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The Reaction of 2,3,4-Trichlorothiophene with Alkyllithium Reagents

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2,3,4-Trichlorothiophene undergoes metal-hydrogen exchange with one equivalent of butyllithium in *THF* at —78 °C to give trichloro-2-thienyllithium in 91% yield. No metal-halogen exchange is observed to have taken place. With *t*-butyllithium under similar conditions, however, the metal-halogen exchange reaction occurs but only to the extent of 8%; the main reaction remains to be the metal-hydrogen exchange. 2,3,4-Trichlorothiophene reacts with two equivalents of butyllithium in ether at —5 °C to give 3,4-dichloro-2,5-dilithiothiophene in 96% yield.

(Keywords: 3,4-Dichloro-2,5-dilithiothiophene; Lithium-chlorine exchange; Lithium-hydrogen exchange; Trichloro-2-thienyllithium; 2,3,4-Trichlorothiophene)

Die Reaktion von 2,3,4-Trichlorthiophen mit Alkyllithium-Reagentien

2,3,4-Trichlorthiophen geht mit einem Äquivalent Butyllithium (in *THF* bei —78 °C) einen Metall-Wasserstoff-Austausch ein, wobei Trichlor-2-thienyllithium in 91% Ausbeute entsteht; es wird keinerlei Metall-Halogen-Austausch beobachtet. Andererseits tritt mit *t*-Butyllithium unter ähnlichen Bedingungen sehr wohl Metall-Halogen-Austausch ein, allerdings nur zu 8%; die Hauptreaktion bleibt der Metall-Wasserstoff-Austausch. 2,3,4-Trichlorthiophen reagiert mit 2 Äquivalenten Butyllithium (in Ether bei —5 °C) mit 96% Ausbeute zu 3,4-Dichlo-2,5-dilithiothiophen.

Introduction

We reported recently[1] that 2,3,4-trichlorothiophene (**1**) reacts with metallic magnesium in *THF* to give a 1 : 1 mixture of trichloro-2-

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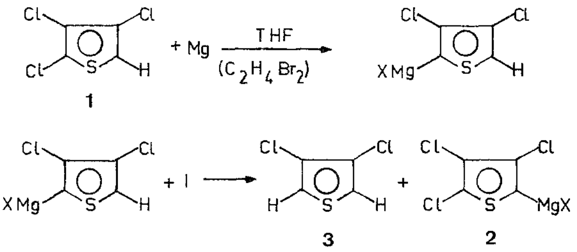
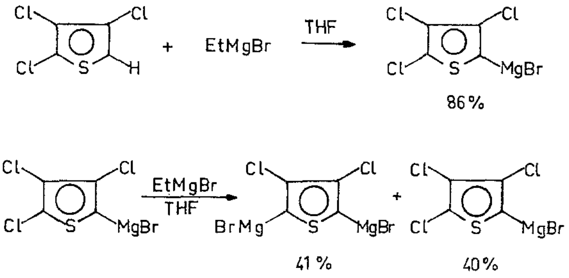
thienylmagnesium halide (**2**) and 3,4-dichlorothiophene (**3**). The reaction is believed to have taken place in steps as shown below:



2,3,4-Trichlorothiophene on the other hand reacts with one equivalent of ethylmagnesium bromide in *THF* to give trichloro-2-thienylmagnesium bromide in 86% yield. With two equivalents of ethylmagnesium bromide 2,3,4-trichlorothiophene affords a mixture of trichloro-2-thienylmagnesium bromide (40%) and 2,5-bis(bromomagnesium)-3,4-dichlorothiophene (41%)[2].



We report here the reaction of 2,3,4-trichlorothiophene with some alkyllithium reagents.

Experimental

The general conditions for organometallic reactions, equipment and materials used were as described before[3–6]. All temperatures quoted are uncorrected. The yields of various compounds were based on the starting amount of 2,3,4-trichlorothiophene.

The Reaction of 2,3,4-Trichlorothiophene with one Equivalent of Butyllithium

To a solution of 2,3,4-trichlorothiophene[1,4] (12.5 mmol) in *THF* (25 ml) at —78 °C was added butyllithium (12.5 mmol) over a period of 15 min. The mixture was stirred at this temperature for 3 h. During this time *Gilman* Test II[7] became negative. Durene (10 mmol) was added as the internal standard for quantitative glc and the mixture stirred for another 1 h. An aliquot was withdrawn, hydrolysed with dilute HCl and extracted with ether. Glc of this extract indicated that 2,3,4-trichlorothiophene (99%) was present in the reaction mixture. No 3,4-dichlorothiophene could be detected. Another aliquot was reacted with chlorotrimethylsilane and then examined by glc. The peak due to 2,3,4-trichlorothiophene had almost disappeared and trichloro-2-thienyltrimethylsilane[4] was formed as the major product (87%). The remaining part of the organolithium reagent was carbonated at —78 °C by adding solid carbon dioxide and slowly allowing the reaction mixture to come to room temperature. The customary work-up followed by recrystallisation from chloroform gave trichloro-2-thiophenecarboxylic acid (91%), m.p. 225-226 °C (reported[8] m.p. 224 °C), identical (ir) with an authentic sample prepared as described before[4].

