a clear liquid, 1.12 g (65.9%), bp 70–72 °C (0.6 mm), which was diluted with carbon tetrachloride and analyzed by NMR spectroscopy. The following resonances were observed: δ 7.03 (s, 1 H, H-5), 6.18 (s, 1 H, H-3), 4.55 (s, 2 H, CH_2), and 1.17–1.21 [m, 9 H, $-C(CH_3)_3$], 4-*tert*-butylfurfuryl thiocyanate; 7.08 (s, 1 H, H-5), 6.28 (s, 1 H, H-3), 4.41 (s, 2 H, CH_2), and 1.17–1.21 [s, 9 H, $-C(CH_3)_3$], 4-*tert*-butylfurfuryl isothiocyanate; 5.86 (s, 1 H, H-3), 2.48 (s, 3 H, CH_3), and 1.17–1.21 [s, 9 H, $-C(CH_3)_3$], 2-thiocyano- or isothiocyano-4-*tert*-butyl-5-methylfuran. The ir spectrum (CCl_4) of the mixture showed bands at 2960, 2920, 2900, 2860, 2150, 2055, 1788, 1770, 1470, 1460, 1360, 1246, 1232, 1212, 1205, 1128, 1086, 966, and 945 cm^{-1}. The following isomer ratios were observed at 37 °C: normal thiocyanate, 43%; normal isothiocyanate, 43%; abnormal product, 14%.

Anal. Calcd for $C_{10}H_{13}NOS$: C, 61.54; H, 6.66; N, 7.18; S, 16.92. Found: C, 61.41; H, 6.74; N, 7.05; S, 16.65.

Preparation of 4-Isopropyl-2-(chloromethyl)furan (1c), Scheme IV. The alkylation of 2-furaldehyde with isopropyl chloride was carried out according to the procedure of Gilman and Calloway.[28a] 2-Furaldehyde (48.00 g, 0.50 mol) was added dropwise, with stirring, to a suspension of aluminum chloride (80.00 g, 0.60 mol) in 1000 ml of carbon disulfide. A solution of isopropyl chloride (39.30 g, 0.50 mol) in 250 ml of carbon disulfide was then added to this mixture and it was stirred for 24 h at ambient temperature. The mixture was poured onto 100 g of cracked ice and extracted with three 200-ml portions of ether. The extracts were then washed with 200 ml of saturated sodium bicarbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solvent and distillation of the residue in vacuo through a spinning band column afforded three fractions. The first fraction consisted of unreacted 2-furaldehyde (**23**), bp 34–36 °C (4 mm) [lit.[28a] bp 161–162 °C (760 mm)]. The second fraction, 14.5 g (21.0% yield), bp 65–68 °C (2.2 mm) [lit.[28a] bp 101–103 °C (21 mm)], was identified as 4-isopropyl-2-furaldehyde (**24**): ir (CCl_4) 2980, 2930, 2870, 2830, 2740, 1685, 1500, 1460, 1380, 1365, 1250, 1140, 1070, 970, and 940 cm^{-1}; NMR (CCl_4) δ 9.58 (s, 1 H, –CHO), 7.40 (s, 1 H, H-5), 7.06 (s, 1 H, H-3), 2.83 [hep, 1 H, $-CH(CH_3)_2$, J = 7 Hz], and 1.23 [d, 6 H, $-CH(CH_3)_2$, J = 7 Hz]. The third fraction, 2.53 g (2.51%), bp 78–80 °C (0.45 mm), was identified as 4,5-diisopropyl-2-furaldehyde (**25**): ir (CCl_4) 2960, 2930, 2870, 2810, 2800, 2740, 2690, 1685, 1675, 1590, 1520, 1455, 1410, 1380, 1360, 1325, 1245, 1160, 1145, 1135, 1100, 1055, 1040, 980, and 970 cm^{-1}; NMR (CCl_4) δ 9.42 (s, 1 H, –CHO), 6.95 (s, 1 H, H-3), 2.95 [hep, 1 H, $-CH(CH_3)_2$, J = 7 Hz], and 1.16 [m, 12 H, $-CH(CH_3)_2$, J = 7 Hz].

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.33; H, 8.88. Found: C, 73.52; H, 8.70.

