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CLEAVAGE OF THE ETHER BOND

X *. THE ACTION OF ORGANOCALCIUM HALIDES ON 1,3-BENZOXATHIOLE AND 1,3-BENZODIOXOLE DERIVATIVES

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Summary

Some reactions of 1,3-benzoxathiole and 1,3-benzodioxole derivatives with organocalcium halides are described. GLC analysis of the reaction products of 1,3-benzoxathiole shows that ether bond cleavage mainly occurs, with formation of substitution, elimination and reduction products; there is also a small amount of reductive cleavage of the thioether bond. Cleavage of only one ethereal bond occurs in the reactions of 1,3-benzodioxole. A probable reaction mechanism is discussed.

Introduction

Our recent studies of the reactions of Grignard reagents with 1,3-benzoxathiole and 1,3-benzodioxole derivatives showed that organomagnesium derivatives behave as nucleophiles, bases and hydride ion donors [1] to give substitution, elimination and reduction products, respectively.

Organo-magnesium and -calcium derivatives have been found [2] to give different products in their reactions with ketones, reduction being the main process which occurs with Ca derivatives while the alcohol resulting from addition is only a minor product. A radical mechanism has been invoked to explain these results [2].

We have now investigated the reactions of 1,3-benzoxathiole and 1,3-benzo-

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dioxole derivatives with organocalcium compounds to determine whether ether and/or thioether bond cleavage occurs.

Results and discussion

Alkyl- and aryl-calcium halides were treated with 1,3-benzoxathiole (I) and 1,3-benzodioxole derivatives (II) (both unsubstituted and substituted in the 2-position). The reaction products were analyzed by gas—liquid chromatography (GLC) and characterized by comparison with authentic samples. Gaseous olefins were characterized as dibromo derivatives. The reaction was carried out in benzene or toluene to avoid competitive attack of the organocalcium derivative on the solvent in which it was initially prepared (THF) [2,3].

On the basis of the results, given in Tables 1—3, it can be seen that: (i). The yields resulting from these cleavage reactions are much lower than those obtained with the corresponding organomagnesium derivatives. (ii). The variety of products, as shown by GLC, is greater than with Grignard reagents. (iii). The main path is cleavage of the C—O bond, but products deriving from cleavage of the C—S bond are found. (iv). The same substitution, elimination and reduction products,

TABLE 1

THE REACTIONS OF METHYLCALCIUM IODIDE WITH 1,3-BENZOXATHIOLE AND 1,3-BENZODIOXOLE DERIVATIVES IN BENZENE SUSPENSION

Starting material	Products	Fraction [a,b] (%)		Material balance [a,c] (%)
1,3-Benzoxathiole (Ia)	2-Ethylthiophenol (IIIa)	(s)	88	
	2-Methylthiophenol (IIIb)	(r_{OH})	7	45
	2-Methoxybenzenethiol (Va)	(r_{SH})	5	
2,2-Dimethyl-1,3-benzoxathiole (Ib)	2-(t-Butylthio)phenol (IIIc)	(s)	60	
	2-Isopropylidenethiophenol (IVa)	(e)	26	33
	2-Isopropylthiophenol (IIId)	(r_{OH})	8	
	2-Isopropoxybenzenethiol (Vb)	(r_{SH})	6	
Spiro[1,3-benzoxathiole-2,1′-cyclohexane] (Ic)	2-[(α-Methylcyclohexyl)thio]phenol (IIIe)	(s)	55	
	2-Cyclohexylidenethiophenol (IVb)	(e)	32	30
	2-Cyclohexylthiophenol (IIIf)	(r_{OH})	9	
	2-Cyclohexyloxybenzenethiol (Vc)	(r_{SH})	4	
1,3-Benzodioxole (II)	2-Ethoxyphenol (VIa)	(s)	93	
	2-Methoxyphenol (VIb)	(r_{OH})	7	48

[a] All percentages were obtained by GLC analysis. [b] s and e = substitution and reduction products respectively; r_{OH} and r_{SH} = reduction products by C—O and C—S bond cleavage respectively. [c] Material balance = percentage of reacted starting material.

