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THE REACTIONS OF GRIGNARD REAGENTS WITH ORGANIC PEROXIDES AND DISULPHIDES

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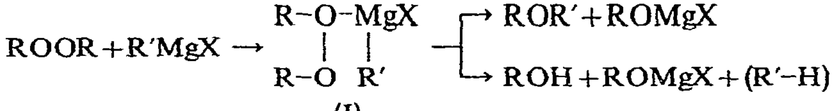
SUMMARY

The cleavage of dialkyl peroxides by Grignard reagents has been investigated. The influence of the structure of the reactants on reaction rates and product ratios has been studied. These reactions have been interpreted as radical processes and the ratio of alcohol and ether produced appears to be determined by the relative rates of radical combination and disproportionation. The reactions of dialkyl disulphides with Grignard reagents give exclusively monosulphides as products. Organolithium compounds have been shown to be more reactive than Grignard reagents in cleaving the disulphides, these reactions also have been interpreted as radical processes.

INTRODUCTION

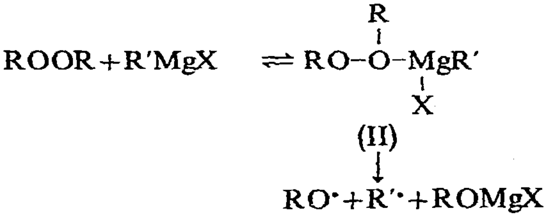
The reaction of Grignard reagents with di-tert-butyl peroxide was originally investigated by Campbell[1] and his co-workers who proposed that the initial step in this reaction was the formation of a peroxide–Grignard reagent complex (I) which could then decompose by either route (1) or (2).



$$\mathrm{ROOR+R'MgX} \rightarrow \begin{array}{c} \mathrm{R{-}O{-}MgX} \\ |\quad\ \ | \\ \mathrm{R{-}O\quad R'} \end{array} \begin{array}{ll} \rightarrow \mathrm{ROR'+ROMgX} & (1) \\ \rightarrow \mathrm{ROH+ROMgX+(R'{-}H)} & (2) \end{array}$$

(I)

The reaction of Grignard reagents with di-tert-butyl peroxides was subsequently investigated by Morrison and his co-workers[2-5]. They too suggested that this reaction followed two pathways, the first being identical to route (1), the other a concerted homolytic cleavage of the O–O and R–Mg bonds within the Lewis acid complex (II), and they proposed the following reaction scheme to account for the observed products:



$$\mathrm{ROOR+R'MgX} \rightleftharpoons \mathrm{RO{-}}\overset{\mathrm{R}}{\underset{}{\mathrm{O}}}\mathrm{{-}}\underset{\mathrm{X}}{\mathrm{MgR'}}\ \ \mathrm{(II)} \rightarrow \mathrm{RO^{\bullet}+R'^{\bullet}+ROMgX} \qquad (3)$$

$$2\,R'^{\bullet} \longrightarrow R'\text{–}R' \tag{4}$$

$$R'+R' \longrightarrow (R'+H)+(R'\text{–}H) \tag{5}$$

$$RO^{\bullet}+R' \longrightarrow ROH+(R'\text{–}H) \tag{6}$$

$$RO^{\bullet}+\text{ether solvent} \longrightarrow ROH \tag{7}$$

$$ROH+R'MgX \longrightarrow ROMgX+R'H \tag{8}$$

The possibility that the ether might be produced by combination of an alkyl and an alkoxy radical rather than by route (1) was considered. However, this idea was rejected because the heavy metal catalysed reactions which were presumed to be completely homolytic gave very low yields of the ethers[5]. The authors pointed out that they had no explanation for the apparent reluctance of alkoxy radicals to combine with alkyl radicals except that "it seems to be the nature of the radicals". Apparently this is not the case, since it has recently been shown by Sheldon and Kochi[6] that the decomposition of peroxy esters gives alkoxy and alkyl radicals which readily undergo cage recombination to form ethers. Whilst it has not yet been established whether ether formation is a heterolytic or homolytic process in the reaction of Grignard reagents with peroxides, we have made the assumption that this is a radical reaction and our results have been interpreted on this basis.

