The Reactions of Aroyl Peroxides with Grignard Reagents. II. Relative Reactivities of Substituted Benzoyl Peroxides.[1]

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Benzoyl peroxide was found to react with Grignard reagents (RMgBr) in tetrahydrofuran at 0°C to form PhCOOR and PhCOOMgBr. The latter which was isolated as a complex containing two molecules of the solvent, can be coordinated by benzoyl peroxide to form an orange-colored complex. Similar complexes were found to be formed in the cases of some substituted benzoyl peroxides. The initial stage of the reaction was studied with the technique of competitive reaction. The results can be explained by assuming the coordination of the carbonyl oxygen atom of benzoyl peroxide to the Grignard magnesium atom. The effect of the substituent of the peroxide on the reaction was discussed.

The reactions of the carbanionic reagents with the peroxidic linkage are interesting, but scarcely any have been investigated so far.[2] We found that, when benzoyl peroxide was added to the tetrahydrofuran (THF) solution of phenylmagnesium bromide (PhMgBr), a pink color and the ESR signal were observed simultaneously.[3] This aroused our interest, and we investigated the reaction of aroyl peroxides with Grignard reagents. A stable complex containing benzoyl peroxide has been reported.[4] The initial stage of the reaction was investigated using the technique of competitive reaction, and the results are reported in this paper.

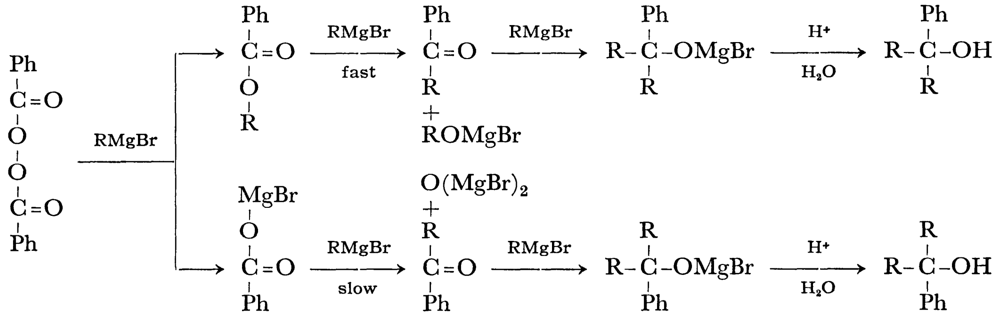
Results and Discussions

When benzoyl peroxide (BPO, 0.00184 mol in 50 m*l* THF) was mixed with nearly equimolar PhMgBr (0.612M, 3 m*l*) in THF (20 m*l*) under nitrogen stream at 0°C, about two thirds of BPO decomposed suddenly and the reaction mixture turned orange after being left to stand for about 2 hr. The products were benzoic acid (85—93%), phenyl benzoate(55—60%), small amounts of phenol, benzophenone and triphenylcarbinol. The orange color did not fade by contact with air, and it was confirmed to be not due to molecular bromine. Considering the products obtained in the preliminary experiment, we can construct the following reaction scheme (1) and (2)(R=Ph), though the reaction (2) is not yet confirmed.[5]

These formulas suggest that at least five moles of Grignard reagent is necessary to decompose one mole of benzoyl peroxide completely to form carbinol. When benzoyl peroxide in THF was added to the stirred solution of ten times moles of PhMgBr (solvent THF) under nitrogen stream, a pink color appeared after a few minutes. The color deepened gradually and did not fade after being left to stand overnight. Thus, the pink color and ESR signal can be attributed to the product resulting from interaction of PhMgBr with benzophenone which is produced during the course of the reaction.[6]

On the Complex Containing Peroxide. In the preceding paper,[4] it was reported that two complexes were isolated from the reaction between BPO and PhMgBr, white (Complex I) and orange (Complex II). The formulas previously proposed are written in an over-simplified form.[7] We should examine whether complexes similar to Complex II are formed in the reaction between analogous peroxides and other Grignard reagents.

When methyl- or ethylmagnesium bromide in THF was added to the solution of equimolar BPO, the mixture turned to a similar orange and Complex II was obtained. Substituted benzoyl peroxides such as



(1)

(2)

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[1] This work was carried out in the Department of Chemistry, Faculty of Science, Kyoto University.

