On the Halogen—Metal Exchange Reaction between Mixed Dihalothiophenes and Alkyllithium

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The halogen-metal exchange of 2-bromo-4-iodo-, 2-chloro-4-bromo-, 2-chloro-3-iodo-, and 2-chloro-3-bromothiophene and butyllithium has been studied. Exchange occurred in all cases first with the β-halogen. 2-Bromo-4-thienyllithium rearranged even at $-100\,°C$, while the other β-thienyllithium compounds were stable enough at $-70\,°C$ to be of preparative use. Upon warming 2-chloro-3-thienyllithium underwent rearrangements, while 2-chloro-4-thienyllithium ring-opened.

Halogen-metal exchange between bromo- or iodothiophenes and alkyllithium derivatives is one of the most important preparative reactions in thiophene chemistry.[1,2] The reaction is very rapid at $-70\,°C$ and it is also known that an α-bromine [3] or α-iodine [4] exchanges much faster than a corresponding β-halogen. This has for instance been demonstrated in the halogen-metal exchange reaction between 2,3-dibromothiophene or 2,4-dibromothiophene with butyllithium at $-70\,°C$, in which cases only the α-bromines are exchanged.[3] It is also well known from the classical investigations by Wittig et al. and Gilman et. al. that iodides react much faster than bromides. (For a review cf. Ref. 5.)

Chlorothiophenes give halogen-metal exchange only when there is no free α-position. Such exchange has been observed with 2,5-dichlorothiophene [6] and with tetrachlorothiophene [6,7] and also with β-chlorine derivatives such as 2,5-dimethyl-3,4-dichlorothiophene.[8] 2-Chlorothiophene on the other hand is metal-

ated to 5-chloro-2-thienyllithium.[6] No halogen-metal interconversion has been observed with fluorothiophenes.[9]

During our work certain complications have been observed in these halogen-metal exchanges. Thus it was found that when the lithium atom does not replace the most acidic hydrogen, rearrangement by a series of rapid halogen-metal exchanges and metalations leads to the most stable lithium derivative, as for instance observed for 4-bromo-3-thienyl- and 4-bromo-2-thienyllithium.[3] It has also been found that at higher temperatures certain 3-thienyllithium derivatives ring-open to lithium thioenynes.[10-13] On the other hand, the high stability of ortho-bromothienyllithium derivatives such as 3-bromo-2-thienyllithium [14] is markedly different from that of ortho-bromophenyllithium.[15] These compounds showed no tendency to eliminate lithium bromide to give dehydrothiophene. Many different attempts to trap dehydrothiophenes have failed,[16-19] and it has been shown that the cine-substitution occurring during the amination of halothiophenes does not involve aryne pathways.[18] Recently, however, Reinecke and Newson [20] claimed the intermediacy of five-membered hetarynes in the thermolysis of heterocyclic anhydrides. We were therefore interested to study the halogen-metal exchange of mixed dihalothiophenes with the more reactive halogen in the β-position. If 2-halo-3-thienyllithium derivatives could be obtained, these should be suitable intermediates for the formation of 2,3-dehydrothiophene.

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In a short communication some years ago we described the reaction between 2-bromo-3-iodothiophene and ethyllithium.[21] At $-100\,°C$ halogen-metal exchange occurred in the β-position, giving 2-bromo-3-thienyllithium in at least 84 % yield, characterized as 2-bromo-3-thiophenecarboxylic acid. Upon hydrolysis, 95 % of 2-bromothiophene was obtained.

However, attempts to detect 2,3-dehydrothiophene by carrying out the halogen-metal exchange in the presence of furan were unsuccessful. 2-Bromo-3-thienyllithium, however, was very prone to undergo rearrangement to a thermodynamically more stable lithium derivative. Thus if the halogen-metal exchange was carried out at $-70\,°C$, 3-bromo-2-thienyllithium was the main product.[21] A reaction scheme for the transformation of 2-bromo-3-thienyllithium to 3-bromo-2-thienyllithium was suggested.

