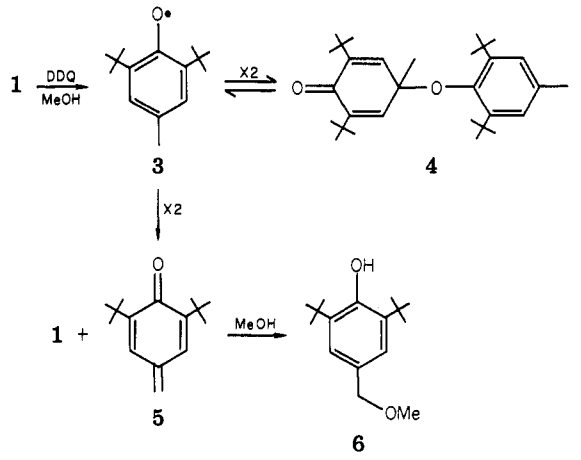
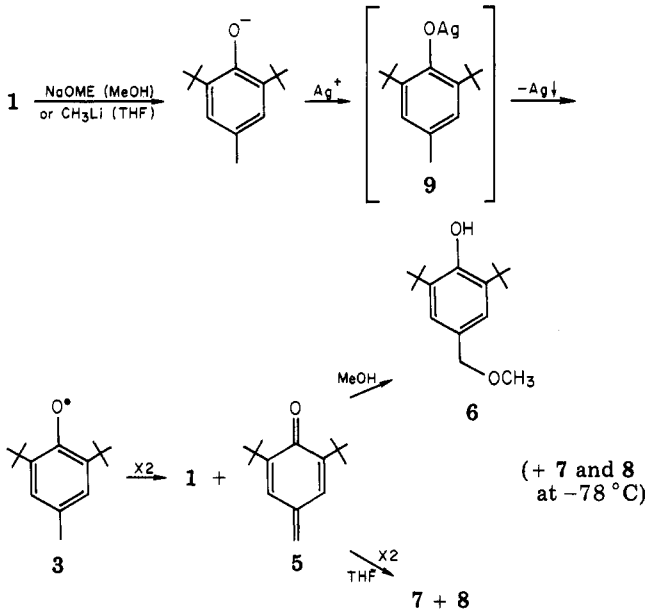
Scheme I



Scheme II



4 H), 4.75 (br s, 2 H), 6.80 (s, 4 H); TLC R_f 0.54.

Acknowledgment. The author expresses his gratitude to Professors Albert Bobst and Estel Sprague of this department for their help in obtaining and interpreting the ESR spectrum and to one of the referees for calling our attention to ref 4.

Registry No. 1, 17688-83-4; 3, 6858-01-1; 4, 2179-51-3; 5, 2607-52-5; 6, 87-97-8; 7, 1516-94-5; 8, 809-73-4; Ag(I), 14701-21-4.

