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On the Halogenation of Halothiophenes with *N*-Chloro- and *N*-Bromosuccinimide

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Isomer distribution and halogen exchange in the reaction of *N*-chlorosuccinimide and *N*-bromosuccinimide with some bromo- and iodothiophenes have been studied. It was found that from a preparative point of view these reagents are to be preferred to molecular chlorine or bromine.

The use of *N*-bromosuccinimide (NBS; Wohl-Ziegler reaction) for benzylic and allylic brominations is well established [1] and the mechanism of the reaction is known (for a review *cf.* Ref. 2). However, as early as 1944 Buu-Hoi [3] found that reactive aromatics, such as thiophene, gave aromatic substitution with NBS in carbon tetrachloride. Schmid found that in the presence of acids, nuclear bromination could also be obtained with benzene and toluene.[4] Recently, the nuclear halogenation of fluorene and acenaphthene with NBS has been studied.[5]

In the thiophene series NBS in inert solvents or in acetic acid or acetic acid-chloroform has been used in a few investigations for the bromination of for instance bromo-, methyl-, and phenylthiophenes,[6–8] as well as for deactivated thiophenes.[9] Also, *N*-chlorosuccinimide (NCS) has been used for nuclear chlorination of thiophenes.[10]

However, no systematic investigation of the use of NBS and NCS for the bromination and chlorination of especially halothiophenes, has been carried out.

We were especially interested to ascertain the tendency of these reagents to give halogen exchange, which often complicates the reaction of certain halothiophenes with molecular chlorine or bromine (for reviews, *cf.* Refs. 11, 12), and also the selectivity of these reagents in the substitution of 2- and 3-substituted halothiophenes. We needed mixed halothiophenes in connection with our study of the halogen-metal exchange reaction of such compounds with alkyllithia.[13,14] Some mixed halothiophenes have previously been prepared by introducing the lighter halogen first or by the use of organomercury or Grignard reagents as intermediates, especially for the introduction of iodine.[15–17]

CHLORINATION WITH *N*-CHLOROSUCCINIMIDE (NCS)

The chlorination of 2- and 3-bromothiophene, 2- and 3-iodothiophene, 2,3-, 2,4-, and 2,5-dibromothiophene with NCS was studied. Product analysis was carried out by GLC. Products of less than 1 % abundance in the reaction mixtures are not reported, if they are not of special interest.

The reaction of 2-bromothiophene with one equivalent of NCS in refluxing acetic acid gave a mixture consisting of 83 % of 2-bromo-5-chlorothiophene, 11 % of 2,5-dibromothiophene, and 6 % of 2,5-dichlorothiophene. In a preparative run, a 55 % yield of pure 2-bromo-5-chlorothiophene was obtained by fractional distillation. It has previously been obtained by bromination of 2-chlorothiophene with molecular bromine.[18] Somewhat surprisingly, 2-iodothiophene gave even a cleaner result: after refluxing for 4 h in acetic acid with one equiv.

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of NCS, a mixture consisting of 95 % of 2-chloro-5-iodothiophene, 5 % of 2,5-dichlorothiophene, and less than 1 % of diiodothiophene was obtained. Fractional distillation *in vacuo* gave a 55 % yield of pure 2-chloro-5-iodothiophene. This compound has previously been obtained by Steinkopf *et al.* *via* the mercury derivative.[19] We found that the most convenient method was to iodinate 2-chlorothiophene with iodine-iodic acid according to the general method of Wirth *et al.*,[20] which gave 2-chloro-5-iodothiophene in 53 % yield.