[2] N. C. Yang and S.-O. Lawesson, *J. Amer. Chem. Soc.*, **81**, 4230 (1959).

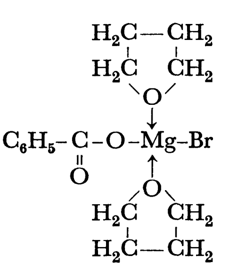
[3] K. Maruyama and M. Ōkubo, unpublished work.

[4] M. Ōkubo, K. Maruyama, and J. Ōsugi, This Bulletin, **42**, 1162 (1969).

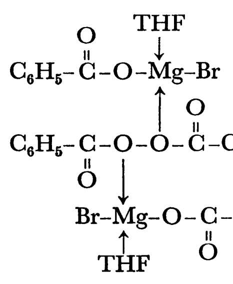
[5] Reaction (2) was confirmed later to proceed but much more slowly than reaction (1). See Experimental.

[6] More details on this phenomenon will be published elsewhere. See K. Maruyama, This Bulletin, **37**, 897 (1964).

[7] Their more precise structures will be discussed in the following paper.



(Complex I)



(Complex II)

p-methyl-, *p,p'*-dimethyl-, *p*-methoxy-, *p,p'*-dimethoxy-, *p*-fluoro-, and *p,p'*-difluorobenzoyl peroxides revealed a similar behavior when they were treated with equimolar PhMgBr. Of these, symmetrically substituted peroxides easily formed orange crystals when the reaction mixtures were left to stand for about 2 hrs at room temperature. However, with the unsymmetrically substituted peroxides, crystallization was difficult even though the solutions colored similarly. Furthermore, when *t*-butyl perbenzoate[2] in THF was added dropwise to the equimolar PhMgBr solution, it turned orange during the course of the reaction and faded by the time the addition was completed. This is also an indication of the transient formation of a similar complex to Complex II.

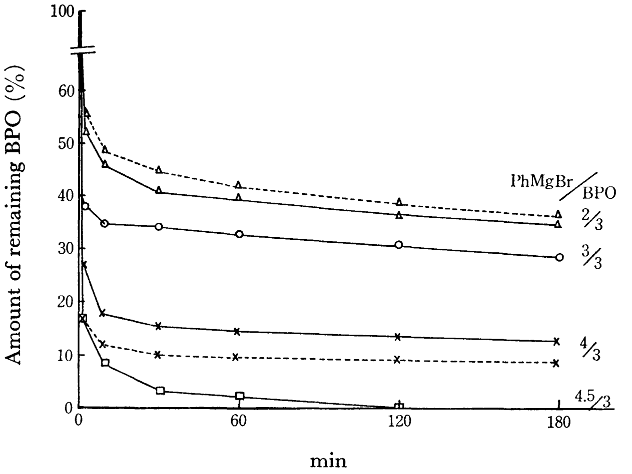
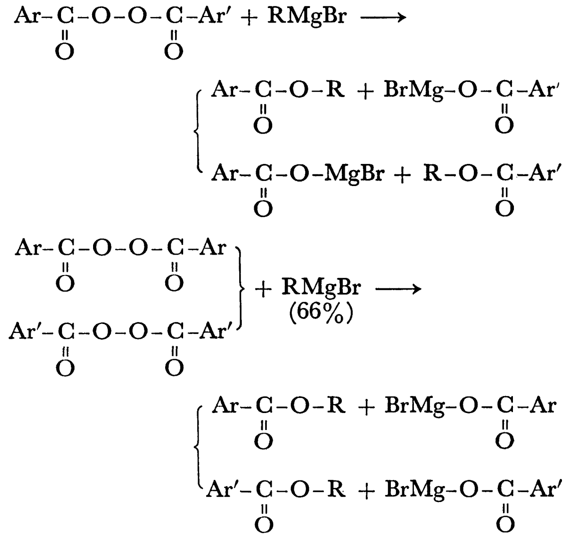


Fig. 1. Effect of molar ratio.
Temperature, 0°C Concentration, 0.007 mol/*l* (PhMgBr/BPO=3/3)

