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Homolytic Aromatic Isopropyloxycarbonyloxylation Induced by Oxygen[*1]

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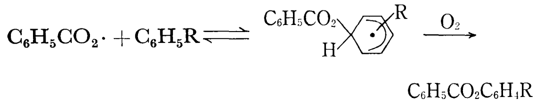
Thermal decomposition of diisopropyl peroxydicarbonate in benzene was carried out at several temperatures ranging from 40 to 70°C under an atmosphere of nitrogen, air or oxygen; the presence of oxygen caused the production of isopropyl phenyl carbonate. For this aromatic isopropyloxycarbonyloxylation induced by oxygen, a mechanism is proposed, which involves reversible addition of an isopropyloxycarbonyloxy radical to an aromatic nucleus to give a cyclohexadienyl intermediate, followed by oxidation with oxygen to produce the carbonate ester. The reaction in a mixture of benzene and hexadeuteriobenzene showed isotope effects for the formation of the ester, $k_H/k_D=2.1—2.3$, thus supporting the reversibility of the addition step of the isopropyloxycarbonyloxy radical to benzene.

In a previous communication[1] we reported that the decomposition of benzoyl peroxide in aromatic solvents under oxygen resulted in the aromatic benzoyloxylation and proposed a mechanism, in which the reversible addition of a benzoyloxy radical to an aromatic nucleus takes place to give a benzoyloxycyclohexadienyl radical, followed by oxidation with molecular oxygen to afford aryl benzoate.



In order to obtain further evidence for this mechanism we have extended the study to other aromatic acyloxylation. Thermal decomposition of diisopropyl peroxydicarbonate in benzene under an atmosphere of nitrogen, oxygen or air was carried out, and the effect of temperature and the isotope effect, utilizing hexadeuteriobenzene, in the aromatic isopropyloxycarbonyloxylation induced by oxygen was examined.

Experimental

Materials. Commercial diisopropyl peroxydicarbonate (purchased from Nippon Oils and Fats Co., Ltd.; purity as determined by iodometric titration, 100%) was used without further purification. Thiophene-free benzene was dried over calcium chloride and fractionated through a Vigreux column. Hexadeuteriobenzene (supplied by Showa Denko Co., Ltd.) was used without further purification.

Gas Chromatography. Gas chromatographic analysis was carried out with a Perkin-Elmer 154D Vapour Fractometer. Isopropyl phenyl carbonate was determined with the use of a 2 m-column of 10% Apiezon M grease on Diasolid H (40 mesh) at 170°C or a 2 m-column of 10% HV DC Silicone grease on Diasolid H at 167°C with *p*-chloroanisole as an internal standard. A mixture of phenyl and phenyl-d_5 isopropyl carbonates was collected from reaction mixtures using the abovementioned column of Silicone grease at 132°C, and subjected to mass spectrometric analysis.

Decomposition of Diisopropyl Peroxydicarbonate in Benzene. A solution of diisopropyl peroxydicarbonate (8 mmol) in benzene (300 m*l*) was placed in a three-necked flask, fitted with a stirrer, a thermometer, a gas inlet tube and a condenser. An appropriate gas (nitrogen, oxygen or air) after purification was bubbled through the solution to produce the desired atmosphere and the bubbling was continued during the whole reaction time. The flask was immersed in an oil bath maintained at a constant temperature (40—70±1°C). The peroxide was allowed to decompose completely and the reaction mixture was concentrated to 5—10 m*l* by distillation of benzene through a Vigreux

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[*1] Most part of this article was presented at the 21st (April, 1968, Osaka) and the 22nd (April, 1969, Tokyo) Annual Meetings of the Chemical Society of Japan.

[1] T. Nakata, K. Tokumaru and O. Simamura, *Tetrahedron Lett.*, **1967**, 3303.

