

Substituted Geminal Dithienyltetrahydrofurans via an Intramolecular Williamson Reaction

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Substituted dithienylbutenes were first prepared by Kleeman *et al.*¹ who described the synthesis of 3-bromo-1,1-bis(3-thienyl)-1-propene. In our laboratory a similar reaction was carried out with 2-lithio-5-methylthiophene and ethyl 4-bromobutyrate (Scheme 1) and it was observed that the nature of the reaction product was dependent upon the reaction temperature. When the temperature was kept below ca. 10 °C the expected product (1) was formed after the reaction had been quenched with water. When the reaction mixture was allowed to reach room temperature 2,2-bis(5-methyl-2-thienyl)tetrahydrofuran (2) was obtained. The formation of 2 is probably due to the increased reactivity of the alkoxide at room temperature and the intramolecular nature of this Williamson reaction.

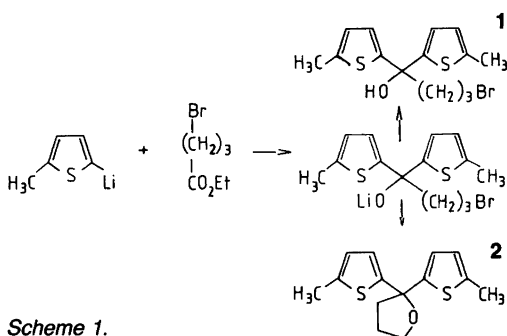
The same procedure, when used for other lithiothiophenes, also yields tetrahydrofurans, thus the method has generally application. Table 1

shows some tetrahydrofurans which were prepared using the appropriate starting materials.

Asymmetrically substituted dithienyl compounds can be prepared by treating 2-(4-chlorobutyryl)thiophene with 2-thienyllithium. The yields are not as high as those in the reactions described above owing to the considerable amount of cyclopropyl 2-thienyl ketone formed. Thus 2-(3-bromo-2-thienyl)-2-(2-thienyl)tetrahydrofuran (6) was prepared in 34 % yield.

The above-mentioned tetrahydrofurans have been used to introduce other functional groups into the thiophene ring. 2,2-Bis(2-thienyl)tetrahydrofuran has been nitrated with nitric acid in acetic anhydride² to yield 2,2-bis(5-nitro-2-thienyl)tetrahydrofuran (7) in 68 % yield. The position of the nitro groups was determined by nuclear Overhauser experiments.

2,2-Bis(3-bromo-2-thienyl)tetrahydrofuran (4) has been treated with CuCl–DMF³ to yield 2,2-bis(3-chloro-2-thienyl)tetrahydrofuran (8). Compound 4 has also been converted into the lithium derivative⁴ with BuLi–Et₂O–70 °C which was then allowed to react with acetaldehyde. The resulting 2,2-bis-[3-(1-hydroxyethyl)-2-thienyl]tetrahydrofuran was oxidized with pyridinium chlorochromate–CH₂Cl₂⁵ to the corresponding ketone (9) in 87 % overall yield. The asymmetric compound (6) has been converted into the azide⁶ 10 using BuLi–Et₂O; –65 °C–dry ice–aq. HCl. All compounds showed satisfactory microanalyses and NMR spectra. Most of the dithienyltetrahydrofurans underwent ring opening to the corresponding butenols (Scheme 2).



Scheme 1.

SHORT COMMUNICATION

Table 1. Novel tetrahydrofurans^a prepared from the appropriate starting materials.

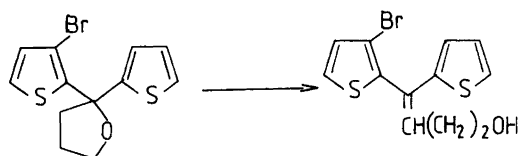
Compound	M.P./°C	Yield/%	
3	2,2-Bis(5-bromo-2-thienyl)-	82	68
4	2,2-Bis(3-bromo-2-thienyl)-	88–92	60
5	2,2-Bis(2-thienyl)-	45–46	70

^aAll compounds showed satisfactory microanalyses and NMR spectra.

Experimental

NMR spectra were recorded on a Bruker WM-400 spectrometer.

In a typical experiment 2.2 equiv. of butyllithium (2.5 mol l⁻¹ in hexane) and diethyl ether were cooled to -65°C and 2 equiv. of 2-methylthiophene in diethyl ether were added slowly. After 1 h at -65°C, 1 equiv. of ethyl 4-bromobutyrate in diethyl ether was added and the reaction mixture was kept at -65°C for 3 h. Quenching the reaction at -10°C with water and subsequent extraction with diethyl ether yielded **1** in 97% yield. When the reaction mixture was kept at room temperature overnight and then treated with water, **2** was formed in 85% yield and showed the following chemical shifts: ¹H NMR (400 MHz; CDCl₃): 2.02 (2 H, quintet, *J* 8 Hz), 2.39 (6 H, s), 2.50 (2 H, t, *J* 8 Hz), 6.52 (2 H, d, *J* 4 Hz), 6.65 (2 H, d, *J* 4 Hz).



Scheme 2.

Tetrahydrofuran ring-opening reaction. In a typical experiment 10 mmol of dithienyltetrahydrofuran were dissolved in 70 ml of isopropyl alcohol and 10 ml of concentrated aqueous HCl on a steam bath. The solution was kept on the steam bath until the starting material has been consumed, as indicated by TLC. The desired butenols were recovered as oils in high yields.

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