The chlorination of 3-bromothiophene with NCS (reflux 5 h in acetic acid) proceeded with very high selectivity in the 2-position, as the product contained much less than 1 % of 4-bromo-2-chlorothiophene and 96 % of 3-bromo-2-chlorothiophene. More important by-products were 2,3-dichlorothiophene (1 %) and 3-bromo-2,5-dichlorothiophene (3 %). The sensitivity factor of 2,3-dichlorothiophene was set equal to that of 2,5-dichlorothiophene. Fractional distillation gave a 65 % yield of pure 3-bromo-2-chlorothiophene. This is certainly the best method for the preparation of this compound, which has been used as starting material in connection with the synthesis of dithienocycloheptanones.[10] When two equivalents of NCS were used, 3-bromo-2,5-dichlorothiophene was, as expected, the main product (87 %). In addition, the product contained 5 % of 3-bromo-2-chlorothiophene, 2 % of tetrachlorothiophene, less than 0.1 % of 2,3-dichlorothiophene, and 6 % of a bromotrichlorothiophene, which was not identified. Its sensitivity factor was set equal to that of 3-bromo-2,5-dichlorothiophene. By fractional distillation *in vacuo* a 55 % yield of pure 3-bromo-2,5-dichlorothiophene was obtained. The behavior of 3-iodothiophene was similar to that of the 3-bromo derivative upon chlorination with one equivalent of NCS (reflux 3.5 h in acetic acid). The product consisted of 90 % of 3-iodo-2-chlorothiophene together with 8 % of 2,5-dichloro-3-iodothiophene, 2 % of 2,3-dichlorothiophene, and much less than 1 % of 2-chloro-4-iodothiophene. The sensitivity factor of 2,3-dichlorothiophene was again set equal to that of 2,5-dichlorothiophene. In spite of the bulkiness of the substituent in the 3-position, substitution thus occurs selectively in the 2-position. This is not unexpected, as it has been found that iodination of 3-iodothiophene with iodine and iodic acid gave a mixture consisting of 99.5 % of 2,3-diiodothiophene and 0.5 % of 2,4-diiodothiophene.[21] Fractional distillation of the chlorination products gave a 53 % yield of 2-chloro-3-iodothiophene. When two equivalents of NCS were used (reflux in acetic acid, 4 h), the main component was 2,5-dichloro-3-iodothiophene (72 %) together with 23 % of 2-chloro-3-iodothiophene, 4 % of 2,3,5-trichlorothiophene, less than 1 % of 2,3-dichlorothiophene, and 2 % of a mono-iodotrichlorothiophene. Its sensitivity factor was set equal to that of 2,5-dichloro-3-iodothiophene. By fractional distillation *in vacuo* pure 2,5-dichloro-3-iodothiophene was obtained in 39 % yield. For preparative purposes, it is more convenient to iodinate 2,5-dichlorothiophene with iodine and iodic acid, which gives a 70 % yield.[22]

Other examples of the preparative usefulness of this iodination method are the preparation of 2-bromo-3,5-diiodothiophene in 53 % yield from 2-bromo-3-iodothiophene, of 3-bromo-2-iodothiophene in 66 % yield from 3-bromothiophene, and of 2-chloro-5-iodothiophene from 2-chlorothiophene in 53 % yield.

The chlorination of the dibromothiophenes with NCS was not as selective. After refluxing in acetic acid for 24 h with one equivalent of NCS, 2,3-dibromothiophene gave a mixture consisting of 59 % of 5-chloro-2,3-dibromothiophene, 24 % of 2,3,5-tribromothiophene, 14 % of 3-bromo-2,5-dichlorothiophene, and 4 % of a dibromodichlorothiophene. Its sensitivity factor was set equal to that of 3-bromo-2,5-dichlorothiophene. Fractional distillation *in vacuo* gave 36 % of pure 5-chloro-2,3-dibromothiophene. After reflux for 6 h with one equivalent of NCS, 2,4-dibromothiophene gave 77 % of 2-chloro-3,5-dibromothiophene, 13 % of 3-bromo-2,5-dichlorothiophene, and 10 % of 2,3,5-tribromothiophene. Fractional distillation gave 43 % of pure 2-chloro-3,5-dibromothiophene.