STARTING MATERIALS

2-Bromo-4-iodothiophene was prepared in 36 % yield from 2,4-diiodothiophene,[4] through halogen-metal exchange followed by reaction with bromine. A possible route to 2-bromo-4-iodothiophene consisting of halogen-metal exchange of 5-bromo-2,3-diiodothiophene followed by hydrolysis was inferior due to the low yield obtained in the bromination of 2,3-diiodothiophene.[28]

4-Bromo-2-chlorothiophene has been prepared from 4-bromo-2-thienyllithium through the reaction with chlorine [9] or with hexachloroethane.[30] Since we had 5-chloro-2,3-dibromothiophene [28] available, we reacted it with butyllithium followed by hydrolysis which gave 4-bromo-2-chlorothiophene in 53 % yield.

For identification purposes the unknown 3-bromo-2-chloro-5-thiophenecarboxylic acid was prepared from 2-chloro-3,5-dibromothiophene through halogen-metal exchange with butyllithium followed by reaction with carbon dioxide. The isomeric 3-bromo-5-chloro-2-thiophenecarboxylic acid was analogously obtained from 5-chloro-2,3-dibromothiophene.[28]

RESULTS

As could be expected from the previous results with 2-bromo-3-iodothiophene, halogen-metal exhange of 2,5-dibromo-3-iodothiophene led to extensive rearrangement and several compounds were formed upon hydrolysis. This reaction therefore cannot be used for the preparation of 2-bromo-4-iodothiophene. Thus as 2-bromo-3-iodothiophene, 2,5-dibromo-3-iodothiophene also gives exchange of the β-iodine faster than of α-bromine.

When 2-bromo-4-iodothiophene was allowed to react with butyllithium it was found that the intermediate 2-bromo-4-thienyllithium was more unstable than 2-bromo-3-thienyllithium and underwent rapid rearrangement even at $-100\,°C$. The results were here somewhat more difficult to reproduce, and in Table 1 the analytical results obtained are given. GLC analyses were carried out both after ethanolysis and after reaction with carbon dioxide followed by esterification with diazomethane.

From Table 1 it can be seen that a large excess of butyllithium suppresses the rearrange-

Table 1. Product distributions in the reactions of 2-bromo-4-iodothiophene with butyllithium in ether after protonation or carbonation followed by acidification and esterification

Temp./°C	X	2-Bromo-4-X-thiophene/%	3-Bromo-5-X-thiophene/%	3-Iodo-5-X-thiophene/%	2,4-Dibromo-5-X-thiophene/%	Excess of BuLi/%
<-60	H	8	48	39	5	110
<-60	H	66	22	11	trace	150
<-100	H	9	24	35	33	10
<-100	H	60	trace	19	21	10
<-100	H	24	12	32	32	10
<-60	CO_2CH_3	trace	21	62	16	10
<-100	CO_2CH_3	64	2	26	8	10
<-100	CO_2CH_3	92	1	7	—	10
<-100	CO_2CH_3	78	6	17	—	10

ments of initially formed 2-bromo-4-thienylli-
thium. The observation of methyl 3,5-dibromo-
2-thiophenecarboxylate is somewhat unex-
pected, as it implies the formation of 3,5-
dibromo-2-thienyllithium through metalation
at −100 °C. Metalation is usually slow at this
temperature, but this observation is in accord-
ance with the faster metalation of 2,4-di-
bromothiophene compared to 2,3-dibromo-
thiophene.[3] Thus 2-bromo-4-iodothiophene is
obviously not a suitable starting material
for the preparation of 2-bromo-4-thienyllithium
and products derived from it.

3-Bromo-2-chloro-[28] and 2-chloro-3-iodothio-
phene,[28] on the other hand, showed no tendency
to rearrange when treated with alkyllithium
at −70 °C. Protonation of the intermediate
2-chloro-3-thienyllithium gave only 2-chloro-
thiophene, and reaction with carbon dioxide
2-chloro-3-thiophenecarboxylic acid in good
yield.