TABLE 1

YIELDS OF ALCOHOLS AND ETHERS FORMED IN THE REACTIONS OF PEROXIDES (4×10^{-3} mole) WITH GRIGNARD REAGENTS (24×10^{-3} mole)

Peroxide	Grignard reagent	Products			
		Ether	Yield (Mole × 10^3)	Alcohol	Yield (Mole × 10^3)
t-BuOO-t-Bu	n-BuMgCl	t-BuO-n-Bu	2.70	t-BuOH	5.20
t-BuOO-t-Bu	n-BuMgBr	t-BuO-n-Bu	2.42	t-BuOH	5.50
t-BuOO-t-Bu	n-BuMgI	t-BuO-n-Bu	1.82	t-BuOH	6.17
t-BuOO-t-Bu	AllylMgBr	t-BuOAllyl	3.10	t-BuOH	4.70
n-BuOO-n-Bu	t-BuMgCl	t-BuO-n-Bu	0.90	n-BuOH	6.80
n-BuOO-t-Bu	t-BuMgCl	t-BuO-n-Bu	0.53	n-BuOH	3.40 } 7.50
		t-BuO-t-Bu	0.00	t-BuOH	4.10
t-BuOO-t-Bu	t-BuMgCl	t-BuO-t-Bu	0.00	t-BuOH	7.90
t-BuOO-n-Bu	n-BuMgCl	t-BuO-n-Bu	1.38	t-BuOH	2.50 } 5.17
		n-BuO-n-Bu	1.21	n-BuOH	2.67
n-BuOO-n-Bu	n-BuMgCl	n-BuO-n-Bu	2.50	n-BuOH	5.50
t-BuOO-t-Bu	RMgBr[a]	t-BuOR[a]	3.46	t-BuOH	4.45

[a] $R=CH_2=CMeCH_2–$

We have carried out some preliminary investigations on the reactions of a series of organic peroxides and disulphides with various Grignard reagents. The purpose of our study was to evaluate these reagents for use as chemical probes for elucidation of the structure of polymer networks in which the polymer chains are joined by peroxide and sulphur bridges. Our main objective was to determine whether the peroxide and disulphide reacted quantitatively, consequently we investigated only the products derived from these compounds and did not examine in any detail the products formed solely from the Grignard reagent. We also examined the relative rates of a few of these reactions.

RESULTS AND DISCUSSION

The yields of alcohol and ether products resulting from the reactions of Grignard reagents with peroxides are summarised in Table 1, the relative rates are given in Fig. 1.

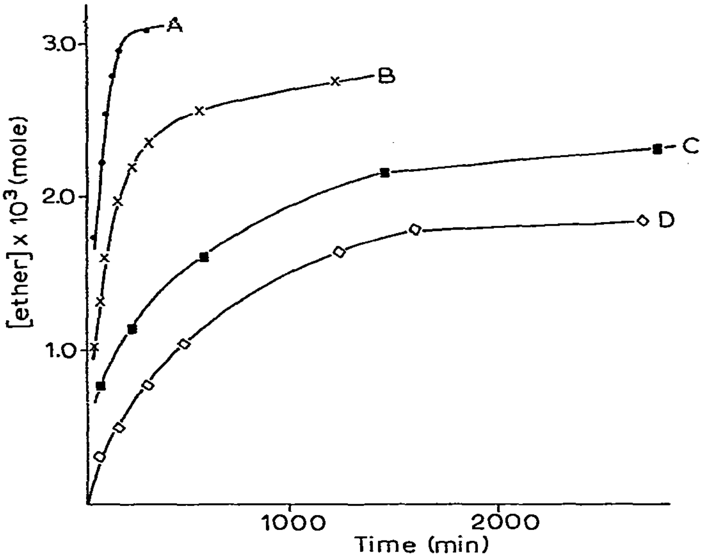


Fig. 1. Rate of formation of ether in the reactions of di-tert-butyl peroxide (4.0×10^{-3} mole) in diethyl ether with 24×10^{-3} mole each of A, allylmagnesium bromide; B, n-butylmagnesium chloride; C, n-butylmagnesium bromide; D, n-butylmagnesium iodide.