4-Isopropylfurfuryl Alcohol (26), Scheme IV. A solution of compound **24** (13.00 g, 0.10 mol) in 150 ml of anhydrous ether was reduced with lithium aluminum hydride (4.95 g, 0.13 mol) in 300 ml of anhydrous ether. The ether solution was washed first with a saturated sodium bisulfite solution and then with 10 ml of 5% aqueous sodium carbonate solution. The ether was removed on a rotary evaporator and the residual liquid was distilled in vacuo to yield 2.45 g (17.4%) of **26**: bp 65–66 °C (6 mm); ir (CCl_4) 3610, 3360, 2960, 2910, 2880, 1460, 1380, 1360, 1255, 1165, 1130, 1115, 1080, 1040, 1010, 960, and 910 cm^{-1}; NMR δ 7.06 (s, 1 H, H-5), 6.11 (s, 1 H, H-3), 4.40 (s, 2 H, CH_2), 3.50 (s, 1 H, –OH), 2.75 [hep, 1 H, $-CH(CH_3)_2$, J = 7 Hz], and 1.25 [d, 6 H, $-CH(CH_3)_2$, J = 7 Hz].

Anal. Calcd for $C_8H_{12}O_2$: C, 68.57; H, 8.57. Found: C, 68.46; H, 8.53.

4-Isopropyl-2-(chloromethyl)furan (1c), Scheme IV. A solution of compound **26** (2.45 g, 0.016 mol) in 2.5 ml of anhydrous ether was treated with thionyl chloride (2.14 g, 0.018 mol) and pyridine (1.58 g, 0.019 mol) in 1.5 ml of ether. The reaction mixture was diluted with additional ether and the precipitated solid was then removed by filtration. The ether extracts were neutralized with aqueous potassium hydroxide and dried with anhydrous sodium carbonate. Removal of the solvent under reduced pressure on a rotary evaporator and distillation of the residue in vacuo gave 1.21 g (42.3% yield) of **1c**: bp 55–56 °C (6 mm); ir (CCl_4) 2980, 2920, 2880, 1465, 1425, 1370, 1360, 1290, 1270, 1250, 1170, 1140, 1110, 1070, 960, 950, 875, and 700 cm^{-1}; NMR (CCl_4) δ 7.02 (s, 1 H, H-5), 6.15 (s, 1 H, H-3), 4.38 (s, 2 H, CH_2), 2.70 [hep, 1 H, $-CH(CH_3)_2$, J = 7 Hz], and 1.17 [d, 6 H, $-CH(CH_3)_2$,

J = 7 Hz]; mass spectrum m/e (rel intensity) 158 (M^+, 1.69), 123 ($C_8H_{11}O^+$, 100).

Anal. Calcd for $C_8H_{11}ClO$: C, 60.51; H, 6.94; Cl, 22.10. Found: C, 60.23; H, 6.65; Cl, 21.98.

Preparation of 3-*tert*-Butyl-2-(chloromethyl)furan (1d), Scheme V. 5-Bromo-2-furoic acid (572.91 g, 3.0 mol) was esterified with 1500 ml of absolute ethanol and 30 ml of concentrated sulfuric acid to yield 501.1 g (70%) of **27:** bp 62–63 °C (3 mm) [lit.[31a] bp 134–136 °C (34 mm)]; ir (CCl_4) 2985, 1715, 1580, 1465, 1366, 1351, 1290, 1205, 1142, 1120, 1110, 1010, 950, and 925 cm^{-1}; NMR (CCl_4) δ 7.18 (d, 1 H, H-3), 6.60 (d, 1 H, H-4), 4.39 (q, 2 H, $-CO_2CH_2CH_3$, J = 7 Hz), and 1.40 (t, 3 H, $-CO_2CH_2CH_3$, J = 7 Hz).

Compound **27** (87.6 g, 0.4 mol) was alkylated using *n*-octadecyl bromide (133.2 g, 0.4 mol) and aluminum chloride (106.8 g, 0.8 mol) in 600 ml of carbon disulfide[32] to yield 30.0 g (36.0%) of **28:** bp 110–125 °C (2 mm) [lit.[32] bp 130–142 °C (5 mm)]; ir (CCl_4) 2960, 2925, 2905, 2870, 1730, 1715, 1590, 1490, 1455, 1365, 1345, 1300, 1245, 1215, 1170, 1140, 1095, 1015, 1005, and 960 cm^{-1}; NMR (CCl_4) δ 7.06 (s, 1 H, H-3), 4.29 (q, 2 H, J = 7 Hz), 1.33 (t, 3 H, J = 7 Hz), and 1.33 [s, 9 H, $-C(CH_3)_3$].

