Studies of the Synthesis of Furan Compounds. XXVIII.[1] Syntheses and Steric Configurations of 3-(5-Nitro-2-furyl)-2-(2-furyl)acrylonitrile and Its Bromine Derivatives[2]

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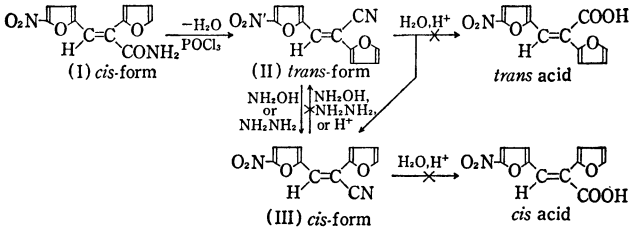
(Received February 2, 1972)

In continuing a previous report[3] concerning the syntheses and steric configurations of 3-(5-nitro-2-furyl)-2-(2-furyl)acrylic acid derivatives, *trans* and *cis* 3-(5-nitro-2-furyl)-2-(2-furyl)acrylonitrile and their related compounds have been synthesized. The isomerization was involved in the conversion of *cis*-3-(5-nitro-2-furyl)-2-(2-furyl)acrylamide (I) to *trans*-3-(5-nitro-2-furyl)-2-(2-furyl)acrylonitrile (II) upon the treatment of phosphoryl chloride. II was converted to its *cis* isomer (III) by treating it with hydroxylamine, hydrazine hydrate, or hydrochloric acid. II and III were treated with bromine at 5—10°C in carbon tetrachloride to afford dibromo compounds, (3*S* : 5*S* and 3*R* : 5*R*)-(IV) and (3*S* : 5*R* and 3*R* : 5*S*)-3-(5-nitro-2-furyl)-3-bromo-2-(5-bromo-2,5-dihydro-2-furylidene)propionitrile (V) respectively. When the bromination was carried out at a higher temperature (70—73°C), a monobromo compound, *cis*-3-(5-nitro-2-furyl)-2-(5-bromo-2-furyl)acrylonitrile (VI), was obtained from both II and III. VI was also produced by heating IV or V in refluxing acetone. The structures and configurations of these compounds were discussed on the basis of their experimental and spectral data.

3-(5-Nitro-2-furyl)acrylonitrile has been prepared by various methods,[1,4-6] and it gives an amidoxime derivatives upon treatment with hydroxylamine.[1,7] In a similar treatment of 3-(5-nitro-2-furyl)-2-(2-furyl)acrylonitrile with hydroxylamine, the corresponding amidoxime-type compound was not obtained, but a configurational interconversion was observed. In this report, the systheses and steric configurations of *trans* and *cis* 3-(5-nitro-2-furyl)-2-(2-furyl)acrylonitrile and their bromine derivatives will be described.

Results and Discussion

3-(5-Nitro-2-furyl)-2-(2-furyl)acrylonitrile (II) was easily obtained in a good yield from 3-(5-nitro-2-furyl)-2-(2-furyl)acrylamide[8] (I) by treatment with phosphoryl chloride at 50—60°C according to the method described in a previous report.[1] When treated with hydroxylamine at 60—70°C, II was converted to its isomer (III); the results of an elemental analysis of this isomer agreed with the value calculated for II. In this isomerization, the hydroxylamine seems to serve as an isomerization catalyst, much like the hydrazine.[3] In fact, the same isomerization also occurred when II was treated with hydrazine hydrate. Further, the isomerization by a hydroxylamine or hydrazine catalyst was confirmed to be irreversible. In order to compare the structures of II and III with those of the corresponding mother acids and identify them, II and III were both heated with hydrochloric acid. The desired acids, however, were not obtained; II was converted to III, while III remained unchanged.



Scheme 1. Preparation and isomerization of II and III.