TABLE 2

THE REACTIONS OF PHENYLCALCIUM BROMIDE WITH 1,3-BENZOXATHIOLE AND 1,3-BENZODIOXOLE DERIVATIVES IN TOLUENE SUSPENSION

Starting material	Products derived from starting material	Fraction ^{a,b} (%)		Products derived from the organocalcium compound	Material balance ^{a,c} (%)
2,2-Dimethyl-1,3-benzoxathiole (Ib)	2-Isopropylidenethiophenol (IVa)	(e)	92	Biphenyl benzene	28
	2-Isopropylthiophenol (IIId)	(r_{OH})	5		
	2-Isopropoxybenzenethiol (Vb)	(r_{SH})	3		
Spiro[1,3-benzoxathiole-2,1'-cyclohexane] (Ic)	2-Cyclohexylidenethiophenol (IVb)	(e)	90	biphenyl benzene	25
	2-Cyclohexylthiophenol (IIIf)	(r_{OH})	6		
	2-Cyclohexyloxybenzenethiol (Vc)	(r_{SH})	4		
1,3-Benzodioxole (II)	2-Benzyloxyphenol (VIc)	(s)	91	biphenyl benzene	37
	2-Methoxyphenol (VIb)	(r_{OH})	9		

[a,b,c] See footnotes Table 1.

TABLE 3

THE REACTIONS OF ALKYL- AND ARYL-CALCIUM HALIDES WITH 2,2-DIMETHYL-1,3-BENZOXATHIOLE [a]

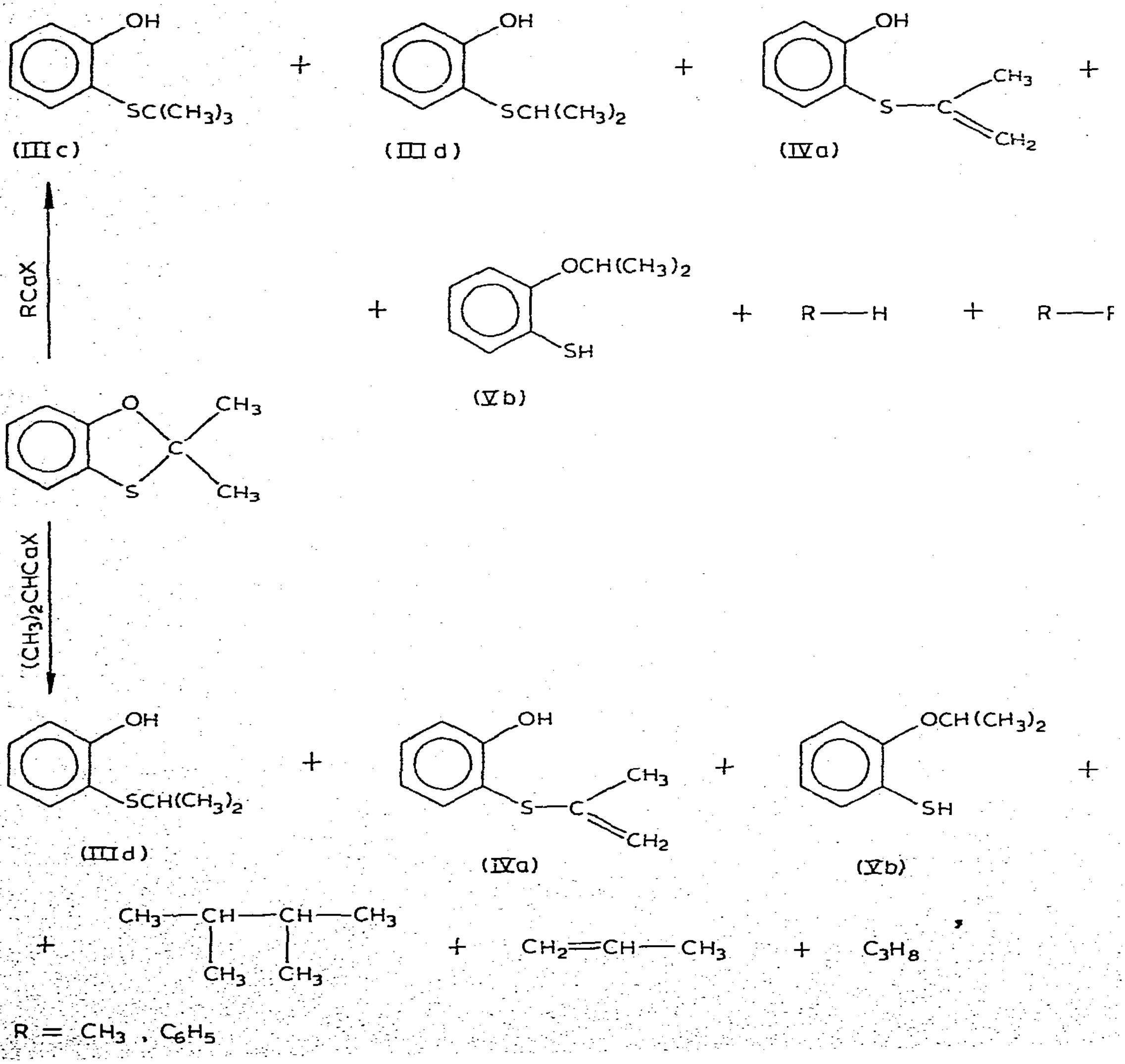
Organocalcium reagent	Subst. (%)	Elim. (%)	Redn.		Products derived from the organocalcium compound	Solvent	Material balance (%)
			ArOH (%)	ArSH (%)			
C_6H_5CaBr	0	90	6	4	Biphenyl benzene	Toluene	25
$CH_3(C_6H_5)CHCaBr$	0	70	24	6	2,3-Diphenylbutane Ethylbenzene Styrene	Benzene	21
$(CH_3)_2CHCaBr$	0	38	54	8	2,3-Dimethylbutane Propane Propene	Benzene	19
$(CH_3)_3CCaBr$	0	25	68	7	2,2,3,3-Tetramethylbutane 2-Methylpropane 2-Methylpropene	Toluene	18

