and activation energies were derived from $k = f \exp(-A/RT)$ between 20 and 70°. Substituents on the benzene ring had little influence on the rate of cis-to-trans isomerization, unless obviously ortho to the diazo group, *e.g.*, when X was 2-Cl-4-NO_2. The isomerization rates increased when bulkier groups R were attached to the sulfur atom, but the activation energies decreased as expected.

Van Zwet and Kooyman[2] gave two possible mechanisms for the thermal cis-to-trans isomerization, namely *via* rotation about the N–N bond or *via* ionization and recombination. For azobenzene derivatives, Talaty and Fargo[4] proposed a third mechanism with a linear transition state in which one or both nitrogen atoms undergo a change in hybridization to the sp state. The arguments for this third mechanism were the low activation energies of 21–24 kcal/mol in combination with the absence of large solvent effects. Since the benzenediazo sulfides of Table I have activation energies of 21–28 kcal/mol and generally small solvent effects,[2] the same mechanism of thermal cis-to-trans isomerization *via* a linear transition state seems to hold.

The effect of substituents X on the absorption spectra (Table II) also suggests a resemblance to azobenzenes. Both classes of compounds have the main absorption peaks of the 4-NO_2 derivatives considerably shifted to the visible with respect to the unsubstituted compounds. This has been attributed to polar resonance structures,[5] but the solvent effects are not entirely consistent with that interpretation. The main absorption peak of 4-nitro-benzenediazo-*tert*-butyl sulfide was found at 351 nm in ethanol but at 388 nm in benzene. Similar effects were reported in ref 2.

Experimental Section

The purity of the cis and trans benzenediazo sulfides was tested by silica gel thin layer chromatography with cyclohexane eluent and by nmr and ir. The nmr spectra were recorded in our analytical department by Mr. H. M. van den Bogaert on a Varian A-60 spectrometer in carbon tetrachloride with tetramethylsilane as internal standard. Analyses were performed by the TNO Organic Chemistry Institute at Utrecht. In the synthetic work assistance was given by Mr. Th. C. J. M. Hegge. The absorption spectra were recorded with a Unicam SP800 spectrophotometer, the triphenylmethyl sulfides in ethyl acetate, the others in 98% ethanol. Isomerization rate constants were determined by photoisomerizing the ethanolic solutions of the trans isomers at 405 nm and spectrophotometrically following the thermal reverse isomerization from the resultant cis isomer to the trans form. The stoppered cells were placed in a constant temperature housing. Since both isomers are light-sensitive, the experiments were carried out in yellow safe-light to prevent photoisomerization.

Anilines and Diazonium Tetrafluoroborates.—Most of the anilines were commercial products. Two of them, 3-Cl-4-$N(CH_3)_2$-aniline and 3,5-Cl_2-4-$N(CH_3)_2$-aniline, were prepared by known methods[6,7] which were improved in that the $N(CH_3)_2$ group was introduced by passing gaseous $HN(CH_3)_2$ into the solution of the bromobenzene derivative in dimethylformamide.[8] The diazonium boron tetrafluorides were prepared as reported earlier.[8]

Benzenediazo Sulfides.—The benzenediazoalkyl sulfides were obtained as follows. The alkylthiol (0.1 mol) was added to a solution of 0.1 mol of diazonium·BF_4 in 250 ml of acetone cooled to 0°. The pH was adjusted with the help of pH paper to a value of between 5 and 6 adding dropwise about 160 ml of 2.5% aqueous NaOH in about 1 hr.

If the cis isomer did not crystallize it was extracted with benzene. The extract was dried (Na_2SO_4) and the solvent removed at reduced pressure at 20°. The residual product was dissolved in 250 ml of isooctane. If the cis isomer did crystallize, it was directly dissolved in isooctane. The solution was kept at 90° for 2 hr to achieve the cis-to-trans isomerization. The solvent was removed at reduced pressure. The crude products were recrystallized from ethanol, yields 50–80% (Table III).

The benzenediazotriphenylmethyl sulfides were prepared by the method given in ref 2 (p 1004).

(4) E. R. Talaty and J. C. Fargo, *Chem. Commun.*, 65 (1967).
(5) W. G. B. Huysmans, Thesis, Leiden, 1964, p 34.
(6) E. E. Ayling, J. H. Gorvin, and L. E. Hinkel, *J. Chem. Soc.*, 755 (1942).
(7) A. van Loon, P. E. Verkade, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **79**, 977 (1960).
(8) L. K. H. van Beek, J. Boven, and J. Helfferich, *ibid.*, **87**, 737 (1968).