Compound **28** (30.0 g, 0.11 mol) was hydrolyzed with ethanolic potassium hydroxide (10.0 g, 0.18 mol) to yield 8.68 g (32.1%) of **29:** mp 164–165 °C (lit.[32] 164–165 °C); ir (CCl_4) 2960, 2865, 1685, 1590, 1490, 1460, 1415, 1360, 1345, 1245, 1215, 1178, 1005, and 960 cm^{-1}; NMR (CCl_4) δ 11.06 (s, 1 H, –OH), 7.26 (s, 1 H, H-3), and 1.36 [s, 9 H, $-C(CH_3)_3$].

2-Bromo-3-*tert*-butylfuran (30), Scheme V. Compound **29** (34.50 g, 0.14 mol), quinoline (53.00 g, 0.75 mol), and copper chromite (6.00 g, 0.026 mol) were heated under nitrogen in a distillation apparatus. The distillate was then redistilled in vacuo to give **30** as a clear liquid: 12.00 g (42.5% yield); bp 63–64 °C (6 mm); ir (CCl_4) 2980, 2905, 2870, 1490, 1475, 1410, 1390, 1365, 1355, 1170, 1150, 1100, 1060, 990, and 890 cm^{-1}; NMR (CCl_4) δ 7.25 (d, 1 H, H-4, J = 2 Hz), 6.26 (d, 1 H, H-5, J = 2 Hz), and 1.30 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_8H_{11}BrO$: C, 49.38; H, 6.41; Br, 37.38. Found: C, 49.72; H, 6.06; Br, 37.24.

3-*tert*-Butyl-2-furoic Acid (31), Scheme V. Compound **30** (11.10 g, 0.055 mol) was added dropwise, under nitrogen, to a solution of 5% *n*-butyllithium (4.74 g, 0.0736 mol) in 20.6 ml of hexane and 80 ml of anhydrous ether. The reaction mixture was cooled, stirred for 4 h, and poured over dry ice. After completion of the reaction, 15 ml of wet ether and then 25 ml of 5% aqueous acetic acid were added to the mixture. Stirring was continued for 1 h. The acid layer was separated and extracted with two 20-ml portions of ether. The combined ether extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the ether under reduced pressure and recrystallization of the residue from aqueous ethanol gave 4.00 g (44% yield) of **31** as a white solid: mp 120–121 °C; ir (CCl_4) 3000, 2980, 2950, 2930, 2880, 1680, 1565, 1485, 1480, 1425, 1310, 1280, 1265, 1085, 1050, and 890 cm^{-1}; NMR (CCl_4) δ 12.33 (s, 1 H, $-CO_2H$), 7.35 (d, 1 H, H-5), 6.51 (s, 1 H, H-4), and 1.36 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_9H_{12}O_3$: C, 64.22; H, 7.14. Found: C, 64.39; H, 7.25.

3-*tert*-Butylfurfuryl Alcohol (32), Scheme V. A solution of compound **31** (4.00 g, 0.024 mol) in 100 ml of anhydrous ether was treated with lithium aluminum hydride (1.11 g, 0.029 mol) in 250 ml of anhydrous ether, as described in the preparation of **26,** to yield 2.50 g (60.0%) of **32,** as a clear liquid: bp 75.5–77 °C (6.5 mm); ir (CCl_4) 3610, 3300, 2980, 2930, 2910, 2870, 1505, 1465, 1390, 1365, 1220, 1170, 1150, 1130, 1080, 915, 895, 885, and 720 cm^{-1}; NMR (CCl_4) δ 7.26 (d, 1 H, H-5, J = 2 Hz), 6.23 (s, 1 H, H-4, J = 2 Hz), 4.50 (s, 2 H, CH_2), 2.66 (s, 1 H, –OH), and 1.25 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_9H_{14}O_2$: C, 70.13; H, 9.09. Found: C, 70.34; H, 9.08.

3-*tert*-Butyl-2-(chloromethyl)furan (1d), Scheme V. A solution of freshly distilled **32** (2.44 g, 0.015 mol) and pyridine (1.45 g, 0.018 mol) in 5 ml of ether was treated with thionyl chloride (1.99 g, 0.17 mol) as described in the preparation of **1a.** Removal of the solvent and distillation of the residue in vacuo gave 1.88 g (65.0% yield) of **1d** as a clear liquid: bp 67.5–68 °C (7.5 mm); ir (CCl_4) 2980, 2900, 2870, 1475, 1460, 1360, 1260, 1220, 1170, 1150, 1070, 1010, 895, and 720 cm^{-1}; NMR (CCl_4) δ 7.20 (d, 1 H, H-5, J = 2 Hz), 6.23 (d, 1 H, J = 2 Hz), 4.65 (s, 2 H, CH_2), and 1.33 [s, 9 H, $-C(CH_3)_3$].