The IR spectra of II and III showed a C≡N stretching absorption band at about 2240 cm^{-1}. In the UV spectra, as is shown in Fig. 1, two absorption maxima of II, one near 300 mμ and the other near 400 mμ, were observed; the former one showed a hypsochromic shift upon comparison with the corresponding one of III. The extinction coefficient of the former was larger and that of the latter was smaller than in III. The NMR spectra (Fig. 2) indicate precisely that the olefinic proton and the CN group are on the same side of the ethylene double bond in the molecule of III, since the olefinic proton of III reveals a signal in a lower magnetic field than that of II (Δ_{tc} 0.44 ppm), as a result of the magnetic anisotropy of the C≡N bond. Thus, the configuration of III was determined to be *cis*, and that of II, to be *trans*, necessarily.[9] Saikachi *et al.*[8] gave a *trans* symbolism in the configurational nomenclature to the general 3-(5-nitro-2-furyl)-2-(2-furyl)acrylic acid and its amide, I, even though their two furan rings are on the same side of the ethylene bond. In a recent experiment, Kato prepared two isomeric 5-[2-(5-nitro-2-furyl)-1-(2-furyl)-vinyl]-2-amino-1,3,4-thiadiazoles from 3-(5-nitro-2-furyl)-2-(2-furyl)acrylic acid and determined the steric configurations of the 1,3,4-thiadiazoles, the starting acids, and their esters,[3] according to the nomenclature[8] mentioned above; it was necessary to correlate and/or compare the starting acids and esters with those described by Saikachi *et al.* We consider

1) Part XXVII of this series: I. Hirao and Y. Kato, This Bulletin, **45**, 2055 (1972).
2) Presented at the 25th Annual Meeting of the Chemical Society of Japan, Tokyo, October, 1971.
3) Y. Kato, This Bulletin, **44**, 489 (1971).
4) M. Ikeda, *Ann. Rept, Fac. Pharm. Kanazawa Univ.*, No **3**, 25 (1953).
5) A. Sugihara, *Yakugaku Zasshi*, **86**, 525 (1966).
6) H. Saikachi and S. Nakamura, *ibid.*, **88**, 110 (1968).
7) I. Saikawa and A. Takai, *ibid.*, **85**, 948 (1965).
8) H. Saikachi and A. Tanaka, *ibid.* **83**, 147 (1963).
9) If we use the nomenclature presented by Saikachi and Tanaka,[8] II is *cis*, and III, *trans*.

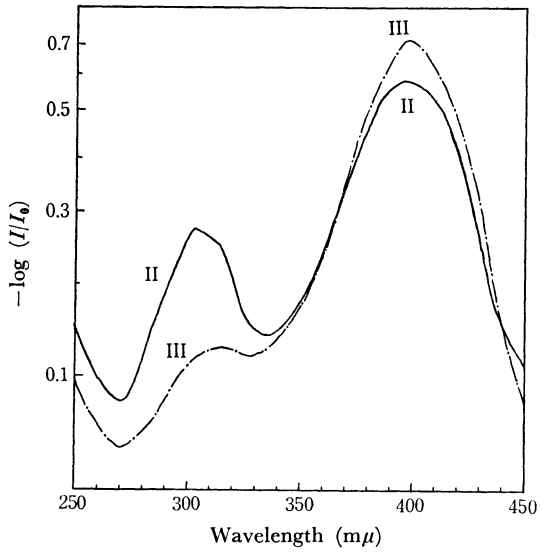


Fig. 1. UV spectra of II and III (in ethanol).
II: 9.3 μg/ml, III: 7.6 μg/ml.

