[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Reaction of Oxygen with Organometallic Compounds. A New Synthesis of Hydroperoxides[1]

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Organic hydroperoxides can be prepared in good yield (30–90%) by the slow addition of Grignard reagents to oxygen-saturated solvents at about −70°. Their isolation confirms the Porter and Steele reaction sequence for the oxidation of Grignard reagents, and provides a convenient synthesis for alkyl hydroperoxides, yields increasing in the order prim. < sec. < tert. Acetylenic Grignard reagents, however, react with oxygen only very slowly at room temperature, and aromatic Grignard reagents apparently yield peroxides which are detectable, but too unstable to be isolated. Since aldehydes and diphenylamine do not interfere with the reaction, it seems unlikely that a radical chain process is involved.

A familiar property of Grignard reagents is their rapid reaction with molecular oxygen, a reaction first investigated by Bodroux[3] and Bouveault[4] in 1903. Although the yield of alcohols from aliphatic Grignard reagents is generally good (60–90%), the reaction is of little synthetic value, since the transformation is not often desired, and can be accomplished by other means. Yields of phenols from arylmagnesium halides are lower (10–22%), and many by-products are formed. Thus, from phenylmagnesium bromide the following have been isolated with indicated maximum yields[5,6]: benzene (23%), ethanol (11%), biphenyl (21%), methylphenylcarbinol (20%), quinone, *p,p'*-terphenyl, diphenyl ether and *p,p'*-biphenol. The significance of these by-products are considered further below.

Because a reaction for converting aryl halides to phenols has considerable potential utility, the oxidation of aromatic Grignard reagents has been investigated more extensively, and is reviewed in detail by Kharasch and Reinmuth.[7] By employing phenetole or benzene in place of ether as solvent, coöxidizing a mixture of aliphatic and aromatic Grignard reagents, or replacing molecular oxygen by H_2O_2 or an organic hydroperoxide, quite satisfactory yields are possible.

The first information concerning the path of the Grignard reagent–oxygen reaction was obtained by Wuyts,[5,8] who found that oxidized solutions of ethylmagnesium bromide in ether–toluene solution liberated iodine from acidic KI solution, and postulated an intermediate peroxide to explain his observation. Solutions oxidized at 0 and −70°, gave peroxide values of 0.7–6%, with the best results being obtained at −70° and relatively high dilution. Solutions of phenylmagnesium bromide gave less than 0.2% peroxide even under these optimum conditions. With this evidence in mind, Porter and Steele[6] have proposed the reaction sequence for the oxidation

$$\mathrm{RMgX} + \mathrm{O_2} \longrightarrow \mathrm{ROOMgX} \qquad (1)$$

$$\mathrm{ROOMgX} + \mathrm{RMgX} \longrightarrow 2\mathrm{ROMgX} \qquad (2)$$

Although this course of the reaction has been generally accepted by subsequent investigators, the intermediate hydroperoxide has not heretofore been isolated.[9]

Our interest in the oxidation of Grignard reagents was aroused since it is one of the most rapid reactions of organic materials with oxygen. Further, if the Porter and Steele reaction sequence were correct, and the reaction could be interrupted at the hydroperoxide stage, it should provide a useful synthesis for a variety of organic peroxides difficultly accessible by other means. This last supposition has been happily confirmed with alkyl, cycloalkyl and benzyl Grignard reagents, and it has proved possible to prepare a variety of aliphatic hydroperoxides by this path.

Reaction of *t*-Butylmagnesium Chloride with Oxygen, Verification of the Porter–Steele Reaction Path.—*t*-Butylmagnesium chloride was chosen for our initial work since *t*-butyl hydroperoxide is a well characterized and reasonably stable material which should be easily identifiable. Preliminary experiments, however, showed that when dry air was bubbled into an ethereal solution of *t*-butylmagnesium chloride at 0° until the Grignard reagent was consumed, the reaction mixture gave a negative peroxide test with KI in acetic acid, and, after hydrolysis, *t*-butyl alcohol was the only identifiable product. Inspection of equations 1 and 2, indicates that one is dealing with two consecutive reactions, and hydroperoxide can be obtained only if the Grignard–oxygen reaction (1) can be made rapid compared with its reaction with the hydroperoxide salt (2). An obvious way of accomplishing this is to increase the ratio of oxygen to hydroperoxide salt in the reaction mixture by reverse addition of Grignard reagent to oxygen saturated ether. Further, in view of Wuyts' observations,[5,8] it seemed desirable to carry out the oxidation at as low a temperature as possible.

The expectation was realized, and in an experiment involving reverse addition at −75°, a 35% yield of *t*-butyl hydroperoxide was isolated.

At this point we performed a developmental

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[1] For a preliminary report of this investigation, *cf.* THIS JOURNAL, **75**, 4372 (1953).

[2] Taken from a portion of a dissertation submitted by Sheldon A. Buckler to the Graduate Faculties of Columbia University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. This work was supported in part by the Office of Ordnance Research, U. S. Army.

[3] F. Bodroux, *Compt. rend.*, **136**, 158 (1903); *Bull. soc. chim.*, [3] **31**, 33 (1904).

[4] L. Bouveault, *ibid.*, [3] **29**, 1051 (1903).

[5] H. Wuyts, *Bull. soc. chim. Belg.*, **36**, 222 (1927).

[6] C. W. Porter and C. Steele, THIS JOURNAL, **42**, 2650 (1920).

[7] M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, pp. 1264–1274.

[8] H. Wuyts, *Compt. rend.*, **148**, 930 (1909).

[9] Schmidlin's detection, *Ber.*, **39**, 631 (1906), of triphenylmethyl peroxide on the oxidation of triphenylmethylmagnesium chloride has no bearing on the reaction scheme, since this product is obtained from oxygen and any source of triphenylmethyl radicals.

study to ascertain the optimum conditions for the preparation of the hydroperoxide. A series of small scale experiments were run in which concentration, rate of addition, and temperature were varied. The results are given in Table I.