Base-Catalyzed Reaction of Methyl α-Cyano-β-(2-thienyl)acrylate

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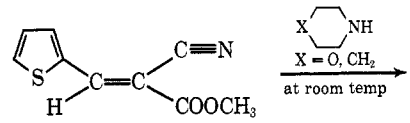
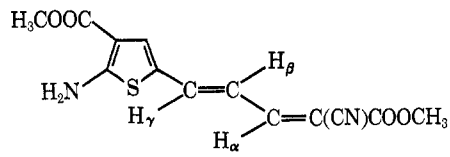
In extension of our previous studies on base-catalyzed ring opening–closure reaction of α-cyano-β-furylacrylic esters, which led to the formation of γ-(4-alkoxycarbonyl-5-aminofuryl)acroleins,[2] we wish to report the one-step synthesis of rather complex thiophenes. When methyl α-cyano-β-(2-thienyl)acrylate (**1**) was allowed to stand overnight in morpholine or in piperidine at room temperature, a colored product resulted in 56 and 69% yields, respectively. The product obtained was assigned as the structure of methyl 2-cyano-5-(4-methoxycarbonyl-5-amino-2-thienyl)-2,4-pentadienoate (**2**), on the basis of ir, nmr, and mass spectral data.



1

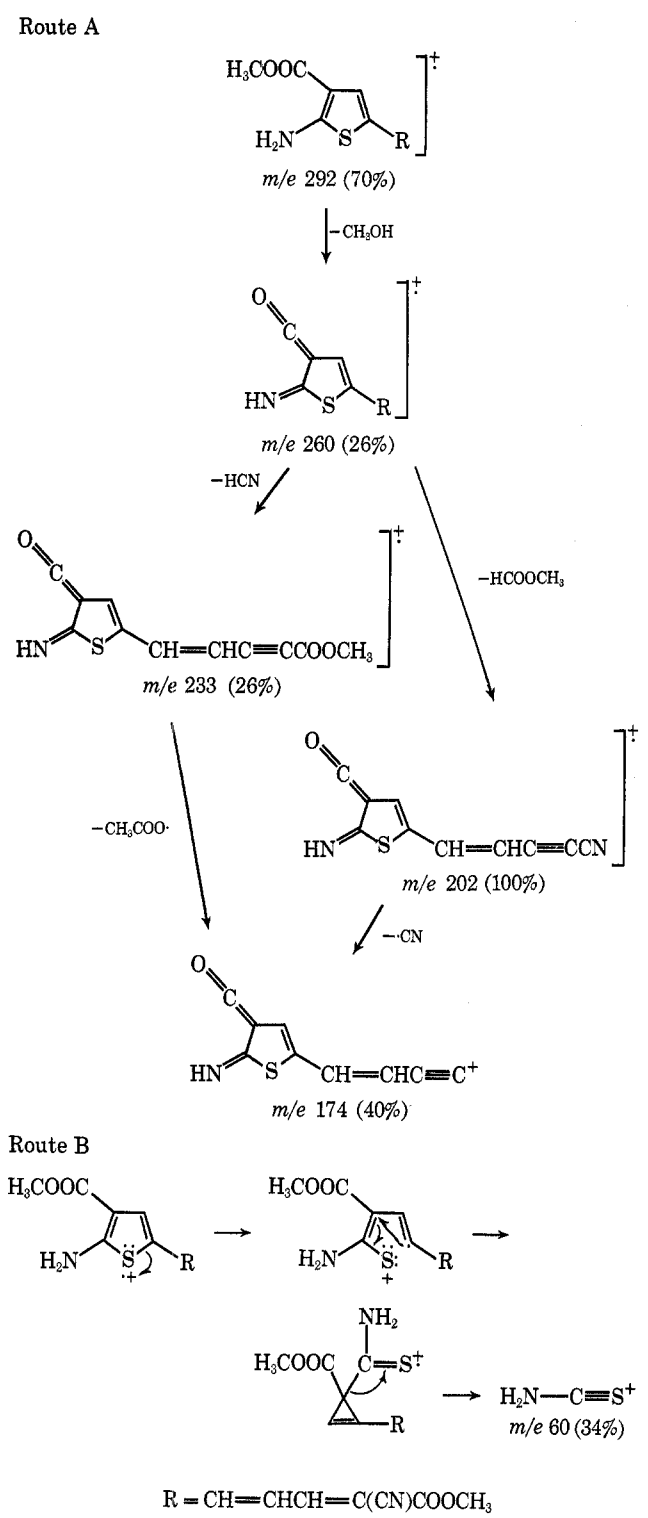


2

On the other hand, when methyl cyanoacetate (**4**) and thiophene-2-carboxaldehyde were mixed in morpholine or in piperidine directly, the same product **2** was also obtained in the range of 29–51% yields even when a 1:1 molar proportion of the reactants was used. The yields, in these reactions, were improved slightly by the use an excess of **4**, thus giving 32–71% **2**. It is impossible to isolate the expected cyanoacrylate **1** in any case. Furthermore, aminals[3–5] are commonly produced by the reaction of a secondary amine with an aldehyde;