Reaction of 2-Amino-3-cyano-4-methylfuran as a Dienamine and a Diene

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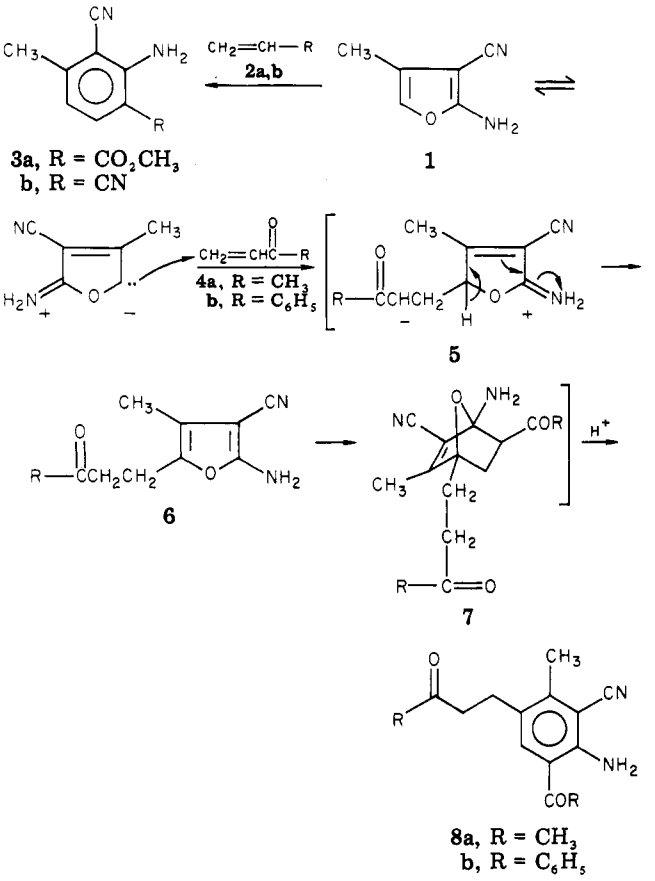
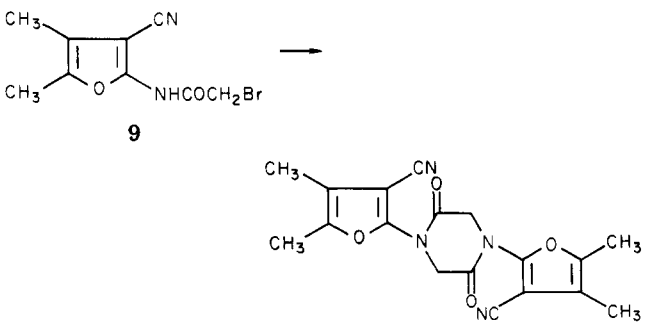
Received December 7, 1981

Previous studies in the use of furan *o*-aminonitriles as precursors for the synthesis of anthranilic acid derivatives and condensed heterocyclic compounds have shown [1] that 4,5-disubstituted 2-amino-3-cyanofurans react with various

Scheme I



olefins in a Diels–Alder fashion. This reaction has now been extended to 2-amino-3-cyano-4-methylfuran (1)[2] with comparable results with methyl acrylate and acrylonitrile (Scheme I). However, 1 was observed to undergo a novel enamine reaction[3] when treated with methyl or phenyl vinyl ketones (Scheme I). The dienamine tautomer adds to the vinyl ketone by Michael addition,[6] leading to the



Upon mild acidic hydrolysis, compound 9[4] gave the starting 4,5-dimethyl-2-amino-3-cyanofuran, whereas a peak at 352 in the mass spectrum supported the diketopiperazine assignment for 10.

(1) Nixon, W. J., Jr.; Garland, J. T.; Blanton, C. D., Jr. *Synthesis* **1980**, 56.

(2) Gewald, K. *Chem. Ber.* **1966**, *99*, 1002.

(3) Furan an pyrrole *o*-aminonitriles have been shown[4] by NMR spectroscopy to behave as dienamines in trifluoroacetic acid with electrophilic addition at C_5. In one case, C-acylation of a furan *o*-aminonitrile (i.e., 2-amino-3-cyano-4,5-dimethylfuran) was claimed[4] to occur via the enamine, which was subsequently converted to a furo[2,3-*b*]pyrrole derivative. In fact, N-acylation was observed, and the product previously designated as a furopyrrole[4] was shown[5] to be *N*,*N*′-bis(3-cyano-4,5-dimethyl-2-furyl)-2,5-diketopiperazine:

(4) Wie, C. T.; Sunder, S.; Blanton, C. D., Jr. *Tetrahedron* Lett. **1968**, 4605.

(5) Nixon, W. J., Jr. Ph.D. Dissertation, University of Georgia, July, 1972.

(6) Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Org. React.* **1959**, *10*, 179.

0022-3263/82/1947-2483$01.25/0

4,5-disubstituted furan *o*-aminonitrile (**6**). This latter product was not isolated but, under the conditions employed, rapidly reacts with the vinyl ketone in a Diels–Alder manner (**7**) as previously demonstrated.[1] Treatment of the Diels–Alder adduct (**7**) with acid gave in modest yield the anthranilonitrile derivative (**8**), which was characterized by elemental analysis and NMR spectroscopy. Compound **8a** was also characterized by ^{13}C NMR and mass spectroscopy.

Interestingly, when **1** was treated with methyl acrylate or acrylonitrile, the only products (**3a,b**) obtained under these coonditions were those expected to arise via the Diels–Alder adduct. No evidence for the prior reaction of the methyl acrylate or acrylonitrile in a Michael addition was detected. Since vinyl ketones are known[6] to be better Michael acceptors than acrylates or acrylonitriles, this appears to account for the formation of **3** and **8**.

