A Novel Debromination in the Thiophen Series

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Summary Di-, tri-, and tetra-bromothiophens readily undergo partial debromination when treated with sodium alkoxides in dimethyl sulphoxide.

IN an attempt to prepare 2,5-dimethoxythiophen by adaption of the literature method for the synthesis of monomethoxythiophens,[1] 2,5-dibromothiophen was treated with sodium methoxide and cupric oxide in methanol. The reaction gave the known[1] 2-bromo-5-methoxythiophen in low yield, and none of the desired 2,5-dimethoxy-compound.

In the hope of effecting nucleophilic displacement of bromine, 2,5-dibromothiophen was then treated with sodium methoxide in dimethyl sulphoxide (DMSO), a solvent known to increase alkoxide nucleophilicity.[2] At room temperature 2-bromothiophen was formed rapidly in an exothermic reaction, with no methoxythiophens detectable in the product. The reaction of several bromothiophens with bases in DMSO was therefore studied, and the results with methoxide are summarised in the Table.

Under conditions which effected debromination in the thiophen series both 2-chloro- and 2-bromo-pyridine rapidly gave high yields of 2-methoxypyridine while 3-bromopyridine did not react at all.

The mechanism of the debromination is under investigation. It may be that the DMSO anion, arising in reaction (1), is involved since phenoxide, which is not a sufficiently

$$\text{Base}^- + CH_3SOCH_3 \longrightarrow \text{BaseH} + {}^-CH_2SOCH_3 \quad (1)$$

strong base to bring this about, fails to cause reduction, whereas isopropoxide and t-butoxide are as effective as methoxide. The slow reduction of 2,5-dibromo- to 2-bromothiophen by sodium hydride–DMSO supports this view.

Moreover, when DMSO was replaced by dimethylformamide, the reaction of 2,5-dibromothiophen with methoxide followed a different path. The major products were 3,4-dibromo- and 2,3,4-tribromo-thiophen, with minor amounts of 2- and 3-bromothiophen. A similar rearrangement of 2-bromothiophen to 3-bromothiophen under the influence of sodamide has been reported.[3]

TABLE

Starting thiophen	Thiophen formed[a] (% yield)
2,5-Dibromo	2-Bromo (65%)[b]
	2-Bromo (75%)[c]
2,3-Dibromo	3-Bromo (67%)[c]
2,3,5-Tribromo	2,4-Dibromo (major product) +2,3-Dibromo and 3-bromo (minor products)
2,3,4,5-Tetrabromo	3,4-Dibromo (1 part) +2,3,4-tribromo (4 parts)[b]
	3,4-Dibromo (3 parts) +2,3,4-tribromo (2 parts)[c]

[a] The identity of all products confirmed by g.l.c. and spectroscopic comparison with authentic specimens. [b] With 1 mol. equiv. of methoxide. [c] With 2 mol. equiv. of methoxide.

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[1] J. Sicé, *J. Amer. Chem. Soc.*, 1953, 75, 3697.
[2] See *e.g.*, A. J. Parker, *Adv. Org. Chem.*, 1965, 5, 1.
[3] M. G. Reinecke and H. W. Adickes, *J. Amer. Chem. Soc.*, 1968, 90, 511.