(1) Laboratory of Chemistry, Utsunomiya University, Utsunomiya, Japan.
(2) H. Yasuda, T. Hayashi, and H. Midorikawa, *J. Org. Chem.*, **35**, 1234 (1970).
(3) C. Mannich and H. Davidsen, *Chem. Ber.*, **69**, 2106 (1936).
(4) A. Dornow and W. Schacht, *ibid.*, **82**, 464 (1949).
(5) R. Duloa, E. Elkik, and A. Veillard, *Bull. Soc. Chim. Fr.*, 967 (1960).

SCHEME I



however, 1,1-di(*N*-morpholine)- or 1,1-di(*N*-piperidino)-thienylmethanes could not be isolated in each reaction.

Elemental analysis and a mass spectral determination establish the molecular formula of **2** as $C_{13}H_{12}O_4N_2S$. Hydrogenation of **2** over palladium/carbon led to colorless oily mixtures of nondistillable materials. The ir and nmr spectra of **2** (see Experimental Section) provide support for the required structural feature. In the nmr spectrum a rather large coupling constant between two olefinic protons suggests the *trans* configuration about C=C bond. The structure of **2** is amply supported by mass spectral data. Based upon recent studies of the mass spectral fragmentation of thiophenes,[6] routes A and B have suggested for the observed fragmentation of **2** (Scheme I). A number of the postulated transformations received support from the metastable ions. Elimination of methanol appears to be the primary mode (route A) of molecular ion (*m/e* 292) fragmentation. Formation of the *m/e* 260 ion is a transformation characteristic anthranilic acid.[7] Loss of HCN or $HCOOCH_3$ from the *m/e* 260 ion could then lead to the ions at *m/e* 233 and 202. The *m/e* 174 ion might then arise from the *m/e* 233 ion by loss of $CH_3COO\cdot$, and from the *m/e* 202 ion by loss of $\cdot CN$. Pertinent aspects of the remaining mass spectrum can be interpreted by formation of the *m/e* 60 ion from the molecular ion as suggested by route B.

The formation of **2** from the cyanoacrylate **1** with morpholine or piperidine is of mechanistic interest. We proposed that the overall reaction may be rationalize by the sequence outlined in Scheme II. It is plausible that the initial attack of the base will occur both at the β carbon atom of the α,β unsaturation and the 5 position of thiophene ring in **1**. Thus, the addition of the base to the β carbon results in the formation of the amino ester intermediate **3**. This amino ester formation resembles the attack of secondary amines on the 1,2 or 2,3 double bond of 1-cyanoallenes, giving the corresponding enamines.[8] Similar addition has also been observed in the reaction of norbornanones with morpholine.[9] In general, cleavage of substituted tertiary amines gives the iminium cation and the anion structure as the results of α elimination.[10-15] It therefore appears that the formation of **4** and quaternary iminium hydroxide intermediate **5** can be visualized as proceeding through cleavage of the ester **3** by water molecule, which contains in the basic medium. When nucleophilic attack by the base appears to have occurred at the 5 position, the reaction would give the enamine intermediate **6**. This, then would cyclize between the SH and C≡N groups to afford the enamine **7**, which readily hydrolyzes to the β-thienylacrolein derivative **8**. The resulting product **8** could condense with **4** to give the required product **2**. This mechanism is closely similar to that previously reported.[2] Unfortunately, intermediates **5** and **8** could not be detected in the present investigation.

Experimental Section

Nmr spectra were recorded on a JNM-C-60 HL high-resolution nmr spectrometer in DMSO-d_6 with TMS as an internal standard. Ir spectra were determined in the KBr disks using a Perkin-Elmer 521 spectrophotometer. Mass spectra were obtained on a JNM-O1S spectrometer operating at 75 eV. Uv spectra were measured with a Cary Model 14 spectrometer.

