

2. Pentamethylacetone gave no enolization and 49% addition with the methyl Grignard reagent.

3. It has been confirmed that steric hindrance around the carbonyl retards both the enolization

and addition reactions. Thus 2,2-dimethyl-4-ethyl-3-hexanone gave 5% enolization and 19% addition with the methyl Grignard reagent.

STATE COLLEGE, PENNSYLVANIA

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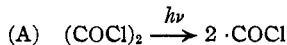
[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Carboxylation. III. The Peroxide-catalyzed Reaction of Oxalyl Chloride with the Side-chains of Aralkyl Hydrocarbons. A Preliminary Study of the Relative Reactivity of Free Radicals

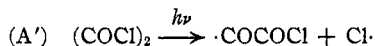
BY M. S. KHARASCH, STEPHEN S. KANE¹ AND HERBERT C. BROWN

It has been suggested that the photochemical carboxylation² of the paraffin hydrocarbons with oxalyl chloride proceeds in the following manner.

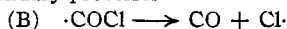
Primary process



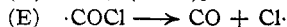
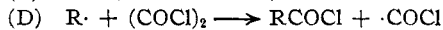
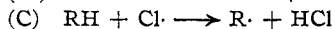
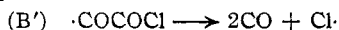
and/or



Secondary processes



and/or



The experimental evidence upon which this mechanism is based has already been discussed.³

Study of the carboxylation of a number of representative hydrocarbons indicates that this reaction is general for the paraffins, the cycloparaffins and their halogen derivatives. However, attempts to extend this photochemical reaction to the carboxylation of the side chains of representative aralkyl hydrocarbons have thus far met with little success.

This observation can be interpreted in either of two ways: (1) the aromatic hydrocarbons containing side-chains are opaque to the radiation necessary for the chain-initiating step, which is the photolysis of the oxalyl chloride (A); or (2) the aralkyl free radicals which are formed (C) require a relatively high energy of activation to break the carbon-to-carbon bond in oxalyl chloride (D).

(1) This paper is part of a dissertation submitted by Stephen S. Kane to the Faculty of the Division of Physical Sciences of the University of Chicago in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) The authors have adopted the term carboxylation to describe the introduction of the chloroformyl ($\cdot COCl$) group; see the first paper of this series (reference in footnote 3).

(3) Kharasch and Brown, *THIS JOURNAL*, **64**, 329 (1942).

Considerable support for the belief that the first of these interpretations is of importance in the photochemical carboxylation reaction was furnished by a study of the carboxylation of cyclohexane in the presence of various diluents. Carbon tetrachloride, chloroform, and similar inert diluents exert but small effects upon the rate of carboxylation of cyclohexane. The slight decrease observed, approximately 20%, can easily be accounted for by decreased concentration of the reactants. On the other hand, the presence of comparable quantities of benzene in the reaction mixture causes a five-fold drop in the rate. It is evident, therefore, that in the *photochemical* carboxylation of the aralkyl hydrocarbons, the poor yields are largely due to the effect of the aromatic nucleus upon the radiation required to initiate the carboxylation reaction.

It is noteworthy, however, that this interpretation does not eliminate the second of the two possibilities mentioned above: namely, that the low degree of reactivity⁴ of the aralkyl free radicals might also contribute to the sluggishness of the aralkyl hydrocarbons in the photochemical carboxylation reaction under discussion. The observation that the carboxylation reaction could be initiated thermally in the dark by the addition of several mole per cent. of an organic peroxide³ offered a means of investigating this question.

