

was added in 1-g. portions over a 30-min. period below 30°. Isolation of the product by the method described above afforded 6.6 g. (66.0%) of relatively pure XIV, m.p. 110–112°. The analytical sample was obtained as white prisms from ethyl acetate–hexane, m.p. 111.5–112°.

Anal. Calcd. for C₁₀H₁₈N₂O: C, 65.89; H, 9.96; N, 15.37. Found: C, 66.01; H, 10.09; N, 15.18.

11,11-Dimethyl-4-oxo-3-aza-11-azoniabicyclo[4.4.1]undecane Iodide (XV). A solution of 10.6 g. (0.059 mole) of XIV and 19.0 g. (0.135 mole) of methyl iodide in 250 ml. of absolute ethanol was refluxed for 2 hr., cooled, and filtered to give 8.6 g. of product, m.p. 246–252°. By concentrating the mother liquor, there was obtained an additional 8.6 g. (total yield of 92.0%) of methiodide, m.p. 245–250°. Recrystallization of the combined fractions from aqueous ethanol–ether gave pure white crystals, m.p. 262–263°; ν^{Nujol} 3225 (NH) and 1660 cm.⁻¹ (amide carbonyl).

Anal. Calcd. for C₁₁H₂₁IN₂O: C, 40.69; H, 6.67; N, 8.63. Found: C, 40.65; H, 6.61; N, 8.68.

Hofmann Elimination of XV. A solution of 18.65 g. (0.058 mole) of XV in water was passed through a column of Amberlite IRA-400 (hydroxide form). One liter of eluate was collected and concentrated. The

residue was pyrolyzed to give 11.28 g. (100%) of a crystalline distillate. Three recrystallizations of this material from ethyl acetate–hexane gave an analytical sample, m.p. 128–129°; ν^{CHCl_3} 3400 (NH) and 1640 cm.⁻¹ (amide carbonyl). The ultraviolet spectrum showed only end absorption.

Anal. Calcd. for C₁₁H₂₀N₂O: C, 67.30; H, 10.27; N, 14.27. Found: C, 67.28; H, 10.40; N, 13.96.

Reaction of XVI with Perchloric Acid. A solution of 0.50 g. (2.55 mmoles) of XVI in 5 ml. of absolute ethanol was treated with an ethanolic solution of perchloric acid (1:1). The mixture was heated for 5 min. on a steam bath and cooled, and the precipitate was filtered. There was obtained 0.69 g. (91.5%) of white crystals, m.p. 158–159°; ν^{Nujol} 3350 (NH) and 1610 cm.⁻¹ (amide carbonyl). The ultraviolet spectrum showed only end absorption.

Anal. Calcd. for C₁₁H₂₁ClN₂O₅: C, 44.52; H, 7.11; N, 9.44. Found: C, 44.59; H, 7.14; N, 9.33.

Acknowledgment. We are indebted to the National Science Foundation for partial support of this research. L. A. P. gratefully acknowledges permission granted by The Upjohn Company, Kalamazoo, Michigan, to publish the conversion of II to Ib which was studied while he was in their employ.

Friedel–Crafts Oxygenation of Toluene with Diisopropyl Peroxydicarbonate¹

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Contribution from the Department of Chemistry, Case Institute of Technology, Cleveland, Ohio. Received November 12, 1964

Cresols were prepared in about 50% yield from toluene by direct oxygenation with diisopropyl peroxydicarbonate in the presence of aluminum chloride. Several reaction variables were studied including time, temperature, ratio of reactants, and nature of the catalyst. Electrophilic oxygenation is proposed on the basis of the cresol isomer distribution (ortho, 34%; meta, 11%; para, 55%), the relative reactivity value of 9.6 for $k_{\text{toluene}}/k_{\text{benzene}}$, the necessity of a catalyst, and the absence of products which would be derived from free-radical reactions. Evidence indicates that the oxygenated product is present in the reaction mixture mainly in the form ArO-CO₂AlCl₂. This procedure provides the first case of direct oxygenation of toluene in reasonably good yield with essentially no undesirable side reactions.

Introduction

The literature contains numerous examples of aromatic oxygenation³ with peroxides, e.g., hydrogen peroxide, peracids, and diaroyl peroxides. In many

of these cases the evidence points to participation of free-radical intermediates.⁴ However, analogous reactions which proceed by an electrophilic pathway have received relatively little attention. The historical treatment will be limited largely to those investigations which apparently fall in the latter category.

