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The Synthetic Utility of Heteroaromatic Azido Compounds. I. Preparation and Reduction of Some 3-Azido-2-substituted Furans, Thiophenes, and Selenophenes

S. GRONOWITZ,* C. WESTERLUND and A.-B. HÖRNFELDT

Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund 7, Sweden

The reaction of 3-bromo-2-formylfuran, -thiophene and -selenophene with sodium azide in dimethyl sulfoxide gave the corresponding 3-azido-2-formyl substituted heterocycles, which were transformed to the azido-cyanides and azido-carboxylic acids. Reduction of the 3-azido-2-formyl derivatives with hydrogen sulfide gave the hitherto unknown 3-amino-2-formyl derivatives, which were quite stable, and constitute excellent starting materials for the synthesis of fused heterocyclic systems.

The 3-amino-2-formyl derivatives exist in the hydrogen bonded *trans* conformations, which is evident from the long-range coupling between the formyl proton and the proton in the 4-position.

The azido group of arylazido compounds is a versatile synthon in organic synthesis. Its value depends largely on two synthetic transformations. The first one is its easy reduction by various means to the corresponding primary amino group. This reaction is especially important in those cases where the amino derivatives are hard to obtain in other ways. However, it should be borne in mind that arylazido compounds are often prepared *via* diazotization of the corresponding amino derivatives. The second transformation is its decomposition, thermally or photolytically, to give a nitrene. In general, nitrenes are generated photolytically as triplets and thermally as singlets, which can then decay to triplets. Nitrenes are highly reactive species which can react in a number of different ways, for example by intramolecular isomerization to imines, by dimerization to azo compounds, by insertion into a C—H bond, by addition to unsaturated systems yielding heterocyclic compounds, *etc.* As a special case there are also decompositions which proceed *via* a synchronous intramolecular mechanism. This means that no free nitrenes are generated along the reaction pathway.

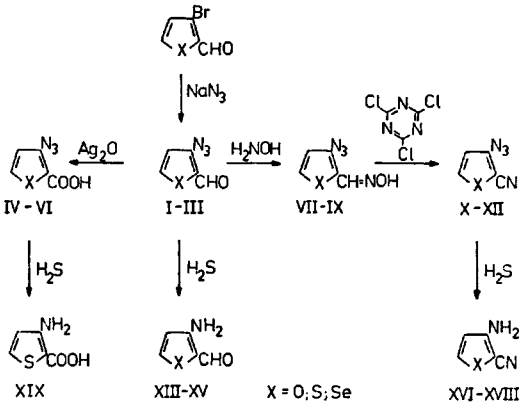
The distinction between these two synthetic transformations is not a sharp one since there are borderline cases, but this division seemed to us to be a practical approach. (Fo review *cf.* Ref. 1.) This paper will deal with the synthesis and reduction of some 3-azido-2-substituted furans, thiophenes and selenophenes. The use of the resulting 3-amino-2-formylfuran, -thiophene, and -selenophene for synthesis of furo-, thieno- and selenolo[3,2-*b*]pyridines will be reported in a following paper. Work on the synthetic utility of thermal decompositions of the azido compounds described in this paper is under way.

Preparation of some 3-azido-2-substituted furans, thiophenes and selenophenes

A sensible approach to this class of compounds was to use aromatic nucleophilic substitution with appropriate 2-substituted 3-bromofurans, -thiophenes and -selenophenes as substrates. The 3-bromo-2-formyl derivatives in these series were all known,[2-4] and they were chosen as suitable starting materials. The formyl group was expected to facilitate the nucleophilic substitution owing to its electron-attracting power.

* To whom correspondence should be addressed.

Thus the 3-bromo-2-formyl derivatives were treated with sodium azide in dimethyl sulfoxide at 60—65 °C for 1—2 days (see Scheme 1).



Scheme 1.

This gave the expected 3-azido-2-formylfuran (I), 3-azido-formylthiophene (II) and 3-azido-2-formylselenophene (III) in moderate yields (45—60 %). These azido compounds are quite stable, crystalline solids. A sample of 3-azido-2-formylfuran (I) showed no sign of decomposition after standing in air, light and at room temperature for four weeks. This is in marked contrast with the observed instability of 5-azido-2-formylfuran, prepared from 5-nitro-2-formylfuran, which is the only example in the literature of an azido derivative in these heterocyclic series.[5] This compound is reported to be stable for a longer time only at 0—4 °C. Samples of 3-azido-2-formylthiophene (II) and 3-azido-2-formylselenophene (III) gave a slight discoloring under the conditions described above. However, no change in the IR spectra of these compounds was evident.