The attempted chlorination of 2,5-dibromothiophene was quite unsuccessful. After 5 h reflux in acetic acid with one equivalent of NCS, 39 % of 2-bromo-5-chlorothiophene, 11 % of 2,3,5-tribromothiophene, 5 % of 2,5-dichlorothiophene, and 44 % of a mixture of at least two of the possible 2,3,5-substituted chlorodibromothiophenes (3-chloro-2,5-dibromo-, 2-chloro-3,5-dibromo-, and 5-chloro-2,3-dibromo-

thiophene) were formed. It was not possible to resolve this peak and the values given in this case are not calibrated. Nor was it possible to isolate any pure 3-chloro-2,5-dibromothiophene by fractional distillation. This compound should therefore most easily be prepared by dibromination of 3-chlorothiophene.

BROMINATIONS WITH *N*-BROMOSUCCINIMIDE (NBS)

We have also studied the bromination of 2- and 3-iodothiophene and of 2,3-diiodothiophene with NBS in acetic acid. When 2-iodothiophene was refluxed in acetic acid with one equivalent of NBS for 1.5 h, a mixture consisting of 88 % of 2-bromo-5-iodothiophene, 8 % of 2,5-dibromothiophene, and 4 % of 2,5-diiodothiophene was obtained, from which 38 % of pure 2-bromo-5-iodothiophene was isolated by fractional distillation. This compound has previously been prepared by Steinkopf *et al.*[17] from the Grignard reagent of 2,5-dibromothiophene and iodine.

If 2-iodothiophene was reacted with two equivalents of NBS, either at room temperature or at reflux, the main product was 2,5-dibromothiophene together with traces of 2-bromo-5-iodothiophene and other more high-boiling products, which were not characterised. This indicates that the second equivalent of NBS prefers to eliminate the iodine instead of entering the β-position.

The reaction of 3-iodothiophene with NBS was much more homogeneous. After 30 min reflux, a mixture consisting of 98 % of 2-bromo-3-iodothiophene, 1 % of 2,3-dibromothiophene, 1 % of 2,5-dibromo-3-iodothiophene, and much less than 1 % of 2-bromo-4-iodothiophene was obtained. Fractional distillation *in vacuo* gave an 83 % yield of pure 2-bromo-3-iodothiophene.

With two equivalents of NBS, 3-iodothiophene gave 2,5-dibromo-3-iodothiophene as the main product (90 %), together with 9 % of a mixture of 2,3,5-tribromothiophene and 3-iodo-2-bromothiophene, and 1 % of 2,3-dibromothiophene after 19 h at room temperature. By fractional distillation *in vacuo*, 2,5-dibromo-3-iodothiophene was isolated in 44 % yield. This method of synthesis is to be preferred, as we only managed to obtain an 11 % yield in the iodination of 2,5-dibromothiophene with iodine-iodic acid.

We also found in this bromination reaction that higher temperature and longer reaction time influenced the reaction (Table 1), and led to a decrease in the yield of 2,5-dibromo-3-iodothiophene.

The separation of all the products with GLC was not possible in this case and therefore no calibration was carried out.

Bromination of 2,3-diiodothiophene with NBS, either in acetic acid or in a 1:1 mixture of acetic acid-chloroform did not proceed cleanly. The mixture consisted of 59 % of 5-bromo-2,3-diiodothiophene, 22 % of 2,5-dibromo-3-iodothiophene, 13 % of 2,3,5-triiodothiophene, and 6 % of 2-bromo-3-iodothiophene. Only a low yield of pure 5-bromo-2,3-diiodothiophene could be obtained by fractional distillation *in vacuo*.

Table 1. Bromination of 3-iodothiophene with two equivalents of NBS in acetic acid.

