Heteroatom Chemistry
Volume 8, Number 1, 1997

Synthesis of 3-Amino-4-(thienyl-2)furazan

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Received 30 January 1996; revised 17 April 1996

ABSTRACT

3-Amino-4-(thienyl-2)furazan **(3)** *has been synthesized from 2-acetylthiophene* **(4)** *by several routes. Nitrosation of* **4,** *followed by oximation of the resulting oxime salt* **5,** *gave a 6:1 mixture of the E,E and E,Z isomers of thienylglyoxime* **(1).** *Estimation of differences and analogies of these isomers' reactivity have been carried out. Oxidation and dehydration of* **1** *gave furoxan* **11** *and furazan* **2,** *respectively. Conversion of* **2, 12, 13,** *and* **11a, b** *into the target amine* **3** *by base-promoted reaction with hydroxylamine has been reported. © 1997 John Wiley & Sons, Inc.*

INTRODUCTION

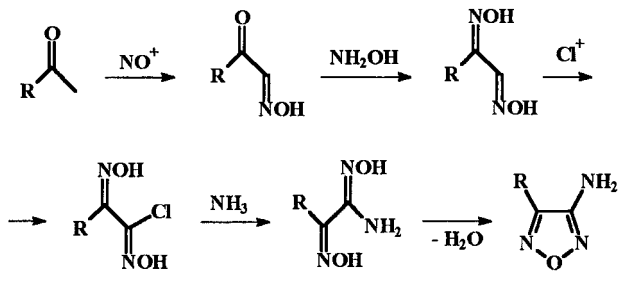
Aminofurazans are well known to be essential constituents in a diverse range of nonnatural products of potential chemotherapeutic and agrochemic interest. The ring family, for example, includes the H_2-receptor histamine antagonist [1], the M_1 selective muscarinic agonist [2], and pesticides [3]. It is, therefore, not surprising that aminofurazans have provided a challenge to both synthetic chemists (in the design of new approaches to the furazan derivatives) [4] and medicinal chemists (in the search for novel, more active analogs). Aryl, alkyl, and amino derivatives have been well investigated. Heteroaryl derivatives have been less investigated, but they are also of interest as versatile building blocks for the construction of target molecules. In connection with our program dealing with the chemistry of aminofurazans [5], we have been exploring various methods for the preparation of these compounds. In an earlier report, we described the reaction of crude 2-(thienyl-2)glyoxime (**1**) with succinic anhydride to produce unsubstituted (thienyl-2)furazan (**2**) [6]. We now wish to describe some approaches to the synthesis of 3-amino-4-(thienyl-2)furazan (**3**).

RESULTS AND DISCUSSION

We commenced our investigations with the commercially available 2-acetylthiophene (**4**). A perusal of the literature indicated a common multistep sequence for the transformation of methyl ketones to aminofurazans, as outlined in Scheme 1.

Using previously reported procedures [7], nitrosation of **4** with an alkyl nitrite in the presence of a suitable sodium-alkoxide afforded salt **5** as a deep red-brown crystalline solid (Scheme 2). 2-Thio-

Scheme 1



SCHEME 1

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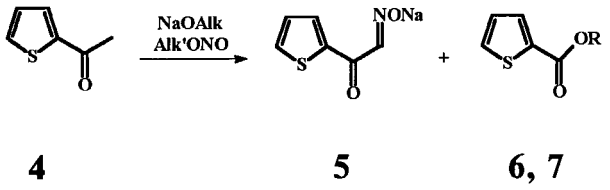
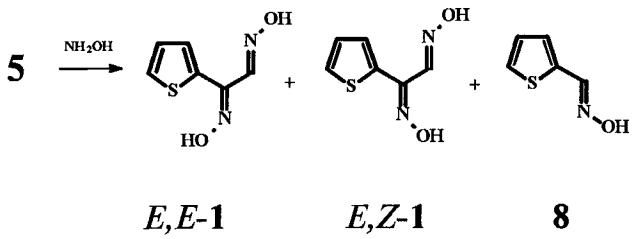
Scheme 2