Methyl α-Cyano-β-(2-thienyl)acrylate (1).—To a mixture of thiophene-2-carboxaldehyde (6.0 g, 0.054 mol) and methyl cyano-

(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.
(7) K. Biemann, *Angew. Chem.*, **74**, 102 (1962).
(8) P. M. Greaves and S. R. Landor, *Chem. Commun.*, 322 (1966).
(9) R. D. Bach, *J. Org. Chem.*, **33**, 1647 (1968).
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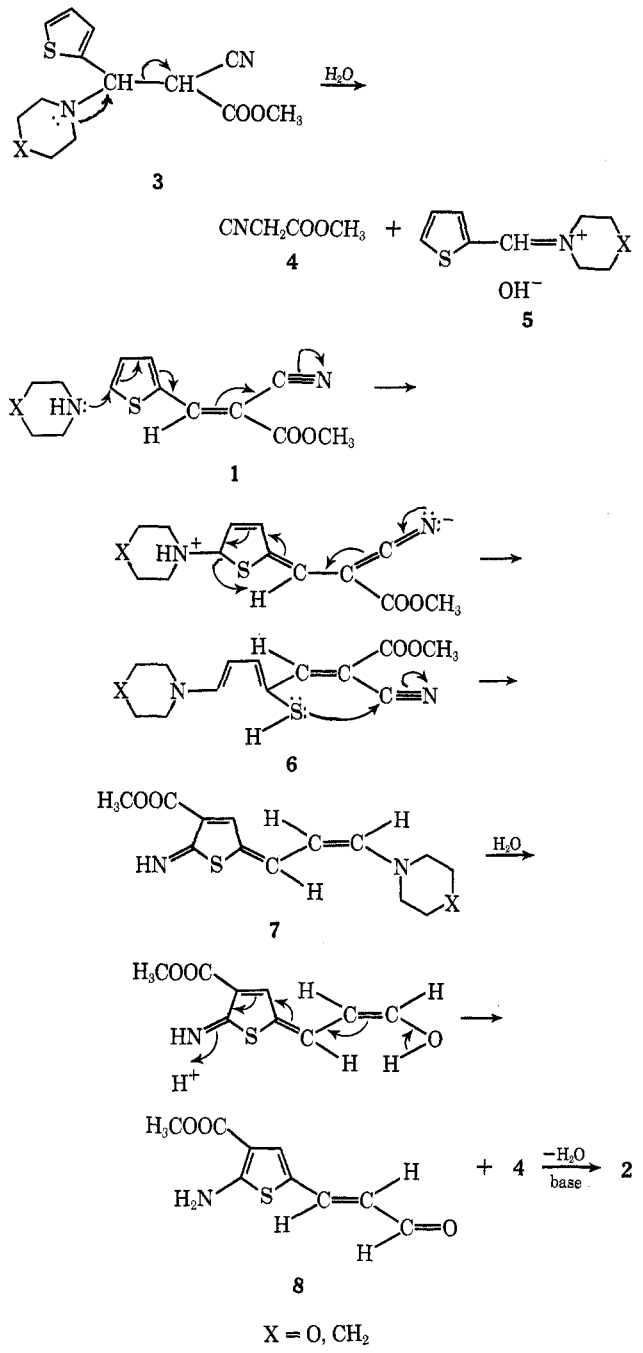
SCHEME II



acetate (6.4 g, 0.065 mol) was added piperidine (0.1 ml), and the mixture was allowed to stand for 4 hr at room temperature. The solid that separated was collected on a filter, washed with diluted methanol, and dried. One recrystallization from methanol gave 8.4 g (96%) of 1 as faintly yellow needles, mp 111–112°.

Anal. Calcd for $C_9H_7O_2NS$: C, 55.96; H, 3.63; N, 8.25. Found: C, 56.39; H, 3.61; N, 8.04.