Unfortunately, the scope of this nucleophilic aromatic substitution seems to be quite limited. 2-Bromo-3-formylthiophene, 5-bromo-2-formylthiophene and 4-bromo-3-formylthiophene did not give azides under the above-mentioned conditions, nor did 3-bromo-2-cyano-, 2-acetyl-3-bromo- or 3-bromo-2-carboxythiophene. Greater success, however, was achieved with 3-bromo-2-nitrothiophene and 3-bromo-4-formyl-2-nitrothiophene, which smoothly gave the expected azides (unpublished results).

Since the aromatic azido group is known to be quite stable in non-reducing environment, it was possible to make some transformations which retained or raised the oxidation level of the formyl group, leaving the azido function intact.

Thus it was possible to oxidize the formyl group to a carboxylic group using silver(I) oxide (see Scheme 1). This gave 3-azido-2-carboxyfuran (IV), 3-azido-2-carboxythiophene (V) and 3-azido-2-carboxyselenophene (VI) in good yields (65—90 %).

The 3-azido-2-formyl derivatives were easily transformed to the corresponding aldoximes (VII, VIII, IX) in the usual manner (see Scheme 1). These could be dehydrated to nitriles by a slight variation of the method of Chakrabarti and Hotten,[6] using 2,4,6-trichloro-s-triazine. They used a small excess of 2,4,6-trichloro-s-triazine calculated for reaction of all three chlorine atoms (0.36—0.50 mol triazine/mol aldoxime). In this work this proportion was found to give a gummy precipitate, which was difficult to separate and wash. If, however, a larger proportion of triazine was used (*ca.* 0.75 mol triazine/mol aldoxime), a precipitate, which was easy to separate and wash, was formed. Thus 3-azido-2-cyanofuran (X), 3-azido-2-cyanothiophene (XI) and 3-azido-2-cyanoselenophene (XII) were obtained in good yields (80—87 %).

These 3-azido-2-substituted derivatives are quite stable compounds. However, no regular melting points could be obtained for the 2-aldoximes (VII, VIII, IX) or the 2-carboxylic acids (IV, V, VI) since these decomposed slowly on heating above *ca.* 110 °C without melting. The 2-cyano derivatives, on the other hand, had distinct melting points.

Preparation of some 3-amino-2-substituted furans, thiophenes and selenophenes

It was of interest to try to prepare some simple, previously unknown, 3-amino-2-substituted derivatives from the corresponding 3-azido derivatives. Several methods for achieving this are known. However, we found that a sparingly used method for reducing azido compounds to the corresponding primary amines consisting in treatment with hydrogen sulfide in alkaline or neutral solutions [7–10] was the superior one. This is a reaction which compares favourably with many of the more currently used

methods for this transformation, namely the use of sodium borohydride,[11] lithium aluminium hydride,[12] sodium dithionite,[13] alkaline arsenite,[14] or different catalytical methods.[15,16] The advantages of using hydrogen sulphide in this respect can be summarized as follows.

(1) The preparative procedure is easy to carry out.

(2) The method is very mild and the reaction can be carried out in neutral solutions at or slightly below room temperature. It should be pointed out that the reaction rate is accelerated in the presence of base.

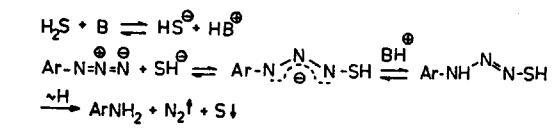
(3) The reducing agent is not prone to react with other parts of the molecule under these conditions.

(4) Excess of reducing agent can be removed simply by blowing a stream of air through the solution for relatively short time.

(5) The reaction gives high yields of the corresponding amines, at least in those cases where no secondary reactions can take place, and it is so "clean" that the reaction mixture after removal of precipitated sulfur can be used directly for further reactions without isolating the amino compounds.

The observations recorded above have been made on reductions of the azido compounds described in this work. However, it seem quite reasonable that they can be generalized to other systems.

Scheme 2 suggests a possible mechanism for this kind of reduction in an alkaline medium.



Scheme 2.

This mechanistic proposal is mainly based on analogy with the mechanism for reduction of azido compounds with alkaline arsenite, proposed by Ugi and co-workers.[14]

Thus the 3-azido-2-formyl compounds were treated with hydrogen sulfide in ethanol and in presence of a small amount of some base such as piperidine (see Scheme 1). This gave 3-amino-2-formylfuran (XIII), 3-amino-2-formylthiophene (XIV) and 3-amino-2-formylselenophene (XV) in good yields (83—89 %). All three compounds were crystalline solids, even though it was rather difficult to obtain 3-amino-2-formylfuran (XIII) in a crystalline form. A sample of 3-amino-2-formylfuran (XIII) had completely disintegrated on standing in air, light and at room temperature for four weeks. The 3-amino-2-formylthiophene (XIV) became rather heavily discoloured under the same conditions. However, no change in the IR spectrum of the compound was evident. 3-Amino-2-formylselenophene (XV), in contrast to those above, showed no sign of decomposition under these conditions.