SCHEME 2

Scheme 3



SCHEME 3

phenecarboxylic acid **6** (R = H) and the ester **7** (R = Alkyl) were by-products of the reaction. These product ratios were found to depend on the experimental conditions. Indeed, after treatment of **4** with NaOMe and MeONO at 0°C, salt **5**, acid **6**, and ester **7** were isolated in yields of 22, 34, and 27%, respectively. Similar results were obtained with *i*-C_3H_7ONO in place of MeONO. On the other hand, when the experiment was repeated employing *i*-C_3H_7ONa, under otherwise identical conditions, **5**, **6**, and **7** were obtained in yields of 73, 12, and 6%, respectively. The most successful nitrosation was achieved with BuONO and *i*-C_3H_7ONa when an 80% yield of **5** was obtained.

Treatment of **5** with hydroxylamine hydrochloride in the presence of sodium acetate afforded **1** [8] as a 6:1 mixture of two isomers (*E*,*E*-**1**/*E*,*Z*-**1**) and an oxime **8** (Scheme 3). Preparative chromatography of this mixture afforded an 8% yield of **8**, a 12% yield of *E*,*Z*-**1**, and a 70% yield of *E*,*E*-**1**. The structures of the glyoxime conformers were determined based on ^{1}H-NMR spectroscopy (here, the literature on NMR of monosubstituted glyoximes [9] was very helpful), mass spectroscopy, and X-ray crystallography [10].

Several procedures have been described for halogenation of glyoximes to α-haloglyoximes. We first attempted the chlorination (in conc. hydrochloric acid) procedure developed by Ungnade and Kissinger [11] for the conversion of both *E*,*E*-**1** and *E*,*Z*-**1** to the desired chloro derivative **9**. It should be noted that the formation of **9**, the intermediate in the reaction sequence shown in Scheme 1, proceeded in poor yield (ca. 0.5%), an intractable product mixture being observed. At room temperature or at 0°C, a reaction mixture of both *E*,*Z*-**1** and *E*,*E*-**1** with bromine water was also observed to turn dark brown over 5 hours, but no detectable product was formed.

Because these reactions were unsuccessful, an alternate route was required. A possible reaction sequence for transformation of **1** to **3** is shown in Scheme 4.

The glyoxime conformation is known [12] to determine its reactivity, which, as a rule, differs strongly for each member of a pair of conformers. Thus, treatment of *E*,*Z*-**1** with N_2O_4 in dry diethyl ether at 0°C gave 4-(thienyl-2)furoxan **11a** [13] in 22% yield and in 6–8% yield at 20–25°C. In the case of the analogous reaction of *E*,*E*-**1**, the expected product, furoxan **11a** or **11b**, was not formed. Only intractable product mixtures were observed, and no unreacted glyoxime was recovered. Ammonolysis of **11a** in water produced the expecting amine **13** in poor yield (5%).