It will be observed that in the reactions of di-tert-butyl peroxide with n-butylmagnesium halides the rate of formation of the mixed ether is in the order RMgCl > RMgBr > RMgI and the final yields of ether follow the same order. This reactivity order may reflect the stability of the peroxide Grignard complexes or alternatively it might be a measure of the ease of electron transfer from the Grignard reagent to the peroxide. The effect of the halide on the yield of ether is most probably due to its influence on the lifetime of the radicals within the protective cage.

Allylmagnesium bromide reacts more rapidly than the n-butylmagnesium halides and gives a better yield of ether. The more rapid reaction would be expected considering the greater ease of radical formation in the allyl system and the greater yield of ether is a reflection of the greater difficulty of removing a hydrogen atom from an allyl radical than from an alkyl radical. The highest yield of ether was found in the reaction of β-methallylmagnesium bromide with di-tert-butyl peroxide. In this system there is no possibility of abstracting a β-hydrogen from the Grignard reagent and the only possible radical cage process is combination of an alkoxy radical and an alkyl radical. The observation that the yield of tert-butanol exceeds that of the mixed ether establishes that the tert-butoxy radicals do not abstract hydrogen exclusively from the alkyl radical [eqn. (6)] but must also obtain hydrogen from the solvent [eqn. (7)]. A similar observation was made previously by Epstein[5].

It has been shown by Herbstman[3] that in the reaction of di-tert-butyl peroxide with alkyl Grignard reagents the ether/alcohol product ratio depends markedly on the nature of the alkyl group. Primary Grignard reagents give the highest yields of ethers, whereas tertiary Grignards give predominantly alcohols, little or no ether being formed. We have confirmed that in the reaction of di-tert-butyl peroxide with tert-butylmagnesium chloride the alcohol is the sole product formed from the peroxide. This is understandable, as we proceed along the series of Grignard reagents, primary, secondary, tertiary the radicals generated should compete more effectively with the solvent in hydrogen donation to the tert-butoxy radicals and disproportion should increase relative to combination. The structure of the peroxide also is of some importance in determining the disproportionation/combination ratio. Although in the reaction of tert-butylmagnesium chloride with di-tert-butyl peroxide complete disproportionation is observed, in the reactions of the same reagent with di-n-butyl peroxide and tert-butyl n-butyl peroxide a 11% and 6% yield of ether is formed respectively. In the light of these observations a high yield of ether would be expected from the reaction of n-butylmagnesium chloride with di-n-butyl peroxide. In fact this reaction gives a lower yield of ether than the reaction of n-butylmagnesium chloride with di-tert-butyl peroxide. Apparently both the bulk of the alkoxy radical and its stability play a part in determining the extent of radical combination. The less stable n-butoxy radical will react more rapidly than the tert-butoxy radical with the solvent cage and fewer n-butoxy radicals will be available for combination with the alkyl radicals. This factor would also explain why a lower yield of symmetrical than unsymmetrical ether is obtained in the reaction of n-butyl tert-butyl peroxide with n-butylmagnesium chloride.

The reaction between disulphides and Grignard reagents has been investigated briefly by Wuyts[7]. We have now carried out a more extensive investigation of the reactions of simple disulphides with a variety of Grignard reagents to determine the

TABLE 2

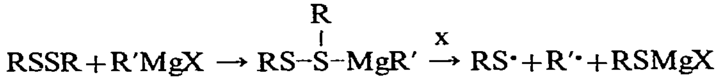
YIELDS OF MONOSULPHIDE AND THIOL FORMED IN THE REACTIONS OF DISULPHIDES (4×10^{-3} mole) WITH GRIGNARD REAGENTS (24×10^{-3} mole)