Accordingly, a study of the peroxide-catalyzed carboxylation of a number of aralkyl hydrocarbons was undertaken. It is significant that low yields (about 5–10%) of the corresponding acid chlorides were obtained with such representative aralkyl hydrocarbons as toluene, *m*-xylene, and mesitylene. In these reactions, the inhibitory ef-

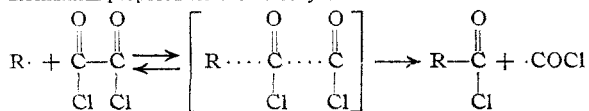
(4) That is, low compared with the highly reactive normal alkyl free radicals.

fect exerted by the nucleus in the photochemical reaction is absent, since cyclohexane readily participates in the peroxide-catalyzed carboxylation reaction in the presence of as much as 50 mole per cent. of benzene. Therefore, the authors are led to the conclusion that the low reactivity of the aralkyl free radicals (resulting in comparatively short chain lengths) must be an important factor in the low conversions noted in the reaction of oxalyl chloride with aralkyl hydrocarbons. In other words, the reaction of the comparatively inactive aralkyl free radicals with oxalyl chloride (D) is so slow that the free radicals have greatly increased opportunity to disappear by participation in side reactions.⁵

An interesting question which is raised by these considerations is that of the relative reactivity of free radicals. If the organic free radicals differ markedly in chemical reactivity (as the results of the carboxylation studies indicate), it would be of considerable interest then to obtain information concerning their relative reactivity. This paper describes some preliminary experiments to establish a method for carrying out such studies.

There is at hand considerable experimental evidence to support the conclusion that the decomposition of the diacyl peroxides in solution proceeds through the formation of organic free radicals as intermediates.⁶ The free radicals formed in this way may either react with the solvent or disappear by disproportionation, combination or other side reactions. The relative amount of any species of free radical which disappears by reaction with the solvent depends largely upon the nature of that solvent. Hence, by a judicious choice of solvent it should be possible to divide the free radicals into two groups which differ markedly in the extent of their attack upon the solvent in question. Obviously, these two groups could be further subdivided by the use of other solvents. In this way, a large number of organic

(5) This reactivity of the free radical must be intimately connected with the energy required for the formation of the activated complex, as indicated in the following equation, which is a more detailed representation of the processes involved in step D of the mechanism proposed for the carboxylation reaction:



That is, a free radical of "high" reactivity must require considerably less energy for the formation of the activated complex (shown in brackets above) than a free radical of "low" reactivity.

(6) Hey and Waters, *Chem. Rev.*, **21**, 169 (1937).

free radicals might finally be arranged in the order of their relative activities.

As a preliminary study of the practicability of the method outlined, an investigation of the decomposition of several representative diacyl peroxides in carbon tetrachloride was undertaken.⁷ Appreciable quantities of methyl, *n*-propyl and isopropyl chlorides were isolated from the reaction products of carbon tetrachloride, with diacetyl, di-*n*-butyryl and di-isobutyryl peroxides, respectively. On the other hand, no *t*-butyl or benzyl chloride could be found in the corresponding thermal decomposition products of di-trimethylacetyl or di-phenylacetyl peroxides in carbon tetrachloride. These results are interpreted, in accordance with the argument previously outlined, to mean that the methyl, *n*-propyl and isopropyl free radicals are of a higher order of reactivity than the benzyl or *t*-butyl free radicals. To the group of more active free radicals phenyl may be added, since dibenzoyl peroxide decomposes in carbon tetrachloride solution to form phenyl chloride and hexachloroethane⁸; triphenylmethyl, which crystallizes unchanged from carbon tetrachloride solution,⁹ evidently belongs to the less reactive class.

These results are summarized in Table I.

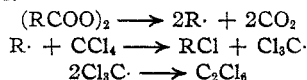
TABLE I
PRELIMINARY RESULTS ON A RELATIVE REACTIVITY SERIES
OF ORGANIC FREE RADICALS

	Free radical
Class I ^a	
More reactive free radicals	phenyl C ₆ H ₅ · methyl CH ₃ · <i>n</i> -propyl CH ₃ CH ₂ CH ₂ · isopropyl (CH ₃) ₂ CH·
Class II ^a	
Less reactive free radicals	benzyl C ₆ H ₅ CH ₂ · <i>t</i> -butyl (CH ₃) ₃ C· triphenylmethyl (C ₆ H ₅) ₃ C·

^a The arrangement of the free radicals within each of the two groups has not yet been verified experimentally.