Anal. Calcd for $C_9H_{13}ClO$: C, 62.21; H, 7.54; Cl, 20.53. Found: C, 62.50; H, 7.84; Cl, 20.44.

Preparation of 4-Bromo-2-(chloromethyl)furan (1e), Scheme VI. 2-Furaldehyde (96.0 g, 2.00 mol) was treated with 94 ml of bromine (279.9 g, 3.50 mol) in the presence of aluminum chloride[34] (292 g, 2.20 mol) to yield 105 g (72%) of **33:** mp 36–37 °C (lit.[34] mp 36–37 °C); ir (CCl_4) 3370, 3140, 2830, 2760, 1690, 1570, 1460, 1370, 1325, 1270, 1200, 1175, 1105, 990, 985, 965, 955, and 840 cm^{-1}; NMR (CCl_4) δ 8.10 (s, 1 H, –CHO), and 6.98 (s, 1 H, H-3).

Compound **33** (53.00 g, 0.22 mol) was oxidized with a solution of silver nitrate (79.50 g, 0.47 mol) and sodium hydroxide[35] (58.30 g, 1.45 mol) in 150 ml of water to give 39.00 g (65.7% yield) of **34:** mp 167–168 °C (lit.[10] 168–169 °C); NMR (CCl_4) δ 11.17 (s, 1 H, $-CO_2H$) and 7.23 (s, 1 H, H-3).

A solution of compound **34** (39.00 g, 0.15 mol) in 700 ml of 2:7 aqueous ammonium hydroxide was treated with zinc dust[36] (30.00 g, 0.46 mol) to give 14.00 g (49.3% yield) of **35,** mp 115–127 °C (lit.[36] mp 126–127 °C). The crude product was used in the next reaction without further purification.

4-Bromofurfuryl Alcohol (36), Scheme VI. A solution of crude 4-bromo-2-furoic acid (14.00 g, 0.075 mol) in 100 ml of anhydrous ether was treated with lithium aluminum hydride (4.40 g, 0.12 mol) in 400 ml of the same solvent as described in the preparation of **26.** The residual liquid was distilled in vacuo to give two fractions. The first fraction (bp 42–44 °C, 2.5 mm) was identified as 2-furfuryl alcohol by comparison of its ir and NMR spectra with those of an authentic sample of this compound. The second fraction (bp 63–64 °C, 2.5 mm) afforded 3.31 g of **36** (40% yield): ir (CCl_4) 3620, 3300, 3160, 2925, 2880, 1595, 1515, 1530, 1385, 1360, 1225, 1210, 1150, 1130, 1015, and 910 cm^{-1}; NMR (CCl_4) δ 7.46 (s, 1 H, H-5), 6.23 (s, 1 H, H-3), 4.38 (s, 2 H, CH_2), and 3.80 (s, 1 H, –OH).

Anal. Calcd for $C_5H_5BrO_2$: C, 34.12; H, 2.83; Br, 44.64. Found: C, 34.10; H, 3.07; Br, 44.93.

4-Bromo-2-(chloromethyl)furan (1e), Scheme VI. A solution of freshly distilled 4-bromofurfuryl alcohol (4.80 g, 0.030 mol) and pyridine (2.85 g, 0.036 mol) in 5 ml of ether was treated with thionyl chloride (4.20 g, 0.035 mol) as described in the preparation of **1a.** The residual liquid was distilled in vacuo to give 3.20 g (74.0% yield) of **1e:** bp 31–32 °C (2.5 mm); ir (CCl_4) 3160, 3120, 2960, 1590, 1510, 1430, 1355, 1270, 1235, 1215, 1145, 1125, 1090, 1015, 950, 930, and 880 cm^{-1}; NMR (CCl_4) δ 7.37 (s, 1 H, H-5), 6.37 (s, 1 H, H-3), and 4.45 (s, 2 H, CH_2).

Anal. Calcd for C_5H_4BrClO: C, 30.86; H, 20.58; Br, 40.53; Cl, 18.23. Found: C, 30.72; H, 20.32; Br, 40.36; Cl, 18.01.