The synthesis of 3-amino-2-formylthiophene (XIV) has been claimed by Büttner in his Ph.D. thesis.[17] He obtained the alleged compound by condensation of α,β-dichloropropionitrile with mercaptoacetaldehyde. He reports the substance to be a yellow oil with a boiling point of 79 °C/0.001 mmHg and that it very rapidly decomposes in air. This indicates that Büttner did not obtain 3-amino-2-formylthiophene (XIV).

ortho-Amino aldehydes are compounds of great synthetic value as starting materials for many different fused systems. Through the Friedländer reactions (for review *cf.* Ref. 18) they give quinolines or isosteric molecules. The use of the 3-amino-2-formyl derivatives described in this paper in the Friedländer synthesis is the subject of a following paper.

Since none of the simple 3-amino-2-cyano derivatives in these heterocyclic series was known earlier, and since they should be valuable starting materials, especially for annelating pyrimidine rings to the furan, thiophene or selenophene nucleus,[19–21] similar reductions as described above were carried out with the 3-azido-2-cyano derivatives as substrates (see Scheme 1). This gave 3-amino-2-cyanofuran (XVI), 3-amino-2-cyanothiophene (XVII) and 3-amino-2-cyanoselenophene (XVIII) in excellent yields (90—95 %).

It was also of interest to try to prepare the 3-amino-2-carboxylic acids in these series. These compounds are analogues of anthranilic acid, which gives them a potential pharmacological interest. 3-Amino-2-carboxythiophene (XIX) was known earlier and had been prepared by hydrolyzing the corresponding methyl ester obtained by the Fiesselmann ring-closure reaction.[22,23] When 3-azido-2-carboxythiophene (V)

was subjected to hydrogen sulfide as described above in slightly alkaline medium, 3-amino-2-carboxythiophene (XIX) could be isolated in medium yield (61 %) (see Scheme 1). When the two other azides (IV and VI) were exposed to the same conditions they were also reduced, which was evident from the evolution of nitrogen. However, no well-defined products could be isolated from these reactions. The reason for these failures, at least in the case of the furan derivative, might be the easy ring-opening of compounds of this type,[24,25] and other complex reactions.

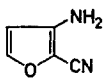
Spectral data

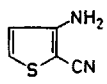
The IR spectra of the azido compounds prepared in this work showed N_3-asymmetric stretching absorption in the region of *ca.* 2090—2140 cm^{-1}. All the amines showed characteristic absorptions in the region of 3120—3470 cm^{-1} due to NH stretching vibrations.

The ^1H NMR data for most of the prepared compounds are given in the experimental part. The NMR data for the amino aldehydes and two of the amino nitriles are given in Tables 1 and 2.

The unsubstituted 3-amino derivatives of these heterocyclic series are known to be quite unstable. The reason for this instability seems to be their tendency to isomerize to the corresponding imines, which then can react in a number of ways. This tendency is greatest in the furan owing to its lesser aromatic stabilization. However, if electron-attracting groups are substituted into these rings, the stability of the amino compounds increases markedly. The reason for this is that the substituent acts as an "electron sink",[26] or in certain cases can form intra- or intermolecular hydrogen bonds with the amino group. It is well known from early NMR investigations that simple aminothiophenes exist in the amino form.[27] 5-Aminophenyl-2-phenyl-3-amino-4-thiophene carboxhydrazides are an exception, and are claimed to exist in the imino form.[28] In no case do the 3-amino-2-substituted derivatives described in this paper give rise to NMR spectra which could be interpreted as due to imino compounds, at least not in a measurable degree. Wie *et al.*[29] have reported that the NMR spectrum of for example 2-amino-3-cyano-4,5-dimethylfuran in trifluoroacetic acid indicates ring protonation. The ring protonation was evident from the observed coupling with the methyl protons. In order to find out if this was also the case for 3-amino-2-cyanofuran (XVI) and 3-amino-2-cyanothiophene (XVII), their NMR spectra were recorded in trifluoroacetic acid. The results are given in Table 1. No formation of additional lines or couplings was observed in this solvent. The only differences were that the bands attributed to the amino protons were absent and that a larger downfield shift of the ring protons compared to that in deuteriochloroform had occurred in this medium. The last effect is to be expected when the strongly electron-

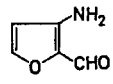
Table 1. ^1H NMR chemical shifts (δ) and coupling constants (Hz) of 3-amino-2-cyanofuran (XVI) and -thiophene (XVII) in deuteriochloroform and trifluoroacetic acid at 60 MHz.