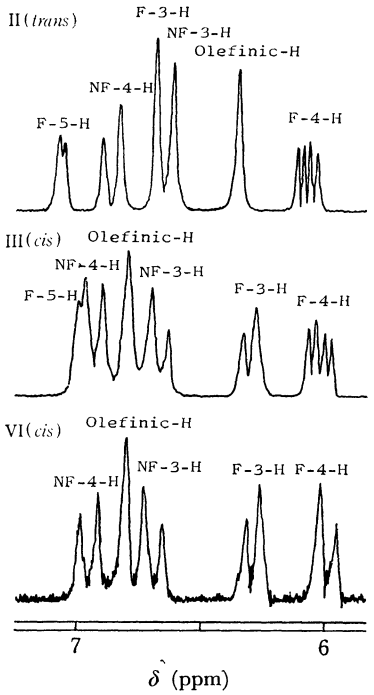
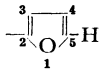
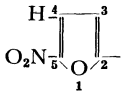


Fig. 2. NMR spectra of II, III, and VI (in CCl_3COOH).

F-5-H: C_5-H of furan ring 

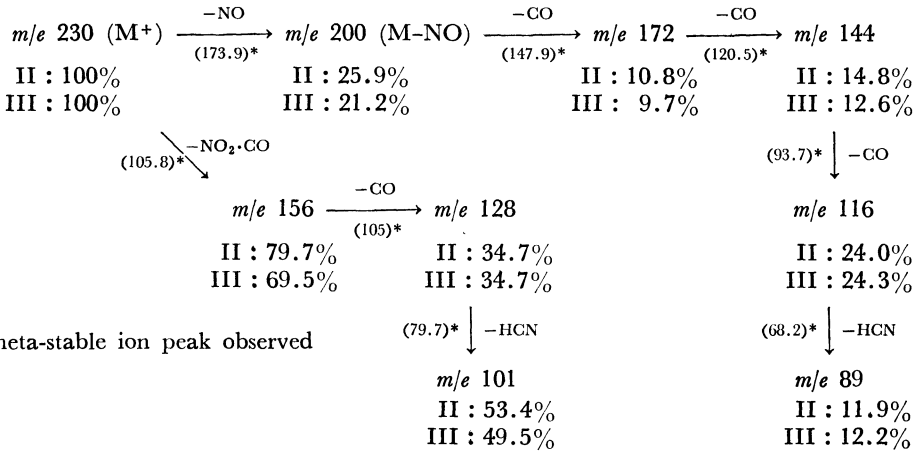
NF-4-H: C_4-H of 5-nitrofuran ring 

that it is most reasonable and suitable to conclude that the configurations of such an acid and I are *cis*. Furthermore, the symbolism of the compounds previously presented by Kato should also be corrected, changing *cis* to *trans*, and *trans*, to *cis*.

In the above dehydration reaction, it was found that a particularly facile isomerization[3,10] was involved in the conversion of I (*cis*) to II (*trans*) by the action of phosphoryl chloride.

The mass spectral data exhibited no difference between II and III. As is shown in Scheme 2, the molecular ion (M^+, *m/e* 230) is the most prominent (the base peak) and forms a distinct ion peak at mass 200 upon the elimination of NO. The M—NO ion successively loses three carbon monoxides to give the *m/e* 172, 144, and 116 ions. The ion with mass 89 results from the *m/e* 116 ion by the loss of HCN. On the other hand, the molecular ion loses NO_2 and CO fragments by a one-step process to give an ion at mass 156. This ion undergoes the elimination of CO and the subsequent loss of HCN to form *m/e* 128 and 101 ions successively.

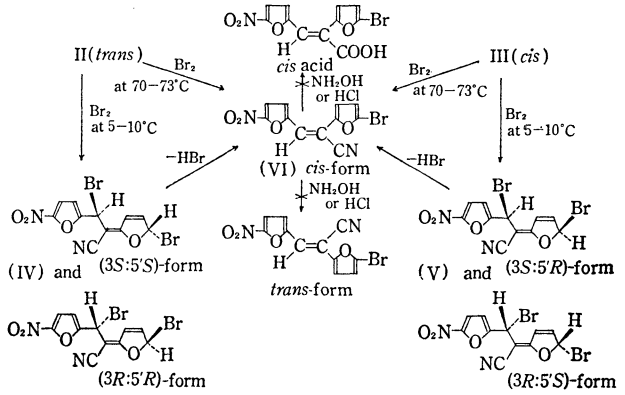
On the treatment of II and III with bromine at 5—10°C in carbon tetrachloride, two dibromo compounds, IV and V respectively, were obtained, while in the bromination carried out at 70—73°C a monobromo compound (VI) was produced from both II and III. Moreover, IV and V were found to be unstable both in air and in solvents, and they gave only VI, with the release of hydrogen bromide. For example, this elimination reaction occurred satisfactorily



Scheme 2. The fragmentation of II and III.