Hydrogen peroxide in the presence of concentrated sulfuric acid⁵ or boron trifluoride etherate⁶ has been used to effect oxygenation of mesitylene, toluene, and *m*-xylene in low yields. Derbyshire and Waters postulated the involvement of hydroxonium ion.

A similar mechanism was proposed in the case of peroxy acids for both the uncatalyzed⁷ and Lewis acid catalyzed reactions. Chambers, Goggin, and Musgrave,⁷ who reviewed earlier work on the reaction of peracetic acid with aromatics, examined the behavior of trifluoroperacetic acid toward *m*-xylene, mesitylene, and pseudocumene. The concept of electrophilic attack is consistent with the isomer distribution observed with *m*-xylene. Phenol ethers have also been

(1) From the Ph.D. thesis (1965) of S. T. M.; presented at the symposium in honor of Sir Christopher K. Ingold, Vanderbilt University, Nashville, Tenn., Aug. 1964.

(2) Union Carbide Co. Fellow, 1963–1964.

(3) This word has been chosen to designate direct introduction of RO (R = hydrogen, alkyl, acyl, etc.) into the aromatic nucleus.

(4) E.g., see J. R. L. Smith and R. O. C. Norman, *J. Chem. Soc.*, 2897 (1963); D. I. Davies, D. H. Hey, and G. H. Williams, *ibid.*, 1878 (1958).

(5) D. H. Derbyshire and W. A. Waters, *Nature*, **165**, 401 (1950).

(6) J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 24 (1962).

(7) R. D. Chambers, P. Goggin, and W. K. R. Musgrave, *J. Chem. Soc.*, 1804 (1959).

used as substrates with this reagent.⁸ These reactions are generally characterized by modest yields of mono-oxygenated products since further oxidation was prone to occur. Benzene and toluene, in contrast, gave only tars. Hart and co-workers,⁹ in recent investigations of the boron trifluoride catalyzed reaction of trifluoro-peracetic acid with aromatics, reported fair to good yields of hydroxylated products from mesitylene, isodurene, and prehnitene. The formation of cyclohexadienones, isolated from hexaalkylbenzenes and prehnitene, indicated the intermediacy of positively charged entities.

In the presence of a Friedel-Crafts catalyst, diaroyl peroxides are known to form esters with aromatics,^{10,11} particularly of the activated type. Orientation pointed to an electrophilic mechanism.¹⁰

The objectives of this work were to effect Friedel-Crafts oxygenation of toluene with diisopropyl peroxydicarbonate and to study the mechanistic aspects.

Results and Discussion

The standard conditions (diisopropyl peroxydicarbonate:aluminum chloride:toluene = 1:2:20 (molar), 0°, 3 hr.) gave a mixture of crude phenols of which 96% were cresols, a 49% yield based on the peroxide (53% when corrected for losses incurred during work-up). The cresols were identified by the infrared spectrum, g.l.c. retention time, elemental analysis, boiling point, and odor. Infrared spectroscopy provided the isomer distribution: 34% *ortho*, 11% *meta*, 55% *para*. A higher boiling material (2%) was obtained as a by-product which had a retention time and infrared spectrum similar to those of the cymenols. The distillation residue constituted 2% of the phenols.

The neutral portion contained mainly cymenes (primarily *meta*) characterized by the infrared spectrum, g.l.c. retention time, and elemental analysis. In addition, some 3,5-diisopropyltoluene was present which was identified by the infrared spectrum.

A number of variables were examined in order to determine their effect on the reaction. It was found that the yield of cresols was very dependent on the ratio of aluminum chloride to peroxide, at least a 2:1 molar ratio being required for good results (Table I). In

Table I. Effect of Catalyst:Peroxide Ratio^a

AlCl ₃ : peroxide, mole ratio	Product yield		
	Crude phenolic, g.	Cresols g.	%
3	4.6	4.0	53
2	4.2	3.7	49
1	1.7	1.5	18

^a At 0° for 3 hr. with 0.07 mole of peroxide and 1.4 moles of toluene.

relation to the temperature variable, the -30 to 25° region was investigated. Best yields were observed at 0 to 25° (Table II). The amount of cresol increased

(8) J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 627 (1962).

(9) C. A. Buehler and H. Hart, *J. Am. Chem. Soc.*, **85**, 2177 (1963); A. J. Waring and H. Hart, *ibid.*, **86**, 1454 (1964).

(10) J. T. Edward, H. S. Chang, and S. A. Samad, *Can. J. Chem.*, **40**, 804 (1962).