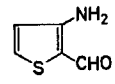


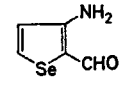


δ	XVI $CDCl_3$	XVI CF_3COOH	XVII $CDCl_3$	XVII CF_3COOH
NH_2	~4.2	not detectable	~4.7	not detectable
H-4	6.17	6.95	6.56	7.43
H-5	7.23	7.80	7.28	7.98
$J_{4,5}$	2.00	2.00	5.30	5.30

Table 2. ^1H NMR chemical shifts (δ) and coupling constants (Hz) of 3-amino-2-formylfuran (XIII), -thiophene (XIV), and -selenophene (XV) in deuteriochloroform at 60 MHz.







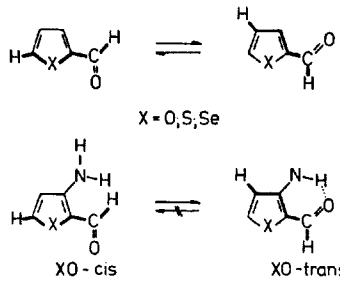
δ	XIII	XIV	XV
NH_2	~5.4	~6.4	~6.5
CHO	9.58	9.55	9.57
H-4	6.11	6.94	6.89
H-5	7.29	7.20	8.17
$J_{4,5}$	1.80	5.25	5.7
$J_{5,CHO}$	—	—	—
$J_{4,CHO}$	0.75	0.7	0.65

donating amino group is replaced by the strongly electron-attracting ammonium group. This seems to indicate that 3-amino-2-formylfuran (XVI) and 3-amino-2-formylthiophene (XVII) in their protonated forms exist largely as ammonium salts.

Several studies of the conformation of 2-formyl derivatives of furan, thiophene and selenophene have been made.[30–34] At room temperature 2-formylfuran exists in 70 % as O,O-*cis* and 30 % as O,O-*trans*,[31] 2-formylthiophene completely as S,O-*cis*.[32] and 2-formylselenophene exists most probably also completely as the Se,O-*cis* form [34] (*cf.* Scheme 3). However, Russian workers [33] have claimed 2-formylselenophene to be a 1:1 mixture of *cis* and *trans* conformers. The increased stability of the *cis* isomer in 2-formylthiophene and 2-formylselenophene has been ascribed to bonding interaction through space between the *d*-orbital of the heteroatom and the electron pair of the carbonyl group.[35,36] Indication for such bonding has recently been obtained by ^{77}Se NMR for 2-formylselenophene.[36]

Substituents in the rings can alter the proportions between *cis* and *trans* conformers in different ways. The NMR spectra of such compounds, especially those unsubstituted in the 4- and 5-positions of the ring, can give an estimate of the amount of each conformer present. The long-range couplings between the aldehyde proton and the ring protons are here extremely useful. In the X,O-*cis* conformation, the aldehyde proton couples with the 5-proton, and in the X,O-*trans* conformation with the 4-proton according to the "zig-zag" convention (see Scheme 3). All three 3-amino-2-formyl derivatives described in this paper show exclusively a long-range coupling to the 4-proton (see Table 2), that is to say that they all exist largely in an X,O-*trans* conformation in deuteriochloroform. The chemical shift assignments are based on the known substituent-caused shifts in 3-amino and 2-formyl derivatives and their approximate additivity, and on the known differences between the α- and β-proton resonances in these heterocyclic systems.

The reason for the dominance of the *trans* conformation is that the aldehyde group is locked in this position by strong intramolecular hydrogen bonding (see Scheme 3). Only two examples of such an intramolecular association in these heterocyclic series, leading exclusively to the X,O-*trans* conformation have been previously reported in the literature, namely the case of 2-formyl-3-hydroxythiophene and 2-formyl-2-hydroxyselenophene.[37,38] However, it has been shown that in the former case the intramolecular hydrogen bond could be broken by using acetone as solvent.[31] No such change in the NMR spectra of 3-amino-2-formylthiophene (XIV) could, however, be observed on going from deuteriochloroform to deuterioacetone as solvent.



Scheme 3.

EXPERIMENTAL PART

3-Azido-2-formylfuran (I). 5.0 g (0.029 mol) of 3-bromo-2-formylfuran [2] and 5.0 g (0.077 mol) of sodium azide were dissolved in 100 ml of dimethyl sulfoxide. The reaction mixture was slowly stirred for 48 h at 65 °C, whereupon it was cooled and poured into 150 ml of water. The water solution was extracted with four 30 ml portions of ether. The combined ether phases were dried over magnesium sulfate and evaporated to dryness. The crude product was recrystallized from methanol which gave 1.8 g (45 %) of product, which melted with slight decomposition at about 115 °C. IR spectrum (KBr): N_3=2140 cm^{-1}, CO=1650 cm^{-1}, NMR spectrum ($CDCl_3$): δ 6.53 (H-4), 7.60 (H-5), 9.67 (CHO), $J_{4,5}$ 2.00 Hz, $J_{5,CHO}$ 0.60 Hz. [Found: C 43.9; H 2.21; N 30.6; m.wt. 137. Calc. for $C_5H_3N_3O_2$: C 43.8; H 2.21; N 30.7; m.wt. 137.11.]