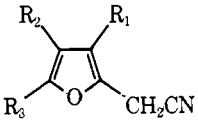
Preparation of Ethyl 5-(Chloromethyl)-3-furoate (1f), Scheme VII. 3,4-Difurandicarboxylic acid (10.00 g, 0.064 mol), copper chromite (1.5 g, 0.0054 mol), and 25 ml of quinoline[37] were heated under nitrogen in a distillation apparatus. The distillate was extracted several times with saturated aqueous sodium carbonate solution. The sodium carbonate extracts were then washed with ether and acidified with 1:1 aqueous hydrochloric acid. Thorough extraction of the acidified solution with ether and evaporation of the ether under reduced pressure gave 1.05 g (12.6% yield) of 3-furoic acid (**38**): mp 120–121 °C (lit.[37] mp 121–122 °C); NMR (CCl_4) δ 12.33 (s, 1 H, CO_2H), 8.17 (s, 1 H, H-2), 7.50 (s, 1 H, H-5), and 6.83 (s, 1 H, H-3).

Compound **38** (0.95 g, 0.0067 mol) was esterified with 5 ml of absolute ethanol and 0.1 ml of concentrated sulfuric acid to yield 0.62 g (65.7%) of **39:** bp 95–95.5 °C (52 mm); ir (CCl_4) 2980, 2960, 2940, 1725, 1590, 1575, 1570, 1500, 1475, 1440, 1400, 1365, 1305, 1160, 1080, 1000, and 875 cm^{-1}; NMR (CCl_4) δ 7.80 (s, 1 H, H-2), 7.37 (s, 1 H, H-5), 6.66 (s, 1 H, H-3), 4.21 (q, 2 H, $-CO_2CH_2CH_3$, J = 7 Hz), and 1.34 (t, 3 H, $-CO_2CH_2CH_3$, J = 7 Hz).

Ethyl 5-(Chloromethyl)-3-furoate (1f), Scheme VII. A mixture of **39** (0.52 g, 0.0026 mol), paraformaldehyde (0.015 g, 0.005 mol), and anhydrous zinc chloride (0.12 g, 0.009 mol) in 2 ml of chloroform was kept at 25 °C while hydrogen chloride was passed into the reaction flask for 2 h. By the end of the reaction, the paraformaldehyde had completely dissolved. The contents of the flask were then poured into 20 ml of cold water. The chloroform layer was separated, washed with three 10-ml portions of water, and dried over calcium chloride. Evaporation of the solvent and distillation of the residue in vacuo afforded 0.38 g (59.0% yield) of **1f:** bp 118–119 °C (3 mm); ir (CCl_4) 2980, 2960, 2930, 2900, 1475, 1460, 1375, 1365, 1305, 1260, 1230, 1200, 1145, 1100, 1075, 970, 965, 945, 840, and 710 cm^{-1}; NMR (CCl_4) δ 7.93 (s, 1 H, H-2), 6.69 (s, 1 H, H-4), 4.52 (s, 2 H, CH_2), 4.25 (q, 2 H, $-CO_2CH_2CH_3$, J = 7 Hz), and 1.31 (t, 3 H, $-CO_2CH_2CH_3$, J = 7 Hz).

Preparation of 5-(Chloromethyl)-3-furonitrile (1g), Scheme VI. 5-Hydroxymethyl-3-furonitrile (40), Scheme VI. A mixture of freshly distilled 4-bromofurfuryl alcohol (**36,** 9.96 g, 0.062 mol), cuprous cyanide (8.40 g, 0.094 mol), and 3 ml of *N,N*-dimethylformamide were heated at reflux for 4 h. The reaction mixture was poured into a solution of sodium cyanide (8.00 g, 0.17 mol) in 24 ml of water and 10 ml of benzene was then added to it. The aqueous layer was extracted three times with 10 ml of benzene. The combined benzene extracts were washed with water and dried over anhydrous sodium sulfate. Removal of the benzene under reduced pressure and distil-

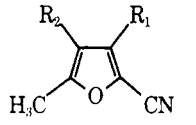
Table II. NMR Spectra of Substituted Furanacetonitriles[a]



Registry no.	Compd	CH_2	R_1	R_2	R_3
2745-25-7	2a	3.68	6.28	6.28	7.37
59413-85-3	2b	3.63	6.25	1.21[b]	7.08
59413-86-4	2c	3.66	6.11	1.23[c]	7.33
				2.91	
59413-87-5	2d	3.78	1.23[b]	6.26	7.25
59413-88-6	2e	3.75	6.40		7.38
59413-89-7	2f	3.78	6.61	1.38[d]	7.90
				4.30	
59413-90-0	2g	3.81	6.61		7.34

[a] δ values. [b] $C(CH_3)_3$. [c] $CH(CH_3)_2$. [d] $CO_2CH_2CH_3$.