Effect of the Molar Ratio. Complex I was obtained when the molar ratio of PhMgBr : BPO was 1.5 : 1.0, while Complex II was obtained when it was 1 : 1.[4] Thus it is clear that the molar ratio of the two reactants has a remarkable effect on the course of reaction. Effect of the molar ratio on the consumption of BPO in the reaction system is shown in Fig. 1. The solid lines in Fig. 1 show the results obtained from the experiments when the amount of PhMgBr is fixed to 0.007 mol/*l* and that of BPO is varied, while the dotted lines show the results for the fixed amount of BPO and the varied amounts of PhMgBr. The difference between the solid and dotted lines for the same molar ratio shows the effect of concentration of the Grignard reagent. It should be noted that all the curves have creases between the initial and the second stages of the reaction. If the molar ratio is 3 : 3, the crease appears at the point where 35—37% of BPO remained, and hereafter the decomposition of BPO is markedly slowed down. The slow decomposition of BPO in the second stage may be attributed to the fact that benzoyl peroxide is stabilized through its complex formation with the reaction products, namely Complex I. If the molar ratio is 2 : 3, the crease rises up to 52—57% of remaining BPO, and the curve then goes down gradually to 33% of remaining BPO. If the molar ratio is 4 : 3, the crease falls down to 17—25% of remaining BPO. If 1.5 times molar Grignard reagent to the peroxide is used, BPO is completely decomposed after 2 hr. Though it is not shown in Fig. 1, when the two reactants were mixed at −15°C, the crease of the curve for the molar ratio of 2 : 3 rose up to about 66% of remaining BPO, and that for 4 : 3 to about 30%. If the molar ratio is 2 : 3, the reaction mixture turns orange very soon after mixing. Two conclusions can be derived from these facts; (i) Complex II is formed most effectively if the molar ratio is 2 : 3 and this ratio agrees with the composition of Complex II, (ii) twice moles of the Grignard reagent seems to be necessary for the rapid decomposition of one mole of Complex II.



$$\mathrm{Ar{-}\underset{\underset{O}{\|}}{C}{-}O{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar' + RMgBr \longrightarrow \left\{\begin{array}{l} Ar{-}\underset{\underset{O}{\|}}{C}{-}O{-}R + BrMg{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar' \\ Ar{-}\underset{\underset{O}{\|}}{C}{-}O{-}MgBr + R{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar' \end{array}\right.}$$

$$\left.\begin{array}{l}\mathrm{Ar{-}\underset{\underset{O}{\|}}{C}{-}O{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar} \\ \mathrm{Ar'{-}\underset{\underset{O}{\|}}{C}{-}O{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar'}\end{array}\right\} + \underset{(66\%)}{\mathrm{RMgBr}} \longrightarrow \left\{\begin{array}{l} \mathrm{Ar{-}\underset{\underset{O}{\|}}{C}{-}O{-}R + BrMg{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar} \\ \mathrm{Ar'{-}\underset{\underset{O}{\|}}{C}{-}O{-}R + BrMg{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ar'} \end{array}\right.$$

Table 1. Competitive reactions of substituted BPO with MeMgBr

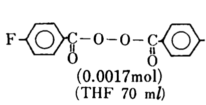
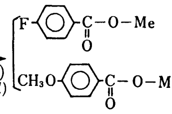
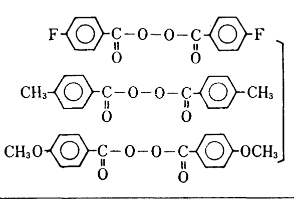
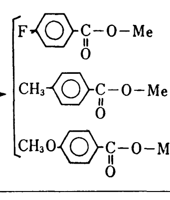
Exp. No.	Peroxide	RMgBr	Ester	Molar ratio of esters
1.	 (0.0017mol) (THF 70 ml)	MeMgBr (0.0017mol) (THF 20 ml)		1.00 0.82
2.		MeMgBr (66%)		1.00 1.38 3.15