Table 1. YIELD OF ISOPROPYL PHENYL CARBONATE AND CARBON DIOXIDE FROM DECOMPOSITION OF DIISOPROPYL PEROXYDICARBONATE IN BENZENE[a)] (In mol% of the peroxide)

Exp. No.	1	2[b)]	3[b)]	4	5	6	7	8	9
Reaction temp. (°C)	60	60	60	40	40	50	50	70	70
Atmosphere	N_2	O_2	Air	N_2	O_2	N_2	O_2	N_2	O_2
Reaction time (hr)	22	22	24	96	144	43	46	6.5	8
CO_2	183	136	—	185	65	186	111	184	181
i-PrOCOOPh	1	57	15	0.7	123	0.6	95	0.8	15
CO_2 group accounted for	184	193	—	186	188	187	206	185	196

a) Diisopropyl peroxydicarbonate (1.6 g) was allowed to decompose in benzene (300 m*l*).

b) Biphenyl (about 3%) was detected by VPC.

column on a water bath. The concentrated solution was subjected to gas chromatographic analysis to determine isopropyl phenyl carbonate. Determination of carbon dioxide was carried out by passing the exist gas from the top of a condenser attached to the reaction flask successively through a trap cooled with dry ice-ethanol, a tube with anhydrous calcium chloride and one with Ascarite, which was finally weighed.

Decomposition of Diisopropyl Peroxydicarbonate in a Mixture of Benzene and Hexadeuteriobenzene. Diisopropyl peroxydicarbonate (*ca.* 2 mmol) was dissolved in an equimolar mixture (25 m*l*) of benzene and hexadeuteriobenzene and allowed to decompose completely at 60°C under an atmosphere of oxygen or air. The reaction mixture was concentrated carefully to a volume of 1—2 m*l* by using a spinning band distillation column. From a portion of the concentrated solution a mixture of phenyl and phenyl-d_5 isopropyl carbonate was collected by gas chromatography. Both the concentrated solution and the collected ester-mixture were analyzed by using a Hitachi mass spectrometer RMU-E6 with ionizing beam of 70 eV to determine the ratio of phenyl to phenyl-d_5 isopropyl carbonates by comparison of the relative intensities of the following pairs of ion peaks:[2)] *i*-$PrOCOOC_6H_5^+$ at *m/e* 180 and *i*-$PrOCOOC_6D_5^+$ at *m/e* 185; $C_6H_5OCO^+$ and $C_6H_5OCHCH_3^+$ at *m/e* 121 and $C_6D_5OCO^+$ and $C_6D_5OCHCH_3^+$ at *m/e* 126; $C_6H_5OH^+$ at *m/e* 94 and $C_6D_5OH^+$ at *m/e* 99.

Results and Discussion

The results of the decomposition of diisopropyl peroxydicarbonate in benzene at several temperatures (40—70°C) under nitrogen, oxygen or air are summarized in Table 1 and Fig. 1.

While decomposition of diisopropyl peroxydicarbonate in benzene at 60°C under nitrogen gave carbon dioxide and isopropyl phenyl carbonate in 183 and 1%, respectively, passage of oxygen through the reaction mixture under otherwise the same reaction conditions caused a remarkable increase in the yield of isopropyl phenyl carbonate (57%) with the corresponding decrease of carbon dioxide (136%). The balance of the CO_2 group originally contained in the peroxide was accounted for nearly quantitatively under nitrogen and oxygen (92 and 97%, respectively). These results are satisfactorily explained by a mechanism similar to that proposed for the aromatic benzoyloxylation induced by oxygen[1)]

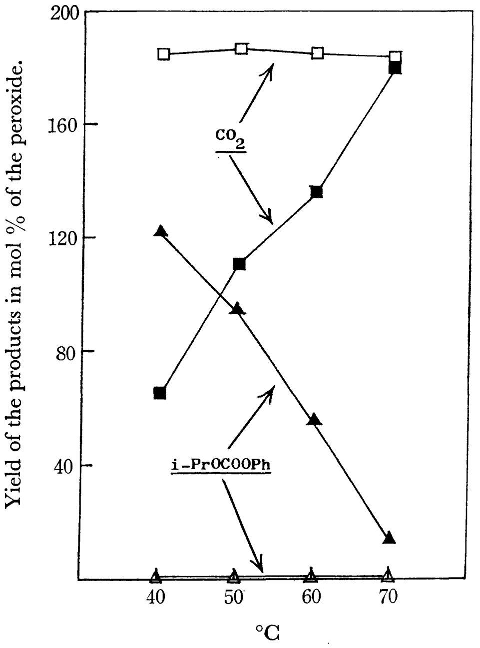
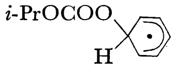