TABLE I

EFFECT OF VARYING CONDITIONS ON THE YIELD OF *t*-BUTYL HYDROPEROXIDE FROM *t*-BUTYLMAGNESIUM CHLORIDE

Run	Reagent, *N*	Temp., °C.	Time of addn., min.[a]	Yield, %[b]
1	1.62	−65	40	34
2	1.62	−71	120	78
3	0.56	−71	40	86
4	1.74	−69	70	46
5	0.53	−74	80	91
6	.53	− 7	80	28
7	.66	−71	40	82[c]
8	.66	−71	40	60[d]
9	.54	−71	40	88[e]
10	.54	−71	40	88[f]

[a] Of 50 ml. of reagent to 50 ml. of O_2 saturated ether except as indicated. [b] By titration. [c] 0.033 mole of acetone present. [d] Oxidation carried out in 50 ml. of acetone. [e] 0.027 mole of *n*-butyraldehyde present. [f] 0.027 mole of diphenylamine present.

These results show that the reaction is greatly dependent upon the conditions of oxidation. The dependence upon temperature is evident from a comparison of runs 5 and 6. This result might be due either to a decreased concentration of oxygen at the higher temperature or to a more favorable competition of reaction 2 at the higher temperature. The latter is probably more important since the solubility of oxygen in ether does not increase greatly at lower temperatures.[10] The effect of time of addition is seen by a comparison of runs 1 and 2 while that of concentration is apparent from the results of runs 1 and 3. Optimum yields plainly require slow addition of rather dilute solutions of the Grignard reagent. Since oxygen was replenished simply by bubbling gas through the solution, these conditions may have been required simply to maintain oxygen saturation in the system. In addition, reaction 2 may be a polymolecular process involving more than one molecule of the Grignard reagent, analogous to the addition of Grignard reagents to ketones,[11] so that the highest yield of hydroperoxide is obtained under conditions where the concentration of Grignard reagent in the system is kept low.

The extreme rapidity of the initial reaction with oxygen has been remarked by Marvel[12] and is borne out by experiments 7–10 in which the oxidation was carried out in the presence of acetone, *n*-butyraldehyde and diphenylamine. Only when pure acetone was used as solvent for the oxygen was the yield significantly reduced. Further, when equimolecular quantities were used, acetone and butyraldehyde were recovered in 59 and 90% yield, respectively.

Although Grignard reagents react rapidly with most organic peroxides, it seemed desirable to verify that reaction 2 actually could take place under our reaction conditions. A solution of the magnesium salt of *t*-butylhydroperoxide was prepared by inverse oxidation, flushed with nitrogen, and an equivalent of Grignard reagent added. Hydrolysis after stirring for an hour gave a 70% yield of *t*-butyl alcohol based upon all the reagents employed. This experiment, plus the actual isolation of the intermediate hydroperoxide, provides a convincing demonstration that the Porter and Steele reaction sequence is essentially correct.

Inverse Oxidation of Other Aliphatic Organometallic Compounds.—We have next investigated the oxidation of a variety of aliphatic organometallic reagents to determine the utility of this reaction for hydroperoxide synthesis. The reagents were oxidized under conditions which were most successful for *t*-butylmagnesium chloride, with results summarized in Table II.

TABLE II

PREPARATION OF ALIPHATIC HYDROPEROXIDES

Reverse addition of 50 ml. of reagent to 50 ml. of O_2 saturated ether at −75° in 43 minutes

Reagent	Normality	Yield of[a] hydroperoxide, %
t-ButylMgCl	0.56	86[b]
t-AmylMgCl	.35	92
2-*n*-OctylMgCl	.50	91
"Bornyl"MgCl	.55	90
CyclohexylMgCl	.52	66
CyclohexylMgBr	.69	30
EthylMgCl	.48	57
EthylMgBr	.54	28
BenzylMgCl	.50	30
n-ButylMgCl	.60	57
n-ButylLi	.38	36
Di-*n*-butylZn	.47	48

[a] By titration. [b] Addition in 40 minutes.

From the results obtained this reaction constitutes a new synthesis of primary, secondary and tertiary hydroperoxides. Best results are obtained with the more highly substituted compounds and, although somewhat lower yields are obtained with primary reagents, our conditions may not be the most favorable for preparation of hydroperoxides from these substances, and higher yields might be obtained by slower addition of a more dilute reagent.

The reason for this variation in yield with structure under essentially standard conditions is not evident from our experiments, but may arise from the more rapid reaction of the less sterically hindered hydroperoxide salts with Grignard reagent.

All the hydroperoxides were isolated and characterized with the exception of ethyl and *n*-butyl hydroperoxides, the former, in particular, being quite explosive. Formations of the hydroperoxides in these cases was demonstrated by the fact that they could be extracted with strong base. Benzyl and "bornyl" hydroperoxides[13] are new compounds,

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(10) J. C. Gjaldbaek, *Acta Chem. Scand.*, **6**, 623 (1952).

(11) C. G. Swain and H. B. Boyles, THIS JOURNAL, **73**, 840 (1951).

(12) M. T. Goebel and C. S. Marvel, *ibid.*, **55**, 1693 (1933).

(13) This reaction product of the Grignard reagent from bornyl chloride is apparently a mixture of bornyl and isobornyl hydroperoxides. Its preparation and properties are discussed in another paper, C. Walling and S. Buckler, THIS JOURNAL, **77**, 6039 (1955).

and 2-octyl hydroperoxide has only been reported since the completion of this work.[14]

The reaction of benzylmagnesium chloride is especially interesting since attempts to prepare benzyl hydroperoxide by autoxidation of large quantities of toluene have proven unsuccessful.[15] This hydroperoxide is stable upon isolation and is converted to benzaldehyde by short treatment with alkali, as described for the *p*-methyl analog.[15]

$$C_6H_5CH_2OOH \xrightarrow{OH^-} C_6H_5CHO + H_2O \qquad (3)$$

Similarly, 2-octyl hydroperoxide gives 2-octanone on somewhat longer treatment with base. This is a general reaction of peroxides containing α-hydrogens, which has been discussed by Kornblum[16] and, as might be expected, benzyl C–H bonds are particularly labile.