Disulphide	Grignard reagent	Products			
		Monosulphide	Yield (Mole × 10^3)	Thiol	Yield (Mole × 10^3)
n-BuSS-n-Bu	n-BuMgCl	n-BuS-n-Bu	4.02	n-BuSH	4.01
AllylSSAllyl	n-BuMgCl	AllylS-n-Bu	4.08	AllylSH	3.85
t-BuSS-t-Bu	n-BuMgCl	t-BuS-n-Bu	Nil	t-BuSH	Nil
t-BuSS-t-Bu	t-BuMgCl	t-BuS-t-Bu	Nil	t-BuSH	Nil
n-BuSS-n-Bu	t-BuMgCl	n-BuS-t-Bu	3.88	n-BuSH	4.13
t-BuSS-t-Bu	n-BuLi	t-BuS-n-Bu	4.00	t-BuSH	3.97
n-BuSS-n-Bu	AllylMgBr	n-BuSAllyl	3.92	n-BuSH	3.62
AllylSSAllyl	AllylMgBr	AllylSAllyl	3.98	AllylSH	3.84
t-BuSS-t-Bu	AllylMgBr	t-BuSAllyl	Nil	t-BuSH	Nil

effect on this reaction of changes in both Grignard and disulphide structure. The yields of products are summarised in Table 2. The di-n-alkyl disulphides studied were readily cleaved even with tert-butylmagnesium chloride; on the other hand di-tert-butyl disulphide did not react even with allylmagnesium bromide which had been shown to be very reactive in peroxide cleavage. n-Butyllithium, however, was effective in decomposing di-tert-butyl disulphide, and the reaction was complete within half an hour.

One of the more interesting aspects of the reaction between disulphides and Grignard reagents is that the monosulphide product is formed quantitatively. Apparently, there are no side reactions as in the comparable reactions with peroxides.

Recently it has been shown by Davies[8] that organometallic compounds react with disulphides to give alkyl radicals which can be detected by ESR. Since the combination reaction is the only reaction observed in the disulphide system these results suggest that it is a radical process. Probably as with the peroxides the first step is the formation of a disulphide–Grignard complex, which undergoes cleavage to give a thiol radical and an alkyl radical.



$$\mathrm{RSSR+R'MgX \longrightarrow RS{-}\overset{\overset{R}{|}}{S}{-}MgR' \xrightarrow{x} RS^{\bullet}+R'^{\bullet}+RSMgX}$$

The organolithium compounds may be more effective than the Grignard reagents either because they form more stable complexes or because they transfer an electron more readily to the S–S linkage. Since peroxide bonds are more susceptible to homolytic cleavage than disulphide bonds, if the combination reaction in the disulphide system is a radical process this provides further justification for assuming the combination reaction is a radical reaction in the peroxide system.

EXPERIMENTAL

Materials

Di-tert-butyl disulphide, di-n-butyl disulphide and di-tert-butyl monosulphide were obtained commercially and redistilled before use. Allyl tert-butyl monosulphide[9], allyl n-butyl monosulphide[9], n-butyl tert-butyl ether[10] and β-methallyl tert-butyl ether[11] were prepared as described in the given references.

Di-tert-butyl ether. The preparation was attempted using the method of Lawesson *et al.*[12], this gave a mixture of products which could not be separated. Di-tert-butyl ether was, however, prepared successfully by the method of Erickson[13]. tert-Butyl chloride was added to a suspension of silver carbonate and irradiated for two weeks with a 300 Watt tungsten filament lamp. There was obtained a 28% yield of di-tert-butyl ether, b.p. 106–107°. The purity of the product was established by NMR and GLC.

Preparation of Grignard reagents

The Grignard solutions were prepared by standard techniques and analysed by the method of Gilman *et al.*[14].

Reaction of peroxides and disulphides with Grignard reagents

The reactions were carried out according to the procedure described below for the reaction of di-tert-butyl peroxide with n-butylmagnesium chloride.

Di-tert-butyl peroxide (0.003 mole) was weighed accurately into a 100 ml flask and 2-methyloctane (0.1845 g) and ether (26.4 ml) were added. (The 2-methyloctane was used as an internal standard in the GLC analysis.) The solution was stirred magnetically and the temperature maintained at 20°. The Grignard solution (10 ml, 1.75 *M*) was added, the air in the flask displaced by nitrogen and the flask sealed with a serum cap. Samples were removed at various time intervals and analysed for peroxide and ether by GLC. When the reaction was complete, the flask was cooled and 0.1 *N* hydrochloric acid was added dropwise. The liberated tert-butanol was then determined by GLC. The absolute concentrations of peroxide, ether and alcohol were estimated by comparison with standard solutions of known concentration.

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