Fig. 1. Thermal decomposition of diisopropyl peroxydicarbonate (1.6 g) in benzene (300 m*l*): □, CO_2 under N_2; ■, CO_2 under O_2; △, *i*-PrOCOOPh under N_2; ▲, *i*-PrOCOOPh under O_2.

$$(i\text{-PrOCOO})_2 \xrightarrow{k_1} 2\, i\text{-PrOCOO}\cdot \qquad (1)$$

$$i\text{-PrOCOO}\cdot \xrightarrow{k_2} i\text{-PrO}\cdot + CO_2 \qquad (2)$$

$$i\text{-PrOCOO}\cdot + C_6H_6 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}}$$



(I) (3)

$$(I) + O_2 \xrightarrow{k_4} i\text{-PrOCOOC}_6H_5 + HO_2\cdot \qquad (4)$$

The formation of isopropyl phenyl carbonate, aromatic isopropyloxycarbonyloxylation, consists of two steps, the reversible addition of an isopropyloxycarbonyloxy radical to an aromatic nucleus

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[2)] P. Brown and C. Djerassi, *J. Amer. Chem. Soc.*, **88**, 2469 (1966).

to give an isopropyloxycarbonyloxycyclohexadienyl radical (reaction (3)), which proceeds competitively with decarboxylation (reaction (2)), and its subsequent oxidation by oxygen to afford isopropyl phenyl carbonate (reaction (4)). The proposal of a reversible addition step (reaction (3)) is based on the following reasons. If the addition were not reversible, in the first place, the decomposition, irrespective of the nature of the atmosphere, would give rise to carbon dioxide in approximately constant yield at a given temperature; and secondly, the decomposition under nitrogen might afford the carbonate ester in fairly good yield, by way of, for example, the disproportionation between isopropyloxycarbonyloxycyclohexadienyl radicals (I), similarly to that between phenylcyclohexadienyl radicals to yield biphenyl and dihydrobiphenyl.[3] The fact that the yield of the ester was dependent on the concentration of oxygen dissolved in the reaction mixture as shown (by the result under air) in Table 1 clearly indicates that the oxidation of the isopropyloxycarbonyloxycyclohexadienyl radical by molecular oxygen competes with its reversible dissociation to an isopropyloxycarbonyloxy radical and benzene.

The above mechanism is further supported by the study of the effect of temperature on the yield of the products under nitrogen or oxygen; the results are shown in Fig. 1. Under oxygen, the yield of isopropyl phenyl carbonate increased with lowering the reaction temperature, being 15 and 123% at 70 and 40°C, respectively, whereas the yield under nitrogen was invariably very low (less than 1%). With lowering the temperature, the yield of carbon dioxide did not change under nitrogen (about 185%), but decreased under oxygen with the corresponding increase of the carbonate ester. The effect of temperature on the yield of the ester under oxygen is certainly due to increase in the concentration of oxygen dissolved in the reaction mixture as well as decrease in the rate of decarboxylation from the isopropyloxycarbonyloxy radical with decrease in the reaction temperature.

In order to obtain further evidence for the reversibility of the addition of isopropyloxycarbonyloxy radicals to benzene, decomposition of diisopropyl peroxydicarbonate in large excess of an equimolar mixture of benzene and hexadeuteriobenzene was carried out at 60°C under oxygen and air, the apparent isotope effect for the formation of isopropyl phenyl carbonate being determined. The apparent isotope effect $k_\mathrm{H}/k_\mathrm{D}$ is defined by

$$\frac{k_\mathrm{H}}{k_\mathrm{D}} = \frac{(\text{yield of } i\text{-PrOCOOC}_6\text{H}_5)}{(\text{yield of } i\text{-PrOCOOC}_6\text{D}_5)} \times \frac{[\mathrm{C_6D_6}]}{[\mathrm{C_6H_6}]} \tag{5}$$