Table III. NMR Spectra of Substituted Furyl Nitriles[a]



Registry no.	Compd	R_1	R_2	CH_3
13714-86-8	3a	7.02	6.17	2.34
59413-91-1	3b	1.33[b]	6.03	2.28
59413-92-2	3c	1.23[c]	6.25	2.83
		2.91		
59413-93-3	3d	6.93	1.23[b]	2.41
59413-94-4	3e		6.25	2.37
59413-95-5	3f	1.38[d]	6.47	2.36
		4.30		

[a] δ values. [b] $C(CH_3)_3$. [c] $CH(CH_3)_2$. [d] $CO_2CH_2CH_3$.

lation of the residue in vacuo gave a clear liquid (bp 54–56 °C, 2.5 mm) which was identified from ir and NMR spectra as a mixture of 4-bromofurfuryl alcohol and *N,N*-dimethylformamide. Distillation of the dark residue under high vacuum gave a viscous liquid which solidified in the condenser. Recrystallization of this solid from carbon tetrachloride afforded 0.63 g (9.5% yield) of **40**: mp 81–82 °C; NMR (CCl_4) δ 7.50 (s, 1 H, H-2), 6.27 (s, 1 H, H-4), 4.43 (s, 2 H, CH_2), and 3.60 (s, 1 H, –OH).

Anal. Calcd for $C_6H_5NO_2$: C, 58.54; H, 4.07; N, 11.38. Found: C, 58.63; H, 4.17; N, 11.47.

5-(Chloromethyl)-3-furonitrile (1g), Scheme VI. A solution of 5-(hydroxymethyl)-3-furonitrile (0.57 g, 0.0046 mol) and pyridine (0.45 g, 0.0057 mol) in 15 ml of anhydrous ether was treated with thionyl chloride (0.66 g, 0.0055 mol) as previously described in the preparation of **1a**. Removal of the solvent and distillation of the residue in vacuo gave 0.33 g (50.1% yield) of **1g** as white crystals: mp 50–50.5 °C; ir (CCl_4) 3150, 3120, 2970, 2890, 2240, 1535, 1425, 1355, 1290, 1255, 1160, 1140, 970, 950, and 720 cm^{-1}; NMR (CCl_4) δ 7.27 (s, 1 H, H-2), 6.67 (s, 1 H, H-4), and 4.55 (s, 2 H, CH_2).

Anal. Calcd for C_6H_4ClNO: C, 50.90; H, 2.83; N, 9.89; Cl, 25.07. Found: C, 51.10; H, 2.78; N, 9.94; Cl, 25.19.

Reactions of Substituted 2-(Chloromethyl)furans, 1a–g, with Potassium Cyanide. The general procedure will be illustrated with the reaction of **1c**. A solution of potassium cyanide (0.51 g, 0.008 mol) in 1 ml of water was prepared in a 10-ml Erlenmeyer flask and placed in an Elberbach water bath shaker. The temperature of the bath was maintained at 37.5 ± 0.5 °C. Freshly distilled 4-isopropyl-2-(chloromethyl)furan (0.79 g, 0.005 mol) was then added to the cyanide solution and the reaction flask was shaken for 28 h. At this point, 10 ml of ether was added to the solution. The ether layer was separated and the aqueous layer was extracted with two 10-ml portions of ether. The ether extracts were combined and evaporated under reduced pressure. After dilution of the residue with carbon tetrachloride, the product mixture was determined by NMR spectroscopy. At 37.5 ± 0.5 °C, the length of time required for the reaction to reach completion varied considerably as shown in Table I.

The reaction of **1d** with aqueous potassium cyanide was also carried out at 70 °C. In this instance, isomeric nitriles **2d** and **3d** as well as an additional product identified as 4-*tert*-butyl-5-methyl-2(5*H*)-furanone (**7**) were observed. The latter compound was separated by preparative vapor phase chromatography: ir (CCl_4) 2970, 2900, 2870, 1780, 1755, 1730, 1620, 1475, 1460, 1395, 1370, 1360, 1290, 1240, 1200, 1195, 1170, 1090, 1060, 950, and 860 cm^{-1}; NMR (CCl_4) δ 5.68 (d, 1 H, H-3, $J_{3,5}$ = 1.5 Hz), 5.46 (q, 1 H, H-5, $J_{CH_3,H\text{-}5}$ = 7, $J_{3,5}$ = 1.5 Hz), 1.53 (d, 3 H, 5-CH_3, $J_{CH_3,H\text{-}5}$ = 7 Hz), and 1.23 [s, 9 H, $-C(CH_3)_3$]; mass spectrum *m/e* (rel intensity) 154 (M^+, 1.0), 139 ($C_8H_{11}O_2^+$, 5), 110 ($C_8H_{14}^+$, 16), 95 ($C_7H_{11}^+$, 44), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 66), and 39 ($C_3H_3^+$, 41).