However, as the lithium of 2-chloro-3-
thienyllithium does not substitute the most
acidic hydrogen, rearrangement to the thermo-
dynamically more stable lithium derivatives
can be expected.[3] If 2-chloro-3-thienyllithium,
prepared at −70 °C, was allowed to reach
room temperature slowly and stirred over-
night, interesting differences were observed

Scheme 1. X = Br or I.

Table 2. Product distributions in the reactions
of 3-bromo-2-chloro- and 2-chloro-3-iodothio-
phene [a] with butyllithium in ether at −70 °C
followed by temperature rise, carbonation,
acidification, and esterification. A, methyl 2-
chloro-5-thiophenecarboxylate; B, methyl 2-
chloro-3-thiophenecarboxylate; C, methyl 2-
chloro-3-bromo-5-thiophenecarboxylate.

A/%	B/%	C/%
18	71	10
53	5	42
31	45	23
32	68	—
25	75	—
13	87	—

[a] The first three results were obtained with 3-
bromo-2-chlorothiophene and the following three
with 2-chloro-3-iodothiophene. [b] The sensitivity
factor of methyl 2-chloro-5-thiophenecarboxylic
acid was set equal to that of methyl 2-chloro-3-
thiophenecarboxylic acid.
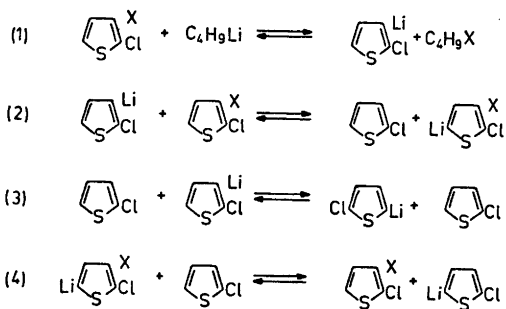
depending upon whether the 2-chloro-3-thi-
enyllithium was derived from 3-bromo-2-
chlorothiophene or 2-chloro-3-iodothiophene.
In the former case, rearrangement appeared
to be more extensive and large relative amounts
of 5-chloro-2-thienyllithium and especially of
3-bromo-2-chloro-5-thienyllithium were formed
(Table 2). The lithium derivatives were as
previously characterized by reaction with
carbon dioxide followed by methylation. In
the latter case no formation of 2-chloro-3-
iodo-5-thienyllithium was observed.

This is somewhat unexpected, since according
to the general mechanism previously suggested[3]
for such rearrangements, 2-chloro-3-halo-5-
thienyllithium should be an intermediate in
the formation of 5-chloro-2-thienyllithium (*cf.*
reaction formulae (1)−(3) in Scheme 1). It
is possible that reaction (3) is much faster than
reaction (2) when X = I, and therefore only
a very low concentration of 2-chloro-3-iodo-5-
thienyllithium will be formed, or that this
lithium derivative is removed by a reaction
such as (4) to a much greater extent than when
X = Br. As is also evident from Table 2, it
was quite difficult to obtain reproducible
proportions of the compounds formed. As
stressed previously,[3] this depends upon the
fact that small and difficultly controllable
differences in the experimental conditions
cause great differences in the final product
proportions. For instance small amounts of
2-chlorothiophene formed by unintentional
hydrolysis will catalyze the rearrangement to
5-chloro-2-thienyllithium (eqn. 3). Also differ-
ences in the reaction rate of the various lithium
derivatives with the "trapping" reagents might
contribute to the difficulties in obtaining

reproducible results. No ring-opening to acetylenic derivatives was observed with 2-chloro-3-thienyllithium. The same is also true for 2-chloro-5-methyl- and 2,5-dichloro-3-thienyllithium.[29]