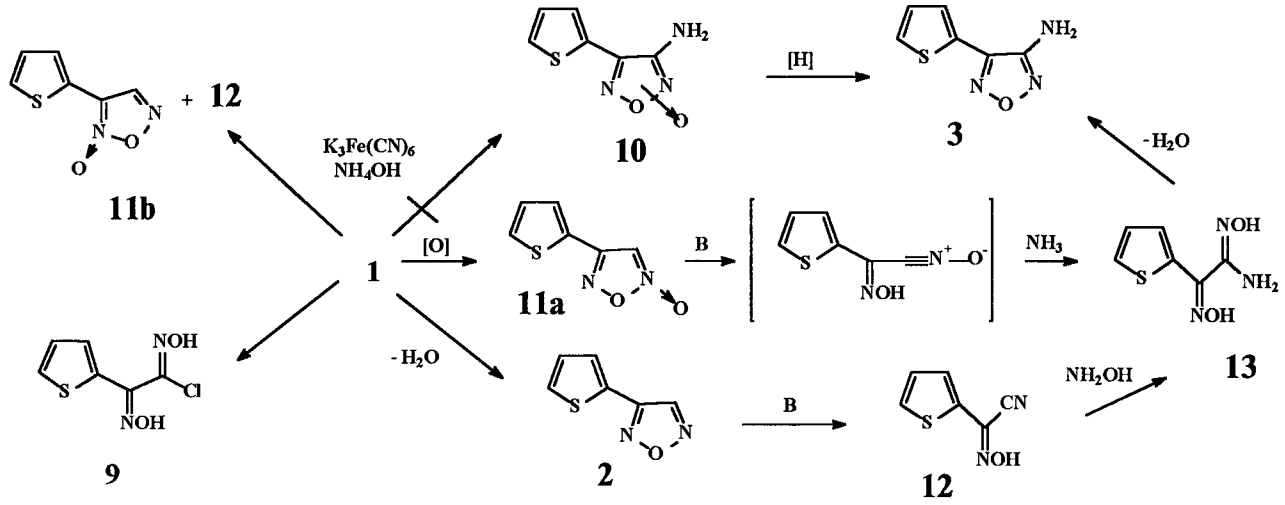
The literature reports that the reaction of monosubstituted glyoximes with $K_3Fe(CN)_6$ in aqueous NH_4OH solution represents the best method for the synthesis of aminofuroxans [14]. We utilized a similar procedure, and the reaction with *E*,*Z*-**1** appeared to be complete in 0.5 hour. However, this method failed for the preparation of the amine **10**. Instead, the only compound isolated (77%) corresponded to the nitrile **12** that was identical to an authentic sample that had apparently been synthesized from **2** in the presence of base (**B**), under conditions similar to those earlier used for furazan opening [15].

Another unexpected finding resulted when the reaction of the other isomer was attempted. Thus, when compound *E*,*E*-**1** was exposed to the same reaction conditions along with **12**, a new compound was produced, but again, formation of **10** and/or its 4-amino isomer did not occur. The new compound showed the same mass as compound **11a**, but its ^{1}H-NMR spectrum was slightly different. Based on literature analogies [6,16], this compound has been assigned the structure of 3-(thienyl-2)furoxan (**11b**).

Both *E*,*E*-**1** and *E*,*Z*-**1**, when melted with succinic anhydride, underwent ring closure to furazan **2** in similar yields, 62 and 67%, respectively. It is apparent that the conformation of the initial glyoxime in this case had practically no influence on the reaction. Probably equilibration of these glyoximes occurred at the increased temperatures used in the cyclization.

Conversion of **12** to the aminoglyoxime **13** was accomplished by heating the substrate in the presence of an excess of hydroxylamine. The reaction of

Scheme 4



SCHEME 4

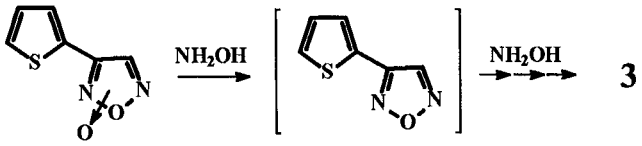
the furazan **2** under identical conditions occurred similarly, producing **13** (68%).

Finally, the synthesis of 3-amino-4-(thienyl-2)furazan (**3**) was accomplished. Ring closure of the aminoglyoxime **13** to **3** was performed conveniently and in high yield (77%) simply by using NaOH/ethylene glycol/150°C [17] (Scheme 4). It should be noted that the precursors to **13**, the furazan **2** and the nitrile **12**, are themselves readily transformed under refluxing with a mixture of an aqueous solution of KOH and NH_2OH to give **3** in 61 and 68% yields, respectively.