The NMR spectra of the nitriles obtained in these reactions are shown in Tables II and III.

Registry No.—**1a**, 617-88-9; **1b**, 59413-96-6; **1c**, 59413-97-7; **1d**, 59413-98-8; **1e**, 59413-99-9; **1f**, 59414-00-5; **1g**, 59414-01-6; **6a**, 22727-21-5; **7**, 17644-74-5; **8**, 59414-02-7; **9**, 59414-03-8; **10**, 59414-04-9; **11**, 59414-05-0; **12**, 59414-06-1; **13**, 59414-07-2; **14**, 59414-08-3; **15**, 59414-09-8; **16**, 59414-10-7; **17**, 59413-60-7; **18**, 59413-61-5; **19**, 59413-62-6; **20**, 59413-63-7; **21**, 52432-89-0; **22**, 59413-64-8; **23**, 98-01-1; **24**, 16015-07-9; **25**, 33554-12-0; **26**, 59413-65-9; **27**, 6132-37-2; **28**, 59413-66-0; **29**, 59413-67-1; **30**, 59413-68-2; **31**, 59413-69-3; **32**, 59413-70-6; **33**, 2433-85-4; **34**, 2434-03-9; **35**, 3439-02-9; **36**, 59413-71-7; **37**, 3387-26-6; **38**, 488-93-7; **39**, 614-98-2; **40**, 59413-72-8; 2-methyl-3-furancarboxaldoxime, 59413-73-9; 1-(4-*tert*-butyl-2-furoyl)aziridine, 59413-74-0; 4-*tert*-butyl-2-furoic acid anhydride, 59413-76-2; 4-*tert*-butyl-2-furoyl chloride, 59413-75-1; rhodanine, 141-84-4; 4-*tert*-butyl-2-furaldehyde hydrazone, 59413-77-3; 3-*tert*-butyl-5-methyl-2-furaldehyde oxime, 59413-78-4; potassium cyanide, 151-50-8; diethylamine, 109-89-7; piperidine, 110-89-4; morpholine, 110-91-8; thiourea, 62-56-6; diethyl malonate, 105-53-3; diethyl methyl malonate, 609-08-5; ethyl acetoacetate, 141-97-9; sodium azide, 26628-22-8; 2-(azidomethyl)-4-*tert*-butylfuran, 59413-79-5; 2-azido-4-*tert*-butyl-5-methylfuran, 59413-80-8; potassium thiocyanate, 333-20-0; 4-*tert*-butylfurfuryl thiocyanate, 59413-81-9; 4-*tert*-butylfurfuryl isothiocyanate, 59413-82-0; 2-thiocyano-4-*tert*-butyl-5-methylfuran, 59413-83-1; 2-isothiocyano-4-*tert*-butyl-5-methylfuran, 59413-84-2; 5-bromo-2-furoic acid, 585-70-6.

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Synthesis of α-Alkoxyacrylonitriles Using Substituted Diethyl Cyanomethylphosphonates

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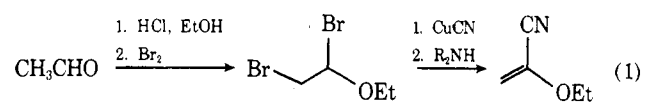
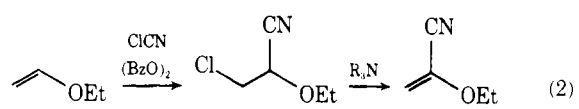
The synthesis of the thiophenoxy, methoxy, and *tert*-butoxy derivatives of diethyl cyanomethylphosphonates $(EtO)_2POCH(Z)CN$ **3** involved either the phenylsulfenylation of the anion of diethyl cyanomethylphosphonate (**4**) to afford **3a** (Z = SPh), the photolysis of the diazo derivative of **4** in methanol to afford **3b** (Z = OMe), or, preferably, the Arbusov reaction of methoxy- or *tert*-butoxybromoacetonitrile with triethyl phosphite to afford **3b** (Z = OMe) or **3c** (Z = O-*t*-Bu), respectively. The latter two phosphonate reagents **3b** and **3c** serve in the Horner–Emmons modification of the Wittig reaction to provide α-alkoxyacrylonitriles RR'C=C(OR")CN **1** from carbonyl compounds RR'C=O in excellent yield.