It is perhaps too early to draw any theoretical

(7) Selection of carbon tetrachloride as the solvent in these preliminary experiments was dictated by a number of observations made at various times in this Laboratory that the decomposition of peroxides in this substance proceeds smoothly in accordance with the following equations:



The possibility of isolating and identifying both the organic chloride and the hexachloroethane offers a simple means of checking the results of any experiment. Cf. Böseken and Gelissen, *Rec. trav. chim.*, **43**, 869 (1924); Kharasch, Kane and Brown, *This Journal*, **63**, 526 (1941).

(8) Böseken and Gelissen; unpublished work of Kharasch and Walling.

(9) Gomberg and Cone, *Ber.*, **37**, 2036 (1904).

conclusions from the chemical structures of the two groups of radicals. However, it is of considerable interest that this division of the free radicals closely follows the relative electronegativity series¹⁰ of organic groups.¹¹ Thus the more reactive radicals are related to the more electronegative groups and the less reactive radicals to the less electronegative groups.

At first glance, it may appear somewhat surprising to find that the electronegativity series of organic groups, set up by a study of the hydrolytic splitting of unsymmetrical organomercurials, should correspond so closely to the arrangement of the free radicals according to their relative reactivities, as determined by the ease with which they react with carbon tetrachloride. Yet this correlation cannot be entirely fortuitous. The factors which tend to give an organic group such as phenyl or methyl a relatively high place in the electronegativity series, *i. e.*, which increase the tendency of the group to exist as a negative ion, probably also give the corresponding free radical a relatively high affinity for electrons.¹² Consequently, the free radical would fall into the more reactive class. By an obvious extension of the argument, the less electronegative groups may be identified with the less reactive free radicals. Whether other factors cause minor divergences between the two series remains to be settled by further experimentation. Until more definite information is available, however, the comprehensive classification of organic groups in the electronegativity series can probably be used as a rough indication of the relative reactivity of the organic free radicals. It is hoped to elaborate on these ideas in subsequent publications from this Laboratory.

Experimental Part

Attempt to Carboxylate the Aralkyl Hydrocarbons Photochemically.—A typical procedure utilizing toluene will be described. A mixture of 16.8 g. (0.2 mole) of

toluene and 12.7 g. (0.1 mole) of oxalyl chloride was placed in an elongated flask and illuminated under the conditions previously described for the carboxylation of the paraffinic hydrocarbons.¹³ After twenty hours, the reaction mixture was fractionated. Less than 0.4 g. of higher boiling material was isolated. With ammonia this material gave only a slight test for acid chloride groups. There was some indication of the presence of dibenzyl. Similar results were obtained with *m*-xylene, mesitylene, *p*-chlorotoluene, tetralin and β -methylnaphthalene. Under similar conditions, in a reaction mixture of cyclohexane and oxalyl chloride, approximately 50% of the oxalyl chloride is converted to the carboxylic acid derivative.

Photochemical Carboxylation of Cyclohexane in Presence of Diluents.—A number of reaction mixtures were made up using 0.1 mole of oxalyl chloride, 0.1 mole of cyclohexane and 0.1 mole of the diluent (benzene, carbon tetrachloride, chloroform, methylene chloride); these were illuminated for twenty hours by the standard procedure.¹³ The yields of cyclohexane carboxylic acid chloride from those reaction mixtures containing the halogenated methanes as diluents were only slightly less (approximately 80%) than those obtained from reaction mixtures free from diluents. On the other hand, the yield of the acid chloride from the reaction mixture containing benzene as diluent was markedly lower—only 15% of the usual yield.