Products	Yield (%) Room temp. 19 h	Reflux 2 h	Reflux 5 h
2,3-Dibromothiophene	1	2	2
2-Bromo-3-iodothiophene 2,3,5-Tribromothiophene	9	23	29
2,5-Dibromo-3-iodothiophene	90	75	69

DISCUSSION

The mechanism of halogenations with NCS and especially NBS has been much discussed [2] and it now seems accepted that these reagents can be considered as sources of molecular chlorine and bromine, which are continuously formed in very low steady-state concentrations.[23] The bromine thus formed may either give radicaloid allylic or benzylic bromination, addition to double bonds or electrophilic (or radicaloid) aromatic substitution, depending upon substrate, solvent and catalyst.[23] In the presence of acids and polar solvents, nuclear substitution is often favoured. The great preparative advantage of NCS and NBS over

molecular chlorine and bromine for the bromination of thiophenes lies most probably in the fact that no strong acids are formed which can cause decomposition of the heterocyclic derivatives. It also seems unlikely that addition products can be formed with these reagents. Such addition products complicate the chlorination [24] and possibly the bromination [25] with molecular chlorine and bromine, respectively. The formation of compounds such as 2,5-dibromothiophene in the reaction of 2-bromothiophene with NCS or of 2,3,5-triiodothiphene in the reaction of 2,3-diiodothiophene with NBS may be due to the formation of Br^+ and I^+ (or Br – Cl and I – Cl) from electrophilic halogen exchange of the substrates followed by electrophilic substitution in the 5-position. This is in agreement with the formation of 2,5-dichlorothiophene and 2-bromo-3-iodothiophene in the two above-mentioned reactions.

The advantage of the NCS and NBS halogenations also became apparent from experiments with other halogenating agents. Thus, sulfuryl chloride, which is the reagent of choice for the preparation of 2-chloro- and 2,5-dichlorothiophene,[27] cannot be used for the chlorination of 3-bromothiophene. A mixture of many compounds, with none predominating, was obtained and no effort was made to identify them. Nor did the reaction of 2,3-diiodothiophene with sulfuryl chloride give any 5-chloro derivative. Also the bromination of 2,3-diiodothiophene with one equivalent of bromine in carbon tetrachloride was quite unsuccessful. No main product was obtained, and 5-bromo-2,3-diiodothiophene could not be detected in the reaction mixture. By reacting 2,3-diiodothiophene with excess bromine, Steinkopf *et al.*[15] obtained 4-iodo-2,3,5-tribromothiophene. When 3-iodothiophene was reacted with two equivalents of bromine in carbon tetrachloride, the main part of the product consisted of one or several hexabromobithienyls together with 2,3,5-tribromothiophene. 2,5-Dibromo-3-iodothiophene could not be detected in the reaction mixture. In acetic acid, on the other hand, the main product was 2,5-dibromo-3-iodothiophene. The different behaviour of NBS and bromine towards 3-iodothiophene is quite striking and casts some doubt on the hypothesis that molecular bromine (or Br^+) is the active agent in both the Br_2 and NBS brominations.

EXPERIMENTAL

General. Gas chromatographic analyses were performed with a Perkin-Elmer 900 apparatus equipped with a flame ionisation detector and connected to a Varian 480 digital integrator. In some cases, however, a disc integrator was used for the evaluation of the gas chromatograms. The columns were made of stainless steel with 3 mm o.d. Nitrogen was used as carrier gas. The following columns were used: 5 % Neopentyl glycolsuccinate (NPBS) on Chrom. W (80/100 mesh), 2.0 m (A). 3 % OV 17 on Gas Chrom. Q (100/120 mesh), 2.5 m (B). 10 % Butane-1,4-diolsuccinate (BDS) on Chrom. W (80/100 mesh), 2.0 m (C) and 10 % Neopentylglycol sebacate on Chrom. W (80/100 mesh), 2.5 m (D).

Products of less than 1 % abundance in the reaction mixtures are not reported, if they are not of special interest. For all products obtained, calibration was, if not otherwise stated, made for the sensitivity factor of each compound to the flame.

NMR spectra were recorded on a Varian A-60 instrument. Tetramethylsilane (TMS) was used as internal standard. A Perkin-Elmer 257 IR spectrometer was used for IR spectra. Mass spectra were recorded on an LKB 9000 mass spectrometer at 70 eV. The mass spectra were mainly used for identification of the molecular ion.

Most of the elemental analyses were performed by the Department of Analytical Chemistry at the University of Lund, Sweden, and a few by Miss Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, West Germany.