[a] The gaseous alkenes were characterized as dibromo-derivatives; the gaseous alkanes were not characterized; The products are: (i) elimination = 2-isopropylidenethiophenol (IVa), (ii) ArOH reduction = 2-isopropylthiophenol (IIId) and (iii) ArSH reduction = 2-isopropoxybenzenethiol (Vb).

previously characterized in the reaction with organomagnesium derivatives, were obtained from cleavage of the C—O bond, whereas C—S bond cleavage is only of a reductive kind, being derived from attack on the aliphatic carbon. (v). The cleavage reactions of 1,3-benzodioxole involve only one oxygen atom in the heterocyclic ring. (vi). We have observed coupling of the organic radical of the organocalcium compound in all the cases examined.

In Scheme 1 we give the possible substitution (IIIc), reduction (IIId) and elimination (IVa) products from the reaction of 2,2-dimethyl-1,3-benzoxathiole with methyl-, phenyl- and isopropyl-calcium halides, together with the product (Vb) arising from reductive cleavage of the C—S bond and the compound resulting from coupling of the organic radical of the organocalcium compound.

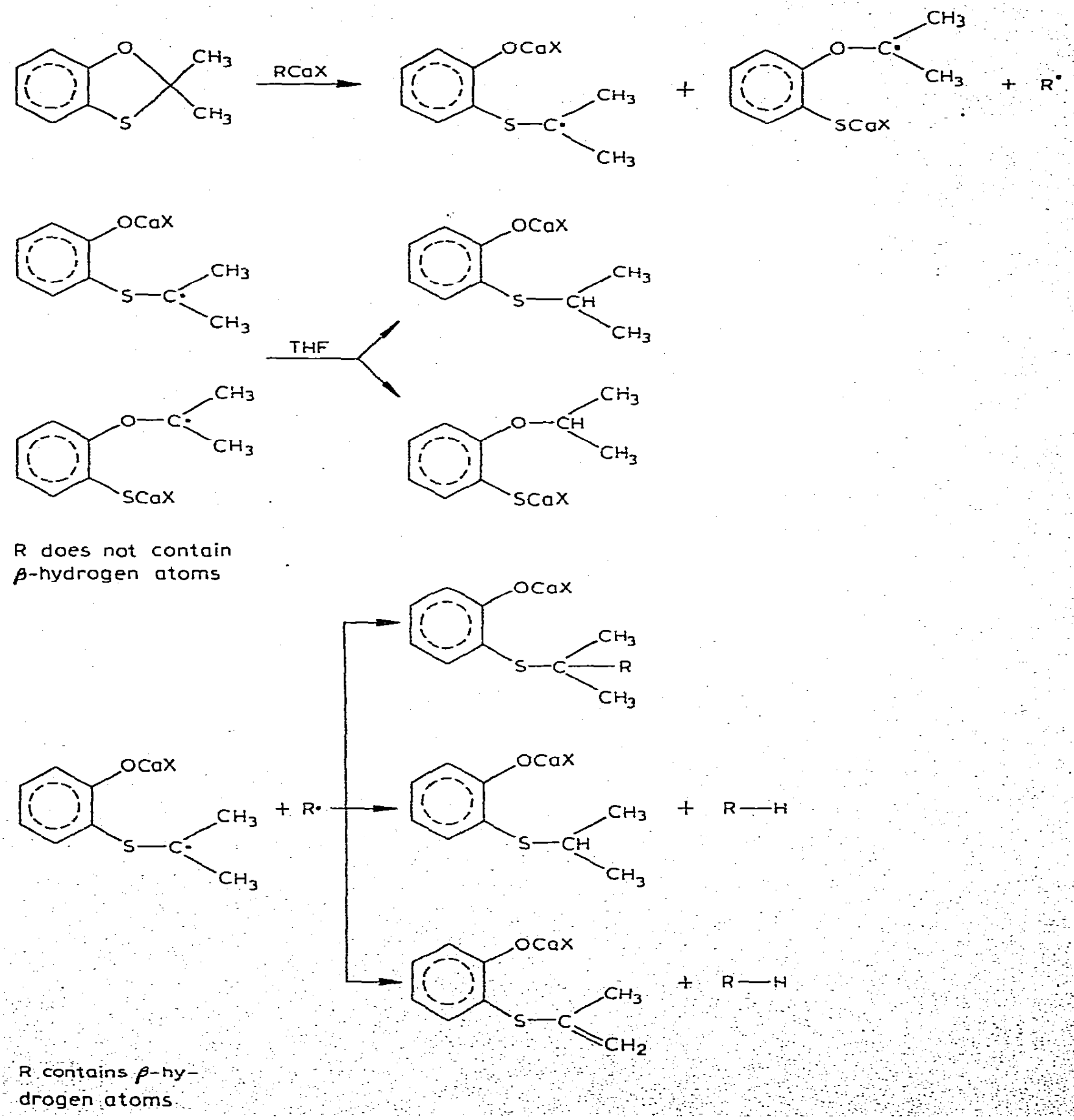
SCHEME 1



In the reaction with methyl- and phenyl-calcium halides (which lack β-hydrogen atoms) (see Tables 1 and 2), the formation of reduction products cannot be explained using the hypothesis suggested for the organomagnesium derivatives [1], but can be explained by assuming the formation of a radical species (as previously found in the case of ketones [2]). The free radical abstracts a hydrogen atom from tetrahydrofuran, (which cannot be completely removed from the reaction medium) to give the reduction product. The presence of 2,2′-octahydrobifuran in the product confirms this hypothesis.