We have also found that formation of **3** (57–59%) occurs smoothly when furoxan **11a** or **11b** is used in a reaction with NH_2OH in an aqueous solution of KOH, a phenomenon that had not been observed previously. Our view of how this unusual product was formed is outlined in Scheme 5. Exposure of the starting furoxan to NH_2OH probably resulted in its reduction to the intermediate furazan **2**. A further reaction with NH_2OH proceeded to give **3** via a series of reactions in the normal manner mentioned earlier. The pathway appears the most reasonable as both of the furoxans gave analogous yields. In contrast, an alternative pathway, occurring via opening of the furoxan ring, would strongly depend on the structure of the initial isomer [12b].

In conclusion, we have developed a procedure for preparing 3-amino-4-(thienyl-2)furazan (**3**). All of the steps are easy to set up, to perform, and to work up. The example illustrates the high synthetic potential of the sequence. The simplicity and availability of the starting materials makes this pathway a powerful method for aminofurazans construction.

Scheme 5



11a (or **11b**) **2**

SCHEME 5

Current efforts in this laboratory are focused on the further applications of this methodology to the formation of aminofurazans.

EXPERIMENTAL

Melting points were obtained on an RCH Kofler apparatus and are uncorrected. ^1H and ^{13}C NMR (residual protiosolvent as an internal standard) were taken on a Bruker AM-300 (300 MHz) spectrometer. Other instruments used were for IR (KBr): Perkin-Elmer 577; for UV: UR-20 spectrophotometer; and for MS (70 eV): Varian MAT CH-6 instrument. Thin-layer chromatography (TLC) was carried out on precoated silica gel plates (Silufol F_{254}). For column chromatography Silica gel 80-100 was used. The columns were packed wet, and all chromatographic fractions were numbered in the sequence of decreasing R_f values.

Na Salt of α-Hydroxyiminoacetylthiophene (**5**). A modification of a known procedure was used [7]. To a precooled (0°C) solution of sodium (3.25 g, 141

mmol) in *i*PrOH was added dropwise with stirring a mixture of 2-acetylthiophene (**4**) (17.8 g, 141 mmol) and BuONO (16.8 g, 148 mmol) at 0°C. The resulting mixture was kept for 3 days at 0°C, and then the precipitate that had formed was filtered off and washed with ether. Crude **5** (20 g, 80%) was thereby obtained as a red-brown microcrystalline solid that was used in subsequent reactions without further purification.

(*Thienyl-2*)*glyoxime* (**1**). A solution of $NH_2OH \cdot HCl$ (7.6 g, 0.11 mol) and $NaOAc \cdot 3H_2O$ (4.1 g, 0.03 mol) in water (20 mL) was added to a suspension of **5** (16.1 g, 0.09 mol) in EtOH (27 mL). The resulting mixture was stirred for 12 hours at 75–80°C. Then the solvents were removed *in vacuo*, and the remaining solid was extracted with chloroform, and the solution was concentrated. The residue was separated by chromatography on a silica gel column by elution with $CCl_4/CHCl_3$ to yield a fast-moving fraction (1 g) that was recrystallized to yield 0.92 g (8%) of **8**: mp 131–132°C (Ref. [18] 132–132.5°C); R_f in AcOEt/$CHCl_3$ (1:4), 0.6; ^{1}H NMR ([D_6]DMSO):δ = 7.28 (4-H), 8.00 (C<u>H</u> = NOH, ^1J = 172 Hz), 8.10, 8.12 (3-H, 5-H), 12.80 (<u>O</u>H).

The second fraction was pure *E*,*Z*-**1** (1.6 g). Recrystallization from chloroform gave 1.5 g (10%) as colorless crystals: mp 164–165°C, R_f in AcOEt/$CHCl_3$ (1:4), 0.47; IR: ν = 3210 cm^{-1}, 3170, 3100, 3010, 2870, 1420, 1260, 1220, 1015, 980; UV (ethanol): λ_{max} = 246 nm, 302; ^{1}H NMR ([D_6]DMSO): δ = 7.29 (4-H), 7.54, 7.58 (3-H, 5-H), 8.44 (C<u>H</u> = NOH, ^1J = 175 Hz), 12.02, 12.07 (OH); MS (70 eV); *m*/*z*: 170 [M^+]; $C_6H_6N_2O_2S$ (170.19). Calcd for C, 42.35; H, 3.55; S, 18.84. Found: C, 42.31; H, 3.60; S, 18.72.