Table 2. Competitive reactions of substituted BPO with PhMgBr

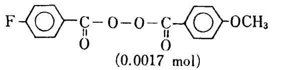
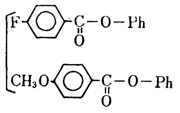
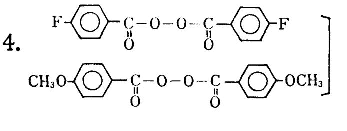
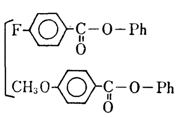
Exp. No.	Peroxide	RMgBr	Ester	Molar ratio of esters
3.	 (0.0017 mol) (THF 70 ml)	PhMgBr (66%)		1.00 0.52
4.		PhMgBr (0.0017 mol) (THF 20 ml)		1.00 0.93

Table 3. Competitive reactions of acyl benzoyl peroxide with PhMgBr

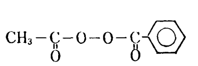
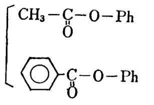
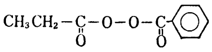
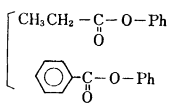
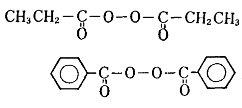
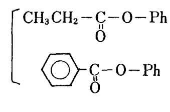
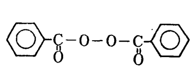
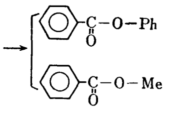
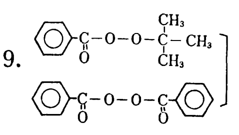
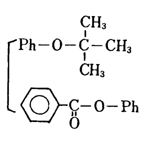
Exp. No.	Peroxide	RMgBr	Ester	Molar ratio of esters
5.	 (0.0017 mol) (THF 70 ml)	PhMgBr (0.0017mol) (THF 20 ml)		3.28 1.00
6.		PhMgBr		3.55 1.00
7.		PhMgBr (66%)		1.60 1.00

Table 4. Other competitive reactions

Exp. No.	Peroxide	RMgBr	Ester	Molar ratio of esters
8.	 +	PhMgBr MeMgBr		1.00 1.32
9.		PhMgBr (66%)		18.1 1.00

Effect of the Structure of Peroxide. The technique of competitive reaction was applied to investigate the first stage of the reaction. The experiments were conducted at −15°C. Although just equivalent moles of two reactants were used for the reaction between unsymmetrical acyl peroxide and the Grignard reagent, 66% equivalent moles of the Grignard reagent to the total moles of peroxides were mixed for the comparison of the reactivities of the two symmetrical peroxides.[8] Relative amounts of esters produced were used as a measure of the reactivity. The results are summarized in Tables 1, 2, 3 and 4.

Since RMgBr in THF is coordinated by solvent molecules, the initial stage of the reaction should be the replacement of THF molecules by peroxide molecules. The results of experiments Nos. 2, 4, and 7 may be used as a measure of the relative facility of the coordination of each peroxide. 2 and 7 show that the electron-donating substituent accelerates the reaction. If the results of 4 and 2 are compared, the difference between the yields of two esters is negligibly small in the case of PhMgBr. This seems to be explained on the basis of the following : —first, the phenyl group which is bulkier than the methyl group would make it difficult for PhMgBr-species to be coordinated by peroxide molecules, and would reduce the difference of the yields of phenyl esters. Second, the donation of π-electrons of the phenyl group would also bring about the same effect. Salinger and Mosher[9] found that the infrared absorption band of C_{Ph}-Mg bond appeared at 370—380 cm^{-1} and that of C_{Me}-Mg bond at 500—535 cm^{-1}, respectively. This means that the C_{Ph}-Mg bond is stronger than the C_{Me}-Mg bond. However, it is conceivable that the phenyl group might donate its π-electrons to the vacant p- and d-orbitals of magnesium atom, and then reduce the positive charge on the magnesium atom. Thus, the facility of the coordination of peroxide molecules to magnesium atom may be more strongly affected in the case of MeMgBr (No. 2) than in the case of PhMgBr (No. 4). The result of No. 8 supports the results.[10] Following the coordination of the peroxide molecule to the Mg-atom, the displacement of carbanionic alkyl or aryl group of Grignard reagent takes place so to form the esters of carboxylic acids. The difference between the values of 0.82(No. 1) and 0.52(No. 3) may also be ascribed to the smaller polarizability of C_{Ph}-Mg bond or to the bulkiness of the phenyl group, both of which may cause a higher selectivity to diaplacement of the carbanionic phenyl group from Mg-atom of Grignard reagent to one of the oxygen atoms in the peroxide molecule. The carbonyl and peroxidic oxygen atoms of peroxide molecules could not be distinguished in the discussions.

