BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 2055—2057 (1972)

Studies of the Synthesis of Furan Compounds. XXVII.[1] Derivatives of 3-(5-Nitro-2-furyl)acrylonitrile

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(Received January 17, 1972)

In a continuation of our previous papers[2,3] concerning the syntheses with 5-nitro-2-furonitrile, 2-(5-nitro-2-furyl)vinyl-1,2,4-oxadiazoles and -1,2,3-triazoles were prepared from 3-(5-nitro-2-furyl)acrylonitrile (I). When I was treated with diazomethane in ether, 4-[2-(5-nitro-2-furyl)vinyl]-1,2,3-triazole (II) was obtained. II gave *N*-acetyl (IIa) and *N*-morpholinomethyl (IIb) compounds when treated with acetic anhydride and when the Mannich reaction was utilized respectively. 3-(5-Nitro-2-furyl)acrylamide oxime (III) was prepared by the usual method from I and hydroxylamine. The treatment of III with benzaldehyde and acid anhydrides or chlorides afforded 3-[2-(5-nitro-2-furyl)vinyl]-5-phenyl-4,5-dihydro-1,2,4-oxadiazoline (IV) and *O*-acyl-3-(5-nitro-2-furyl)acrylamide oximes (IIIa—IIIe) respectively. The *O*-acyl-amide oximes were found to cyclize to 3-[2-(5-nitro-2-furyl)vinyl]-5-alkyl-1,2,4-oxadiazole (V—VII) in their thermal analyses.

3-(5-Nitro-2-furyl)acrylonitrile (I) has been prepared from 3-(5-nitro-2-furyl)acrolein oxime acetate and pyridine,[4] by the dehydration of the corresponding acid amide with *p*-toluenesulfonyl chloride,[5] and by the Wittig reaction of 5-nitrofurfural with cyanomethylenetriphenylphosphorane.[6] However, the above procedures may be supposed to be unsuitable for supplying I as a synthetic raw material from the following points of view: 1) the low yields of the product, 2) the lack in the economy, and 3) the complicated procedure necessary because of the isomerization of the product. Therefore, a better procedure for the preparation of I and the synthesis of its derivatives shall be described in this paper.

Results and Discussion

3-(5-Nitro-2-furyl)acrylonitrile (I) was prepared in a good yield by the reaction of 3-(5-nitro-2-furyl)acrylamide with phosphoryl chloride. When treated with diazomethane in ether, I cyclized to 4-[2-(5-nitro-2-furyl)vinyl]-1,2,3-triazole (II). The structure of this compound was confirmed on the basis of its analytical and IR spectral data. By heating II with acetic anhydride or with 37% formaldehyde and morpholine, *N*-acetyl (IIa) and *N*-morpholinomethyl (IIb) compounds were obtained respectively, though the position of the substituents on the triazole ring was uncertain. 3-(5-Nitro-2-furyl)acrylamide oxime (III) was readily obtained from I and hydroxylamine in the usual way.[2,7,8] The IR spectrum of III exhibited two N–H stretching bands, one at 3448 and the other at 3405 cm^{-1}, besides a broad absorption at 2807 cm^{-1} which might be assumed to be a intramolecular chelated[9] O–H stretching frequency.

3-(5-Nitro-2-furyl)acrylamide was prepared from *trans*-3-(5-nitro-2-furyl)acrylic acid[10] by the usual method. In comparing the NMR spectrum of the acrylamide with that of the *trans*-acrylic acid, the *trans*

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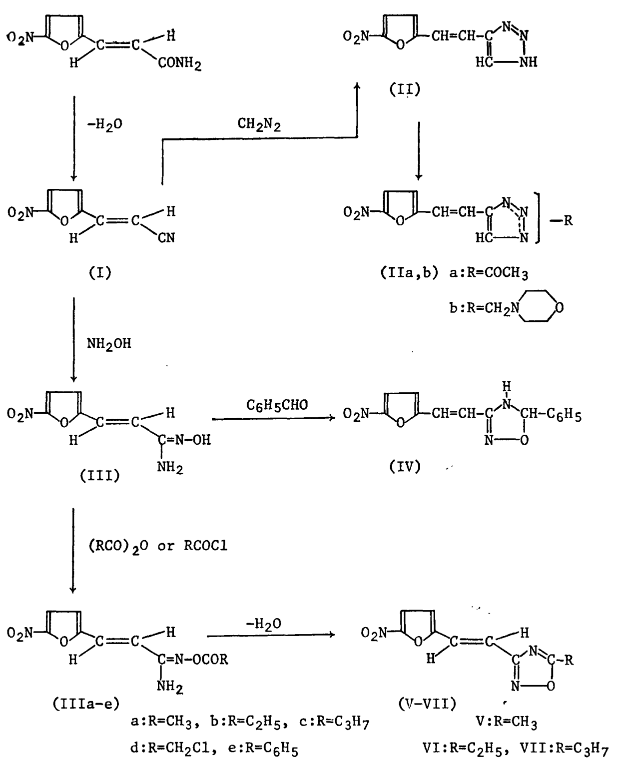