From Table II alkylmagnesium chlorides give better yields of hydroperoxides than the corresponding bromides, *cf.* the ethyl and cyclohexyl compounds. After these alkylmagnesium bromides were oxidized, an orange color was present in the ether layer, which could be destroyed by $Na_2S_2O_3$ solution. It is therefore possible that the decrease in yield is due to the oxidation of bromide ion to bromine by a portion of the hydroperoxide.

n-Butyllithium and di-*n*-butylzinc give somewhat lower yields of peroxide than the corresponding Grignard reagent. In view of this and the greater ease of preparation and handling of Grignard reagents, there is no advantage in using the other organometallic compounds.

Some larger scale preparations were carried out with several of the reagents to get a better idea of the actual synthetic utility of the reaction. A preparation from *t*-butylmagnesium chloride (0.52 mole) gave a 91% yield as determined by titration, and an 82% yield by actual isolation of hydroperoxide. Although the material was carefully fractionated, no di-*t*-butyl peroxide was detected. From benzylmagnesium chloride (0.18 mole), a 37% yield of hydroperoxide was obtained by titration and purified by extraction as the sodium salt and two distillations. The balance of the products were 54% of benzyl alcohol and 2% of benzaldehyde, presumably an artifact formed during the basic treatment.

Attempts to prepare cumene hydroperoxide by this method failed because the corresponding Grignard reagent could not be prepared from α,α-dimethylbenzyl chloride.

To assess the synthetic utility of the Grignard reagent–oxygen reaction it may be compared with the three other general methods of peroxide synthesis.[17]

The classic method of preparing primary and secondary hydroperoxides is by a simple displacement reaction, usually between alkaline hydrogen peroxide and a dialkyl sulfate. Until recently the reaction was limited to 1–4 carbon hydroperoxides, but it recently has been extended and improved by Williams and Mosher,[14,18] using hydrogen peroxide and alkyl esters of methanesulfonic acid in alkaline methanolic solution. Under these conditions 38–45% yields of primary and 20–25% yields of secondary hydroperoxides are realized, even from long chain sulfonic esters.

Tertiary alkyl hydroperoxides have been prepared from the corresponding alcohol and hydrogen peroxide in the presence of sulfuric acid, the reaction presumably being an acid-catalyzed solvolysis, proceeding through the carbonium ion. *t*-Butyl hydroperoxide is obtained in 50–70% yield in this manner.[19] It fails, however, with benzyl-type alcohols since the resulting products are rearranged by acid.[20]

Finally a number of hydroperoxides can be prepared by the direct autoxidation of hydrocarbons by a free radical chain process.[21] Yields vary widely, and attack occurs preferentially at allyl, substituted benzyl and tertiary C–H bonds so that the method is essentially limited to the synthesis of hydroperoxides of these types.

Compared with these methods, the oxidation of Grignard reagents is somewhat more versatile, and may often be the method of choice, particularly for the preparation of secondary alkyl hydroperoxides, and substances such as benzyl hydroperoxide which are inaccessible by other means. On the other hand, it obviously fails with structures which do not yield Grignard reagents, and the other techniques are probably preferable when they give high yields, particularly in large-scale preparations.

The ethereal solutions of the magnesium salts of hydroperoxides obtained in our oxidations also can be used directly for the preparation of other organic peroxides without hydroperoxide isolation. Thus, an oxidized solution of *t*-butylmagnesium chloride was treated with a molar equivalent of benzoyl chloride, stirred at room temperature for two hours, and stored overnight at −20°. After hydrolysis, a 54% yield of *t*-butyl perbenzoate was obtained by distillation.

In a similar fashion, an oxidized solution treated with an equivalent of ethyl bromide and left at room temperature for 19 hours gave a 22% yield of ethyl *t*-butyl peroxide. When excess ethyl sulfate was employed as an alkylating agent under the same reaction conditions, a 20% yield of the same peroxide was obtained. In both cases 48% of unalkylated *t*-butyl hydroperoxide was recovered, indicating that variations in conditions might improve the yield. Although no further work has been carried out on reactions of this sort, they are obviously capable of considerable variation.

Inverse Oxidation of Aryl Grignard Reagents.—Since no simple aryl derivatives of hydrogen peroxide are known, their preparation would be of considerable interest, and the facile reaction of aromatic Grignard reagents with oxygen suggested that they might be obtained by our inverse addi-

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[14] H. R. Williams and H. S. Mosher, THIS JOURNAL, **76**, 2987 (1954).

[15] H. Hock and S. Lang, *Ber.*, **76**, 169 (1943).

[16] N. Kornblum and H. E. DeLaMare, THIS JOURNAL, **73**, 880 (1951).

[17] For a detailed survey see A. V. Tobolsky and R. B. Mesrobian, "Organic Peroxides," Interscience Publishers, Inc., New York, N. Y., 1954.

[18] H. R. Williams and H. S. Mosher, THIS JOURNAL, **76**, 2984 (1954).

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

[20] H. Hock and S. Lang, *Ber.*, **77**, 257 (1944).