3-Azido-2-formylthiophene (II) was prepared as described above for I from 45.0 g (0.236 mol) of 3-bromo-2-formylthiophene [3] and 45.0 g (0.692 mol) of sodium azide in 600 ml of dimethyl sulfoxide. The reaction temperature was 65 °C and the reaction time 24 h. The yellow crude product was recrystallized from methanol, giving 17.5 g (48 %) of 3-azido-2-formylthiophene (II), m.p. 56.6–57.2 °C. IR spectrum (KBr): N_3=2120 cm^{-1}, CO=1660 cm^{-1}, NMR spectrum ($CDCl_3$): δ 7.02 (H-4), 7.73 (H-5), 9.88 (CHO), $J_{4,5}$ 5.15 Hz, $J_{5,CHO}$ 1.20 Hz. [Found: C 39.4; H 1.90; N 27.2; S 20.8; m.wt. 153. Calc. for $C_5H_3N_3OS$: C 39.2; H 1.98; N 27.4; S 20.9; m.wt. 153.17.]

3-Azido-2-formylselenophene (III) was prepared as described above for I from 33.0 g (0.138 mol) of 3-bromo-2-formylselenophene[4] and 26.0 g (0.406 mol) of sodium azide in 600 ml of dimethyl sulfoxide. The reaction temperature was 60 °C and the reaction time 24 h. The brown-red crude product was recrystallized from methanol, giving 16.7 g (60 %) of the product, m.p. 69.0–70.5 °C. IR spectrum (KBr): N_3= 2110 cm^{-1}, CO=1640 cm^{-1}, NMR spectrum ($CDCl_3$): δ 7.35 (H-4), 8.42 (H-5), 9.84 (CHO), $J_{4,5}$ 5.75 Hz, $J_{5,CHO}$ 1.00 Hz. [Found: C 29.9; H 1.75; Se 39.2; m.wt. 201. Calc. for $C_5H_3N_3OSe$: C 30.0; H 1.51; Se 39.5; m.wt. 200.07.]

3-Azido-2-furan carboxylic acid (IV). 1.9 g (0.014 mol) of 3-azido-2-formylfuran (I) was added with stirring to a suspension prepared from 20 ml of water, 4.8 g (0.028 mol) of silver nitrate and 2.3 g (0.058 mol) of sodium hydroxide cooled to 10 °C. The reaction mixture was allowed to attain room temperature and the stirring continued for another 30 min. The solid material was filtered off and washed with 6 ml of water. The combined aqueous phases were acidified with conc. hydrochloric acid, whereupon a white voluminous precipitate was formed, which was filtered off. The crude product was dissolved in warm ether and the resulting solution filtered. The ether solution was dried over magnesium sulphate and concentrated, giving 1.7 g (79 %) of the acid. An analytical sample which was obtained by recrystallization from toluene showed an IR spectrum identical with that of the crude product, m.p. 110 °C (decomp.). IR spectrum (KBr): N_3=2120 cm^{-1}, CO=1670 cm^{-1}. NMR spectrum (DMSO-d_6): δ 6.73 (H-4), 7.87 (H-5); $J_{4,5}$=2.14 Hz. [Found: C 39.2; H 2.05; O 31.0; m.wt. 153. Calc. for $C_5H_3N_3O_3$: C 39.2; H 1.98; O 31.4; m.wt. 153.11.]

3-Azido-2-thiophene carboxylic acid (V) was prepared as described above for IV from 5.0 g (0.033 mol) of 3-azido-2-formylthiophene (II), 44 ml of water 11.5 g (0.0676 mol) of silver nitrate, and 5.4 g (0.14 mol) of sodium hydroxide, yielding 5.0 g (90 %) of the product, m.p. 110 °C (decomp.). An analytical sample which was obtained by recrystallization from toluene showed an IR spectrum identical with that of the crude product. IR spectrum (KBr): N_3= 2110 cm^{-1}, CO=1680 cm^{-1}; NMR spectrum (DMSO-d_6): δ 7.08 (H-4), 7.87 (H-5), and $J_{4,5}$=5.25 Hz. [Found: C 35.9; H 1.80; S 19.0; m.wt. 169. Calc. for $C_5H_3N_3O_2S$: C 35.5; H 1.79; S 19.0; m.wt. 169.17.]