configuration of the acrylamide can be deduced from a coupling constant ($J_{\alpha\beta}$) of the ethylene-bonding α- and β-protons similar to that of the *trans*-acrylic acid ($J_{\alpha\beta}$=15.8 Hz). In the NMR spectra of I and III, the observed $J_{\alpha\beta}$ values were approximately the same as that of the starting acrylamide. Therefore, the geometrical configuration was confirmed to be retained during the process of acrylamide→I→III.

When amide oximes are heated with aldehydes, they are converted to 4,5-dihydro-1,2,4-oxadiazolines.[11] Thus, III reacted with benzaldehyde to afford 3-[2-(5-nitro-2-furyl)vinyl]-5-phenyl-4,5-dihydro-1,2,4-oxadiazoline (IV). On the treatment of III with acid anhydrides or chlorides in the usual manner, *O*-acyl-3-(5-nitro-2-furyl)acrylamide oximes (IIIa—IIIe) were produced. The assignment of the *O*-acyl structures to IIIa—IIIe is based on their IR spectra. As in the case of the *N*-acylamide oxime, only one sharp band is observed in the 3400 cm^{-1} region.[12] On the other hand, in the IR spectra of IIIa—IIIe these compounds showed two absorptions, at about 3460 and 3350 cm^{-1}, presumably due to the N-H stretching of the primary amino group, and a C=O absorption at about 1750 cm^{-1}. Furthermore, the characteristic O-H absorption at 2807 cm^{-1} in the mother compound, III, disappeared.

The results of differential thermal analysis (DTA) and thermogravimetric analysis (TGA) indicated that IIIa—IIIc underwent a cyclization reaction, with the release of a molecule of water; this was supported by the absence of the C=O and NH_2 absorptions in the IR spectra of the heating residues of IIIa—IIIc. The DTA curves show an endothermic peak at 173°C for IIIa, at 161°C for IIIb, and at 156°C for IIIc. These peaks coincide with the melting points of each of the corresponding compounds, and are in agreement with a stage in the reduction of the weight at 172—190°C for IIIa, at 160—187°C for IIIb, and at 155—184°C for IIIc, as shown by the TGA curves. About 8.0, 7.4, and 7.1% losses of the weight were observed for IIIa, IIIb, and IIIc respectively at this stage; these losses correspond to the loss of a molecule of water (theoretical: IIIa 7.5, IIIb 7.1, and IIIc 6.7%). Thus, the cyclization reaction was successfully carried out when IIIa—IIIc were heated at the corresponding melting point in a nitrogen stream to give 5-methyl (V), 5-ethyl (VI), and 5-propyl-3-[2-(5-nitro-2-furyl)vinyl]-1,2,4-oxadiazole (VII) respectively.

The geometrical configurations of the compounds, IIIa—IIIe and V—VII, were concluded to be *trans* by a comparison of the $J_{\alpha\beta}$ values of IIId and VI with that of I or III.