The last fraction was *E*,*E*-**1** (8.6 g). Recrystallization from chloroform gave 8.3 g (54%) as colorless prisms: mp 133–135°C, R_f in AcOEt/$CHCl_3$ (1:4), 0.3; IR: ν = 3350–2700 cm^{-1}, 1585, 1410, 1340, 1300, 1225, 1020, 930; UV (ethanol): λ_{max} = 238 nm, 283; ^{1}H NMR ([D_6]DMSO): δ = 7.18 (4-H), 7.79 (5-H), 7.94 (C<u>H</u> = NOH, ^1J = 168 Hz), 8.16 (3-H), 11.60, 12.80 (<u>O</u>H); MS (70 eV); *m*/*z*: 170 [M^+], $C_6H_6N_2O_2S$ (170.19). Calcd for C, 42.35; H, 3.55; S, 18.84. Found: C, 42.32; H, 3.58; S, 18.77.

3-(*Thienyl-2*)*furazan* (**2**). (A) A mixture of *E*,*E*-**1** (17 g, 0.1 mol) and succinic anhydride (12 g, 0.12 mol) was heated at 120°C (oil bath) until the reaction began. After 5 more minutes, the bath was removed, and the mixture was chilled to room temperature. The fused solid mixture was then crushed and extracted with CH_2Cl_2/pentane (2/1). The solution was boiled with charcoal and filtered, and the filtrate was concentrated to dryness. There was obtained 10.4 g (68.42%) of crude **2**, mp 55–58°C. Sublimation at 70°C and 10 Torr gave analytically pure **2** in 62% yield as colorless crystals, mp 60–60.5°C (Ref. [6] 59–60°C, mixed mp 60°C); on the basis of IR spectroscopy and TLC, the substance corresponded in all respects with the compound described in Ref. [6]. (B) According to the method just described, *E*,*Z*-**1** gave 10.18 g (67%) of pure **2**, mp 60–60.5°C.

α-*Hydroxyimino*-α-(*thienyl-2*)-*acetonitrile* (**12**). (A) A solution of sodium hydroxide (0.35 g, 8.75 mmol) in water (3 mL) was added dropwise with stirring at 0°C to a solution of **2** (1.52 g, 10 mmol) in methanol (5 mL). This was followed by dropwise addition of precooled (nearly 0°C) water (5 mL) and acidified with 1.0 *N* HCl to pH 5. The precipitate of **12** that resulted was filtered off, dried, and recrystallized from benzene. Pure **12** (1.23 g, 81%) was obtained as a yellow microcrystalline solid, mp 135–136°C; IR: ν = 3320 cm^{-1} (OH), 2260 (CN), 1585 (C=N); UV (methanol): λ_{max} = 219 nm, 289, 306; ^{1}H NMR ([D_6]DMSO): δ = 7.18 (4-H), 7.44 (5-H), 7.72 (3-H), 13.68 (OH); MS (70 eV): *m*/*z* = 152 [M^+]; $C_6H_3N_2OS$ (152.17). Calcd for C, 47.36; H, 2.65; S, 21.07. Found: C, 47.29; H, 2.71; S, 21.00. (B) To a solution of *E*,*Z*-**1** (0.32 g, 1.85 mmol) in aqueous NH_4OH (6.1 mL, 8.98 mmol) was added dropwise a solution of $K_3Fe(CN)_6$ (2.44 g, 7.4 mmol) in water (18.5 mL), the temperature being maintained at 10–15°C. After having been stirred for 1 hour at 10–15°C, the entire reaction mixture was extracted with ethyl acetate (4 × 10 mL), dried over $MgSO_4$, and filtered through silica gel. The filtrate was concentrated to dryness *in vacuo* and worked up as in method A to yield 0.21 g (72%) of **12**, mp 135–136°C.