When 4-bromo-2-chlorothiophene was reacted with butyllithium at $-70\,°C$, 2-chloro-4-thienyllithium was obtained, which at this temperature gave no rearrangement yielding 2-chloro-4-(1-cyclohexenyl)thiophene with cyclohexanone,[30] and 2-chloro-4-thiophenecarboxylic acid and 2-chloro-4-iodothiophene with carbon dioxide and iodine, respectively. However, when 2-chloro-4-thienyllithium prepared at $-70\,°C$ was stirred overnight at room temperature, no chlorothiophenecarboxylic acids could be detected after reaction with carbon dioxide. IR analysis indicated that compounds containing triple bonds had been formed. One peak in the gas chromatogram, with longer retention time than that of the starting material, showed in the GLC/MS analysis a molecular ion at $m/e = 138$. The intensities of this peak and those at $m/e = 139$ and $m/e = 140$ indicated this compound to have the composition $C_8H_{10}S$, and the intense fragments at $m/e = 81$ $(M^+ - C_4H_9)$ and $m/e = 82$ $(M^+ - C_4H_8)$ showed the compound to be butylthiodiacetylene. This compound is formed by ring-opening of 2-chloro-4-thienyllithium to lithium 1-chloro-1-buten-3-yne-1-thiolate, which is alkylated by the butyl bromide to give 1-butyl-thio-1-chloro-1-buten-3-yne. This yields the observed 1-butylthiodiacetylene upon elimination of hydrogen chloride.

A similar observation was made when 5-chloro-2-methyl-3-thienyllithium, prepared by halogen-metal exchange between 3-bromo-5-chloro-2-methylthiophene and ethyllithium, ring-opened to yield 1-ethylthio-1,3-pentadiyne.[29]

CONCLUSIONS

Our investigations thus indicate that α-chloro-β-thienyllithium compounds prepared through halogen-metal exchange between α-chloro-β-iodo- or α-chloro-β-bromothiophenes and alkyllithia at $-70\,°C$ are stable enough to allow the preparation of 2-chloro-3-substituted and 2-chloro-4-substituted thiophenes. If the temperature is allowed to rise, 2-chloro-

3-thienyllithium rearranges to thermodynamically more stable lithium derivatives, predominantly 5-chloro-2-thienyllithium, while 2-chloro-4-thienyllithium ring-opens. α-Bromo-β-thienyllithium compounds prepared from α-bromo-β-iodothiophenes rearrange much faster. However, 2-bromo-3-substituted thiophenes can be obtained by carrying out the reaction below $-100\,°C$. No evidence for the formation of 2,3-dehydrothiophene from 2-bromo-3-thienyllithium was found.

EXPERIMENTAL

The equipment for obtaining NMR, IR, and mass spectra has been described in Ref. 28, as well as the GLC equipment used. The following columns were used: 5 % Neopentyl glycolsuccinate (NPGS) 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-diol succinate (BDS) on Chrom. W (80/100 mesh), 2.0 m (C), and 5 % Apiezon L on Chrom. W (80/100 mesh), 2.0 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.

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.

Experiments with lithium compounds and titration of alkyllithium solution were carried out as described in Ref. 13.

The purities of the compounds were checked by gas chromatography and NMR. Acids were esterified with diazomethane before being injected into the gas chromatograph.

Authentic samples of 2-bromo-,[22] 3-bromo-,[23] 3-iodo-,[24] 2,4-dibromothiophene [25] as well as of 2-bromo-4-thiophenecarboxylic acid,[26] 4-bromo-2-thiophenecarboxylic acid,[25] 4-iodo-2-thiophenecarboxylic acid,[4] and 3,5-dibromo-2-thiophenecarboxylic acid [27] were used for identification of the products.

Halogen-metal interconversion with 2,5-dibromo-3-iodothiophene. To an ethereal solution of 5.5 g (0.015 mol) of 2,5-dibromo-3-iodothiophene [28] cooled to $-70\,°C$, 28 ml of 0.55 M (0.015 mol) butyllithium in ether was added at such a rate that the temperature was kept below $-60\,°C$. After stirring for 10 min at $-70\,°C$, the reaction mixture was poured into water. After work-up in the usual manner, GLC analysis showed that several products had been produced, indicating rapid rearrangement reactions. The method was therefore not

suitable for the preparation of 2-bromo-4-iodothiophene. (Column: C.)