3-Azido-2-selenophene carboxylic acid (VI) was prepared as described above for IV form 1.7 g (0.0085 mol) of 3-azido-2-formylselenophene (III), 11 ml of water, 2.9 g (0.017 mol) of silver nitrate, and 1.4 g (0.035 mol) of sodium hydroxide, giving after recrystallization from toluene 1.2 g (65 %) product with m.p. 110 °C (decomp.). IR spectrum (KBr): N_3=2090 cm^{-1}, CO=1660 cm^{-1}. NMR spectrum (DMSO-d_6): δ 7.34 (H-4), 8.44 (H-5); $J_{4,5}$ 5.65 Hz. [Found: C 27.9; H 1.55; Se 36.6; m.wt. 217. Calc. for $C_5H_3N_3O_2Se$: C 27.8; H 1.40; Se 36.5; m.wt. 216.07.]

3-Azido-2-formylfuran aldoxime (VII). 10.0 g (0.142 mol) of hydroxylamine hydrochloride was dissolved in 60 ml of water, whereupon 40 ml of 10 % sodium hydroxide solution was added. To this solution, 4.0 g (0.029 mol) of 3-azido-2-formylfuran (I) in 10 ml of ethanol was added. The reaction mixture was heated to 50 °C with stirring, whereupon it was allowed to attain room temperature and kept at this temperature for another 45 minutes. After cooling to 0 °C the precipitate was filtered off, giving 4.0 g (91 %) of the product. An analytical sample which was obtained by recrystallization from water/ethanol gave an IR spectrum identical with that of the crude product, m.p. 110 °C (decomp.). IR spectrum (KBr): N_3=2110 cm^{-1}. NMR spectrum (DMSO-d_6): δ 6.72 (H-4), 7.69 (H-5), 7.84 (CH), 11.39 (OH); $J_{4,5}$ 2.00 Hz. [Found: C 39.4; H 2.83; O 21.0; m.wt. 152. Calc. for $C_5H_4N_4O_2$: C 39.5; H 2.66; O 21.0; m.wt. 152.13.]

3-Azido-2-formylthiophene aldoxime (VIII) was prepared as described above for VII from 15.0 g (0.0980 mol) of 3-azido-2-formylthiophene (II) in 25 ml of ethanol, 37.0 g (0.529 mol) of hydroxylamine hydrochloride in 225 ml of water and 150 ml of 10 % sodium hydroxide solution, yielding 15.1 g (92 %) of the product. An analytical sample which was obtained by recrystallization from water/ethanol showed an IR spectrum identical with that of the crude product, m.p. 110 °C (decomp.). IR spectrum (KBr): N_3=2120 cm^{-1}. NMR spectrum (DMSO-d_6): δ 7.20 (H-4), 7.80 (H-5), 7.60 (CH), 11.2 (OH); $J_{4,5}$ 5.40 Hz. [Found: C 35.8; H 2.53; S 19.2; m.wt. 168. Calc. for $C_5H_4N_4OS$: C 35.7; H 2.40; S 19.1; m.wt. 168.19.]

3-Azido-2-formylselenophene aldoxime (IX) was prepared as described above for VII from 2.0 g (0.010 mol) of 3-azido-2-formylselenophene (III) in 30 ml of ethanol, 5.0 g (0.071 mol) of hydroxylamine hydrochloride in 30 ml of water and 20 ml of 10 % sodium hydroxide solution, yielding 1.9 g (88 %) of the product. An analytical sample which was obtained by recrystallization from water/ethanol showed an IR spectrum identical with that of the crude product, m.p. 110 °C (decomp.). IR spectrum (KBr): N_3=2110 cm^{-1}. NMR spectrum (DMSO-d_6): δ 7.44 (H-4), 8.45 (H-5), 7.75 (CH), 12.00 (OH); $J_{4,5}$ 6.05 Hz, and $J_{5,CH}$ 0.85 Hz. [Found: C 27.9; H 1.89; Se 36.6; m.wt. 216. Calc. for $C_5H_4N_4OSe$: C 27.9; H 1.88; Se 36.7; m.wt. 215.09.]

3-Azido-2-cyanofuran (X). 3.5 g (0.023 mol) of 3-azido-2-formylfuran aldoxime (VII) was dissolved in 55 ml of methylene chloride and 2.0 g of pyridine. The reaction mixture was treated with nitrogen gas for 10 min, whereupon 31.2 g (0.0168 mol) of 2,4,6-trichloro-s-triazine was added in one batch with stirring and continued nitrogen inlet. The stirring and nitrogen inlet

were then continued for 90 minutes and the temperature kept at 30 °C with a water bath. The reaction mixture was filtered and the solid phase was washed twice with 10 ml portions of methylene chloride. The crude product obtained by concentration of the filtrate was recrystallized from methanol/water giving 2.7 g (87 %), m.p. 61.5–62.5 °C. IR spectrum (KBr): CN= 2200 cm^{-1} and N_3=2110 cm^{-1}. NMR spectrum ($CDCl_3$): δ 6.50 (H-4), 7.51 (H-5); $J_{4,5}$ 2.10 Hz. [Found: C 44.6; H 1.61; O 12.2; m.wt. 134. Calc. for $C_5H_2N_4O$: O 44.8; H 1.51; O 11.9; m.wt. 134.11.]