Experimental

All the melting points are uncorrected. The elemental analyses were carried out with a Yanagimoto CHN Corder, MT-2 type. The infrared absorption spectra (IR) were performed on a JASCO Model IRA-2 grating infrared spectrophotometer. The nuclear magnetic resonance spectra (NMR) were determined by means of a Japan Electron Optics NMR spectrometer, JNM-C-60HL (60 MHz). All the spectra were measured in DMSO-d_6 (concentration, 7—8 wt%), with tetramethylsilane as the internal reference; the peak positions were expressed in δ-values. The thermal analyses were carried out with a Chyo Balance and with Rigaku Denki Thermoflex in a nitrogen stream.

trans-*3-(5-Nitro-2-furyl)acrylonitrile (I).* A mixture of 18.2 g (0.1 mol) of *trans*-3-(5-nitro-2-furyl)acrylamide, 35 m*l* of phosphoryl chloride, and 2—3 drops of *N*,*N*-dimethylaniline was heated at 65—70°C for 1.5 hr. After cooling, the reaction mixture was poured onto crushed ice, and the precipitates were collected by filtration, washed with cold water, and dried. They were then recrystallized from ethanol to afford 14 g (84.7%) of the pure nitrile (I) as yellow needles; mp 110°C. IR (KBr) cm^{-1}: 2218 (C≡N). NMR (DMSO-d_6) δ: 6.41 (d, 1H, J=16.3 Hz, ethylene bond C_α-H), 7.18 (d, 1H, J=4.0 Hz, furan ring C_3-H), 7.57 (d, 1H, J=16.3 Hz, ethylene bond C_β-H), and 7.67 (d, 1H, J=4.0 Hz, furan ring C_4-H).

Found: 51.49; H, 2.01; N, 17.05%. Calcd for $C_7H_4N_2O_3$: C, 51.22; H, 2.44; N, 17.07%.

The NMR data of the ethylenic protons of the *trans*-acrylic acid and acrylamide were obtained as follows:

trans-acrylic acid: α-H 6.53, β-H 7.42, J=15.8 Hz. acrylamide: α-H 6.68, β-H 7.23, J=15.8 Hz.

4-[2-(5-Nitro-2-furyl)vinyl]-1,2,3-triazole (II). To a stirred suspension of I (5 g, 30 mmol) in 100 m*l* of ether, we added an ethereal solution containing 32 mmol of diazomethane. The mixture was refluxed for 4 hr, and then the insoluble material was filtered off. The filtrate was taken to dryness *in vacuo*, and the residue was washed with boiling ligroin. Recrystallization from benzene gave 1 g (16.2%) of II as ochreous granules which melted at 133—134°C. IR (KBr) cm^{-1}: 3500 (N-H).

Found: C, 46.61; H, 2.86; N, 27.38%. Calcd for $C_8H_6N_4O_3$: C, 46.60; H, 2.91; N, 27.18%.

4-[2-(5-Nitro-2-furyl)vinyl]-N-*acetyl-1,2,3-triazole (IIa).* A mixture of II (0.3 g, 1.5 mmol) and acetic anhydride (0.5 g)

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[11] F. Tiemann, *Ber.*, **22**, 2412 (1889).

[12] F. Floy, R. Lenears, and C. Moussebois, *Helv. Chim. Acta*, **45**, 437 (1962).

in 10 ml of dioxane was refluxed for 2 hr. The resulting solution was taken to dryness *in vacuo*, and the residue was washed with water and then dried. Crystallization from benzene gave 0.28 g (76%) of IIa as yellow needles; mp 146—148°C. IR (KBr) cm^{-1}: 1670 (C=O).

Found: C, 48.14; H, 3.43; N, 22.69%. Calcd for $C_{10}H_8N_4O_4$: C, 48.38; H, 3.22; N, 22.58%.

4-[2-(5-Nitro-2-furyl)vinyl]-N-*morpholinomethyl-1,2,3-triazole (IIb).* A mixture of II (0.3 g, 1.5 mmol), 37% formaldehyde (0.15 g), morpholine (0.15 g), *N,N*-dimethylformamide (0.15 g), and dioxane (10 ml) was stirred at 10—12°C for 1 hr. The resulting mixture was poured onto ice water, and the precipitates were collected on a filter. Recrystallization from methanol afforded pale yellow granules (IIb) which melted at 62—63°C and which weighed 0.2 g (43.7%).