2-Bromo-4-iodothiophene. To 120 ml of 0.90 M (1.08 mol) butyllithium in ether cooled to −70 °C, 33.6 g (0.100 mol) of 2.4-diiodothiophene [4] dissolved in 100 ml of ether was added in a slow stream. After stirring for an additional 20 min, bromine, dried with concentrated sulfuric acid, was added, while the temperature was kept at −70 °C. The bromine was added in portions, and at regular intervals aliquots were analyzed by GLC after hydrolysis. When the ratio between 3-iodothiophene and 2-bromo-4-iodothiophene no longer declined according to their relative concentrations in the reaction mixture, the addition of bromine was interrupted. After pouring the reaction mixture into water, the ether phase was separated and the water phase extracted with ether. The combined ether phases were washed with sodium thiosulfate solution, dilute sodium hydroxide solution, and water, and dried over magnesium sulfate. Distillation gave 10.5 g (36 %) of 2-bromo-4-iodothiophene, b.p. 106−108 °C/10 mmHg. The product was further purified by preparative gas chromatography (BDS 20 % on Chrom. W, 9 mm × 2 m). (Column: C.) NMR (CCl_4): δ 6.95 (H3 or H5, d, 1 H) and 7.20 (H5 or H3, d, 1 H). J (H3, H5) 1.5 Hz. [Calc. for C_4H_2BrIS (288.9): C 16.6; H 0.70; I 43.9. Found: C 17.0; H 0.84; I 43.6.]

Halogen-metal interconversion with 2-bromo-4-iodothiophene. 5.0 ml of 1.12 M (5.6 mmol) butyllithium in ether was cooled to −70 °C, whereupon 1.1 g (3.8 mmol) of 2-bromo-4-iodothiophene dissolved in 5 ml of ether was added at such a rate that the temperature was kept below −60 °C. After stirring for an additional 20 min, carbon dioxide gas, dried by bubbling through concentrated sulfuric acid, was led into the reaction mixture during 45 min at −70 °C. If protonation was desired instead, ethanol was added after stirring for 20 min. Work-up and analyses were performed as in the halogen-metal interconversion reactions with 2-bromo-3-iodothiophene (*cf,* above). When the reaction was performed at about −110 °C, the same method was used while keeping the temperature below −100 °C. The results of the analyses are given in Table 1 (Columns: A, C).

2-Chloro-3-thiophenecarboxylic acid. A. *From 2-chloro-3-iodothiophene.* To 50 ml of 0.90 M (0.045 mol) butyllithium in ether at −70 °C, 10 g (0.041 mol) of 2-chloro-3-iodothiophene dissolved in ether was added at such a rate that the temperature was kept below −55 °C. After stirring for 15 min, the reaction mixture was poured onto dry ice in ether. When the bubbling of the carbon dioxide had finished, the mixture was hydrolyzed with water and acidified with hydrochloric acid. After extracting the water phase with ether, the combined ether phases were extracted several times

with dilute sodium hydroxide. The combined water phases were acidified with hydrochloric acid, whereupon the acid precipitated. After recrystallization from water-ethanol (1:1) and drying, 3.4 g (51 %) of 2-chloro-3-thiophenecarboxylic acid was obtained with m.p. 162−163 °C; lit. value:[31] 163 °C (Column: C). NMR (DMSO): δ 7.38 (H4 or H5, d, 1 H), 7.50 (H5 or H4, d, 1 H), and 9.08 (COOH, s, 1 H). J (H4, H5) 5.8 Hz. B. *From 3-bromo-2-chlorothiophene.* The same method as above utilizing 3-bromo-2-chlorothiophene gave a 58 % yield of 2-chloro-3-thiophenecarboxylic acid (Column: C).