3-(*Thienyl-2*)*furoxan* (**11b**). To a solution of *E*,*E*-**1** (0.32 g, 1.85 mmol) in aqueous NH_4OH (6.1 mL, 8.98 mmol) was added dropwise a solution of $K_3Fe(CN)_6$ (2.44 g, 7.4 mmol) in water (18.5 mL), the temperature being maintained at 0°C. After having been stirred for 1 hour at 0°C, the entire reaction mixture (containing some solid that was difficult to separate by filtration) was extracted with ethyl acetate (4 × 10 mL), then dried over $MgSO_4$ and filtered. The residue was separated by chromatography on a silica gel column by elution with $CHCl_3$ → $CHCl_3$/ethyl acetate to yield a fast-moving fraction (0.057 g) that was recrystallized from CH_2Cl_2/pentane to yield 0.045 g (13%) of pure **11b**, mp 106–107.5°C. R_f ($CHCl_3$), 0.58; IR: ν = 3120 cm^{-1}, 2970, 1625, 1530, 1490, 1450, 1400, 1360, 1275, 1220, 1035, 975, 910, 880, 840, 790, 720; ^{1}H NMR (CD_3CN): δ = 7.27 (4-H), 7.74, 7.75 (3-H, 5-H), 8.88 (furoxan); MS (70 eV):

m/z = 168 [M^+], 152 [$M^+ - O$], 138 [$M^+ - NO$], 125 [$M^+ - HCNO$], 122 [$M^+ - O - NO$], 109 [$ThCN^+$], 108 [$M^+ - 2NO$]. $-C_6H_4N_2OS$ (168.17). Calcd for C, 42.85; H, 2.40; S, 19.06. Found: C, 42.89; H, 2.33; S, 19.02.

A second, slower-moving fraction of **12** (0.06 g, 21%), mp 135–136°C, was also collected.

4-(Thienyl-2)furoxan (**11a**). To a solution of *E*,*Z*-**1** (0.136 g, 0.8 mmol) in dry ether (9.5 mL) was added a solution of N_2O_4 (0.8 mmol) in dry ether (4.85 mL) at 0°C, and the mixture was stirred for 1 hour. Evaporation of the solvent under vacuum yielded a solid, whose column chromatography on silica gel, by elution with $CHCl_3/CCl_4$ (1/1), gave 0.03 g (22%) of **11a**; mp 70–72°C; IR: ν = 3120 cm^{-1}, 1590, 1450, 1410, 935, 885; ^1H NMR ([D_6]acetone): δ = 7.16 (4-H), 7.66, 7.71 (3-H, 5-H), 8.12 (furoxan); MS (70 eV): m/z = 168 [M^+]; $C_6H_4N_2OS$ (168.17). Calcd for C, 42.85; H, 2.40; S, 19.06. Found: C, 42.80; H, 2.34; S, 19.00.

α-Amino-β-(thienyl-2)glyoxime (**13**). (A) A mixture of hydroxylamine (0.66 g, 20 mmol) and nitrile **12** (1.52 g, 10 mmol) in methanol (5 mL) was refluxed for 30 minutes. The reaction mixture was cooled with an ice bath, and the resulting solid was separated by filtration and dried. The yield of crude **13** was 1.41 g (76%), mp 158–160°C; MS (70 eV): m/z = 185 [M^+]. The crude compound was used in subsequent reactions without further purification.

(B) To a solution of hydroxylamine (0.66 g, 20 mmol) in methanol (5 mL) was added dropwise with stirring compound **2** (1.52 g, 10 mmol). The resulting mixture was refluxed for 30 minutes and worked up as in method A to yield 1.26 g (68%) of **13**, mp 158–160°C.