[21] L. Bateman, *Quart. Revs.*, **8**, 147 (1954).

tion technique. However, experiments with phenylmagnesium bromide and chloride yielded reaction mixtures which developed deep colors on warming to −20° and gave peroxide titrations of only 1–3%. On working up the reaction mixture, phenol was isolated in 43–46% yield. Similar results were obtained with *p*-bromophenylmagnesium bromide and mesitylmagnesium bromide, and an attempt also was made to isolate phenyl perbenzoate by treating the oxidized phenylmagnesium bromide with benzoyl chloride at −78°, but without success. In spite of our failure to isolate any aryl hydroperoxide, we did obtain evidence that peroxides are actual reaction intermediates. Freshly oxidized solutions were flushed with nitrogen, and sodium iodide in isopropyl alcohol containing acetic acid was added at below −70°. On warming the solution, the liberated iodine was titrated, the amounts corresponding to 3, 5.2 and 9.3% peroxide for mesityl, phenyl and *p*-bromophenylmagnesium bromides, respectively. Apparently, aryl hydroperoxide salts are very unstable, even at these low temperatures, and also may compete with oxygen for additional Grignard reagent more successfully than do their aliphatic analogs.

A large scale inverse oxidation of phenylmagnesium bromide (0.3 mole) was carried out to compare yields of isolated products with those obtained by direct oxidation. After hydrolysis, the products were separated into neutral and acidic fractions. From the latter was obtained 41% of phenol, leaving a small residue (1–2%) from which no other substances could be identified. The neutral layer gave 7% of methylphenylcarbinol, and steam distillation of the residue gave 11% of diphenyl. The residue from this operation was small and no other products were isolated. Because of the fairly large quantities of ether involved, no attempt was made to isolate benzene or ethanol.

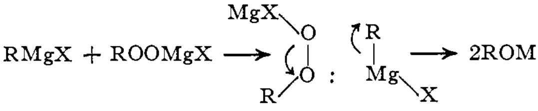
A comparison of the yields of these products with those obtained by normal oxidation shows that the yield of phenol is doubled, while the yields of byproducts are considerably diminished.

Oxidation of Acetylenic Grignard Reagents.—Grignard has reported the preparation of phenyl ketene and acetic acid (under unspecified conditions) by the oxidation of the Grignard reagents from phenylacetylene and acetylene.[22] However, several experiments carried out on the Grignard reagents derived from 1-pentyne and 1-octyne confirmed the observation of Kroeger and Nieuwland[23] that acetylenic Grignard reagents are relatively stable toward oxygen. Inverse oxidation of octynylmagnesium bromide and chloride yielded only 1-octyne upon hydrolysis, and stirred ether solutions of octynylmagnesium bromide in an oxygen-filled apparatus connected with a gas buret showed absorption of less than 1 mole % of oxygen after an hour at either 0 or 26°.

In a larger experiment, oxygen was bubbled through a pentynylmagnesium bromide solution for 12 hours. On working up the products, 4.3% of *n*-valeric acid was isolated plus a small amount of a hydrocarbon, by analysis and molecular weight a trimer of 1-pentyne, $C_{15}H_{20}$, but of unknown structure. Octynylmagnesium bromide gave rather similar results. Accordingly, acetylenic Grignard reagents were not investigated further.

The Mechanism of the Oxygen–Grignard Reagent Reaction.—Atlhough this investigation has been concerned more with the synthetic scope of the inverse oxygen–Grignard reagent reaction than with reaction mechanisms of the individual steps in the Porter and Steele reaction sequence, some comments on the latter are in order in light of our experimental observations.

Reaction 2, between hydroperoxide salt and further Grignard reagent, which occurs in the ordinary course of Grignard reagent oxidations is presumably analogous to other reactions between peroxides and organometallic reagents discussed by Campbell, Burney and Jacobs.[24] In their scheme, the reaction proceeds through the rearrangement of an initial complex, and in our case might be formulated as



$$\mathrm{RMgX + ROOMgX \longrightarrow \begin{matrix} \mathrm{MgX{-}O} & & \mathrm{R} \\ | & & | \\ \mathrm{R{-}O} & : & \mathrm{Mg{-}X} \end{matrix} \longrightarrow 2ROMgX} \qquad (3)$$

recognizing that the structure of the intermediate is essentially schematic. Alternatively, such a complex might require attack by a second mole of Grignard reagent but, in any case, an essentially polar reaction is indicated in which the alkyl group supplies the electron pair for attachment to oxygen.

The initial oxygen–Grignard reagent reaction (1) is more interesting and obscure. Molecular oxygen is a diradical, and autoxidation processes in general appear to be radical reactions, involving either a chain process, yielding hydroperoxides, as in the autoxidation of hydrocarbons,[21] or electron transfer as in the autoxidation of the anions of hydroquinones,[25] in which oxygen is reduced to H_2O_2. In addition some photochemical autoxidations are known often involving a photosensitizer,[26] which give transannular peroxides by a non-chain process. Grignard reagents participate in both polar and radical processes.[27]

The autoxidation of the anion of 2-nitropropane has been studied by Russell,[28] who has postulated an intermediate hydroperoxide anion, formed by a chain process involving electron transfer and suggests a similar mechanism for the reaction of Grignard reagents with oxygen.

$$\mathrm{R\cdot + O_2 \longrightarrow R{-}O{-}O\cdot} \qquad (4)$$

$$\mathrm{R{-}O{-}O + R^- \longrightarrow ROO^- + R\cdot} \qquad (5)$$

Doering and Haines[29] have investigated the alkoxide ion catalyzed autoxidation of ketones and esters, concluding that the enolate ion is the reactive species, and that an intermediate hydroperoxide anion decomposes to the isolated products. However, they do not attempt

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[22] V. Grignard and L. Lepayre, *Bull. soc. chim.*, [4] **43**, 141, 930 (1928).

[23] J. W. Kroeger and J. A. Nieuwland, THIS JOURNAL, **58**, 1861 (1936).

[24] T. W. Campbell, W. Burney and T. L. Jacobs, *ibid.*, **72**, 2735 (1950).

[25] T. H. James, J. M. Snell and A. Weissberger, *ibid.*, **60**, 2084 (1938).

[26] G. O. Schenk, *Angew. Chem.*, **64**, 12 (1952).

[27] *Cf.* ref. 7, Chapter 5.