General procedure for NCS chlorination. To 0.050 mol of halothiophene in approximately 200 ml of acetic acid a small amount of a total of 6.7 g (0.050 mol) of NCS was added. The temperature was raised to reflux, whereupon the rest of the NCS was added in portions. After refluxing for 1 h, the reaction mixture was poured into water and extracted with ether. The combined ether phases were washed with water, dilute sodium hydroxide solution and more water. After drying over magnesium sulfate, the ether was evaporated, the product analyzed by GLC and the product distilled.

2-Bromo-5-chlorothiophene was obtained in 55 % yield from 2-bromothiophene,[26] b.p. 63 – 67 °C/11 mmHg (Column A). Lit. value [18] 69.5 – 70.0 °C/18 mmHg.

2-Chloro-5-iodothiophene was obtained in 55 % yield from 2-iodothiophene,[20] b.p. 89 – 90 °C/10 mmHg (Column A). Lit. value [19] 95 – 96 °C/14 mmHg.

3-Bromo-2-chlorothiophene was obtained in 62 % yield from 3-bromothiophene [28] (0.50 mol in 400 ml of acetic acid), b.p. 69 – 73 °C/11 mmHg (Column A). Lit. value [10] 68 – 72 °C/9 mmHg.

2-Chloro-3-iodothiophene was obtained in 53 % yield from 3-iodothiophene [29] (0.30 mol.

300 ml acetic acid), b.p. 96–98 °C/11 mmHg (Column A). NMR (CCl_4): δ 6.91 and 6.99. J_{45} 5.8 Hz. Calc. for C_4H_2ClIS (244.5): C 19.6; H 0.82; I 51.9. Found: C 19.8; H 0.92; I 51.9.

3-Bromo-2,5-dichlorothiophene was obtained in 55 % yield from 3-bromothiophene [28] using two equivalents of NCS, b.p. 89–92 °C/11 mmHg (Column A). Calc. for C_4HBrCl_2S (232.0): C 20.7; H 0.43; S 13.8. Found: C 20.7; H 0.39; S 13.8.

2,5-Dichloro-3-iodothiophene was obtained in 39 % yield from 3-iodothiophene [29] using two equivalents of NCS, b.p. 112–114 °C/11 mmHg (Column A). Calc. for C_4HCl_2IS (278.9): C 17.2; H 0.36; I 45.5 Found: C 17.6; H 0.48; I 45.3.

5-Chloro-2,3-dibromothiophene was obtained in 36 % yield from 2,3-dibromothiophene [31] (1.50 mol in 1500 ml acetic acid and 1.57 mol NCS), b.p. 106–109 °C/11 mmHg (distilled through a 35 cm long column filled with glass helices (Column B). Calc. for C_4HBr_2ClS (276.4): C 17.4; H 0.36; S 11.6. Found: C 17.5; H 0.33; S 11.6.

2-Chloro-3,5-dibromothiophene was obtained in 43 % yield from 2,4-dibromothiophene,[32] b.p. 104–108 °C/10 mmHg (Column B). Calc. for C_4HBr_2ClIS (276.4): C 17.4; H 0.36; S 11.6. Found: C 17.5; H 9.42; S 11.4.

From *2,5-dibromothiophene* [26] and *NCS* no 3-chloro-2,5-dibromothiophene could be identified with certainty, because of difficulties in the separation of the products in the reaction mixture (Column C).

General procedure for NBS bromination. To 0.100 mol of halothiophene in approximately 160 ml acetic acid 0.104 mol of NBS was added in portions. When the reaction did not start spontaneously, it was heated to 35–40 °C. After stirring for 2 h during which time the temperature did not exceed 40 °C, the reaction mixture was poured into water and worked up as described for the NCS chlorination.

2-Bromo-5-chlorothiophene was obtained in 47 % yield from 2-chlorothiophene,[27] b.p. 59–60 °C/9 mmHg (Column A): Lit. value [18] 69.5–70.0 °C/118 mmHg. NMR (CCl_4): δ 6.67 and 6.74, J_{34} 4.0 Hz.