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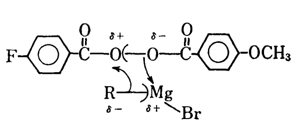
[8] As the initial stage of reaction is very fast, even the less reactive peroxide was readily decomposed almost completely when the 100% equivalent moles of the Grignard reagent to the total moles of peroxides were used. When 2/3 mol of PhMgBr were used, unreacted BPO (1/3 mol) was converted into Complex II completely by the interaction with PhCOOMgBr (Complex I) produced.

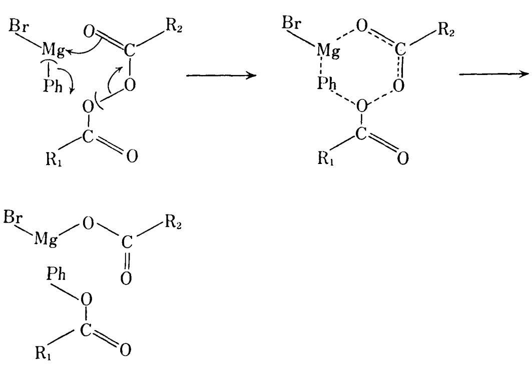
[9] R. M. Salinger and H. S. Mosher, *J. Amer. Chem. Soc.*, **86**, 1782 (1964).

[10] The $p\pi$-$p\pi$ and $p\pi$-$d\pi$ delocalizations which have been proposed to explain the lower reactivities of vinyl-substituted boranes and silanes may be the same as the π-donation discussed here. cf. J. J. Eisch, "The Chemistry of Organometallic Compounds," Macmillan Co., New York (1967), Chap. IV.

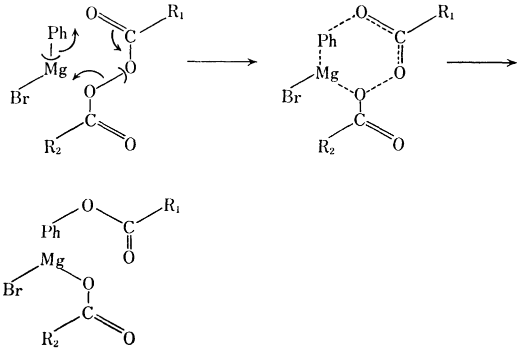
The results of the intramolecular competitive reactions, Nos. 1, 3, 5, and 6 are considered to provide information on the facility of displacement of alkyl or aryl groups. At this stage, the possibility of the so-called four-center-type reaction as shown in formula (3) may be small, since the actual Grignard reagent must have considerable bulkiness due to the coordination of solvent molecules. Thus, the six-membered ring structure for the transition state is more probable. If the carbonyl oxygen coordinates to Mg-atom, the mechanism is expressed as shown in formula (4). Another possible mechanism in which the peroxidic oxygen atom coordinates to Mg-atom is shown in formula (5). Both mechanisms lead to the same products. However, it may be difficult for the latter to occur when the result of experiment No. 9 is taken into account. The fact that *t*-butyl perbenzoate is known to react with equimolar PhMgBr to produce exclusively *t*-butyl phenyl ether,[2] is explained solely by assuming the transition state in which the magnesium atom of the Grignard reagent is coordinated by the carbonyl oxygen atom as shown in formula (6). The predominant formation of *t*-butyl phenyl ether over phenyl benzoate in No. 9 is thus interpreted on the same assumption. The fact that di-*t*-butyl peroxide cannot react with PhMgBr under the same conditions,[2,11] means that peroxidic oxygen atoms are difficult to coordinate to the magnesium atom. Thus, the transition state can best be expressed by formula (4).