Found: C, 51.52; H, 5.07; N, 23.30%. Calcd for $C_{13}H_{15}N_5O_4$: C, 51.15; H, 4.92; N, 22.95%.

trans-*3-(5-Nitro-2-furyl)acrylamide oxime (III).* To a stirred, warmed (50—55°C) mixture of I (1.64 g, 10 mmol), *N,N*-dimethylaniline (2 drops), and ethanol (50 ml) was added a solution of hydroxylamine hydrochloride (2.1 g, 30 mmol) and sodium hydroxide (0.96 g, 24 mmol) in 10 ml of water over a period of 15—20 min. After the addition, the mixture was stirred at 60°C for an additional hour. On cooling, the precipitated product was filtered and dried. Recrystallization from ethanol afforded 1.58 g (80.2%) of III as orange needles; mp 217—218°C. IR (KBr) cm^{-1}: 3448, 3405 (NH_2), and 2807 ($O-H\cdots NH_2$). NMR (DMSO-d_6) δ: 5.78 (s, 2H, NH_2 proton), 6.61 (d, 1H, J=16.3 Hz, ethylene bond C_α–H), 7.00 (d, 1H, J=4.0 Hz, furan ring C_3–H), 7.05 (d, 1H, J=16.3 Hz, ethylene bond C_β–H), and 7.68 (d, 1H, J=4.0 Hz, furan ring C_4–H).

Found: C, 42.77; H, 3.37; N, 21.49%. Calcd for $C_7H_7N_3O_4$: C, 42.64; H, 3.55; N, 21.32%.

3-[2-(5-Nitro-2-furyl)vinyl]-5-phenyl-4,5-dihydro-1,2,4-oxadiazoline (IV). A 10-mmol (1.97 g) portion of III was heated with benzaldehyde (50 ml) at 100°C for 4 hr. The resulting solution was taken to dryness *in vacuo*, and the residue was washed with ether and then dried. Recrystallization from methanol gave 1.6 g (56.1%) of IV as ochre-colored needles; mp 158—159°C.

Found: C, 59.09; H, 3.77; N, 14.73%. Calcd for $C_{14}H_{12}N_3O_4$: C, 58.94; H, 2.86; N, 14.73%.

trans-O-*Acetyl-3-(5-nitro-2-furyl)acrylamide oxime (IIIa).* A mixture of acetic anhydride (20 ml) and III (0.99 g, 5 mmol) was heated at 60—65°C for 0.5—1 hr. After cooling, water was added to decompose the surplus acid anhydride, and the precipitated product was filtered, washed with water, and dried. It was then recrystallized from dioxane to give 0.88 g (73.4%) of IIIa as yellow leaflets; mp 171—172°C. IR (KBr) cm^{-1}: 3457, 3350 (NH_2), and 1745 (C=O). Thermal analysis: 173°C (DTA; endothermic), 172—190°C (TGA; weight loss 8.0%).

Found: C, 45.03; H, 3.80; N, 17.26%. Calcd for $C_9H_9N_3O_5$: C, 45.19; H, 3.76; N, 17.57%.

trans-O-*Propionyl-3-(5-nitro-2-furyl)acrylamide oxime (IIIb).* This was prepared by the method used for IIIa, using 20 ml of propionic anhydride. Work up as above afforded 0.91 g (72%) of pure IIIb as yellow leaflets; mp 157—158°C (from dioxane). IR (KBr) cm^{-1}: 3455, 3350 (NH_2), and 1745 (C=O). Thermal analysis: 161°C (DTA; endothermic), 160—187°C (TGA; weight loss 7.4%).

Found: C, 47.09; H, 4.32; N, 16.15%. Calcd for $C_{10}H_{11}N_3O_5$: C, 47.43; H, 4.37; N, 16.60%.

trans-O-*Butyryl-3-(5-nitro-2-furyl)acrylamide oxime (IIIc).* The procedure described above for IIIa was employed using butyric anhydride (35 ml). The resulting solution was kept standing at room temperature until the product was isolated. The product was obtained as yellow leaflets; mp 153—154°C (from dioxane); weight, 1.1 g (78.7%). IR (KBr) cm^{-1}: 3455, 3350 (NH_2), 2970, 2885 (CH_2, CH_3), and 1745 (C=O). Thermal analysis: 156°C (DTA; endothermic), 155—184°C (TGA; weight loss 7.1%).