(11) D. Z. Denney, T. M. Valega, and D. B. Denney, *J. Am. Chem. Soc.*, **86**, 46 (1964).

Table II. Effect of Temperature^a

Temp., °C.	Product yield		
	Crude phenolic, g.	Cresols g.	%
-30	3.9	3.3	43
0	4.6	4.0	53
25	4.4	3.8	50

^a For 3 hr. with peroxide:aluminum chloride:toluene = 1:3:20 (molar) (ca. 0.07 mole of peroxide).

slightly on increasing the reaction time from 1.5 to 3 hr., and then remained essentially constant for longer times (Table III). Short periods could not be examined

Table III. Effect of Reaction Time^a

Time, hr.	Product yield		
	Crude phenolic, g.	Cresols g.	%
1.5	3.9	3.3	43
3	4.2	3.7	49
6	4.3	4.1	51

^a At 0° with peroxide:aluminum chloride:toluene = 1:2:20 (molar) (ca. 0.07 mole of peroxide).

conveniently since the exothermic reaction precluded rapid addition of the peroxide. Doubling the amount of toluene served only to decrease the over-all yield, presumably because of additional losses during work-up, with little alteration in the per cent of high-boiling phenol and residue (Table IV).

Table IV. Effect of Toluene Concentration^a

Toluene: peroxide, molar ratio	Product yield		
	Crude phenolic, g.	Cresols g.	%
20	4.15	3.7	49
40	3.45	3.1	41

^a At 0° for 3 hr. with aluminum chloride:peroxide = 1:2 (molar) (ca. 0.07 mole of peroxide).

From a study of various candidate catalysts, the indicated order of reactivity was obtained: AlCl₃ > BF₃, AlBr₃ > SbCl₅ > FeCl₃, SnCl₄, H₃PO₄ (Table V). Introduction of coordinating solvents, namely ethyl ether, nitromethane, or tetramethylene sulfone, markedly decreased the product yield with aluminum chloride or boron trifluoride. It is well established that reactions of the Friedel-Crafts type are affected by the catalyst strength. For example, acylation of toluene with acetyl chloride revealed the following decrease in catalyst potency¹²: AlCl₃ > SbCl₅ > FeCl₃ > SnCl₄. Hence, the order is similar to that obtained in the present study. However, the catalyst rating is known to depend on conditions, particularly the nature of the

(12) O. C. Dermer, D. M. Wilson, F. M. Johnson, and V. H. Dermer, *ibid.*, **63**, 2881 (1941).

Table V. Catalyst Variation^a

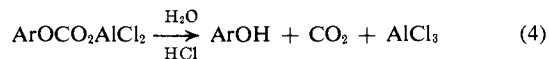
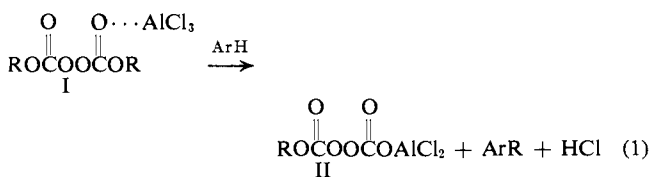
Catalyst	Product yield		
	Crude phenolic, g.	Cresols	
		g.	%
AlCl ₃	4.15	3.7	49
BF ₃ ^b	3.8	1.8	24
AlBr ₃	1.95	1.7	22
AlCl ₃ -CH ₃ NO ₂ ^c	1.6	1.0	12
SbCl ₅	0.8	0.3	4
AlCl ₃ -(CH ₂) ₄ SO ₂ ^c	0.5	0.3	4
BF ₃ ·Et ₂ O	0.2
FeCl ₃	<0.1
SnCl ₄	<0.1
H ₃ PO ₄ (80%)	<0.1

^a At 0° for 3 hr. with 1.4 moles of toluene and 0.07 mole of peroxide (peroxide:catalyst = 1:2). ^b The gas was slowly passed into the reaction mixture during 3 hr. ^c 1:1 molar ratio.

reaction.¹³ Russell¹⁴ proposed the order AlBr₃ > FeCl₃, SbCl₅ > BF₃, SnCl₄ from an investigation of the reactions: alkane isomerization, alkylation of benzene, and polymerization of styrene.