3-Amino-4-(thienyl-2)furazan (**3**). (A) A suspension of sodium hydroxide (4 g, 0.1 mol) and compound **13** (18.5 g, 0.1 mol) in ethylene glycol (20 mL) was stirred at 150°C for 30 minutes. The mixture was then cooled to room temperature and diluted with water. The resulting mixture was kept overnight at −5°C, and the product was filtered off and recrystallized from *i*PrOH/H_2O (10/1) to yield 12.86 g (77%) of **3** as colorless crystals, mp 114.5–115°C; IR: ν = 3430 cm^{-1}, 3310, 3220, 3100, 1620, 1530, 1480, 1410, 1325, 1280, 995, 945; UV (methanol): λ_{max} = 254 nm, 291; ^{13}C NMR ($CDCl_3$): δ = 155.3 (C–NH_2), 143.4 (C–Th), 129.7 (C-5), 129.1 (C-3), 129.0 (C-4), 127.1 (C-2); MS (70 eV): m/z = 167 [M^+], 137 [$M^+ - NO$], 110, 97, 83, 69; $C_6H_4N_2OS$ (167.19). Calcd for C, 43.11; H, 3.01; S, 19.18. Found: C, 43.06; H, 3.13; S, 19.09.

(B) A suspension of **12** (15.2 g, 0.1 mol), $NH_2OH \cdot HCl$ (13.9 g, 0.2 mol) and KOH (11.78 g, 0.21 mol) in water (70 mL) was refluxed and stirred for 2 hours. The mixture was then cooled to 20°C and extracted with ether (4 × 50 mL). The organic layer was washed with water, dried ($MgSO_4$), and filtered. The filtrate was concentrated *in vacuo*. The residue was purified by recrystallization. Compound **3** (11.36 g, 68%) was thereby obtained as a colorless solid, mp 114–115°C.

(C) Compound **3** was synthesized according to procedure B starting from furazan **2**; yield 61%.

(D) The furoxan **11a** or **11b** (16.8 g, 0.1 mol) was added with stirring to a solution of $NH_2OH \cdot HCl$ (13.9 g, 0.2 mol) and KOH (11.78 g, 0.21 mol) in water (70 mL) at 10–15°C. The mixture was then heated for 2.5 hours at 95–100°C and worked up as in Method B to yield 9.52–9.85 g (57–59%) of pure **3**, mp 114–115°C.

REFERENCES

[1] G. Sorba, R. Fruttero, A. DiStilo, A. Gasco, M. Orsetti, *Arch. Pharm. (Weinheim, Ger.), 325,* 1992, 151 and references therein.

[2] P. Sauerberg, P. H. Olesen, S. Nielsen, S. Treppendahl, M. J. Sheardown, T. Honore, C. H. Mitch, J. S. Ward, A. J. Pike, F. P. Bymaster, B. D. Sawyer, H. E. Shannon, *J. Med. Chem., 35,* 1992, 2274.

[3] W. Sirrenberg, R. Lantzsch, A. Marhold, U. Wachendorff-Neumann, A. Elbert (Bayer AG): *Eur. Pat. Appl. EP* 561250, 1993; *Chem. Abstr., 120,* 1994, P54545w.

[4] For a review on the chemistry of aminofurazans, see V. G. Andrianov, A. V. Eremeev, *Khim. Geterotsikl. Soedin.,* 1984, 1155. English translation in *Chem. Heterocycl. Compd. (USSR),* 1984, 937.