Stability of 2-chloro-3-thienyllithium. 57 ml of 0.51 M (0.029 mol) butyllithium in ether was cooled to −70 °C, whereupon 5.0 g (0.025 mol) of 3-bromo-2-chlorothiophene [28] dissolved in ether was added, keeping the temperature below −55 °C. After stirring for 10 min the cooling bath was removed and the reaction mixture was stirred at room temperature overnight. The reaction mixture was carbonated and worked up in the usual manner. The resulting acid mixture was esterified with diazomethane. GLC/MS showed the formation of methyl 2-chloro-5-thiophenecarboxylate, methyl 2-chloro-3-thiophenecarboxylate, and methyl 3-bromo-2-chloro-5-thiophenecarboxylate. The NMR spectrum of the acid mixture also indicated the formation of 2-chloro-5-thiophenecarboxylic acid ($J = 4.1$ Hz) and 2-chloro-3-thiophenecarboxylic acid ($J = 5.8$ Hz). IR analysis of the ether phase did not reveal the formation of any compounds containing carbon-carbon triple bonds, indicating that no ring-opening reaction had occurred.

When 2-chloro-3-iodothiophene was used in a corresponding reaction, methyl 2-chloro-5-thiophenecarboxylate and methyl 2-chloro-3-thiophenecarboxylate were formed. However, in this case, no methyl 2-chloro-3-iodo-5-thiophenecarboxylate was obtained. IR analysis gave the same result as above. The results are given in Table 2 (Column: C).

3-Bromo-2-chloro-5-thiophenecarboxylic acid. To 40 ml of 0.85 M (0.034 mol) butyllithium in ether 8.2 g (0.030 mol) of 2-chloro-3,5-dibromothiophene [28] in 30 ml of ether was added in a slow stream, keeping the temperature below −47 °C. After stirring for an additional 20 min at −70 °C, the reaction mixture was poured onto dry ice in ether. After work-up in the usual manner and recrystallization from water-ethanol (1:1) 4.5 g (62 %) of 3-bromo-2-chloro-5-thiophenecarboxylic acid (m.p. 206−207 °C) was obtained (Column: A). [Calc. for $C_5H_2BrClO_2S$ (241.5): C 24.9; H 0.83; S 13.3. Found: C 24.8; H 0.85; S 13.2.]

4-Bromo-2-chloro-5-thiophenecarboxylic acid. To 40 ml of 0.85 M (0.034 mol) butyllithium in ether cooled to −70 °C 8.6 g (0.031 mol) of 5-chloro-2,3-dibromothiophene [28] in 40 ml of ether was added in a slow stream, keeping the temperature below −42 °C. After stirring

for an additional 20 min at − 70 °C, the reaction mixture was carbonated and worked up in the usual way. The crude acid was recrystallized from water-ethanol (1:1), whereupon 5.0 g (67 %) of 4-bromo-2-chloro-5-thiophenecarboxylic acid (m.p. 198 − 199 °C) was obtained (Column: A). [Calc. for $C_5H_2BrClO_2S$ (241.5): C 24.9; H 0.83; S 13.3. Found: C 24.9; H 0.80; S 13.4.]

4-Bromo-2-chlorothiophene. 450 ml of 0.87 M (0.40 mol) butyllithium in ether was cooled to − 70 °C, whereupon 96.5 g (0.350 mol) of 5-chloro-2,3-dibromothiophene[28] dissolved in 200 ml of ether was added in a slow stream. After stirring for 20 min the reaction mixture was poured into water and worked up in the usual manner. Distillation gave 36.3 g (53 %) of 4-bromo-2-chlorothiophene at 68.0 − 71.5 °C/10 mmHg. Lit. value:[9] 70 − 72 °C/12 mmHg (Column: A).