Furan *o*-aminonitriles can be used to synthesize highly substituted anthranilate derivatives,[1] and **1**, in particular, may be used to prepare anthranilate derivatives (**8**) not readily accessible from previously available furan *o*-aminonitriles.[2,7] Anthranilates are valuable intermediates,[1] and the ability to introduce additional functionality at positions 3 and 5 extends the potential synthetic value gained by the use of furan *o*-aminonitriles as precursors.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 467 grating spectrophotometer. The ^1H NMR spectra were obtained on a 60-MHz Hitachi Perkin-Elmer R20A high-resolution spectrometer using Me_4Si as an internal standard. ^{13}C NMR spectra (Me_4Si) were recorded on a JEOL PTS-100. Mass spectra were determined on a Finnigan 4000 GC–MS Quadrupole mass spectrometer or on a DuPont 21-490 low-resolution mass spectrometer. Microanalyses were performed by Atlantic Microlab, Inc., Atlanta, GA.

3-Acetyl-6-methyl-5-(3-oxobutyl)anthranilonitrile (8a). To a 250-mL round-bottomed flask equipped with a magnetic stirrer, reflux condenser, and a heating mantle was added 3.2 g (30 mmol) of 2-amino-3-cyano-4-methylfuran (**1**),[2] 7 mL of methyl vinyl ketone, and 100 mL of acetone. The reaction mixture was refluxed for 24 h, cooled, and concentrated in vacuo. The yellow-orange gum was dissolved in 50 mL of acetic acid and chilled in an ice–water bath. To the cold solution was added 30 mL of concentrated H_2SO_4. The mixture was stirred at room temperature for 1 h and then poured onto ice. A yellow solid was collected and recrystallized from methanol to yield 2.1 g (29%): mp 158–160 °C; IR (KBr) 3440, 3320, 2200, 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7 (s, 1 H), 6.9 (br, 2 H, exchangeable by D_2O), 2.8 (t, 4 H), 2.6 (s, 3 H), 2.5 (s, 3 H), 2.2 (s, 3 H); ^{13}C NMR ($CDCl_3$) 206.53 (s), 198.85 (s), 149.78 (s), 146.30, (s), 136.85 (d), 125.82 (s), 115.88 (s), 115.46 (s), 97.78 (s), 42.79 (t), 29.50 (q), 27.67 (q), 25.48 (t), 17.88 (q) ppm; mass spectrum, *m/e* 244.1 (M^+), calcd 244.299.

Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.83; H, 6.67; N, 11.42.

3-Benzoyl-6-methyl-5-(3-oxo-3-phenylpropyl)-anthranilonitrile (8b). The title compound was prepared as above from **1** and phenyl vinyl ketone.[8] The gum was purified on a silica gel column using methylene chloride as eluent. Concentration of the solvent gave a yellow solid, which was recrystallized from aqueous methanol to give **8b** (18%) as yellow crystals: mp 120–121 °C; IR (KBr) 3400, 3300, 2200, 1690, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.25–8.0 (m, 11 H), 6.8 (s, 2 H), 2.9–3.1 (2 t, 4 H), 2.55 (s, 3 H).

Anal. Calcd for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60. Found: C, 78.29; H, 5.48; N, 7.56.

Methyl 3-Cyano-4-methylanthranilate (3a). The title compound was prepared as above from **1** and methyl acrylate. The off-white solid was recrystallized from benzene–hexane solution (26%): mp 106–108 °C; IR (KBr) 3420, 3310, 2950, 2200, 1695, 1600 cm^{-1}; ^1H NMR ($CDCl_3$–Me_2SO-d_6) δ 7.9 (d, 1 H, J = 8.5 Hz), 6.5 (d, 1 H, J = 8.5 Hz), 3.85 (s, 3 H), 2.45 (s, 3 H).

Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.15; H, 5.32; N, 14.72.

3-Cyano-4-methylanthranilonitrile (3b). The title compound was prepared as above from **1** and acrylonitrile. The solid was recrystallized from aqueous methanol to yield **3b** (35%): mp 158–159.5 °C; IR (KBr) 3500, 3390, 2220, 2210, 1640 cm^{-1}; ^1H NMR ($CDCl_3$–Me_2SO-d_6) δ 7.5 (d, 1 H, J = 8.0 Hz), 6.45 (d, 1 H, J = 8.0 Hz), 2.5 (s, 3 H).