[28] G. A. Russell, THIS JOURNAL, **76**, 1595 (1954).

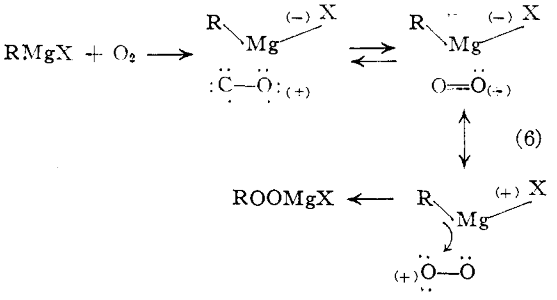
[29] W. von E. Doering and R. M. Haines, *ibid.*, **76**, 482 (1954).

to resolve the question whether the initial reaction follows a radical or polar path.

The very high rate of Grignard reagent oxidation makes a radical chain process attractive, and experiments 9 and 10 in Table I were carried out to see whether added materials could be induced to enter a radical chain. Aliphatic aldehydes are autoxidized readily at low temperatures in the presence of free radicals, but *n*-butyraldehyde had no effect upon the peroxide yield, no butyric acid was detected on reduction of the reaction mixture with bisulfite and the aldehyde was recovered in 90% yield.

Similarly, diphenylamine, a good inhibitor for many hydrocarbon autoxidations when present in only traces, had no effect upon the yield, and although the amine was not recovered, the reaction mixture was only slightly colored. In other experiments, phenylmagnesium bromide was oxidized in the presence of cumene, which also is readily involved in oxidation chains, but no significant amount (<1%) of peroxides was detected.

These results cannot entirely rule out a radical chain process, particularly a chain involving electron transfer as reactions 4 and 5, in which 5 might be very rapid compared with radical attack on any of the added materials, but in the absence of any evidence to the contrary, they certainly make it unlikely. The simplest alternative would be some sort of bimolecular association of oxygen and Grignard reagent, followed by rearrangement, which we may diagram as



(6)

The initial complex is indicated as either a diradical or a species with all electrons paired, perhaps in equilibrium with each other, and, although we prefer to think of the final product formation as occurring through migration of R with its electron pair as indicated, in analogy with the postulated paths for other reactions of Grignard reagents with oxygen-containing compounds, an alternative formulation in which R and O each contribute an electron to the R–O bond is possible.

The reactions of other alkyl organometallic compounds (Table II) can be formulated similarly. The low reactivity of the acetylenic Grignard reagents parallels the low reactivity of phenylethynylmagnesium bromide toward benzonitrile,[30] but the magnitude of the difference is striking.

Finally, the peculiar behavior of aromatic Grignard reagents merits discussion. With the exception of di- and polyphenyls, which are normal byproducts in the preparation of aryl Grignard reagents, the products observed are essentially those which might be expected from the homolytic decomposition of intermediate aryl peroxides, followed by radical attack on the ether solvent. There is good reason to expect that aryl peroxides would be relatively unstable, since scission of the O–O linkage yields a phenyloxy radical, C_6H_5–O·, which should be stabilized by resonance with the π-electron stystem of the aromatic ring. By analogy to the isoelectronic benzyl radical, the effective stabilization should be about 25 kcal./mole,[31] but too little is known about the properties of hydroperoxide salts such as C_6H_5OOMgX (and the other species with which it may be in equilibrium) to make any actual estimate of the O–O bond dissociation energy. Once radicals are formed, induced chain reactions are possible involving both further peroxide and ether, and perhaps complicated by reaction of the intermediate radicals with oxygen. There is no point in speculating on their exact nature, but radical attack on ethers lead to the formation of alcohol and aldehyde derivatives.[32] The latter, in the presence of further Grignard reagent, should turn up finally as phenylmethylcarbinol. Similarly, the quinonoid and phenolic byproducts resemble the peroxide–phenol reaction products described by Waters,[33] and presumably formed by radical paths.

Experimental

Preparation of Organometallic Reagents.—Essentially standard procedures were used for the preparation of organometallic reagents, preparation and storage both being conducted in a nitrogen atmosphere. The Grignard reagents were allowed to stand for 24 hours to allow suspended solids to settle, and were then filtered through glass wool by applying excess nitrogen pressure. A syringe was used in diluting and subsequent handling of these reagents to avoid exposure to reactive species in the air. Grignard concentrations were determined by the method of Gilman and co-workers[34] and employed in calculating yields. Peroxide analyses were performed by the method of Wagner, Smith and Peters.[35]

Investigation of Experimental Variables in Inverse Oxidation of *t*-Butyl MgCl.—The experiments in Table I were conducted in a 100-cc. reaction vessel fitted with a hollow bore stirrer, Trubore bearing, low temperature thermometer, and the drying tube. The reagent was added by means of either a motor-driven 50-ml. syringe, or a dropping funnel. In the latter case, the reagent was protected by an atmosphere of nitrogen. Fifty ml. of anhydrous ether was placed in the apparatus, and cooled by means of a Dry Ice–trichloroethylene or ice–HCl-bath to the desired temperature. Dry oxygen was passed through the bore of the stirrer for a few minutes with vigorous stirring, and addition of the reagent was then started, maintaining the stirring and a steady flow of oxygen. When the addition was completed, runs 2, 3 and 5, Table I (the runs giving highest yields), were clear, while the others contained varying amounts of precipitate. From this it might be concluded that *t*-butylOOMgCl is more soluble in ether than *t*-butylOMgCl.

The solutions were allowed to come to room temperature, poured on a small amount of ice, and 6 *N* HCl added until the aqueous layer was faintly acidic. The layers were

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(30) C. G. Swain, THIS JOURNAL, **69**, 2306 (1947).