10) S. M. Kupchan and A. Afonso, *J. Org. Chem.*, **25**, 2217 (1960); see also R. E. Buckles, G. V. Mock, and L. Locatell, *Chem. Rev.*, **55**, 659 (1955).

when a dioxane solution of IV or V was left standing at room temperature or heated in refluxing acetone. The monobromo compound VI was stable, and it was recovered unchanged when heated with hydroxylamine in aqueous ethanol for 2 hr or with 36% hydrochloric acid for 12 hr.



Scheme 3. Preparation of bromo compounds from II and III.

The thermostability of IV, V, and VI was investigated by thermogravimetric analysis (TGA) and differential thermal analysis (DTA) under a nitrogen atmosphere. As is shown in Fig. 3, the DTA curve of VI shows an endothermic peak and an exothermic peak at 215°C and 222°C respectively; these peaks coincide with the melting and decomposition points of VI. On the other hand, in the DTA curves of IV and V, the endothermic peak at 102°C for IV and that at 113°C for V, and the exothermic one (210°C for IV and V) are in agreement with the initial and the second stages (80—114°C and 180—220°C for IV, 100—120°C and 185—220°C for V) of the reduction in weight of the corresponding TGA curves. About 23% and 21% of the loss of weight occur for IV and V respectively in the initial stage; this corresponds to the loss of a hydrogen bromide molecule from both IV and V (theoretical: 20.8%). The second stage of the reduction in weight agrees with the decomposition point of VI during the pyrolysis.

The IR spectrum of VI showed two C–H stretching absorption bands and a weak C≡N stretching absorption band at 3150, 3063, and 2240 cm^{-1} respectively. In the spectra of IV and V, the absorbances

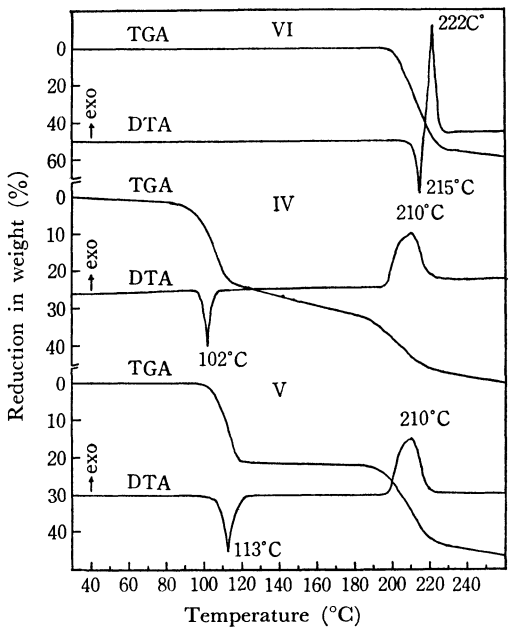
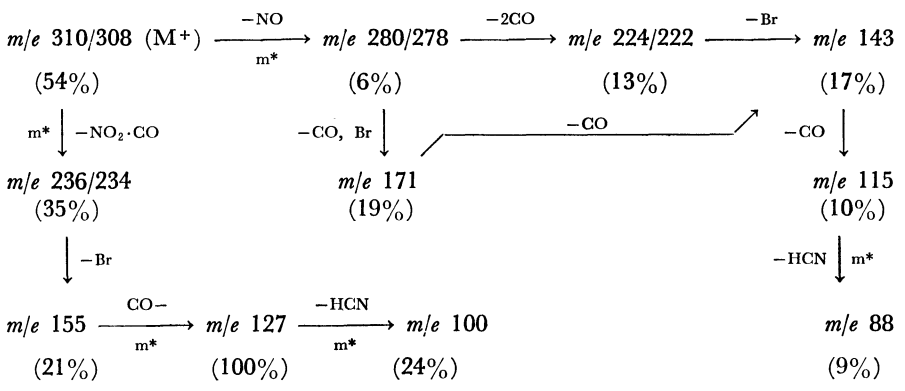