According to the reaction sequence (reactions (3) and (4)) shown above, the ratio between the isotopic esters formed is given by

$$\frac{(\text{yield of } i\text{-PrOCOOC}_6\text{H}_5)}{(\text{yield of } i\text{-PrOCOOC}_6\text{D}_5)} = \frac{k_4{}^\mathrm{H}}{k_4{}^\mathrm{D}} \times \frac{[\mathrm{C_6H_6}]}{[\mathrm{C_6D_6}]} \times K_{\mathrm{H/D}} \times \frac{(1+k_4{}^\mathrm{D}[\mathrm{O_2}]/k_{-3}{}^\mathrm{D})}{(1+k_4{}^\mathrm{H}[\mathrm{O_2}]/k_{-3}{}^\mathrm{H})} \tag{6}$$

where $K_{\mathrm{H/D}}=\dfrac{k_3{}^\mathrm{H}/k_{-3}{}^\mathrm{H}}{k_3{}^\mathrm{D}/k_{-3}{}^\mathrm{D}}$ and superscripts H and D refer to the reactions involving ordinary benzene and deuterated benzene, respectively.

Table 2. Isotope effects in aromatic isopropyloxycarbonyloxylation[a] (60°C)

Exp. No.	Atmosphere	Reactant benzene[b),d)] I_{78}/I_{84}	Isopropyl phenyl carbonate[d)]				Apparent isotope effect
			Sample analysed[c)]	I_{94}/I_{99}	I_{121}/I_{126}	I_{180}/I_{185}	
1	O_2	0.996	A	2.29	2.10	2.30	2.1—2.3
			B	2.23	2.10	2.34	
2	O_2	0.996	A	2.27	2.10	2.34	2.1—2.3
			B	2.22	2.08	2.36	
3	Air	1.06$_2$	A	1.91	1.75	1.90	1.6—1.8
			B	1.87	1.68	1.91	
4	Air	1.00$_3$	A	1.64	1.50	1.60	1.5—1.7
			B	1.67	1.38	1.75	

a) Diisopropyl peroxydicarbonate was allowed to decompose at 60°C in an equimolar mixture of benzene and hexadeuteriobenzene under a specified atmosphere. The initial peroxide concentration was 0.07—0.1 mol/*l*.

b) The hexadeuteriobenzene used was found to contain less than 3.3% of pentadeuteriobenzene, by mass spectrometric analysis with ionizing beam of 15 eV.

c) A denotes the carbonate collected from concentrated reaction mixtures by VPC; B, concentrated reaction mixtures.

d) Average of three measurements. I is the intensity of a mass spectrometric peak at *m/e* indicated as subscript of I.

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3) D. F. DeTar and R. A. J. Long, *J. Amer. Chem. Soc.*, **80**, 4742 (1958).

Table 2 contains values, as determined by mass spectrometry, for the ratio of the resulting isotopic esters, which is equal to the apparent isotope effect because of the use of equimolar amounts of benzene and hexadeuteriobenzene. Fairly large isotope effects, 2.1—2.3 under oxygen and 1.5—1.8 under air, were observed. If the rate of dissociation of the isopropyloxycarbonyloxycyclohexadienyl radical (I) is much lower than that of the reaction with oxygen, *i.e.*, $k_4[O_2] \gg k_{-3}$, the apparent isotope effect would be expressed by $k_H/k_D = k_3{}^H/k_3{}^D$. Numerical estimation of this ratio is difficult, since there has hitherto been no experimental results concerning the secondary isotope effect in the homolytic aromatic substitution. Small reverse secondary isotope effects have been noticed for the radical addition to deuterio-olefins,[4] however; it would therefore seem reasonable to assume that $k_3{}^H/k_3{}^D$ is unity or slightly less than unity. The observed apparent isotope effects are distinctly greater than this estimate. On the other hand, if $k_{-3} \gg k_4$ $[O_2]$, Eq. (6) reduces to