(31) M. Szwarc, *Chem. Revs.*, **47**, 75 (1950). By a somewhat different method, N. S. Hush, *J. Chem. Soc.*, 2375 (1953), has estimated the C_6H_5O–H bond dissociation energy of phenol as 84 kcal., corresponding to a similar resonance stabilization. It is pertinent that 2,4,6-tri-*t*-butylphenoxy radicals are apparently stable in solution, although here steric hindrance may aid in preventing their association to peroxide, *cf.* C. D. Cook and R. C. Woodworth, THIS JOURNAL, **75**, 6242 (1953).

(32) P. D. Bartlett and K. Nozaki, *ibid.*, **69**, 2299 (1947); W. E. Cass, *ibid.*, **69**, 500 (1947).

(33) S. L. Cosgrove and W. A. Waters, *J. Chem. Soc.*, 3189 (1949); 388 (1951).

(34) H. Gilman, P. D. Wilkinson, W. P. Fishel and C. H. Meyers, THIS JOURNAL, **45**, 150 (1923).

(35) C. D. Wagner, R. H. Smith and E. D. Peters, *Anal. Chem.*, **19**, 976 (1947).

separated and the aqueous layer extracted with several 25-ml. portions of ether. The total ether layer was made to 250 ml. and 10- or 25-ml. aliquots were titrated for peroxide. That such an analysis is valid in the presence of ether was shown by dissolving a known weight of pure *t*-butyl hydroperoxide in ether and duplicating the extraction procedure, using water containing an equivalent of $MgCl_2$. Analysis gave a value of 101% of the amount added. Duplicate experiments of the oxidation were run in some cases and gave yields which differed by less than 2%. Experiments with changes of solvent (7–10) were carried out in the same manner. From 7 the acetone was recovered in 59% yield as its 2,4-dinitrophenylhydrazone. After hydrolysis the ether layer of 9 was shaken for 0.5 hour with sodium bisulfite solution. The aqueous layer was then made distinctly alkaline with 30% NaOH solution and agitated further. The layers were separated and the aqueous layer was acidified, extracted with ether, and the ether distilled. No residue remained. From the original ether layer, 90% of the butyraldehyde could be recovered as its 2,4-dinitrophenylhydrazone.

Experiment 10 showed little evidence of reaction with diphenylamine, although this material was not recovered. The oxidized solution was slightly colored and on warming to room temperature, only a small amount of tarry material formed.

Inverse Oxidation of Other Aliphatic Organometallic Compounds, Table II.—The oxidations and peroxide analyses were carried out substantially as described for run 3 of Table I, employing 50 ml. of diluted reagent added in 43 minutes to 50 ml. of ether cooled to Dry Ice temperature in the apparatus previously described. Yields were determined by titration.

All preparations except those from *t*-amylMgCl, 2-*n*-octylMgCl and bornylMgCl contained varying amounts of precipitate at the end of the oxidation, and those from alkyl bromides were deep orange after hydrolysis, the color being removed by washing with thiosulfate. **Ethyl and *n*-butyl hydroperoxides** were not isolated. Benzyl hydroperoxide is described below, and the bornyl product is described elsewhere.[13] The remainder of the hydroperoxides were characterized as follows.

Cyclohexyl Hydroperoxide.—After hydrolysis the ether layer from the oxidation of cyclohexylMgCl was concentrated to 30 ml. under reduced pressure employing a 65-cm. packed column. The solution was extracted several times with 5-ml. portions of 30% NaOH, precooling both layers in an ice-bath. The basic extracts and solids were neutralized slowly with 6 *N* HCl with efficient cooling. This aqueous layer was then extracted with three 15-ml. portions of ether, and the combined extracts dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue distilled from a short path apparatus. Obtained was 1.4 g. (52%, corrected for amount titrated) of cyclohexyl hydroperoxide, b.p. 42–43° (0.10 mm.), n^{25}_{D} 1.4645, d^{20}_{4} 1.019; literature,[36] b.p. room temperature (10^{-4} mm.), n^{25}_{D} 1.4638, d^{20}_{4} 1.018; *anal.* 83.0% $C_6H_{11}OOH$.

This material is water white and has a garlic-like odor. This degree of purity is approximately that obtained from autoxidation of cyclohexane, followed by concentration as the sodium salt.[36]

***t*-Amyl Hydroperoxide.**—After hydrolysis of the oxidation product of *t*-amylMgCl, the ether layer was dried over $CaCl_2$ and the ether removed under reduced pressure through a 65-cm. packed column. The residue was distilled *in vacuo* through a short path apparatus to give 1.3 g. (81%, corrected for amount titrated) of *t*-amyl hydroperoxide, b.p. 32–33° (4.3 mm.), n^{25}_{D} 1.4132, d^{20}_{4} 0.902; literature,[37] b.p. 26° (3.5 mm.), n^{20}_{D} 1.4161, d^{20}_{4} 0.903; anal. 83.2% *t*-amyl hydroperoxide. This material was a colorless liquid which did not freeze at −70°.

2-*n*-Octyl Hydroperoxide.—The ether layer obtained after hydrolysis of the oxidation product of 2-*n*-octylMgCl was dried over $MgSO_4$ and the ether removed under reduced pressure through a short-path apparatus to give 2.65 g. (80% corrected for amount titrated) of 2-*n*-octyl hydroperoxide, b.p. 58–59° (0.5 mm.), n^{25}_{D} 1.4269, d^{20}_{4} 0.868; literature,[14] b.p. 78–80° (0.5 mm.), n^{25}_{D} 1.4266; anal. 91.1% $C_8H_{17}OOH$. The discrepancy in boiling points may well arise from our use of a short-path distillation apparatus, and the great pressure gradients possible in distilling equipment at these pressures.

Two hundred mg. of the hydroperoxide was heated with 4 ml. of 2 *N* NaOH solution on the steam-bath for 15 minutes, neutralized, and treated with 2,4-dinitrophenylhydrazine. Upon standing, orange crystals were obtained, m.p. 55–56° after recrystallization from dilute ethanol; the 2,4-dinitrophenylhydrazone of 2-octanone melts at 56°.

