BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 47(5), 1289—1290 (1974)

The Reaction of α-Ethoxybenzyl *t*-Butyl Peroxide with Grignard Reagents

Masao Ōkubo, Hiroshi Saitō, and Toshiaki Tomiyoshi

Department of Chemistry, Faculty of Science and Engineering, Saga University, Honsho-cho, Saga 840

(Received May 25, 1973)

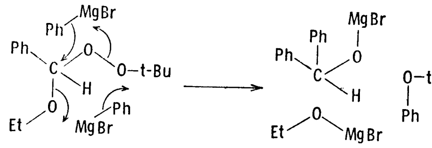
Synopsis. Effect of the ethoxyl group of the peroxide in the title was examined. Reactivities of some peroxides having oxygen- and nitrogen-atom adjacent to O-O linkage against magnesium compounds and alkali iodide were compared, and effect of the coordination of heteroatoms to the cationic species was discussed.

It was previously found that di-*t*-butyl peroxide (I) did not react with phenyl-[1] and methyl-[2]magnesium bromide (PhMgBr and MeMgBr) in tetrahydrofuran (THF) at 60 °C. Peroxide I reacts with Grignard reagents prepared from primary and secondary alkyl halides,[3] but the formation of *t*-butanol and olefins, both of which may be the result of "the reducing action of the β-hydrogen atom" of alkyl groups of reagents,[4] has been reported. These are excluded in this work to avoid complication of the reaction products. On the other hand, benzoyl peroxide (II) and *t*-butyl perbenzoate (III) reacts rapidly with PhMgBr in THF at 0 °C.[1] In these cases, the acceptance of the electron by peroxidic linkage[5] can probably be facilitated by the coordination of the neighboring carbonyl-oxygen to the Mg-atom of PhMgBr. Thus, the authors desired to see the effect of neighboring heteroatoms on the reactivity of peroxides with PhMgBr. α-Ethoxybenzyl *t*-butyl peroxide (IV)[6] was chosen as a model compound with neighboring ethereal oxygen.

Table 1. Molar ratio and extent of reaction (in THF, at 60 °C, 7 hr, under N_2)

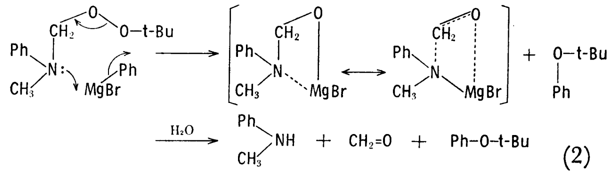
Purity of peroxide (wgt %)	$\frac{[PhMgBr]}{[P.O.]}$	P.O. reacted (%)	Yield of Ph-O-*t*-Bu (%)
70.7	1.8	38.1	67.1
70.7	3.1	68.9	59.1
70.7	4.5	97.4	69.9
85.6	2.0	65.3	63—70
85.6	3.0	85.2	
85.6	4.8	100	

A 85.6%-pure sample of IV was obtained by the repeated treatments of benzaldehyde diethylacetal with *t*-BuOOH at 80 °C.[6] The main products of the reaction of IV with PhMgBr after hydrolysis were benzhydrol and phenyl *t*-butyl ether. The reaction proceeds moderately at 60 °C in THF under an N_2-atmosphere, but the final extent of the reaction varies with the molar ratio of the reactants, as is shown in Table 1. It may be seen that about 4 mol of PhMgBr are necessary for the complete decomposition of IV. The products and their yields obtained using 4.8 molar PhMgBr will now be given. Benzhydrol was obtained quantitatively based on the reacted peroxide. The yield of phenyl *t*-butyl ether was 63—70%, almost independent of the purity (Table 1). *t*-Butanol was about 25%. Ethanol was found to have a 36—50% yield; however, it must really be much higher, as this product is readily lost in treating the reaction mixture. Small amounts of by-products were triphenylmethane and benzhydryl ethyl ether, both of which came from benzaldehyde diethylacetal, the sole contaminant in the sample of IV.