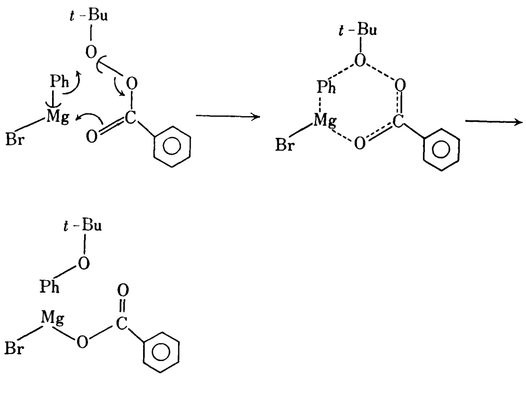
(3)



(4)



(5)



(6)

From this consideration, the more favorable structure for the transition state of No. 5 and No. 6 is expressed by formula (4) in which R_1 is CH_3 or CH_3CH_2 and R_2 is C_6H_5. Similarly, the results of No. 1 and No. 3 are expressed by formula (4) in which R_1 is *p*-FC_6H_4 and R_2 is *p*-$CH_3OC_6H_4$. These results cannot be interpreted if one assumes that the carbonyl group bearing the inductively more electron-donating substituent coordinates predominantly to Mg-atom. On the contrary, as shown in the above discussions, the "electromerically" more electron donating substituent favors the adjacent carbonyl group to coordinate to Mg-atom. Thus, the reaction of aroyl peroxides with the Grignard reagents can be illustrated by considering the electromeric polarizabilities caused by coordination of both the reagents.

Experimental

Grignard Reagents. THF solutions of phenyl-, ethyl- and methylmagnesium bromides were prepared in the usual manner using an excess of magnesium metal. They(about 0.5M, 300 m*l*) were stored in a tightly stoppered bottle and left standing overnight. A portion of clear solution was pipetted out, and its concentration was determined by alkaline titration.[12] Br^- and Mg^{2+} were also titrated by $AgNO_3$ and oxine-chelate[13] methods, respectively. Three values agreed with each other.

Peroxides. Commercial BPO was examined for its peroxide-content by iodometry, and purified, if necessary, by dissolving in chloroform and reprecipitated by methanol. *p,p'*-Difluoro-, *p,p'*-dimethyl- and *p,p'*-dimethoxy derivatives were prepared by treatment of the corresponding acid chlorides with sodium peroxide.[14] *p*-Fluoro-*p'*-methoxy derivative was prepared from sodium *p*-methoxyperbenzoate and *p*-fluorobenzoyl chloride.[15] *p*-Fluoro-, *p*-methyl- and *p*-methoxybenzoyl peroxides were prepared in the same manner from sodium perbenzoate and the corresponding acid chlorides. However, the differences in yields of the corresponding methyl esters on the reactions with MeMgBr were very small and the peroxide were not used.

Acetyl benzoyl peroxide and propionyl benzoyl peroxide were prepared by aerating the mixtures of acetic and/or

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[11] See experimental section. Baeyer and Villiger (*Ber.*, **33**, 3387 (1900)) observed that diethyl peroxide could not be decomposed by even sodium metal.

[12] H. Gilman, P. D. Wilkinson, W. P. Fishel, and C. H. Meyers, *J. Amer. Chem. Soc.*, **45**, 150 (1923).

[13] I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," Macmillan Co., N. Y. (1955), pp. 362, 607.

[14] C. G. Swain, W. H. Stockmayer, and J. T. Clarke, *J. Amer. Chem. Soc.*, **72**, 5426 (1950).

[15] J. E. Leffler and C. C. Petropoulos, *ibid.*, **79**, 3068 (1967).

propionic anhydride and benzaldehyde.[16] Dipropionyl peroxide was prepared by treating propionic anhydride with sodium peroxide.[17] *t*-Butyl perbenzoate was obtained by treating *t*-butyl hydroperoxide with benzoyl chloride and sodium hydroxide.[18] Di-*t*-butyl peroxide was prepared by adding *t*-butyl hydroperoxide to a cooled mixture of *t*-butyl alcohol and sulfuric acid.[19]