2-Bromo-5-iodothiophene was obtained in 38 % yield from 2-iodothiophene,[20] b.p. 107–110 °C/11 mmHg (Column C). Lit. value [17] 116 °C/13 mmHg. NMR (CCl_4): δ 6.67 and 6.95, J_{34} 3.8 Hz.

2-Bromo-3-iodothiophene was obtained in 83 % yield from 3-iodothiophene,[29] b.p. 104–108 °C/8 mmHg (Column A). NMR (CCl_4): δ 6.91 and 7.17, J_{45} 5.6 Hz. Calc. for C_4H_2BrIS (288.9): C 16.6; H 0.70; S 11.1. Found: C 16.7; H 0.81; S 10.9.

2,5-Dibromo-3-iodothiophene was obtained in 44 % yield from 3-iodothiophene [29] using two equivalents of NBS, b.p. 145–150 °C/11 mmHg (Columns A, C). Higher temperatures and shorter reaction times did not improve the yields. Calc. for C_4HBr_2IS (367.8): C 13.1; H 0.27; I 34.5. Found: C 13.2; H 0.24; I 33.5.

5-Bromo-2,3-diiodothiophene was obtained in 5 % yield from 2,3-diiodothiophene.[30] The fractions boiling at 102–119 °C/0.2 mmHg were chromatographed on a column filled with neutral aluminium oxide. Petroleum ether (30–50 °C) was used as eluent. The fractions were checked by GLC. In this way pure title compound, m.p. 45–46 °C was obtained (Column C). Calc. for C_4HBrI_2S (414.8): C 11.6; H 0.24; I 61.2. Found: C 11.9; H 0.28; I 60.0.

2-Chloro-5-iodothiophene. To 11.8 g (0.100 mol) of 2-chlorothiophene,[27] 43 ml of acetic acid, 16 ml of water, 21 ml of carbon tetrachloride, 3.7 g (0.021 mol) of HIO_3, and 0.7 ml of concentrated sulfuric acid, at reflux, 10.2 g (0.040 mol) of iodine was added in portions. After reflux for 3 h, more water and carbon tetrachloride were added. The organic phase was separated, washed with water, sodium thiosulfate solution, and water, and dried over magnesium sulfate. Distillation gave 12.9 g (53 %) of 2-chloro-5-iodothiophene at 86–87 °C/11 mmHg. Lit. value [19] 95–96 °C/14 mmHg (Column A). NMR (CCl_4): δ 6.51 and 6.95, J_{34} 3.8 Hz.

3-Bromothiophene and sulfuryl chloride. To 24 g (0.15 mol) of 3-bromothiophene,[28] 25 ml (0.31 mol) of sulfuryl chloride was added dropwise. After the addition, the mixture was refluxed for 2 h. GLC analysis showed that several products had been formed. Reflux for a further 2 h did not change the result. No peak in the gas chromatogram was dominant. This method is thus not useful for the preparation of 3-bromo-2,5-dichlorothiophene. The products were not identified. (Column D).

2,3-Diiodothiophene and sulfuryl chloride. To 6.7 g (20 mmol) of 2,3-diiodothiophene,[30] 1.6 ml (20 mmol) of sulfuryl chloride was added dropwise. After reflux for 1.5 h, GLC analysis showed that most of the starting material was unreacted. An additional 1.5 ml (19 mmol) of sulfuryl chloride was added, whereupon reflux was continued for 6.5 h. Besides starting material, which was the largest peak, GLC analysis indicated the formation of 2-chloro-3-iodothiophene, 2,5-dichloro-3-iodothiophene and eventually 2,3,5-triiodothiophene. Thus, this method was not useful for the preparation of 5-chloro-2,3-diiodothiophene (Column A).