Fig. 3. The thermal analyses of IV, V, and VI at the heating rate of 3°C/min in a nitrogen stream.

of the C–H and C≡N stretching bands were more intense than those of VI, and the C–H absorption bands were observed at 3135 and 2985 cm^{-1} for IV, and at 3175, 3085, and 3025 cm^{-1} for V. The C≡N absorption bands appeared at 2220 cm^{-1}. The NMR spectra of IV and V were unsatisfactory because of their lower solubility and greater instability in solvents. On the other hand, VI was clearly determined to be *cis*-3-(5-nitro-2-furyl)-2-(5-bromo-2-furyl)acrylonitrile by a comparison of its NMR spectrum with those of II and III (Fig. 2). The mass spectrum also supported the above structure. In Scheme 4, the molecular ion (M^+, *m/e* 310/308) peak is strong; this undergoes two modes of cleavage. One path is the loss of NO_2 and CO fragments by a one-step process to give an ion at mass 236/234, and the other is the loss of NO, giving rise to the *m/e* 280/278 ion. The following fragmentations are virtually identical with that of II or III, but the substituted position of bromine is demonstrated by the elimination porcess of a bromine atom previous to the loss of the last CO.

Considering the above experimental data and the



m*; meta-stable ion peak observed

Scheme 4. The fragmentation of VI.

rule of *trans*-addition in the usual bromination, IV and V can be presumed to be (3*S* : 5*S* and 3*R* : 5*R*)- and (3*S* : 5*R* and 3*R* : 5*S*)-3-(5-nitro-2-furyl)-3-bromo-2-(5-bromo-2,5-dihydro-2-furylidene)propionitrile respectively, though more precise data as to the confirmation of the configuration of IV and V could not be obtained. In conclusion, by the elimination of hydrogen bromide, as has been mentioned above, only a sort of monobromo compound, VI, was obtained from both IV and V. It can be suggested that the elimination is not a simple *trans*-one, but that the configurational interconversion is involved in the releasing process of a bromine anion after a proton has been pulled off.

Experimental

The melting and decomposition points are uncorrected. The elemental analyses were carried out with a Yanagimoto CHN Corder, MT-2 type. The ultraviolet absorption spectra (UV) were performed on a Perkin-Elmer Model 202 spectrophotometer. The infrared absorption spectra (IR) were measured with a JASCO Model IRA-2 grating infrared spectrophotometer. The nuclear magnetic resonance spectra (NMR) were determined with a Japan Electron Optics Lab. JNM-C-60HL spectrometer. All the spectra were measured in trichloroacetic acid at 60 MHz, with hexamethyldisiloxane as the internal reference; the chemical shifts are expressed in δ-values. The mass spectra were taken on a Hitachi RMU-6L mass spectrometer by means of a direct insertion (at 70 eV, 3.2 kV). The thermal analyses were carried out with a Chyo Balance and with a Rigaku Denki Thermoflex in a nitrogen stream.