(1)

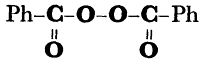
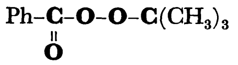
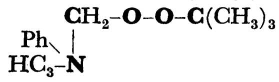
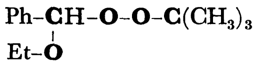
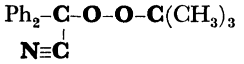
The mechanism of the reaction can be suggested on the basis of these results (Formula 1). Ethereal oxygen coordinates to the Mg-atom, and the ethoxyl anion is withdrawn from the aldehyde-carbon, thus facilitating the attack of the phenyl anion of the other Grignard molecule to produce benzhydrol. One more phenyl anion attacks the butoxyl-oxygen (*t*-Bu—O(—O-+Ph—)MgBr) to produce phenyl *t*-butyl ether. These are the main reactions. The considerable yield of *t*-butanol suggests the possibility of inverse heterolysis (*t*-Bu—O—)O-+Ph—)MgBr). As 4 mol of Grignard reagent are needed to complete the reaction, PhMgBr in Formula 1 should be written as dimers and thus takes a structural configuration favoring the attack of the cationic Mg-atom on the butoxyl-oxygen. Another mechanism in which Grignard molecule directly attacks the O-O linkage, can be rejected because 35 and 15% of peroxide remained unreacted after heating the reaction mixture for more than 7 hr even with two and three molar PhMgBr respectively. Probably, the dimerization process of PhMgBr($2PhMg\text{-}Br \rightleftharpoons Ph_2Mg \cdot MgBr_2 \rightleftharpoons Ph_2Mg + MgBr_2$) favors the release of the phenyl anion. Though there are some uncertainities, the initial abstraction of the ethoxy group has at least been ascertained.



(2)

N-Methyl-*N*-phenylaminomethyl *t*-butyl peroxide (V),[9] which has neighboring nitrogen atom, was also examined. Peroxide V decomposed completely with an equimolar PhMgBr at 60 °C in about 7 hr and formed *N*-methylaniline (73%) and phenyl *t*-butyl ether (81%) (Formula 2). Formaldehyde was detected as 2,4-dinitrophenylhydrazone. α-Cyanodiphenylmethyl *t*-butyl peroxide (VI)[10] was unchanged after having been treated with two molar PhMgBr at 60 °C for 7 hr. Around the O-O linkages peroxide VI structurally resembles triphenylmethyl *t*-butyl peroxide, which is stable to PhMgBr, but it is uncertain why the nitrile group itself does not react. Although these heteroatom-containing peroxides are not crowded to the same extent sterically around the O–O linkages, the adjacent oxygen and/or nitrogen, which can coordinate to the Mg-atom, seems to play an important part in reactions with PhMgBr.

Table 2. Correlation of reactivity

	Structure of P.O.	Mg-reagents		Iodometry		
		PhMgBr	$MgBr_2$ + 	(a)	(b)	(c)
II	 $\mathrm{Ph{-}\underset{\underset{O}{\Vert}}{C}{-}O{-}O{-}\underset{\underset{O}{\Vert}}{C}{-}Ph}$	++	+	○	—	—
III	 $\mathrm{Ph{-}\underset{\underset{O}{\Vert}}{C}{-}O{-}O{-}C(CH_3)_3}$	++	–	×	○	—
I	$(CH_3)_3C{-}O{-}O{-}C(CH_3)_3$	–	–	×	×	○
V	 $\mathrm{(Ph)(H_3C)N{-}CH_2{-}O{-}O{-}C(CH_3)_3}$	+	+	○	–	–
IV	 $\mathrm{Ph{-}\underset{\underset{Et-O}{\vert}}{C}H{-}O{-}O{-}C(CH_3)_3}$	+	–	×	○	—
VI	 $\mathrm{Ph_2{-}\underset{\underset{N\equiv C}{\vert}}{C}{-}O{-}O{-}C(CH_3)_3}$	–	–	×	×	○

Concerning the reaction of Grignard reagents with organic peroxides, we found that $MgBr_2$ and II in THF form an orange-colored complex, which acts as a moderate reagent for the bromine-addition to olefins, especially easily to cyclohexene, at room temperature.[11] In this colored complex, the carbonyl-oxygen of II is considered to coordinate to the Mg-atom and to induce a positive charge on the bromine atom. Thus, the combination of $MgBr_2$ and cyclohexene may be regarded as a magnesium reagent, based on the mechanistic resemblance. Peroxide V slowly afforded 1,2-dibromocyclohexane at 60 °C, but the IV and VI peroxides did not react at the same temperature. The reactivities to these two magnesium reagents of some peroxides containing and not containing adjacent heteroatoms are classified in Table 2. The methods of iodometry used are also included in the table. Method a), using a saturated KI solution and acetic acid, is applied to "highly reactive" peroxides, such as II and *t*-BuOOH.[12] Method b) is applied to "moderately reactive" peroxides such as III,[7] which reacts with alkali iodide alone in acetic acid, but so slowly that a catalytic amount of ferric ion is necessary for iodometry. Method c) is used to titrate "stable" peroxides such as I, which can be decomposed only in refluxing acetic acid.[13]