2-Chloro-4-thiophenecarboxylic acid. 40 ml of 0.82 M (0.033 mol) butyllithium in ether was cooled to − 70 °C, whereupon 6.0 g (0.030 mol) of 4-bromo-2-chlorothiophene dissolved in 30 ml of ether was added in a slow stream keeping the temperature below − 48 °C. After stirring for an additional 20 min, the reaction mixture was poured onto dry ice in ether. Water was added and the ether phase separated and extracted with dilute sodium hydroxide solution. The combined water phases were acidified with hydrochloric acid, whereupon the acid precipitated. Recrystallization from water-ethanol (1:1) gave 2.3 g (47 %) of 2-chloro-4-thiophenecarboxylic acid with m.p. 163 − 164 °C. Lit. value:[26] 156 − 157 °C (Column: B). NMR (acetone): δ 7.39 (H3, d, 1 H), 8.14 (H5, d, 1 H), and J (H3, H5) 1.6 Hz.

2-Chloro-4-iodothiophene. 70 ml of 0.89 M (0.062 mol) butyllithium in ether was cooled to − 70 °C, whereupon 11 g (0.056 mol) of 4-bromo-2-chlorothiophene dissolved in 60 ml of ether was added in a slow stream, keeping the temperature below − 60 °C. After stirring for an additional 25 min, the reaction mixture was poured through a rubber tube into a solution of 14.2 g (0.056 mol) of iodine in 70 ml of ether, also cooled to − 70 °C. Stirring was then continued for 1 h at − 70 °C. The cooling bath was removed, and after the temperature had reached 0 °C, the reaction mixture was poured into water. After separation of the ether phase, the water phase was extracted with ether. The combined ether phases were washed with water, sodium thiosulfate solution, and water, and dried over magnesium sulfate. Distillation gave 6.0 g (44 %) of 2-chloro-4-iodothiophene at 89.5 − 91.5 °C/10 mm (Column: A). NMR (CCl₄): δ 7.14 (H3 or H5, d, 1 H) and 7.36 (H5 or H3, d, 1 H). J (H3, H5) 1.5 Hz. [Calc. for C_4H_2ClIS (244.5): C 19.6; H 0.82; I 51.9. Found: C 19.6; H 0.86; I 50.2.]

3-Iodo-2-thiophenecarboxylic acid. To 15 ml of 1.00 M (0.015 mol) ethyllithium in ether

cooled to − 70 °C, 4.8 g (0.014 mol) of 2,3-diiodothiophene[4] dissolved in ether was added. The temperature was kept below − 60 °C. After stirring for an additional 10 min, the reaction mixture was carbonated and worked up as described for 2-chloro-4-thiophenecarboxylic acid. Recrystallization from water-ethanol (1:1) gave 1.6 g (45 %) of 3-iodo-2-thiophenecarboxylic acid with m.p. 199 − 201 °C. Lit. value:[32] 193 − 195 °C (Column: A). NMR (acetone): δ 7.33 (H4, d, 1 H), 7.77 (H5, d, 1 H), and 7.95 (COOH, s, 1 H). J (H4, H5) 5.1 Hz.

Stability of 2-chloro-4-thienyllithium. To 40 ml of 0.85 M (0.034 mol) butyllithium in ether, 6.2 g (0.031 mol) of 4-bromo-2-chlorothiophene in 70 ml of ether was added, keeping the temperature below − 51 °C. After stirring for an additional 15 min at − 70 °C, the cooling bath was removed and the reaction mixture stirred for 19 h at room temperature. One sample was taken up and hydrolyzed with water, a second sample was carbonated, and a third part was stirred at room temperature for an additional 24 h. By absorption at approximately 2180 cm⁻¹, IR analysis of the ether phase indicated the formation of acetylenic products from ring-opening reactions. Combined GLC-mass spectrometry also indicated the prevalence of acetylenic compounds. The carbonated product was worked up and esterified. However, no methyl thiophenecarboxylates could be observed upon analysis, which also indicates that ring-opening had occurred. Analysis of the part of the reaction mixture which was stirred for a longer period gave the same result (Columns: C, D).

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