trans-*3-(5-Nitro-2-furyl)-2-(2-furyl)acrylonitrile (II).* A mixture of *cis*-3-(5-nitro-2-furyl)-2-(2-furyl)acrylamide (10 g, 40 mmol), 40 m*l* of phosphoryl chloride, and 2 drops of *N,N*-dimethylaniline was heated at 50—60°C for 45 min, cooled, and then poured into crushed ice with agitation. The solidified crude product was collected and purified by recrystallization from methanol to afford 7.8 g (84.4%) of ochreous needles; mp 132—133°C. UV λ_{max}^{EtOH} mμ (ε): 302 (6800) and 396 (15000). IR (KBr) cm,$^{-1}$: 3143, 3050 (C–H), and 2232 (C≡N). NMR (CCl_3COOH) δ: 6.07 (q, 1H, J=1.7 Hz, furan ring C_4–H), 6.36 (s, 1H, olefinic proton), 6.66 (d, 1H, J=*ca.* 3.5 Hz, furan ring C_3–H; overlapped with nitrofuran ring C_3–H), 6.66 (d, 1H, J=4.0 Hz, nitrofuran ring C_3–H), 6.85 (d, 1H, J=4.0 Hz, nitrofuran ring C_4–H), and 7.07 (d, 1H, J=2.1 Hz, furan ring C_5–H). Mass: the spectral fragmentation is indicated in Scheme 2.

Found: C, 57.40; H, 2.57; N, 12.28%. Calcd for $C_{11}H_6N_2O_4$: C, 57.39; H, 2.61; N, 12.17%.

cis-*3-(5-Nitro-2-furyl)-2-(2-furyl)acrylonitrile (III).*

From the Conversion of II to III with Hydroxylamine: To a stirred, warmed (70—75°C) mixture of II (2 g, 8.7 mmol) and 2 drops of *N,N*-dimethylaniline in 50 m*l* of ethanol, we gradually added an aqueous solution of free hydroxylamine (16 mmol in 10 m*l* of water) during a period of 15—20 min. After the addition, the reaction mixture was heated under reflux for 5 hr. Cooling provided a crude product, and then recrystallization was carried out from methanol. Orange-yellow needles; mp 186—187°C. The yield was 1.96 g (98%). UV λ_{max}^{EtOH} mμ (ε): 316 (5900) and 398 (21800). IR (KBr) cm^{-1}: 3138, 3065 (C–H), and 2240 (C≡N). NMR (CCl_3COOH) δ: 6.03 (q, 1H, J=1.7 Hz, furan ring C_4–H), 6.31 (d, 1H, J=3.4 Hz, furan ring C_3–H), 6.66 (d, 1H, J=4.0 Hz, nitrofuran ring C_3–H), 6.80 (s, 1H, olefinic proton), 6.93 (d, 1H, J=4.0 Hz, nitrofuran ring C_4–H), and 6.98 (d, 1H, J=*ca.* 2 Hz, furan ring C_5–H; overlapped with nitrofuran ring C_4–H). Mass: shown in Scheme 2.

Found: C, 57.75; H, 2.61; N, 12.55%. Calcd for $C_{11}H_6N_2O_4$: C, 57.39; H, 2.61; N, 12.17%.

On the other hand, III was not converted to II under the above conditions.

From the Conversion of II to III with Hydrazine Hydrate: A mixture of II (0.6 g, 2.6 mmol), 80% hydrazine hydrate (0.63 g, 10 mmol), and methanol (100 m*l*) was stirred at 0—5°C for 1 hr, at room temperature for 3 hr, and then at 50—60°C for 3 hr. Cooling subsequently provided 0.5 g (83.3%) of a product which melted at 186—187°C. Recrystallization from methanol gave orange-yellow needles; mp 187—188°C. This product was identified as III by an admixture-test and by a comparison of its IR spectrum with that of the sample prepared by the above procedure. Compound III was not converted to II under the above conditions.

From the Conversion of II to III with Hydrochloric Acid: A mixture of II (1 g, 4.4 mmol) and 36% hydrochloric acid (50 m*l*) was heated under reflux for 50 min. Work-up as above gave 0.98 g (98%) of orange-yellow needles. Mp 186°C; undepressed upon admixture with a sample prepared by the above two methods. In a similar manner, III was recovered without any conversion.