As Table 2 shows, diacyl-type (II) and *N*-containing (V) peroxides, both of which react with two magnesium reagents, are titrated by Method a). Perester-type (III) and *O*-containing (IV) peroxides, both of which react only with PhMgBr, are titrated by Method b). Di-*t*-alkyl-type (I) and *CN*-containing (VI) peroxides cannot react with both of the two magnesium reagents; they are titrated only by Method c). This correlation of reactivities seems reasonable when it is taken into account that Grignard reagents behave as ion-pairs and that alkali iodide is also known to exist as ion-pairs at a high concentration in a low dielectric solvent such as acetic acid.[14] The diminution of the rate of reaction of alkali iodide with acyl peroxides in ethanol by adding water,[15] which is a highly dielectric solvent, may thus be the result of the degree of association of the ion-pairs becoming lower and the participation of the counter cation being retarded. The higher reactivity of V than IV may be at least in part due to the higher coordinating ability of nitrogen. The non-reactivity of I and di-triphenylmethyl peroxide to PhMgBr has been ascribed to steric hindrance,[16] but the absence of adjacent heteroatom is probably another important factor.

Experimental

The purity of the IV peroxide was determined by integrating the NMR spectrum of aldehyde-protons of unreacted acetal (5.5 ppm) and of IV (5.8 ppm). In the iodometry, ferric chloride was used as a catalyst;[7] the amount of it was determined so as to obtain the same value as that found by the NMR method.

To a filtered solution of PhMgBr (prepared from 2.9 g of bromobenzene and excess Mg-turnings in 30 ml of THF), 1.0 g of IV (85.6% pure) in 20 ml of THF was added all at once under an N_2-stream. The reaction flask was transferred into a water bath (60 °C) and stirred gently. After 7 hr, the peroxide-content became nearly zero. The reaction products were analyzed by glc.

References

1) M. Ōkubo, K. Maruyama, and J. Ōsugi, This Bulletin, **44**, 125 (1971).

2) Methyl *t*-butyl ether was not detected, and the peroxide was recovered.

3) T. W. Campbell, W. Burney, and T. L. Jacobs, *J. Amer. Chem. Soc.*, **72**, 2735 (1950).

4) H. S. Mosher and E. L. Combe, *ibid.*, **72**, 3944 (1950).

5) K. Tokumaru and O. Simamura, This Bulletin, **36**, 333 (1963).

6) A. Rieche and C. Bischoff, *Chem. Ber.*, **94**, 2457 (1961).

7) L. S. Silbert and D. Swern, *Anal. Chem.*, **30**, 385 (1958).

8) A. E. Tschitschibabin and S. A. Jelgasin, *Ber.*, **47**, 48 (1914).

9) M. S. Kharasch and A. Fono, *J. Org. Chem.*, **24**, 72 (1959).

10) M. S. Kharasch and G. Sosnovsky, *Tetrahedron*, **3**, 105 (1958).

11) M. Ōkubo, H. Kusakabe, T. Hiwatashi, and K. Kishida, This Bulletin, **47**, 860 (1974).

12) J. P. Wibaut, H. B. van Leewen, and B. van der Wal, *Rec. Trav. Chim. Pays-Bas*, **73**, 1033 (1954).

13) R. D. Mair and J. Graupner, *Anal. Chem.*, **36**, 194 (1964).

14) R. A. Robinson and R. H. Stokes, "Electrolytic Solution," Butterworth, London (1959), p. 401.

15) G. Tsuchihashi, S. Miyajima, T. Ōtsu, and O. Simamura, *Tetrahedron*, **21**, 1039 (1965).

16) G. A. Baramki, H. S. Chang, and J. T. Edward, *Can. J. Chem.*, **40**, 333 (1963).