Peroxide-Catalyzed Carboxylation of the Aralkyl Hydrocarbons.—In the main, the experimental procedure was similar to that used for the peroxide-catalyzed carboxylation of the paraffin hydrocarbons.¹⁴ A few modifications were, however, introduced. The hydrocarbon, oxalyl chloride, and dibenzoyl peroxide (3.0, 2.0, and 0.08 moles, respectively) were refluxed for twenty-four hours. The solution was then fractionated through a small column. The oxalyl chloride and most of the unreacted hydrocarbon was removed at ordinary pressure; the higher boiling material was fractionated under reduced pressure (approximately 20 mm.). Particular care was taken to separate benzoyl chloride (formed by the reaction of the peroxide on oxalyl chloride) from the acid chloride produced in the course of the reaction. The acid chloride thus obtained was identified by its boiling point, its neutral equivalent and the melting point of either the corresponding acid, or amide.

Under these experimental conditions, toluene produced an 8% yield of phenylacetyl chloride, *m*-xylene a 10% yield of 3-methylphenylacetyl chloride, mesitylene a 7% yield of 3,5-dimethylphenylacetyl chloride,¹⁵ and *p*-chlorotoluene a 5% yield of 4-chlorophenylacetyl chloride.

No appreciable quantity of the carboxylic acid derivatives could be obtained from diphenylmethane, *p*-nitrotoluene and β -methylnaphthalene.¹⁶

Di-phenylacetyl Peroxide.—Phenylacetyl chloride, b. p. 99–103° (16 mm.), was prepared from phenylacetic acid and phosphorus pentachloride. The peroxide was made by slowly running 5 g. of the acid chloride into a vigor-

(10) Kharasch and Marker, *THIS JOURNAL*, **48**, 3131 (1926); Kharasch and Flenner, *ibid.*, **54**, 674 (1932). For leading references to the application of the electronegativity theory to the interpretation of organic reactions, see Kharasch, Reinmuth and Mayo, *J. Chem. Ed.*, **13**, 7 (1936).

(11) The term "groups" has been substituted for the original term "radicals." At the time the electronegativity series was set up, no particular significance had yet been attached to the term radical. At the present time, however, "radical" is used chiefly to refer to neutral organic aggregates and it seems advisable thus to restrict the use of this term.

(12) The correlation which exists between the electronegativity series and dipole moment data [Brown, *THIS JOURNAL*, **61**, 1483 (1939)] lends further support to the view that the position of an organic group in the electronegativity series is a measure of the affinity of the bonding carbon atom for electrons.

(13) Kharasch and Brown, *ibid.*, **64**, 331–332 (1942).

(14) Kharasch and Brown, *ibid.*, pp. 332–333.

(15) M. p. of the amide (not previously reported) is 154–154.5°. *Anal.* Calcd. for $C_{10}H_{10}ON$: N, 8.59. Found: N, 8.66.

(16) It may be recalled that these substances also failed to undergo the peroxide-catalyzed chlorination reaction with sulfuryl chloride [Kharasch and Brown, *THIS JOURNAL*, **61**, 2142 (1939)].

ously stirred solution of 4 g. of sodium peroxide in 100 cc. of water. The temperature was carefully maintained slightly below 5°. After thirty minutes, the granules formed were filtered off and immediately added to carefully purified carbon tetrachloride.¹⁷ When the mixture was warmed, a vigorous reaction occurred which kept the carbon tetrachloride refluxing for several minutes. The carbon tetrachloride was then removed by distillation under ordinary pressure. The residue, 7 g., distilled from 115–200° (23 mm.). The combined distillate was washed with aqueous alkali and steam distilled. The solid obtained was identified as dibenzyl by its melting point of 52–53° (verified by the melting point of a mixture with an authentic sample). Acidification of the aqueous extract yielded a white crystalline precipitate, which, after recrystallization from water, was identified as phenylacetic acid from its m. p. of 75–76° and its neut. eq. of 140. Neither benzyl chloride nor hexachloroethane could be found in the reaction product.