(*3S* : *5S and 3R* : *5R*)-*3-(5-Nitro-2-furyl)-3-bromo-2-(5-bromo-2,5-dihydro-2-furylidene)propionitrile (IV).* To a stirred, cooled (5—10°C) mixture of II (5 g, 21.7 mmol) and carbon tetrachloride (250 m*l*) was added dropwise a solution of bromine (4 g, 22.3 mmol) in 50 m*l* of carbon tetrachloride. The mixture was stirred below 10°C until the bromine had been absorbed completely. The solid product was collected by filtration, washed with cooled dry petroleum ether, and dried on paraffin wax in a cold box. In this way, a 8.4-g portion (quantitative yield) of a pale yellow powder was obtained; it melted, with decomposition, at 102°C. However, the recrystallization of this product could not be achieved from the solvents or solvent mixtures, and the product could not be stored over 3 days; nevertheless, the freshly-prepared product was pure enough for elemental analysis and was used in the following experiments without further purification. IR (KBr) cm^{-1}: 3135, 2985 (C–H), and 2220 (C≡N).

Found: C, 34.27; H, 1.83; N, 6.82%. Calcd for $C_{11}H_6N_2O_4Br_2$: C, 33.86; H, 1.54; N, 7.18%.

(*3S* : *5R and 3R* : *5S*)-*3-(5-Nitro-2-furyl)-3-bromo-2-(5-bromo-2,5-dihydro-2-furylidene)propionitrile (V).* This was prepared by the method used for IV, using 5 g (21.7 mmol) of III. Work-up as above afforded 8.3 g (quantitative) of V as a pale yellow powder; mp 113°C (decomp.). This product was also unstable and gradually decomposed during storage. IR (KBr) cm^{-1}: 3175, 3085, 3025 (C–H), and 2220 (C≡N).

Found: C, 33.53; H, 1.53; N, 6.83%. Calcd: the same value as IV above.

cis-*3-(5-Nitro-2-furyl)-2-(5-bromo-2-furyl)acrylonitrile (VI).*

Procedure A: A solution of bromine (0.8 g, 5 mmol) in 20 m*l* of carbon tetrachloride was stirred into a warmed (70°C) mixture of 1 g (4.4 mmol) of II (or III) and carbon tetrachloride (50 m*l*) and then the mixture was refluxed for 2 hr. After cooling, the precipitated product was collected, washed with carbon tetrachloride, and then dried. Recrystallization from acetone-dioxane gave 1.2 g (63%) of VI as an orange-red powder, which melted at 218—220°C with decomposition. IR (KBr) cm^{-1}: 3150, 3063 (C–H), and 2240 (C≡N). NMR (CCl_3COOH) δ: 6.00 (d, 1H, J=3.4 Hz, bromofuran ring C_4–H), 6.29 (d, 1H, J=3.4 Hz, bromofuran ring C_3–H), 6.71 (d, 1H, J=4.0 Hz, nitrofuran

ring C_3–H), 6.81 (s, 1H, olefinic proton), and 6.95 (d, 1H, J =4.0 Hz, nitrofuran ring C_4–H). Mass: shown in Scheme 4.

Found: C, 43.17; H, 1.63; N, 8.73%. Calcd for $C_{11}H_5N_2O_4Br$: C, 42.72; H, 1.62; N, 9.06%.

Procedure B: IV or V (each 1 g, 5 mmol) was heated in acetone under reflux for 1 hr, or was dissolved in dioxane and allowed to stand at room temperature for 2 hr. A work-up as above afforded 0.8 g (quantitative) of an orange-red powder; mp 218—220°C (decomp.). This product was identical in its infrared spectrum with an authentic sample of VI.

Found: C, 42.91; H, 1.63; N, 8.81%. Calcd: the same value as VI by *Procedure A*.

This compound, VI, could not be converted to its *trans*-isomer or carboxylic derivative by treatment with hydroxylamine at 70—80°C in aqueous ethanol for 2 hr or by refluxing with 36% hydrochloric acid for 12 hr.

The authors are indebted to Mr. A. Yamamoto and Mr. S. Iwasaki for their experimental assistance.