Anal. Calcd for $C_9H_7N_3$: C, 68.78; H, 4.49; N, 26.73. Found: C, 68.55; H, 4.55; N, 26.63.

2-(Bromoacetamido)-3-cyano-4,5-dimethylfuran (9). To a solution of 4,5-dimethyl-2-amino-3-cyanofuran[2] (27.2 g, 0.2 mol) in 30 mL of acetonitrile and 50 mL of tetrahydrofuran was added dropwise 20.2 g (0.1 mol) of bromoacetyl bromide while maintaining the temperature below 5 °C during the addition. The mixture was stirred continuously for 2 h at this temperature. Upon completion of the reaction, the hydrogen bromide salt of the starting material was removed by filtration (ca. 52% yield). The acetonitrile and tetrahydrofuran were removed in vacuo to yield an orange solid. The product was recrystallized from ethyl acetate–ligroin (58% yield): mp 142–143 °C; IR (KBr) 3175, 3125, 3050, 2250, 1715, 1630, 1550 cm^{-1}; NMR (Me_2SO-d_6) δ 2.0 (s, 2 H), 2.2 (s, 3 H), 4.0 (s, 2 H), 11.40 (s, 1 H, exchangeable with D_2O).

Anal. Calcd for $C_9H_9N_2O_2Br$: C, 42.02; H, 3.50; N, 10.89. Found: C, 42.26; H, 3.66; N, 11.09.

***N,N'*-Bis(3-cyano-4,5-dimethyl-2-furyl)-2,5-diketopiperazine (10).** A solution of **9** (5.0 g, 17.0 mmol) in 500 mL of water was refluxed and stirred for 2 h. Upon cooling a white product was collected, washed with water, and recrystallized from dimethylformamide and water to give a 90% yield of **10**: mp 226–227 °C; IR (KBr) 2975, 2925, 2240, 1700, 1650, 1600 cm^{-1}; NMR (Me_2SO-d_6) δ 2.0 (s, 6 H), 2.35 (s, 6 H), 4.80 (s, 4 H); mass spectrum, *m/e* 352 (M^+), calcd 352.36.

Anal. Calcd for $C_{18}H_{16}N_4O_4$: C, 61.36; H, 4.55; N, 15.91. Found: C, 61.30; H, 4.62; N, 15.73.

Acknowledgment. This research was supported in part by the National Institute of Neurological and Communicative Disorders and Stroke Grant 5R01NS16988. We are grateful to Courtney Pape, Department of Chemistry, University of Georgia, for the ^{13}C NMR and mass spectra.

Registry No. **1**, 5117-87-3; **2a**, 96-33-3; **2b**, 107-13-1; **3a**, 81446-91-5; **3b**, 81446-92-6; **4a**, 78-94-4; **4b**, 768-03-6; **8a**, 81446-93-7; **8b**, 81446-94-8; **9**, 81446-95-9; **10**, 81446-96-0; 4,5-dimethyl-2-amino-3-cyanofuran, 5117-88-4; 4,5-dimethyl-2-amino-3-cyanofuran hydrobromide, 81446-97-1; bromoacetyl bromide, 598-21-0.

(7) Taylor, E. C.; McKillop, A. "The Chemistry of Cyclic Enaminonitriles and *o*-Aminonitriles"; Interscience: New York, 1970.

(8) (a) Gras, J.-L. *Tetrahedron Lett.* **1978**, 2955. (b) The original procedure employed trioxymethylene (*s*-trioxane) as a reagent in the synthesis of vinyl ketones. In our hands, use of this reagent gave low yields (ca. 40%) of the vinyl ketone. However, substitution of paraformaldehyde instead of trioxymethylene lead to 85–90% yield of the phenyl vinyl ketone.

Studies in the Elimination of Substituted Vinyl Halides to Acetylenes

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Received March 2, 1982

The elimination of the elements HX from a vinyl halide is one of the most important and general methods for preparing the carbon–carbon triple bond and has been reviewed several times.[1] In general, one finds that al-

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