Found: C, 49.39; H, 4.95; N, 15.43%. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.44; H, 4.86; N, 15.73%.

trans-O-*Chloroacetyl-3-(5-nitro-2-furyl)acrylamide oxime (IIId).* To a stirred, warmed (50—60°C) mixture of III (0.99 g, 5 mmol), sodium bicarbonate (1.05 g, 12.4 mmol), and dioxane (20 ml), we added, drop by drop, a solution of chloroacetyl chloride (0.57 g, 5.1 mmol) in 10 ml of dioxane. The resulting mixture was stirred for an additional hour, and then it was poured into ice water. The precipitates were collected, washed with water, and dried. Crystallization from ethanol afforded 1.1 g (80.4%) of IIId as yellow-ochre needles; mp 147—148°C. IR (KBr) cm^{-1}: 3465, 3345 (NH_2), 1767 (C=O), and 1285 (CH_2Cl). NMR (DMSO-d_6) δ: 4.46 (s, 2H, $COCH_2Cl$ proton), 6.57 (d, 1H, J= 16.3 Hz, ethylene bond C_α–H), 6.86 (broad s, 2H, NH_2 proton), 7.12 (d, 1H, J=4.0 Hz, furan ring C_3–H), 7.28 (d, 1H, J=16.3 Hz, ethylene bond C_β–H), and 7.68 (d, 1H, J=4.0 Hz, furan ring C_4–H).

Found: C, 39.62; H, 3.15; N, 15.09%. Calcd for $C_9H_8N_3O_5Cl$: C, 39.41; H, 2.92; N, 15.32%.

trans-O-*Benzoyl-3-(5-nitro-2-furyl)acrylamide oxime (IIIe).* This was prepared in the same way as IIId, but using benzoyl chloride (1.4 g). In this way, 1.1 g (73.4%) of IIIe were obtained; mp 197°C. Recrystallization from dioxane gave a yellow powder; mp 200—201°C. Yield: 1.8 g (59.2%). IR (KBr) cm^{-1}: 3470, 3345 (NH_2), and 1726 (C=O).

Found: C, 55.97; H, 3.69; N, 13.46%. Calcd for $C_{14}H_{11}N_3O_5$: C, 55.81; H, 3.65; N, 13.95%.

trans-*3-[2-(5-Nitro-2-furyl)vinyl]-5-methyl-1,2,4-oxadiazole (V).* Compound IIIa (0.55 g, 2.3 mmol) was heated at 173—175°C under a nitrogen stream for 5 min, by which time the evolution of water had ceased. The residue was then recrystallized from ethanol to give 0.23 g (45.6%) of V as yellow-ochre granules; mp 189—190°C.

Found: C, 48.48; H, 3.19; N, 18.73%. Calcd for $C_9H_7N_3O_4$: C, 48.87; H, 3.16; N, 19.00%.

trans-*3-[2-(5-Nitro-2-furyl)vinyl]-5-ethyl-1,2,4-oxadiazole (VI).* The method used here was virtually identical with that described for V; 0.75 g (2.9 mmol) of IIIb was heated at 162—164°C. Work-up as above afforded 0.4 g (58.6%) of VI as yellow needles; mp 123—125°C (from ethanol). NMR (DMSO-d_6) δ: 1.30 (t, 3H, J=7.2 Hz, $-CH_2-C\underline{H}_3$ proton), 2.91 (q, 2H, J=7.2 Hz, $-C\underline{H}_2-CH_3$ proton), 7.12 (d, 1H, J=16.9 Hz, ethylene bond C_α–H), 7.18 (d, 1H, J=4.0 Hz, furan ring C_3–H), 7.43 (d, 1H, J=16.9 Hz, ethylene bond C_β–H), and 7.66 (d, 1H, J=4.0 Hz, furan ring C_4–H).

Found: C, 50.62; H, 3.73; N, 17.67%. Calcd for $C_{10}H_9N_3O_4$: C, 51.06; H, 3.83; N, 17.87%.

trans-*3-[2-(5-Nitro-2-furyl)vinyl]-5-propyl-1,2,4-oxadiazole (VII).* The method used here was virtually identical with that used for V; a 2.1-g (7.9 mmol) portion of IIIc was heated at 155—156°C. Ochre-colored leaflets; mp 67—68°C (from ethanol). Yield: 0.65 g (43.3%). IR (KBr) cm^{-1}: 2971, 2940, and 2880 (CH_2, CH_3).

Found: C, 53.14; H, 4.56; N, 16.71%. Calcd for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.41; N, 16.88%.

The authors are indebted to Mr. S. Iwasaki and Mr. Y. Hanada for their technical assistance, to Mr. T. Uchida for the infrared spectral measurements, and to Mr. Y. Uemura for the elemental analysis.