$$\frac{(\text{yield of } i\text{-PrOCOOC}_6\text{H}_5)}{(\text{yield of } i\text{-PrOCOOC}_6\text{D}_5)} = \frac{k_4{}^H}{k_4{}^D} \times K_{H/D} \times \frac{[C_6H_6]}{[C_6D_6]}$$

and $$k_H/k_D = (k_4{}^H/k_4{}^D) \times K_{H/D}$$

so that a fairly large apparent isotope effect is to be observed owing to the primary isotope effect for the oxidation step (reaction (4)), $K_{H/D}$ being not appreciably different from unity as mentioned above. Whether or not the actual situation corresponds to this extreme condition is not certain, but the observed isotope effects as a whole clearly indicate that the dissociation step competes favorably with the reaction with oxygen to give isopropyl phenyl carbonate, thus corroborating the reversibility of the addition step of the isopropyloxycarbonyloxy radical to an aromatic nucleus.*2

It is worth noting that the present results of isotope effect measurements for the production of the carbonate ester in the presence of oxygen, contrast with the observation of no apparent isotope effect in the presence of cupric chloride as an oxidant in place of oxygen reported by Kurz, Kovacic, Bose and Kugajevsky.[5] In the presence of cupric chloride, isopropyl phenyl carbonate has been proposed to arise by the following oxidative reaction:

$$i\text{-PrOCOOC}_6\text{H}_6\cdot + \text{CuCl}_2 \xrightarrow{k_4'} i\text{-PrOCOOC}_6\text{H}_5 + \text{CuCl} + \text{HCl}$$

The absence of apparent isotope effect leads to the conclusion that $k_4' \cdot [CuCl_2]$ is much larger than k_{-3}, in contrast with the present result that $k_4 \cdot [O_2]$ is smaller than k_{-3}. The fact that $k_4 \cdot [O_2]$ is, thus, much smaller than $k_4' \cdot [CuCl_2]$ is probably attributable both to higher efficiency (k_4') of cupric chloride than oxygen ($k_4' > k_4$) in oxidizing the cyclohexadienyl intermediate and to the higher concentration of cupric chloride used than that of oxygen dissolved in benzene.*3

Finally, it must be pointed out that the present observation of the isotope effect is in keeping with Denney and Klemchuk's finding of isotope effect, $k_H/k_D = 1.32$, for the intramolecular formation of 3,4-benzocumarin from 2-(2-deuteriophenyl)benzoyl peroxide, which led to the postulation of the intramolecular reversible cyclization of the *o*-phenylbenzoyloxy radical to give a cyclohexadienyl intermediate, followed by oxidation to the benzocumarin, without mention of the nature of the oxidant.[6]

The authors wish to thank Drs. M. Fukuyama and M. Anbe of Sagami Research Center for mass spectrometric measurements.

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[4] M. Feld, A. P. Stefani and M. Szwarc, *J. Amer. Chem. Soc.*, **84**, 4451 (1962); M. Takahasi and R. J. Cvetanović, *Can. J. Chem.*, **40**, 1037 (1962).

*2 The observation of somewhat smaller isotope effects for the reaction under air than under oxygen was contrary to the prediction from Eq. (6). The cause for this is unknown.

[5] M. E. Kurz, P. Kovacic, A. K. Bose and I. Kugajevsky, *J. Amer. Chem. Soc.*, **90**, 1818 (1968).

*3 In connection with the aromatic isopropyloxycarbonyloxylation caused by cupric chloride, Kurz and Kovacic examined the effect of several non-metallic oxidants in the reaction of diisopropyl peroxydicarbonate with toluene in acetonitrile at 60°C, and stated that oxygen brought about a small, but real, increase in isopropyl tolyl carbonate (in 6.6% yield), whereas, without any oxidant, the yield was very low (0.7%) (M. E. Kurz and P. Kovacic, *J. Org. Chem.*, **33**, 266 (1968)). In a preliminary experiment carried out during the present investigation, the presence of oxygen in the decomposition of diisopropyl peroxydicarbonate in toluene at 60°C caused a remarkable increase of isopropyl tolyl carbonate (in about 20% yield).

[6] D. B. Denney and P. P. Klemchuk, *J. Amer. Chem. Soc.*, **80**, 3289 (1958).