The Reaction of 2,3,4-Trichlorothiophene with one Equivalent of t-Butyllithium

To a solution of 2,3,4-trichlorothiophene (12.5 mmol) in *THF* (25 ml) at —78 °C was added *t*-butyllithium (12.5 mmol) over a period of 15 min. The mixture was stirred for 2 h. During this period *Gilman* Test II[7] became negative. An aliquot was withdrawn, reacted with dil. HCl, and the organic material was extracted in hexane. A glc analysis of this (with durene as the internal standard) showed that the yield of 2,3,4-trichlorothiophene was 90% and that of 3,4-dichlorothiophene was 8%. Another aliquot when reacted with excess chlorotrimethylsilane and analysed as above showed that (trichloro-2-thienyl)trimethylsilane and (3,4-dichloro-2-thienyl)trimethylsilane were present in 20 : 1 glc area ratio. No bis-silyl derivative was formed. The carbonation of the mixture and the usual work-up gave trichloro-2-thiophenecarboxylic acid (76%), m.p. 225-226 °C as the only isolable acid.

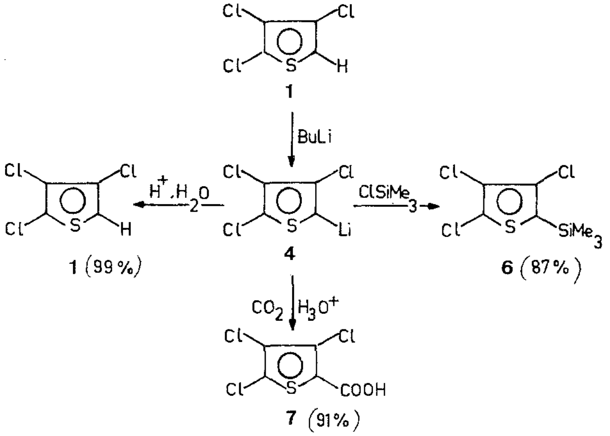
The Reaction of 2,3,4-Trichlorothiophene with two Equivalents of Butyllithium

To a solution of 2,3,4-trichlorothiophene (12.5 mmol) in diethyl ether (100 ml) at —5° to 0 °C was added butyllithium (25 mmol) over a period of 15 min and the reaction mixture was stirred for 6 h. The reaction was monitored by glc. Subsequent to carbonation, hydrolysis and the usual work-up, there was obtained 3,4-dichloro-2,5-thiophenedicarboxylic acid (96%), m.p. 327-328 °C (cited[9]: 328 °C), identified by undepressed mixed m.p. with an authentic sample prepared by a published[9] procedure.

When the above reaction was carried out in *THF* at —78 °C for 18 h, there were obtained, subsequent to carbonation and work-up, trichloro-2-thiophenecarboxylic acid (60%), m.p. 225-226 °C and 3,4-dichloro-2,5-thiophenedicaboxylic acid (15%), m.p. 327-328 °C. The yields of the mono- and dicarboxylic acids changed to 46% and 33% respectively when three molar equivalents of butyllithium per mol of 2,3,4-trichlorothiophene were used under essentially similar reaction conditions. The di/mono ratio did not alter appreciably when the reaction was carried out in *THF* at —5-0 °C for 6 h with two equivalents of butyllithium.

Results and Discussion

2,3,4-Trichlorothiophene (**1**) reacts with one equivalent of butyllithium in *THF* at —78 °C to give trichloro-2-thienyllithium (**4**) in high yield. This lithium reagent on hydrolysis gives **1** in 99%, on trimethylsilylation **6** in 87% and on carbonation **7** in 91% yields. No 3,4-dichlorothiophene is observed to have been formed in the above reactions. This indicates that the metal-hydrogen exchange is occurring at a rate much faster than that of metal-halogen exchange. However, with *t*-butyllithium (one equivalent) the metal-halogen exchange reaction does take place but to a small extent (8%) as is evidenced by the formation of 3,4-dichlorothiophene subsequent to hydrolysis (see Exp.). The major reaction, however, remains to be the metalation reaction (76%).



With two equivalents of butyllithium, 2,3,4-trichlorothiophene in *THF* at —78 °C gives, subsequent to carbonation, 3,4-dichloro-2,5-thiophenedicarboxylic acid (15%) and trichloro-2-thiophenecarboxylic acid (60%). The use of three-fold excess of butyllithium still gave a mixture of the two thiophenecarboxylic acids but the ratio of the yields of di- to mono-carboxylic acid increased by a small amount. Additionally, a similar mixture of trichloro-2-thiophenecarboxylic acid and 3,4-dichloro-2,5-thiophenedicarboxylic acid was obtained when 2,3,4-trichlorothiophene was treated with two equivalents of butyllithium in *THF* at —5° to 0 °C rather than at —78 °C. On the other hand, when the above reaction is carried out in diethyl ether rather than in *THF* at —5-0 °C the yield of 3,4-dichloro-2,5-thiophenedicarboxylic acid increases to 96%. These facts indicate the existence of an equilibrium of the following type:

The yield of the dicarboxylic acid and hence of the dilithio derivative is higher in ether than in *THF* because the dilithio derivative, being only slightly soluble in diethyl ether[9], is precipitated out. This probably is, atleast in part, responsible for the shift of the equilibrium position to the right. Such an equilibrium reaction was invoked by *Smith* and *Gilman*[9] to explain the formation of a mixture of trichloro-2-thiophenecarboxylic acid and 3,4-dichloro-2,5-thiophenedicarboxylic acid from the reaction of tetrachlorothiophene with an excess of butyllithium in *THF*.

The high yield of the dilithium reagent by our method makes it suitable for synthetic work. However, this dilithium reagent may also be prepared by reacting two equivalents of butyllithium with either the more commonly available tetrachlorothiophene[9] or with 3,4-dichlorothiophene[5]. The yield in the latter reaction is 71% but in the former it is 99% which is similar to ours.

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