# Reductive Cleavage of Ether and Thioether Bonds on 1,3-Benzodioxole and 1,3-Benzoxathiole Derivatives



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The reaction of lithium and sodium diethylamide with 1,3-benzodioxoles and 1,3-benzoxathioles is here reported. 1,3-Benzodioxoles exhibit selective cleavage of the ether bond with formation of alkoxyphenols; 1,3-benzoxathioles when reacting with sodium diethylamide lead to 2-alkoxybenzenethiols while with lithium diethylamide give 2-alkoxybenzenethiols together with 2-(alkylthio)phenols.

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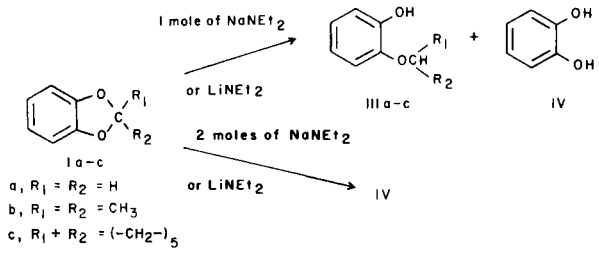
Previously we examined cleavage reactions of the ether bond by Grignard reagents in 1,3-benzodioxole and 1,3-benzoxathiole derivatives. These reactions have been shown to be exploitable for the synthesis of 2-substituted phenols, alkanes and alkenes [1]. Moreover we recently reported the selective cleavage of the thioether bond by sodium and lithium diethylamide [2].

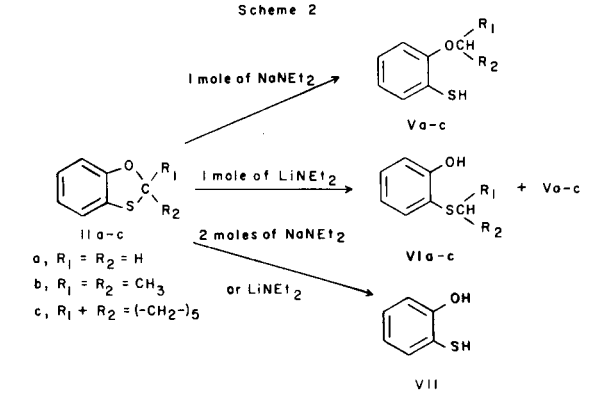
In this work we extend the latter research examining the reaction of 1,3-benzodioxole and 1,3-benzoxathiole derivatives with lithium and sodium diethylamide, with the aim of getting more information about the behaviour of the above mentioned reagents towards cyclic ethers and thioethers, and verifying if this reaction is exploitable for synthetic purposes.

The reactions have been carried out treating one mole of the 1,3-benzodioxoles (Ia-c) or the 1,3-benzoxathioles (IIa-c) with equimolar amounts or two moles of lithium or sodium diethylamide in a mixture of benzene-hexamethylphosphoric acid triamide. The reaction products have been analyzed by glc and identified by comparison with authentic samples.

Scheme 1




Scheme 2




The results, listed in Table I, show that both lithium

Table 1

Action of *N,N*-Diethylamides on 1,3-Benzodioxoles and 1,3-Benzoxathioles

| Starting Material | Amide | Amide to substrate ratio | Products | Yield (%) |
|---|---|---|---|---|
| Ia | $NaNEt_2$ | 1 | IIIa | 55 |
| | | | IV | 21 |
| | | 2 | IV | 85 |
| | $LiNEt_2$ | 1 | IIIa | 35 |
| | | | IV | 16 |
| | | 2 | IV | 68 |
| Ib | $NaNEt_2$ | 1 | IIIb | 48 |
| | | | IV | 30 |
| | | 2 | IV | 88 |
| | $LiNEt_2$ | 1 | IIIb | 32 |
| | | | IV | 19 |
| | | 2 | IV | 65 |
| Ic | $NaNEt_2$ | 1 | IIIc | 51 |
| | | | IV | 33 |
| | | 2 | IV | 83 |
| | $LiNEt_2$ | 1 | IIIc | 33 |
| | | | IV | 24 |
| | | 2 | IV | 66 |
| IIa | $NaNEt_2$ | 1 | Va | 78 |
| | | 2 | VII | 73 |
| | $LiNEt_2$ | 1 | Va | 40 |
| | | | VIa | 20 |
| | | 2 | VII | 64 |
| IIb | $NaNEt_2$ | 1 | Vb | 69 |
| | | 2 | VII | 71 |
| | $LiNEt_2$ | 1 | Vb | 46 |
| | | | VIb | 25 |
| | | 2 | VII | 57 |
| IIc | $NaNEt_2$ | 1 | Vc | 73 |
| | | 2 | VII | 75 |
| | $LiNEt_2$ | 1 | Vc | 49 |
| | | | VIc | 31 |
| | | 2 | VII | 56 |

and sodium amides react similarly with Ia-c giving 2-alkoxyphenols (IIIa-c) and 1,2-benzodiol (IV) by reductive cleavage of one or both the ether bonds (Scheme 1). Higher yields are obtained in the case of the sodium derivative.