Larger Scale Preparation of *t*-Butyl Hydroperoxide.—A one-liter 3-neck flask containing 400 ml. of anhydrous ether and fitted with stirrer, sintered glass oxygen inlet tube, and a graduated dropping funnel, and protected from moisture by a $CaCl_2$ tube, was cooled to −75° and the ether was saturated with O_2. Three hundred ml. of a 1.74 *N* *t*-butylMgCl solution was introduced under the surface of the liquid in the course of 2.75 hours. Vigorous stirring and a steady stream of O_2 was maintained over this period. After the addition was complete, the mixture was stirred for 0.25 hour with O_2 bubbling through.

The mixture was allowed to come to 0°, and poured into a beaker with 200 g. of ice. 6 *N* HCl was added slowly until the aqueous layer was distinctly acidic. The layers were separated and the aqueous layer extracted three times with 90-ml. portions of ether which were combined with the original extracts and dried overnight with 100 g. of $CaCl_2$. Titration of an aliquot of the solution gave a hydroperoxide yield of 91.3%. The ether was removed through a 65-cm. packed column with the bath no higher than 45°. The last traces of ether were removed at slightly reduced pressure and the hydroperoxide distilled through a 20-cm. Vigreux column, b.p. 31–33° (17 mm.). The yield was 38.7 (82.4%). The product was fractionated through a helix packed column of about 15 plates and the material collected has b.p. 34–35° (20 mm.), n^{27}_{D} 1.3980, d^{20}_{4} 0.897, m.p. 0.5–2.0°; literature,[38] b.p. 33–34° at 17 mm., n^{25}_{D} 1.3983, d^{20}_{4} 0.896, m.p. 4.0–4.5°; anal., 98.6%.

Preparation and Characterization of Benzyl Hydroperoxide.—120 ml. of 1.52 *N* benzylMgCl was introduced just over the surface of 250 ml. of anhydrous ether at −75° in the course of 1.75 hours, and stirring continued for 15 minutes. The Grignard solution could not be introduced under the surface since it was found to freeze at this temperature. The mixture was allowed to warm to 0°, poured on ice, acidified, and the layers separated, and the aqueous layer extracted three times with 65-ml. portions of ether. Titration of an aliquot of the combined ether extracts showed a yield of 36.5% hydroperoxide. The ether layer was concentrated *in vacuo* to a volume of 50 ml., and cooled in ice. It was extracted four times with 8-ml. portions of cold 30% NaOH, leaving a neutral ether solution which was subsequently investigated.

The basic suspension was neutralized slowly with dilute HCl while cooling in ice, and extracted three times with 25-ml. portions of ether. The ether solution was dried over $CaCl_2$, and evaporated *in vacuo* leaving 6.15 g. of an oil which was distilled, b.p. 55–57° (0.1 mm.); anal. 87.1% C_6H_5-CH_2OOH. It was a colorless liquid which, though odorless, proved irritating to the nasal passages.

The neutral ether layer was distilled and the fraction b.p. 195–204° was collected (11.0 g.), n^{25}_{D} 1.5360, d^{20}_{4} 1.05. This proved to be mainly benzyl alcohol, contaminated with a small amount of benzaldehyde, probably formed as an artifact during the basic extraction. The yield of benzaldehyde was determined by precipitation as the 2,4-dinitrophenylhydrazone, m.p. 236–237° (no depression with an authentic sample) and found to be 1.8%. The yield of benzyl alcohol was 54%.

Three hundred mg. of the sodium salt of benzyl hydroperoxide was heated on the steam-bath for 5 minutes with 4 ml. of 0.5 *N* NaOH. The solution was extracted with ether, the ether evaporated, and the residue (smelling of benzaldehyde) treated with a solution of 2,4-dinitrophenylhydrazine in acidic aqueous ethanol. It gave an orange derivative, m.p. 237.5–238° after recrystallization from ethanol–ethyl acetate, and gave no melting point depression with an authentic sample of benzaldehyde 2,4-dinitrophenylhydrazone.

Alkylation and Acylation of *t*-Butyl-OOMgCl.—To a solution of *t*-butyl-OOMgCl prepared by oxidizing 35 ml. of 1.20 *N* *t*-butylMgCl at −75°, 4.6 g. (0.042 mole) of ethyl bromide was added in a little ether. The mixture was allowed to warm to room temperature and stand 16 hours. On

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(36) A. Farkas and E. Passaglia, This Journal, **72**, 3333 (1950).

(37) N. Milas and D. Surgenor, *ibid.*, **68**, 643 (1946).

(38) N. Milas and D. Surgenor, *ibid.*, **68**, 205 (1946).

working up there was obtained 0.99 g. (22%) of ethyl *t*-butyl peroxide, b.p. 34° (84 mm.), $n^{24}\text{D}$ 1.3840, d^{20}_4 0.810; literature,[39] b.p. 35° (84 mm.), $n^{20}\text{D}$ 1.3840, d^{20}_4 0.809.

Also obtained was 1.80 g. (48%) of recovered hydroperoxide b.p. 50° (40 mm.), $n^{24}\text{D}$ 1.3970, d^{20}_4 0.898.

In a larger scale experiment employing 2 equivalents of diethyl sulfate in place of ethyl bromide, the yield of ethyl *t*-butyl peroxide was 20% and that of recovered hydroperoxide 48%.

In a similar experiment, 0.042 mole of oxidized Grignard reagent was treated with an equivalent of benzoyl chloride and allowed to stand at room temperature for two hours. Working up and distilling in good vacuum employing a short-path apparatus gave 4.40 g. (54%) of *t*-butyl perbenzoate, b.p. 64–65° (0.04 mm.), $n^{25}\text{D}$ 1.4983, d^{20}_4 1.048; literature,[40] b.p. 76° (2 mm.), $n^{20}\text{D}$ 1.5007, d^{20}_4 1.043.

