Novel Cyclisation of 1-(Alkyl- or phenyl-thio)-4-(methylthio)buta-1,3-dienes to Thiophen Derivatives

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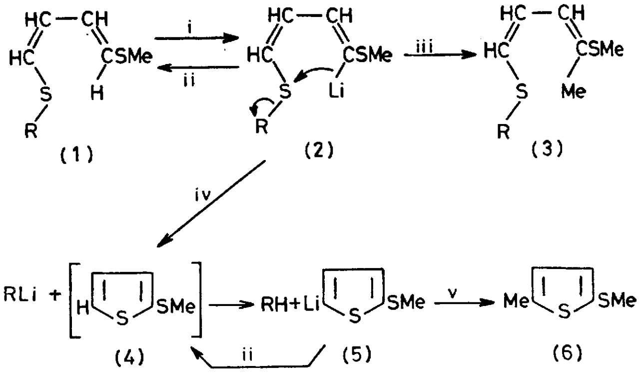
Summary Lithiated bis-sulphides (**2**) in tetrahydrofuran undergo at room temperature, preferably in the presence of some hexamethylphosphoric triamide, a ring closure to 2-(methylthio)thiophen (**4**) *via* nucleophilic attack on sulphur.

In the course of our investigations concerning the metallation of unsaturated ethers and sulphides[1] we have studied the reaction of the 1-*cis*-3-*trans*-bis-sulphides (**1**; R = alkyl or Ph). At low temperatures (−40 °C) these compounds are monometallated with 1 equiv. of n-butyl-lithium in tetrahydrofuran (THF)–tetramethylethylenediamine (TMEDA); the ^{1}H n.m.r. spectra and g.l.c. analyses of the compounds obtained by subsequent methylation with MeI showed that lithium had been introduced exclusively at the *trans* double bond, adjacent to the SMe group.†



Scheme. i, Bu^{n}Li THF, TMEDA, −40 °C; ii, H_2O; iii, MeI, −40 °C; iv, 25—30 °C; v, MeI.

When the methylation of the reaction mixture from (**1**; R = Me or Ph) and butyl-lithium was carried out after it had been kept for a few minutes at about 25 °C, significant amounts of 2-methyl-5-(methylthio)thiophen (**6**) were detected along with the methylated bis-sulphide (**3**). Hydrolysis, instead of methylation, afforded 2-(methylthio)thiophen (**4**) and the starting compound. After lengthening of this interval to 2 h, methylation and hydrolysis resulted in the exclusive formation of the thiophen derivatives (**6**) and (**4**). The addition of 20%

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† All compounds had a purity of at least 96%, as indicated by ^{1}H n.m.r. spectroscopy and g.l.c. analysis.

v/v of hexamethylphosphoric triamide (HMPA) caused rapid cyclisation of the metallated compounds within a few minutes at room temperature. The thiophen derivatives (**6**) and (**4**) were isolated in 75—80% yields. In the case of R = Ph, benzene could be detected in the product mixture obtained after hydrolysis. The facts described above suggest that the reaction takes place *via* the mechanism shown in the Scheme.

The crucial step in this proposed mechanism is the internal nucleophilic attack of the negative sp^2-carbon centre on the sulphur atom of the SR-group leading to expulsion of the more strongly basic RLi, the driving force being the formation of the (aromatic) thiophen derivative (**4**). The latter compound is, of course, immediately metallated at the 5-position by RLi.‡ The ^{1}H n.m.r. spectrum recorded during the reaction showed the conversion of (**2**) into (**5**). In the presence of 20% v/v of HMPA, even the bis-sulphides with R = Et and Bu^t were converted into the thiophen derivatives in 63 and 35% yields, respectively. CIDNP and e.s.r. spectroscopic experiments did not give any indication of a free-radical mechanism.

Nucleophilic elimination of methyl-lithium has recently been observed in reductive aromatization of cyclohexa-1,4-diene ring to a benzene ring.[2] Our reaction is, to the best of our knowledge, totally unprecedented.

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‡ This metallation was also observed in a separate experiment with 2-(methylthio)thiophen and BuLi; reaction with MeI afforded 2-methyl-5-(methylthio)thiophen.

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