3-Azido-2-cyanothiophene (XI) was prepared as described above for X from 13.0 g (0.0774 mol) of 3-azido-2-formylthiophene aldoxime (VIII), 175 ml of methylene chloride, 6.1 g of pyridine and 10.6 g (0.057 mol) of 2,4,6-trichloro-s-triazine. Recrystallization of the crude product from methanol gave 10.0 g (86 %) of the product, m.p. 77.5–79.0 °C. IR spectrum (KBr): CN=2215 cm^{-1} and N_3=2130 cm^{-1}. NMR spectrum ($CDCl_3$): δ 6.96 (H-4), 7.61 (H-5); $J_{4,5}$ 5.20 Hz. [Found: C 39.9; H 1.56; N 36.6; m.wt. 150. Calc. for $C_5H_2N_4S$: C 40.0; H 1.35; N 37.3; m.wt. 150.17.]

3-Azido-2-cyanoselenophene (XII) was prepared as described above for X from 3.3 g (0.015 mol) of 3-azido-2-formylselenophene aldoxime (IX), 35 ml of methylene chloride, 1.2 g pyridine and 2.1 g (0.011 mol) of 2,4,6-trichloro-s-triazine. Recrystallization from methanol gave 2.4 g (80 %) of the product, m.p. 108.0–109.0 °C. IR spectrum (KBr): CN=2190 cm^{-1} and N_3=2100 cm^{-1}. NMR spectrum ($CDCl_3$): δ 7.19 (H-4), 8.27 (H-5); $J_{4,5}$ 5.90 Hz. [Found: C 30.5; H 1.20; Se 40.3; m.wt. 198. Calc. for $C_5H_2N_4Se$: C 30.5; H 1.03; Se 40.1; m.wt. 197.07.]

3-Amino-2-formylfuran (XIII). 1.8 g (0.013 mol) of 3-azido-2-formylfuran (I) was dissolved in 20 ml of methanol and cooled to 10 °C, whereupon 2 drops of piperidine was added. With continued cooling, hydrogen sulfide was bubbled through the reaction mixture, whereupon an exothermic reaction took place with evolution of nitrogen. The rate of the hydrogen sulfide inlet was adjusted so that the reaction temperature was kept below 20 °C. After about 20 min, the evolution of nitrogen had ceased, the solution was cooled to 0 °C and the precipitated sulfur filtered off. The filtrate was poured into 100 ml of water and the water solution was extracted five times with chloroform. The combined chloroform solutions were dried over magnesium sulfate and concentrated; giving 1.2 g (83 %) of an oil which partly crystallized after standing in a freezer for 2 days. An analytical sample which was obtained by recrystallization from ether showed an IR spectrum identical to that of the crude oil, m.p. 45–50 °C. IR spectrum (KBr): NH=3450, 3340, 3210 cm^{-1}, CO=1630 cm^{-1}. NMR spectrum ($CDCl_3$): see Table 2. [Found: C 54.3; H 4.46; O 28.3; m.wt. 111. Calc. for $C_5H_5NO_2$: C 54.1; H 4.55; O 28.8; m.wt. 111.11.]

3-Amino-2-formylthiophene XIV was prepared as described above for XIII from 6.2 g (0.041 mol) of 3-azido-2-formylthiophene (II), 50 ml of ethanol, 2 drops of piperidine and hydrogen sulfide, yielding after precipitation with ice 4.4 g (85 %) of the product. An analytical sample showing an IR spectrum identical with that of the crude product was obtained by recrystallization from ethanol/water, m.p. 68.0–70.0 °C. IR spectrum (KBr): NH=3430, 3320, 3180 cm^{-1}, CO=1610 cm^{-1}. NMR spectrum ($CDCl_3$): see Table 2. [Found: C 47.3; H 4.10; S 25.5; m.wt. 127. Calc. for C_5H_5NOS: C 47.2; H 3.97; S 25.2; m.wt. 127.17.]

3-Amino-2-formylselenophene (XV) was prepared as described above for XIII from 0.92 g (0.0046 mol) of 3-azido-2-formylselenophene (III), 20 ml of ethanol, 1 drop of piperidine and hydrogen sulfide, yielding 0.71 g (89 %) of crude product. An analytical sample showing an IR spectrum identical with that of the crude product was obtained by recrystallization from toluene, m.p. 82.0–84.0 °C. IR spectrum (KBr): NH=3440, 3340–3160 cm^{-1}, CO=1620 cm^{-1}. NMR spectrum ($CDCl_3$): see Table 2. [Found: C 34.7; H 2.92; Se 45.1; m.wt. 175. Calc. for C_5H_5NOSe: C 34.5; H 2.90; Se 45.4; m.wt. 174.07.]