A similar experiment was initially stirred at room temperature for only 0.5 hour, and gave a yield of 27%.

Inverse oxidations of aromatic Grignard reagents were carried out by adding the reagents to an equal volume of oxygen saturated ether at −75° over 43 minutes. In addition to peroxide titrations, yields of phenols also were determined, mesitol by direct isolation and the other phenols as tribromophenol by the method of Herman and Nelson.[41] Results are summarized below.

Reagent	Normality	Yield, % Phenol	Yield, % Peroxide
C_6H_5MgBr	0.73	46.5	1
C_6H_5MgCl	0.53	43	2.5
p-BrC_6H_4MgBr	1.22	39	1.8
MesitylMgBr	0.65	11.5	3.3

In an effort to detect unstable peroxides in the oxidized reaction mixtures, experiments in which 10 ml. of reagent had been added to 50 ml. of ether at −75° were flushed with nitrogen and treated with 30 ml. of a saturated solution of NaI in isopropyl alcohol plus 6 ml. of acetic acid at −75°. The solution was then allowed to come to room temperature, sufficient water was added to dissolve precipitated salts, the layers were separated quickly and the liberated iodine determined.

Reagent	Normality	Time of addition, min.	Peroxide, %
p-BrC_6H_4MgBr	1.20	20	9.3
Phenyl MgBr	1.52	20	5.2
Methyl MgBr	1.30	40	3.0

Large-scale Oxidation of Phenylmagnesium Bromide.—A larger scale experiment was also carried out to determine the effect of inverse addition on the by-products of the oxidation. Two hundred ml. of 1.52 *N* reagent was oxidized, hydrolyzed, and separated into neutral and acidic fractions. The acidic fraction, distilled under reduced pressure, gave 11.8 g. (41.2%) of phenol, b.p. 84° at 20 mm., m.p. 41–42°; literature, b.p. 90° (20 mm.), m.p. 43°. A dark residue (300 mg.) remained from which no further phenols could be isolated.

The neutral fraction, distilled *in vacuo*, gave 2.60 g. (7.1%) of methylphenylcarbinol, b.p. 87° (16 mm.). A derivative was obtained by oxidizing this material at room temperature with CrO_3 solution, extracting with ether, and subsequent preparation of the 2,4-dinitrophenylhydrazone, m.p. 245–247°. The residue from the distillation was steam distilled to give 3.3 g. (10.6%) of biphenyl, m.p. 68–70°. A gummy residue of 0.4 g. remained. No further products could be isolated, and no attempt was made to detect benzene or ethanol.

Oxidation of Acetylenic Grignard Reagents.—Inverse oxidation of octynylMgBr and octynylMgCl produced no titratable peroxides, and exposure of a stirred 0.2 *N* solution octynylMgBr to oxygen in a gas buret showed absorption of less than 1% of the calculated oxygen in one hour at either 0 or 26°.

In a further experiment, 100 ml. of 0.72 *N* octynylMgBr cooled in an ice-bath was bubbled with oxygen for 5 hours, and then hydrolyzed with ice and HCl. The ether layer was extracted with 50 ml. of 5% NaOH solution, the basic extracts acidified, extracted with ether, and the ether evaporated to give a dark residue from which no identifiable product could be obtained. The neutral ether layer was distilled through a helix-packed column, giving 2.60 g. (33%) of 1-octyne, b.p. 126–130°, $n^{25}\text{D}$ 1.4138, giving an immediate precipitate with ammoniacal $AgNO_3$ solution. The residue was distilled *in vacuo* giving 1.1 g. of a liquid, b.p. 112–114° (0.2 mm.). This material had a small peak at 5.85 μ, and a peak at 226 mμ (*E* 920). The molecular weight was found to be 217 (Rast method). 0.106 g. of this substance took up 63.0 ml. (S.T.P.) of hydrogen, using a palladium catalyst, corresponding to 5.8 moles of hydrogen. No carbonyl derivatives could be obtained.

In a similar experiment using 350 ml. of a 1.43 *N* solution of pentynylMgBr the acidic fraction of the products (3.2 g.) on distillation gave 2.2 g. (4.3%) of a colorless liquid with an odor characteristic of valeric acid, b.p. 183–187°, $n^{25}\text{D}$ 1.4080. The infrared spectrum of this material was identical with that of authentic *n*-valeric acid.

Distillation of the neutral fraction gave 3.30 g. of liquid, b.p. 86–88° (14 mm.), $n^{27}\text{D}$ 1.4845. A viscous residue remained which was not further examined. The distillate had a peak at 5.90 μ and 226 mμ (*E* 1390). No carbonyl derivatives could be obtained. 0.548 g. of this substance took up 348 ml. (S.T.P.) of hydrogen corresponding to six moles employing a palladium catalyst. *Anal.* Found: C, 88.0; H, 10.1; mol. wt., 210 (Rast).

Reaction of *t*-ButylMgCl with *t*-Butyl-OOMgCl.—*t*-Butyl-OOMgCl was prepared exactly as in run 2, Table I, employing 50 ml. of 1.69 *N* *t*-butylMgCl (0.084 mole). After flushing well with nitrogen, 39 ml. of 1.69 *N* *t*-butylMgCl was added and the mixture was stirred at room temperature for one hour. It was then hydrolyzed with a cold solution of 38 g. of ammonium chloride in 150 ml. of water, and the layers were separated. The aqueous layer was extracted with ether for 6 hours with a continuous liquid extractor. The ether extracts were dried with $MgSO_4$ and distilled through a packed 15-plate column. The residue yielded 7.83 g. (70%) of *t*-butyl alcohol, b.p. 80–83°, $n^{25}\text{D}$ 1.3850.

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[40] N. Milas and D. Surgenor, *ibid.*, **68**, 642 (1946).

[41] D. F. Herman and W. K. Nelson, *ibid.*, **75**, 3877 (1953).