3-Iodothiophene and bromine. To 21 g (0.10 mol) of 3-iodothiophene [29] in 15 ml of carbon tetrachloride 11 ml (0.21 mol) of bromine in 15 ml of carbon tetrachloride was added during 2 h. After stirring at room temperature for 24 h, the reaction mixture was refluxed for 45 min. More carbon tetrachloride and 30 ml of 5 N sodium hydroxide were added. After reflux for 2 h, the reaction mixture was filtered. The separated solid tarlike product did not dissolve in boiling dioxane, but upon treatment with acetone, red-brown crystals were obtained after filtering. These crystals were only to a small degree soluble in carbon tetrachloride, which, however, was a better solvent than acetone, dimethyl sulfoxide, or chloroform. NMR spectrum showed

no proton absorptions. Combined GLC-mass spectrometry indicated that the crystals consisted of one or more hexabromobithienyls. The filtrate above contained mainly 2,3,5-tribromothiophene. 2,5-Dibromo-3-iodothiophene could not be detected in the reaction mixture.

If acetic acid was used as solvent, no hexabromobithienyl could be observed. In this case, 2,5-dibromo-3-iodothiophene was formed together with other products. GLC analysis indicated that if acetic acid is used as solvent, molecular bromine can be an alternative to the utilization of NBS for the synthesis of 2,5-dibromo-3-iodothiophene (Column B).

2,3-Diiodothiophene and bromine. To 9.0 g (0.027 mol) of 2,3-diiodothiophene [30] in 10 ml of carbon tetrachloride, 1.6 ml (0.031 mol) of bromine dissolved in 10 ml of carbon tetrachloride was added dropwise during a 35 min period. After stirring for 24 h, GLC analysis indicated that only products with retention times shorter than that of 2,3-diiodothiophene had been formed, with the exception of one product with a longer retention time. This product, which possibly was 2-bromo-4,5-diiodothiophene, was however only approximately 3 % of the total product distribution. Thus, this route is not useful for the synthesis of 5-bromo-2,3-diiodothiophene. The other products were not identified (Column B).

2-Bromo-3,5-diiodothiophene. 5.8 g (20 mmol) of 2-bromo-3-iodothiophene, 9 ml of acetic acid, 3.5 ml of water, 4.5 ml of carbon tetrachloride, 0.2 ml of concentrated sulfuric acid, and 0.80 g (4.6 mmol) of iodic acid were heated to reflux; 2.1 g (8.3 mmol) of iodine was then added in portions. After reflux for an additional 4 h, more water and carbon tetrachloride were added. The organic phase was separated and washed with water, sodium thiosulfate solution, and water, and dried over magnesium sulfate. The carbon tetrachloride was evaporated and the residue recrystallised from ethanol, whereupon 2-bromo-3,5-diiodothiophene precipitated. Weight after drying: 4.4 g (53 %). M.p.: 63–64 °C. Column: B. Calc. for C_4HBrI_2S (414.8): C 11.6; H 0.24; I 61.2. Found: C 11.6; H 0.21; I 60.9.

3-Bromo-2-iodothiophene. 41 g (0.25 mol) of 3-bromothiophene,[28] 80 ml of acetic acid, 30 ml of water, 20 ml of carbon tetrachloride, 1.5 ml of concentrated sulfuric acid, 20.4 g (0.080 mol) of iodine, and 8.2 g (0.047 mol) of HIO_3 were stirred at 40 °C until the iodine was consumed (2 h). Water, sodium hydrogen carbonate solution, and 20 ml of carbon tetrachloride were added. The organic phase was separated, washed with sodium hydrogen carbonate solution and dried over magnesium sulfate, whereupon it was chromatographed on a column filled with basic aluminium oxide. Low boiling petroleum ether was used as eluent. After evaporation of the petroleum ether, distillation gave 38 g (66 %) of 3-bromo-2-iodothiophene at 108–110 °C/9 mmHg (Column A). NMR (CCl_4): δ 7.30 (H-4), 7.80 (H-5). J_{45} 5.6 Hz. Calc. for C_4H_2BrIS (288.9): C 16.6; H 0.70; S 11.1. Found: C 16.8; H 0.74; S 11.2.

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