Reaction of 1 with Piperidine.—A mixture of 1 (5.0 g, 0.026 mol) and 30 ml of piperidine containing 1 drop of water was mechanically stirred at room temperature for 40 min. The solution immediately turned a dark reddish brown color and an exothermic reaction took place. Dark brown solid began to precipitate after 15 min. After the mixture was allowed to stand overnight, the colored crystalline product that separated was collected on a filter, washed with methanol, and recrystallized from pyridine–ethanol to give 1.8 g (48%) of 2 as reddish brown short needles, mp 262–263°. The combined filtrate and washes were diluted with water, and the resulting colored solid recrystallized from the same solvent to yield 0.8 g [total 2.6 g (69%)] of pure 2 (the mother liquor in the above recrystallizations must be dry; the expected product 5 or 8 is almost impossible to separate): uv max ($CHCl_3$) 274 mμ (ε 15,000), 313 (8400), 458 (49,000); ir (KBr disk) 3358, 3258 (NH_2), 2214 (α,β-unsaturated C≡N), 1712 (α,β-unsaturated ester C=O), 1688 (α,β-unsaturated ester C=O, directly attached to thiophene ring), 1522, 1438, 1355, and 852 cm^{-1} (thiophene ring); nmr (DMSO-d_6) δ 3.70, 3.73 ($2COOCH_3$), 6.38 (q, H_β, $J_{\alpha\beta}$ = 11.2 Hz, $J_{\beta\gamma}$ = 14.5 Hz, $J_{\alpha\gamma}$ = ~0Hz), 7.62 (d, H_γ, $J_{\beta\gamma}$ = 14.5 Hz), 7.87 (d, H_α, $J_{\alpha\beta}$ = 11.2 Hz), 7.33 (s, thiophene ring H), and 8.24 (b, NH_2).

Anal. Calcd for $C_{13}H_{12}O_4N_2S$: C, 53.42; H, 4.10; N, 9.58; S, 10.95. Found: C, 53.42; H, 4.13; N, 9.53; S, 10.86.

Reaction of 1 with Morpholine.—A mixture of 1 (5.0 g, 0.026 mol) in 30 ml of morpholine containing 1 drop of water was mechanically stirred at room temperature for 40 min. The solution immediately became orange, and a dark brown solid precipitated. The precipitate on standing overnight was collected on a filter, washed with methanol, and recrystallized from pyridine–ethanol to form 2.1 g (56%) of the desired product 2. Evaporation of the combined filtrate and washes gave dark brown tarry matter which could not be purified further.

Reaction of Thiophene-2-carboxaldehyde with Methyl Cyanoacetate (4) in Piperidine. Method A (1:1 Aldehyde–Ester).—To a stirred solution of 4 (1.1 g, 0.011 mol) in piperidine (5 ml) was added dropwise the aldehyde (1.2 g, 0.011 mol) at room temperature, and the stirring was continued for 20 min. The solution became reddish brown and an exothermic reaction took place. The mixture on standing overnight was diluted with methanol (15 ml), and the resulting colored solid recrystallized from pyridine–ethanol to give 0.8 g (51%) of the required product 2. Purification of colored residual oil, followed by evaporation of the basic solvent at diminished pressure, gave no cyano ester 1 or other by-products.

Method B (1:2 Aldehyde–Ester).—In a procedure much like that of A, the aldehyde (1.2 g, 0.011 mol) and 4 (2.2 g, 0.022 mol) in piperidine (5 ml) were stirred for 20 min at room temperature. After the mixture was allowed to stand overnight, it was diluted with methanol (15 ml). The colored solid that separated was collected and recrystallized from pyridine–ethanol to yield 1.1 g (71%) of 2. Evaporation of mother liquor afforded a negligible amount of oily matter which could not be purified further.

Reaction of Thiophene-2-carboxaldehyde with 4 in Morpholine. Method C (1:1 Aldehyde–Ester).—The aldehyde (1.2 g, 0.011 mol) was placed in 1.1 g (0.011 mol) of 4 in morpholine (5 ml) at room temperature. The mixture was stirred for 20 min and then allowed to stand overnight. The mixture became reddish brown, and dark brown solid precipitated. The reaction mixture on dilution with methanol (15 ml) was filtered to remove the crude 2. One recrystallization from pyridine–ethanol gave 0.45 g (29%) of pure 2. The residues on removal of the combined filtrate and washes and of mother liquor were not investigated further.

Method D (1:2 Aldehyde–Ester).—In essentially the procedure of *C*, a mixture of 4 (2.2 g, 0.022 mol) and the aldehyde (1.2 g, 0.011 mol) in morpholine (5 ml) was mechanically stirred for 20 min at room temperature. The reaction mixture on standing overnight was filtered and the residue was washed with methanol. After recrystallization from pyridine–ethanol a 32% yield (0.5 g) of 2 was obtained. The combined filtrate and washes were concentrated *in vacuo* to a dark brown oil, and no purification was attempted.

Attempted Catalytic Hydrogenation of 2.—A mixture of 2 (2.0 g, 0.010 mol) and 5% palladium/carbon catalyst (0.20 g) in ethanol (100 ml) was treated with hydrogen gas. The solution was changed to a colorless one and 0.042 mol of the gas was absorbed. Removal of solvent and the catalyst gave an almost colorless oil which could not be purified by fractional distillation under diminished pressure.

Registry No.—1, 29577-54-6; 2, 29577-55-7.

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