When the organocalcium contains β-hydrogen atoms, it is these that are main-

SCHEME 2



ly responsible for the reductive process; in fact when we repeated these reactions using an organocalcium compound which contained β-hydrogen atoms (see Table 3), we observed an increase in reduction as the number of β-hydrogens increased.

The radical species (see Scheme 2) can give the products of: (i) reduction (if it is able to bond to the organocalcium radical), (ii) substitution and (iii) elimination (if it can transfer a β-hydrogen atom to the organometallic radical). This mechanism can also explain reductive cleavage of the C—S bond and coupling of the radical derived from the organocalcium compound.

However a concerted mechanism, as invoked for organomagnesium compounds, cannot be excluded, particularly in view of the preferential attack at the ether bond [1,4] and the observation that for these cleavages, the ratio of substitution, elimination and reduction products depends on the extent of steric hindrance in both the heterocyclic substrate and the organometallic compound [1].

Besides the reaction products considered above, others have been detected by GLC (though in much smaller yields). Attempts to characterize these are in progress and will be the subject of a further communication.

Experimental

General

GLC analyses were performed with a Perkin—Elmer 881 gas-chromatograph (equipped with a flame ionization detector and a polyethylene glycol 20 M column) using N_2 as the carrier gas.

Starting materials

1,3-Benzoxathiole (Ia), 2,2-dimethyl-1,3-benzoxathiole (Ib), spiro[1,3-benzoxathiole-2,1′-cyclohexane] (Ic) and 1,3-benzodioxole (II) were prepared by standard procedures [5—8].

Phenol and arylthiol derivatives

2-Ethylthio- (IIIa), 2-methylthio- (IIIb), 2-(t-butylthio)- (IIIc), 2-isopropylthio- (IIId), 2-[(α-methylcyclohexyl)thio]- (IIIe), and 2-cyclohexylthio-phenol (IIIf); 2-isopropylidenethio- (IVa) and 2-cyclohexylidenethio-phenol (IVb); 2-methoxy- (Va), 2-isopropoxy- (Vb) and 2-cyclohexyloxy-benzenethiol (Vc); and 2-benzyloxyphenol (VIc) were obtained as previously described [1,5,7,9,10,11]. Commercial 2-ethoxy- (VIa) and 2-methoxy-phenol (VIb) were used as supplied (FLUKA).

Hydrocarbon derivatives

2,3-Diphenylbutane and 2,2,3,3-tetramethylbutane were prepared by procedures described in the literature [12,13]. Biphenyl, ethylbenzene, styrene and 2,3-dimethylbutane were obtained as commercial products (FLUKA).

Halogen and dihalogen derivatives

Iodomethane, bromobenzene, 2-bromopropane, 2-bromo-2-methylpropane and 1,2-dibromopropane were obtained as commercial products (FLUKA). 1-Bromo-1-phenylethane and 1,2-dibromo-2-methylpropane were prepared by standard procedures [14,15].

The 2,2′-octahydrobifuran was prepared by procedures described in the literature [16].

Procedure in cleavage reactions

The organocalcium halide (0.07 mol) was prepared by literature [3,17] methods. The solvent was evaporated off at —10°C in a nitrogen stream and replaced by the same volume of anhydrous toluene or benzene (70 ml). The substrate (0.03 mol) was then added and the mixture refluxed with vigorous stirring for almost eight hours. Evolved gases were bubbled into a cooled solution of bromine in carbon tetrachloride and yielded dibromo derivatives. The reaction mixture was poured into an ice/water mixture, acidified with aqueous sulfuric acid (10%) and separated. After drying with anhydrous sodium sulphate, the mixture was analyzed by GLC and compared with authentic samples. The phenol and arylthiol derivatives were extracted with aqueous sodium hydroxide (10%), separated with 10% sulfuric acid, extracted with diethyl ether and analyzed by GLC. The neutral parts were separately analyzed by GLC. The dibromo derivatives, after removal of carbon tetrachloride, were characterized by comparison with authentic samples.

The results are listed in Tables 1—3.

Acknowledgement

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