In connection with our interest in the chemistry of α,β-unsaturated nitriles,[1] we required a convenient synthesis of α-alkoxy- or α-thioalkoxyacrylonitriles. Cuvigny and Normant[2] have developed a substitution–elimination sequence for the conversion of aldehydes to α-alkoxyacrylonitriles which parallels a synthesis of α-ethoxyacrylonitrile reported earlier by Price[3] (eq 1). A more direct sequence developed by Vasil'eva[4] utilized the free-radical addition of cyanogen chloride to ethyl vinyl ether but suffered from low overall yields of α-ethoxyacrylonitrile (eq 2).

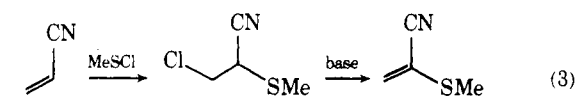


(1)

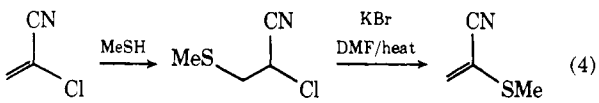


(2)

In contrast to the syntheses of α-alkoxyacrylonitriles in which the cyano group is introduced subsequent to the alkoxy group, the reported approaches to α-thioalkoxyacrylonitriles invert this order for the introduction of cyano and thioether groups. The addition of methylsulfenyl chloride to acrylonitrile and subsequent dehydrochlorination furnished α-thiomethoxyacrylonitrile[5] (eq 3). Alternatively, Gundermann[6] developed an interesting approach in which the 2-chloro-3-thiomethoxynitrile was dehydrochlorinated with concomitant migration of the thioether group to afford α-thiomethoxyacrylonitrile (eq 4).

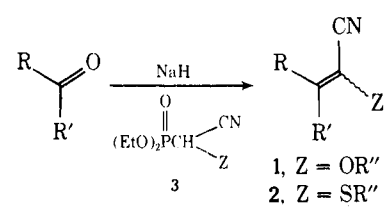


(3)



(4)

To develop a general synthesis of α-alkoxyacrylonitriles **1** and α-thioalkoxyacrylonitriles **2** which would avoid these multistep sequences, we required a Wittig reagent which could introduce the α-alkoxyacrylonitrile or α-thioalkoxyacrylonitrile synthon in a single operation. In particular, we desired the phosphonate Wittig reagents[7] **3** which offer the distinct advantage over phosphorane Wittig reagents of providing water-soluble, phosphate by-products. We now wish to report various synthetic approaches to these phosphonate reagents **3** and their application to the preparation of **1** and **2** (eq 5).



(5)

We have examined three different approaches to the phosphonates **3** (eq 6–8). Initially, we studied the sulfenylation of the anion of diethyl cyanomethylphosphonate (**4**) with phenylsulfenyl chloride and succeeded in obtaining the thiophenoxyphosphonate **3a** as the predominant product (eq 6). Our interest in exploring similarly substituted sulfur derivatives of **4** was dampened by the failure of the anion of **3a** to condense with carbonyl compounds other than nonenolizable aldehydes. For example, although benzaldehyde condensed with the anion of **3a** (1.0 equiv, 10% HMPA–DME, 81 °C, 24 h) to furnish (*E*)- and (*Z*)-2-thiophenoxycinnamonitriles in 68% yield, acetaldehyde failed to provide any of the desired product. The failure of the anion of **3a** to add to the carbonyl group of other aldehydes and ketones was attributed either to the steric bulk of the phosphonate or to the additional thioether stabilization[8] of the anion of **3a** relative to the anion of **4**. We consequently turned to the synthesis of the alkoxy derivatives of **4**.

In a second effort to utilize **4** to secure the methoxyphosphonate **3b**, we investigated the reaction of the anion of **4** with *p*-toluenesulfonyl azide[9a] and *p*-carboxybenzenesulfonyl azide[9b] (**5**). Although the infrared spectrum of crude products displayed a signal at 4.74 μ which indicated successful diazo transfer, we were unable to obtain the azophosphonate **6** in