Di-trimethylacetyl Peroxide.—Trimethylacetic acid was prepared by the Grignard reaction¹⁸ and was transformed into its acid chloride by the use of benzoyl chloride.¹⁹ The peroxide was prepared by the action of sodium peroxide on a solution of the acid chloride in ethyl ether.²⁰ This peroxide decomposed readily in warm carbon tetrachloride. Neither *t*-butyl chloride nor hexachloroethane could be identified in the reaction mixture.

From the less volatile constituents of the reaction product was obtained a liquid which distilled at 166–168°. It contained chlorine (28.54%) and appeared to be a C₈ derivative. Further identification was not attempted; the substance is probably formed by secondary reactions of the *t*-butyl free radicals.

Diacetyl, Di-*n*-butyryl, and Di-isobutyryl Peroxides.—These peroxides were prepared by methods similar to that described for di-trimethylacetyl peroxide. Their decomposition in hot excess carbon tetrachloride proceeded smoothly. From the reaction mixtures the corresponding alkyl chlorides²¹ were isolated in yields of 10 to 20% and

the presence of equivalent quantities of hexachloroethane was demonstrated.

Summary

1. A number of aralkyl hydrocarbons (toluene, *m*-xylene, mesitylene, *p*-chlorotoluene) react with oxalyl chloride in the presence of dibenzoyl peroxide to form the corresponding acid chlorides. (The reaction is $\text{RC}_6\text{H}_4\text{CH}_3 + (\text{COCl})_2 \rightarrow \text{RC}_6\text{H}_4\text{CH}_2\text{COCl} + \text{CO} + \text{HCl}$.) The conversions in the instances mentioned are low; they average 5–10% under conditions such that the carboxylation of representative paraffinic hydrocarbons is practically complete. Under the same conditions, some other aralkyl hydrocarbons (β -methylnaphthalene, diphenylmethane, *p*-nitrotoluene) are not appreciably carboxylated.

2. None of the aralkyl hydrocarbons were observed to undergo photochemical carboxylation with oxalyl chloride to any appreciable extent.

3. An important factor in the inhibition of the photochemical reaction of oxalyl chloride with the aralkyl hydrocarbons appears to be the effect of the aromatic nucleus on the radiation required for the photolysis of the oxalyl chloride, the chain-initiating step.

4. The low conversions in the peroxide-catalyzed reaction are ascribed to the comparatively low reactivity of the aralkyl free radicals, which results in a sluggish reaction of these intermediates with the oxalyl chloride.

5. Means of investigating the relative reactivity of aralkyl free radicals are discussed. Preliminary results indicate that the free radicals phenyl, methyl, *n*-propyl and isopropyl are more reactive than the benzyl, *t*-butyl and triphenylmethyl.

6. There is an interesting correspondence between the order of the free radicals when arranged according to their reactivities and the electronegativity series of organic groups. A plausible interpretation of this correspondence is advanced.

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(17) The carbon tetrachloride used in this work was washed with potassium permanganate solution, dried over Drierite, and distilled through an efficient column.

(18) "Organic Syntheses," Coll. Vol. I, p. 510.

(19) Brown, *THIS JOURNAL*, **60**, 1325 (1938).

(20) Procedure modified from that described by Gambayan, *Ber.*, **42**, 4008 (1909); see also Kharasch, Kane and Brown, *THIS JOURNAL*, **63**, 527 (1941).

(21) It is of considerable interest that *only n*-propyl chloride was obtained in the decomposition of *n*-butyryl peroxide and *only* isopropyl chloride was obtained from isobutyryl peroxide. This result suggests that the organic free radicals in solution do not isomerize to any appreciable extent. This point is of considerable importance for the further development of the chemistry of free radicals in liquid systems and has been discussed in detail in an earlier publication [Kharasch, Kane and Brown, *ibid.*, p. 526].