In the case of IIa-c the reaction with the sodium amide leads to selective cleavage of the thioether bond using a molar ratio of 1:1. When 1,3-benzoxathiole and sodium amide were used in the ratio of 1:2 both the ether and thioether bonds were cleaved. The reaction of the lithium amide shows a much lower selectivity giving cleavage of both the bonds with higher yields of alkoxybenzenethiols (Scheme 2).

The sodium diethylamide that gives higher yields reacts as a more effective cleavage reagent probably because of the less request for solvation of the amidure ion [2]. Conversely, the presence of the phenols (VIa-c) in the reactions with lithium diethylamide was unexpected and in contrast with the results obtained with the open chain ethers. Possibly, in this case an important role is played by the ring strain and the coordination of the lithium cation with the ether oxygen.

## EXPERIMENTAL

Benzene was freshly distilled from the lithium aluminum hydride prior to use; hexamethylphosphoric acid triamide was distilled over calcium hydride and stored in the dark over molecular sieves 4Å. The glc analyses were performed on a Carlo Erba 4200 instrument equipped with SE 52 column (1 m × 0.2 cm, 3% on chromosorb W80-100 M).

### Starting Materials.

1,3-Benzodioxole (Ia-c) and 1,3-benzoxathiole derivatives (IIa-c) were prepared by reported methods [1a, 3-5].

### Authentic Samples.

2-Methoxyphenol (IIIa) and 1,2-benzodiol (IV) were commercial products (Aldrich Chemical Company). 2-Isopropoxy- (IIIb), 2-cyclohexyloxy- (IIIc), 2-(methylthio)- (VIa), 2-(isopropylthio)- (VIb) and 2-(cyclohexylthio)-phenol (VIc), 2-methoxy- (Va), 2-isopropoxy- (Vb), 2-cyclohexyloxy- (Vc) and 2-hydroxy-benzenethiol (VII) were prepared by procedures described in the literature [1a, 6-9].

### General Procedure for the Reactions with Sodium Diethylamide.

Diethylamine (0.04 or 0.08 mole) was added dropwise at 45° under a stream of nitrogen to a stirred suspension of sodium hydride (0.04 or 0.08 mole) in dry benzene (10 or 20 ml) and hexamethylphosphoric acid triamide (0.04 or 0.08 mole). After 15 minutes, the starting material (0.04 mole) in dry benzene (8 ml) was added and the mixture heated under reflux for 12 hours. After cooling the mixture was poured into water, acidified with 10% aqueous hydrochloric acid and extracted with diethyl ether. In the case of the reactions of Ia-c, the combined extracts were dried over sodium sulphate, analyzed by glc and compared with authentic samples.

In the case of the reactions of IIa-c, the extracts were treated with concentrated hydrochloric acid and zinc powder and then steam distilled. The products were extracted from the aqueous mixture with diethyl ether, dried over sodium sulphate, analyzed by glc and compared with authentic samples.

The phenol or benzenethiol derivatives were then extracted with 10% aqueous sodium hydroxide, separated with 10% hydrochloric acid and extracted wtih diethyl ether. After drying over anhydrous sodium sulphate, the solvent was evaporated and the residue chromatographed on a silica gel column using petroleum ether (40-70°)-diethyl ether (5:1) as eluent.

The results are listed in Table 1.

### General Method for the Reactions with Lithium Diethylamide.

A solution of *n*-butyllithium in hexane (29 ml, 0.04 mole, or 58 ml, 0.08 mole) was added dropwise under nitrogen to a stirred solution of diethylamine (0.04 or 0.08 mole) and hexamethylphosphoric acid triamide (0.04 or 0.08 mole). When the addition was complete, a mixture of starting material (0.04 mole) in dry benzene (8 ml) was added at once. The reaction mixture was heated for 12 hours and worked up in the same manner as above described.

The results are listed in Table 1.

### Acknowledgement.

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