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# Dehalogenation of Bromothiophenes with Butyllithium

SVEN-OLOV LAWESSON

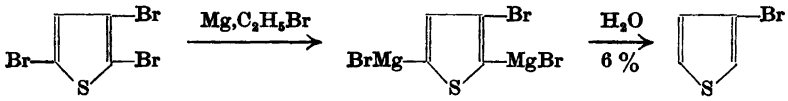
*Department of Organic Chemistry, Chemical Institute, University of Uppsala, Sweden*

Two new methods of preparing 3-bromothiophene and the preparation of a new compound, 3,5-dibromo-2-thiophencarboxylic acid, are described.

A possible route to 2,4-dibromothiophene is outlined.

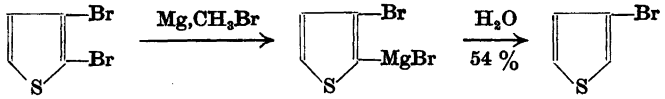
The author, who is investigating thiopheneboronic acids, needs as intermediates all isomers of the bromothiophenes. Some of these are troublesome to synthesize and the identity and purity of the product are not certain and, therefore, some preliminary experiments have been made in order to work out better methods. This paper deals with the preparation of 3-bromothiophene and 2,4-dibromothiophene.

As early as 1934, Steinkopf [1] prepared 3-bromothiophene according to the following reaction:




(Method I)

The yield was very low, but he did not abandon the method, neither did he try to improve it, strange to say. Instead, he prepared 3-bromothiophene by reacting 2,3-dibromothiophene with methylmagnesium bromide [2], *viz.*




(Method II)

Gronowitz [3] has recently improved both the methods of Steinkopf. By refluxing 2,3,5-tribromothiophene with magnesium for 49 hours, using ethyl bromide as entraining agent and then hydrolysing the Grignard reagent, he got 3-bromothiophene in a yield of 51 %. Using Steinkopf's method II, Gronowitz got 3-bromothiophene in a good yield.

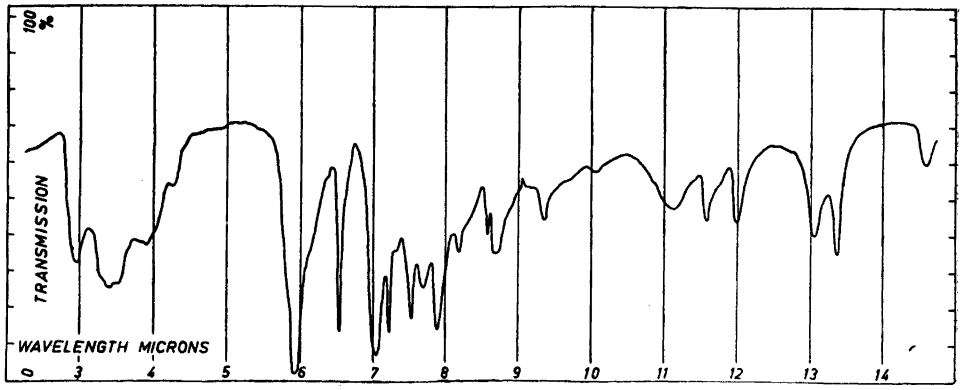



*Fig. 1. The infrared spectrum of 4,5-dibromo-2-thiophenecarboxylic acid (in pressed KBr).*

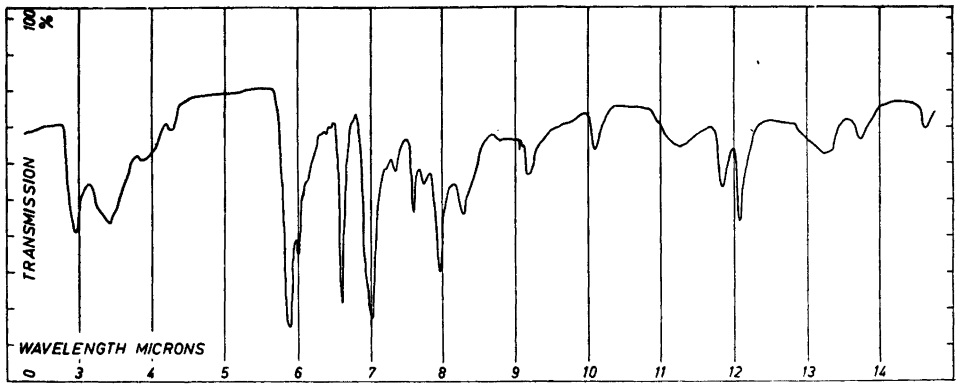
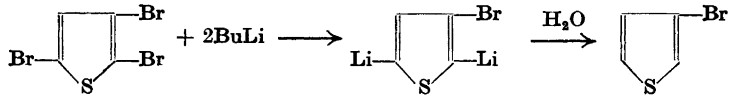



*Fig. 2. The infrared spectrum of 3,5-dibromo-2-thiophenecarboxylic acid (in pressed KBr).*

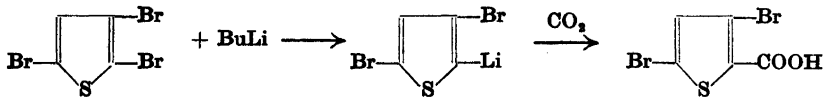
All these methods seem to be tedious and very time-consuming. We have instead brought together one mole of 2,3,5-tribromothiophene [4] and two moles of butyllithium [5] and obtained, after hydrolysing the lithium compound, 3-bromothiophene, through the reaction:




(Method III)

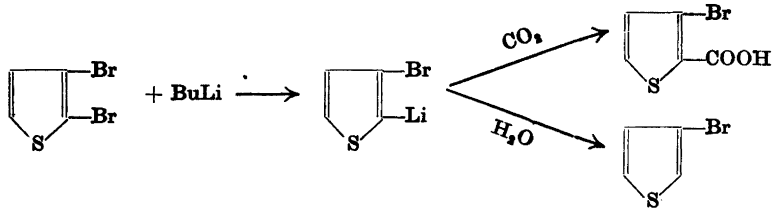
If the reaction was carried out with a 1 : 1 molar ratio of the 2,3,5-tribromothiophene and the butyllithium, at —70°, we obtained, after pouring the solution onto dry ice, a substance with a melting point 15° lower than that of 4,5-dibromo-2-thiophenecarboxylic acid [1]. The IR spectra (Figs. 1 and 2) showed

great differences in the finger-print region between 4,5-dibromo-2-thiophenecarboxylic acid, prepared by brominating 2-thiophenecarboxylic acid, and the new compound. Even in chloroform solution the differences remained, and consequently, the possibility of polymorphism is excluded. As a matter of fact, the occurrence of the following reaction is proposed:




From this it is seen that if instead of pouring the monolithium reagent on dry ice, we hydrolyse it, 2,4-dibromothiophene should be obtained. Investigation in this field is in progress at this Institute.

By treating 2,3-dibromothiophene[6] with an equimolar amount of butyllithium, 3-bromothiophene was obtained in good yields after hydrolysis. If the lithium reagent was poured onto dry ice, 3-bromo-2-thiophenecarboxylic acid[1] was isolated, as a result of the reaction:




(Method IV)

The infrared spectra were recorded with a Perkin-Elmer spectrophotometer (model 21) equipped with NaCl optics.

## EXPERIMENTAL

*3-Bromothiophene* (*Method III*). A solution of 0.2 mole of butyllithium in 250 ml dry ether was added dropwise, over a period of 90 minutes, to an ice-cold solution of 2,3,5-tribromothiophene (32 g, 0.1 mole) in 200 ml of dry ether. The reaction was carried out under nitrogen, with stirring. The resulting yellow suspension was poured into ice-water. The organic layer was separated off and the water phase shaken several times with ether. The combined extracts were washed once with water, dried over sodium sulfate, and then concentrated. The residue was distilled, yielding 10.5 g of 3-bromothiophene, b.p. 58°/20 mm Hg, (identified by means of the IR spectrum), and 2 g of dibromothiophenes, b.p. 94°–96°/15 mm Hg. Yield of 3-bromothiophene: 65 %.

*3,5-Dibromo-2-thiophenecarboxylic acid.* 21 ml of 1.5 M butyllithium in dry ether was added, in a slow stream, to 10 g of 2,3,5-tribromothiophene in 100 ml of ether, at −70°. The solution was stirred for 5 minutes and then treated all at once with an excess of powdered solid carbon dioxide. After the dry ice had evaporated, the mixture was hydrolysed with water, the organic layer separated off, the water solution extracted with ether, and the combined ether layers extracted with dilute sodium hydroxide. Upon acidification of the alkaline solution, a white powder precipitated; this, after recrystallisation from water-ethanol solution, yielded small, faintly yellow-coloured, needles. Weight: 3.2 g, yield 36 %. M.p. 210–212°C.

Anal Subst. 44.30 mg; 3.11 ml of 0.0495 M NaOH
27.60 mg; 9.88 ml of 0.00978 M $Hg(NO_3)_2$
$C_5H_2Br_2O_2S$ Calc. Equiv. wt. 285.95 Br 56.19
Found » » 288.0 Br 55.98

*3-Bromothiophene* (*Method IV*). Butyllithium (0.09 mole) in 150 ml of dry ether was added with stirring over a 45-minute period to 20 g (0.083 mole) of 2,3-dibromothiophene in 150 ml of ether at 0°C. The solution was hydrolysed, and after being worked up as usual was distilled, giving 7.9 g of 3-bromothiophene (b.p. 44°—46°/11 mm Hg). Yield 58 %.

The yield ought to be better, but the optimum conditions have not been worked out, since this method is inferior to method III and more time-consuming.

*3-Bromo-2-thiophenecarboxylic acid.* Into 10 g of 2,3-dibromothiophene in 50 ml of ether, at −40°, was poured 23 ml of 1.5 M butyllithium. The reaction was carried out under nitrogen, with stirring; after 7 minutes, the solution was poured onto dry ice and worked up in the usual way. Recrystallisation from water-ethanol solution gave white needles with m.p. 193°—195°C. Weight: 6 g; yield 70 %.

Anal. Subst., 24.30 mg; 2.37 ml of 0.0495 M NaOH. Equiv. wt. Calc. 207.1; Found 207.2.

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## REFERENCES

1. Steinkopf, W., Jacob, H. and Penz. H. *Ann.* **512** (1934) 136.
2. Steinkopf, W. *Ibid.* **543** (1940) 128.
3. Gronowitz, S. *Arkiv Kemi* **7** (1954) 267.
4. Lawesson, S.-O. *To be published.*
5. Wittig, G. *Angew. Chem.* **53** (1940) 241.
6. Steinkopf, W. and Köhler, W. *Ann.* **532** (1937) 250.

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