[5] (a) V. A. Dorokhov, E. A. Shagova, T. S. Novikova, A. B. Sheremetev, L. I. Khmelnitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1988, 2363; *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.), 37,* 1988, 2128 (b) A. B. Sheremetev, T. S. Novikova, T. M. Melnikova, L. I. Khmelnitskii, *Izv. Akad. SSSR, Ser. Khim.,* 1990, 1193; *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.), 39,* 1990, 1073. (c) V. A. Dorokhov, E. A. Shagova, A. B. Sheremetev, Yu. A. Strelenko, T. S. Novikova, *Izv. Akad. Nauk., Ser. Khim.,* 1992, 174. (d) E. T. Apasov, A. B. Sheremetev, B. A. Dzhetigenov, A. V. Kalinin, V. A. Tartakovsky, *Izv. Akad. Naukr SSSR, Ser. Khim.* 1992, 1916. (e) A. B. Sheremetev, O. V. Kharitonova, *Mendeleev Commun.,* 1992, 157–158. (f) A. B. Sheremetev, Yu. A. Strelenko, *Mendeleev Commun.,* 1993, 120. (g) L. S. Vasilev, A. B. Sheremetev, V. A. Dorokhov, N. K. Khoa, M. O. Dekaprilevich, Yu. T. Struchkov, L. I. Khmelnitskii, *Mendeleev Commun.,* 1994, 57. (h) T. S. Novikova, T. M. Melnikova, O. V. Kharitonova, V. O. Kulagina, N. S. Aleksandrova, A. B. Sheremetev, T. S. Pivina, L. I. Khmelnitskii, S. S. Novikov, *Mendeleev Commun.,* 1994, 138.

[6] Yu. A. Strelenko, A. B. Sheremetev, L. I. Khmel'nitskii, *Khim. Geterotsikl. Soedin.,* 1992, 1101; *Chem. Heterocycl. Compd. (Engl. Transl.),* 1992, 927.

[7] S. Fujise, *Biochem. Zeitsch., 236,* 1931, 241.
[8] C. Musante, V. Parrini, *Sperimentale, Ser. Chim. Biol., 3,* 1952, 140.
[9] Yu. A. Strelenko, O. A. Rakitin, L. I. Khmel'nitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1990, 1023; *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.), 39,* 1990, 978, and references therein.
[10] These structures of *E*,*E*-**1** and *E*,*Z*-**1** were confirmed by an X-ray crystallographic analysis, see L. Chertanova, C. Pascard, A. Sheremetev, *Acta Crystallogr. Sect. B, B50,* 1994, 708.
[11] H. E. Ungnade, L. W. Kissinger, *Tetrahedron, 19,* 1963, Suppl. 1, 143.
[12] (a) D. Dyrssen, *Suensk. Kem. Tidsrift., 75,* 1963, 618; (b) L. I. Khmelnitskii, T. I. Godovikova, S. S. Novikov: *Chemistry of Furoxans. Structure and Synthesis,* Nauka, Moscow, p. 216 (1981) (in Russian).
[13] Compounds containing both thiophene and furoxan rings are known, see M. S. Chang, A. J. Matuszko, *J. Org. Chem., 26,* 1961, 5239; C. R. Meloy, D. A. Shirley, *J. Org. Chem., 32,* 1967, 1255; Y. Iwakura, K. Uno, S. Shiraishi, *Bull. Chem. Soc. Jpn., 41,* 1968, 2954; A. A. Espenbetov, Yu. T. Struchkov, Yu. D. Cturkin, L. V. Pantilova, *Zh. Obshch. Khim., 55,* 1985, 1565; O. O. Mamaeva, M. M. Krayushkin, F. M. Stoyanovich, *Izv. Akad. Nauk, Ser. Khim.,* 1990, 913.
[14] A. R. Gagneux, R. Meier, *Helv. Chim. Acta, 53,* 1970, 1883.
[15] R. A. Olofson, J. S. Michelman, *J. Org. Chem., 30,* 1965, 1854.
[16] T. I. Godovikova, S. P. Golova, Yu. A. Strelenko, M. Yu. Antipin, Yu. T. Struchkov, L. I. Khmelnitskii, *Mendeleev Commun.,* 1994, 7.
[17] I. V. Vigalok, A. V. Ostrovskaya, *Khim. Tekhnol. Elementoorg. Soedin. Polym., 78,* 1978, 48.
[18] S. G. Tandon, S. C. Bhattacharya, *Anal. Chem., 32,* 1960, 194.