3-Amino-2-cyanofuran (XVI). 1.5 g (0.011 mol) of 3-azido-2-cyanofuran (X) was dissolved in 40 ml of ethanol, 6 drops of piperidine were added and the reaction mixture cooled to 10 °C. With continued cooling, hydrogen sulfide was bubbled through the reaction mixture, whereupon an exothermic reaction took place with evolution of nitrogen. The rate of the hydrogen sulfide inlet was adjusted so that the reaction temperature was kept below 30 °C. After about 30 min the evolution of nitrogen had ceased, whereupon the reaction mixture was cooled to 0 °C and the precipitated sulfur filtered off. The filtrate was poured into 150 ml of water and the water solution was extracted four times with chloroform. The combined chloroform solutions were dried over magnesium sulfate and concentrated, giving 1.1 g (93 %) of the product. An analytical sample showing an IR spectrum identical with that of the crude product was obtained by recrystallization from toluene, m.p. 32.5–36.0 °C. IR spectrum (KBr): NH=3440, 3340 and 3210 cm^{-1}, CN=2200 cm^{-1}. NMR spectrum ($CDCl_3$ and CF_3COOH): see Table 1. [Found: C 54.4; H 3.74; O 15.0; m.wt. 108. Calc. for $C_5H_4N_2O$: C 55.6; H 3.74; O 14.8; m.wt. 108.11.]

3-Amino-2-cyanothiophene (XVII) was prepared as described above for XVI from 0.95 g (0.0063 mol) of 3-azido-2-cyanothiophene (XI), 25 ml of ethanol, 2 drops of piperidine, and hydrogen sulfide, yielding 0.75 g (95 %) of the product. An analytical sample showing an IR spectrum identical with that of the crude product was obtained by recrystallization from toluene, m.p. 47.5–50.0 °C. IR spectrum (KBr): NH=3440, 3340 and 3220 cm^{-1}, CN=2190

cm^{-1}. NMR spectrum ($CDCl_3$ and CF_3COOH): see Table 1. [Found: C 48.0; H 3.47; S 25.8; m.wt. 124. Calc. for $C_5H_4N_2S$: C 48.4; H 3.25; S 25.8; m.wt. 124.17.]

3-Amino-2-cyanoselenophene (XVIII) was prepared as described above for XVI from 1.1 g (0.0056 mol) of 3-azido-2-cyanoselenophene (XII), 2.5 ml ethanol, 2 drops of piperidine, and hydrogen sulfide, yielding 0.90 g (93 %) of the product. An analytical sample showing an IR spectrum identical with that of the crude product was obtained by recrystallization from toluene, m.p. 72.5—74.0 °C. IR spectrum (KBr): NH = 3420, 3310—3120 cm^{-1}, CN = 2170 cm^{-1}. NMR spectrum ($CDCl_3$): δ 6.89 (H-4), 7.98 (H-5), 4.7 (NH_2); $J_{4,5}$ 6.00 Hz. [Found: C 35.0; H 2.44; Se 46.3; m.wt. 172. Calc. for $C_5H_4N_2Se$: C 35.1; H 2.36; Se 46.2; m.wt. 171.07.]

3-Amino-2-thiophene carboxylic acid (XIX). 2.7 g (0.016 mol) of 3-azido-2-thiophene carboxylic acid (V) was dispersed in 30 ml of ethanol, and 1.7 g (0.017 mol) of triethylamine was added. The reaction mixture was cooled to 10 °C with an ice-bath and hydrogen sulfide was bubbled through the solution. An exothermic reaction took place with evolution of nitrogen gas. The rate of the hydrogen sulfide inlet was adjusted so that the reaction temperature was kept below 30 °C. After about 45 min the evolution of nitrogen had ceased, whereupon the reaction mixture was poured into 150 ml of water. Precipitated sulfur was filtered off and the filtrate was acidified with dilute hydrochloric acid (pH 2—3). The acid was filtered off and dried, yielding 1.4 g (61 %). An analytical sample showing an IR spectrum identical with that of the crude product was obtained by recrystallization from toluene, m.p. 82 °C (decomp.). (Lit. value 83 °C.[23]) IR spectrum (KBr): NH = 3465 and 3360 cm^{-1}, CO = 1640 cm^{-1}. NMR spectrum (DMSO-d_6): δ 6.62 (H-4), 7.48 (H-5), 8.0 (NH_2); $J_{4,5}$ 5.40 Hz.

The ^1H NMR spectra were obtained with a Varian A-60 high resolution spectrometer. The IR spectra were recorded on a Perkin-Elmer model 257 instrument. Mass spectra were obtained with an LKB 9000 mass spectrometer. Elemental analyses were carried out at the Analytical Department of the Chemical Institute and by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mühlheim/Ruhr.

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