Reactions of Aroyl Peroxides with Grignard Reagents. From reaction schemes (1) and (2), we see that the primary products of the reaction are PhCOOMgBr and PhCOOPh (from BPO and PhMgBr). Phenyl benzoate reacts easily with the remaining Grignard reagent to produce benzophenone, which again reacts to produce triphenylcarbinol. It is necessary, therefore, to avoid these reactions as far as possible. Thus, the reaction flask as shown in Fig. 2 was used throughout this work. After air in the flask was replaced with nitrogen and the equimolar peroxide and Grignard reagent were cooled to the desired temperature, the resevior was turned upside-down with vigorous stirring of the peroxide solution. After mixing, the one m*l* portions of the mixture were pipetted out at definite time intervals and quickly introduced into a CO_2-purged flask containing acetic acid and potassium iodide. The mixture was titrated with a standard thiosulfate solution according to Wibaut.[20] For comparison, di-*t*-butyl peroxide was added to PhMgBr and the mixture was left standing for 2 hr,* but the peroxide was recovered and no product other than benzene was detected.

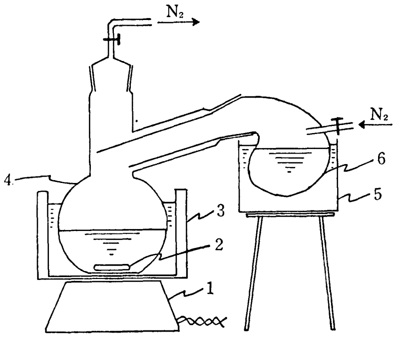

Fig. 2. Reaction flask for rapid mixing.
1. magnetic stirrer
2. stirring rod
3. ice bath
4. reaction flask (peroxide solution)
5. ice bath
6. reservoir (Grignard solution)

The Competitive Reaction. Mixing of perodixe solution with Grignard reagents was conducted by using the devide in Fig. 2. After stirring for 30 min, the reaction mixture was concentrated and decomposed with ammonium chloride. Neutral products were extracted with ether, dried with anhydrous magnesium sulfate, and concentrated to an appropriate volume. For gas-chromatographic analysis, a suitable substance was added as an internal standard. The mixture of known amounts of authentic samples was analyzed under the same gas-chromatographic condition for the calculation of the calibration factor.

In experiments Nos. 2, 4, 7, and 9, in which 66% equivalent amounts of Grignard reagent were used, a considerable amount of peroxides were not decomposed. Since they might interfere with gas-chromatographic analysis, they had to be removed. For this purpose two methods were used. The first was to decompose the peroxide by treating with hydroquinone and palladium-black according to Wieland.[21] Peroxide can easily decomposed to benzoic acid (and its derivatives), and they were removed by alkaline extraction. However, there was some difficulty, since benzoquinone, which is formed from hydroquinone through hydrogen-fransfer, gave a large quantity of precipitates from a concentrated sample solution for gas-chromatographic analysis. The other method was as follows: peroxide which remains as Complex II (or its derivatives) can be almost quantitatively precipitated from the concentrated reaction mixture by addition of a sufficient amount of dry ethyl ether.[4] The precipitate was collected on a glass-filter and washed throughly with dry ether. The filtrate was concentrated for gas-chromatographic analysis.

Reaction of Complex I with PhMgBr. Five milliliters of *ca.* 0.5M PhMgBr was pipetted into a N_2-purged flask and diluted with 20 m*l* of THF. The solution was vigorously stirred and carbon dioxide was introduced. After the absorption of carbon dioxide was completed, 10 m*l* of PhMgBr (0.5M) was added and stirred gently. After a few hours the solution turned wine-red. The color faded after being left standing overnight. The solution was concentrated and decomposed with ammonium chloride. The products were benzoic acid (0.38 g), and the mixture of benzophenone and triphenylcarbinol (1.1 g). The latter was confirmed with TLC.

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[16] Yu. A. Ol'dekop, A. N. Sevchenko, I. P. Zyat'kov, and A. I. El'nitzkii, *Zh. Obshch. Khim.*, **31**, 2904 (1961).

[17] A. Rennubaum and M. Szwarc, *J. Chem. Phys.*, **23**, 909 (1955).

[18] N. A. Milas and D. M. Surgenor, *J. Amer. Chem. Soc.*, **68** 642 (1946).

[19] N. A. Milas and D. M. Surgenor, *ibid.*, **68**, 205 (1946).

[20] J. P. Wibaut, H. B. van Leeuwen, and B. van der Wal, *Rec. trav. chim.*, **73**, 1033 (1954).

[21] H. Wieland, *Ber.*, **54**, 2369 (1921).