It is not certain that the catalyst is the metal halide itself. The active agent may be a proton (or hydrogen of increased acidity) obtained from interaction of the metal halide with a cocatalyst, such as water. This possibility is supported by previous investigations which point to cocatalysis by Brønsted acids in the Friedel-Crafts alkylation¹⁵ of benzene with alkyl halides or ethers in the presence of boron trifluoride catalyst.

A reasonable reaction scheme which is consistent with the experimental findings is



Alternatively, oxygenation might precede alkylation.



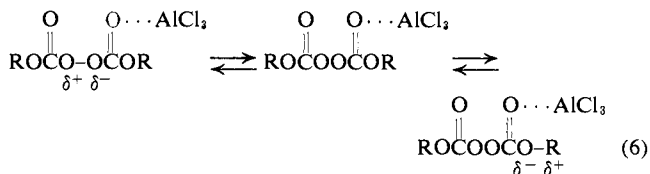
It is likely that a peroxide-catalyst complex plays a crucial role since no reaction occurred in the absence of aluminum chloride. In addition, when diisopropyl peroxydicarbonate was added to aluminum chloride in cyclohexane, a brown flocculent mass was formed. However, no evidence concerning the structure of the brown material could be obtained because of the rapid reaction with atmospheric moisture during attempted identification. Complexes similar to I have been

(13) G. A. Olah in "Friedel-Crafts and Related Reactions," Vol. I, G. A. Olah, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter XI.

(14) G. A. Russell, *J. Am. Chem. Soc.*, **81**, 4834 (1959).

(15) G. F. Hennon and R. A. Kurtz, *ibid.*, **65**, 1001 (1943); R. L. Burwell, Jr., and L. M. Elkin, *ibid.*, **73**, 502 (1951).

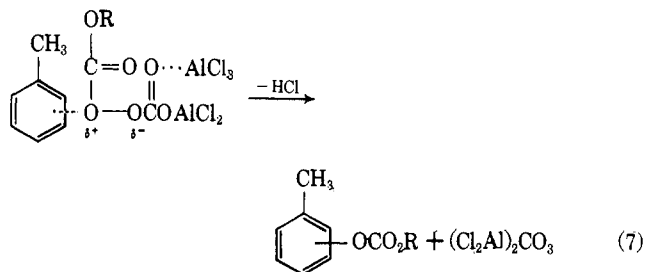
proposed previously in the carboxy inversion of benzoyl peroxide with antimony pentachloride,¹¹ and in the Friedel-Crafts oxygenation of aromatics with a substituted benzoyl peroxide.¹⁰ Aluminum chloride has been shown to complex with a variety of carbonyl-containing compounds, including esters.¹⁶ Evidence in the case of esters and ketones indicates that coordination involves the carbonyl oxygen.¹⁶ Accordingly, there would be a resultant increase in the electrophilic character of both an isopropyl group and a peroxide oxygen.



Alkyl esters are known to effect alkylation under Friedel-Crafts conditions.^{17, 18} Although acylation is a possible competing reaction, the factors cited are known to facilitate alkylation¹⁸: (a) stability of the alkyl group as a carbonium ion, *i.e.*, tertiary > secondary, > primary, and (b) lower temperatures. Furthermore, the aluminum derivative II brings to mind the stoichiometry proposed for acylation with acid anhydrides.¹⁹

The predominant *ortho, para* orientation with toluene suggests an electrophilic substitution mechanism. Subjecting a cresol mixture to simulated reaction conditions established the validity of the isomer distribution. No isomerization was found. The relatively large amount of *meta* isomer indicates that the attacking species possesses high activity²⁰ and therefore low selectivity. The selectivity factor, *S_i*, which can be calculated from orientation data, serves as a measure of activity.^{21, 22}

Brown and co-workers^{21, 23, 24} postulated a concerted displacement mechanism for the Friedel-Crafts methylation of toluene. Since the selectivity factor (1.0) for the diisopropyl peroxydicarbonate-toluene-aluminum chloride reaction is close to the value for methylation (0.84), a similar mechanism for oxygenation appears reasonable.



(16) N. N. Greenwood and K. Wade, pp. 585 and 586 of ref. 13.

(17) F. A. Drahowzal in "Friedel-Crafts and Related Reactions," Vol. II, Part 1, G. A. Olah, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, Chapter XX.

(18) C. A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1941, p. 673 ff.

(19) P. H. Groggins, R. H. Nagel, and A. J. Stirton, *Ind. Eng. Chem.*, **26**, 1317 (1934).

(20) H. C. Brown and K. L. Nelson, *J. Am. Chem. Soc.*, **75**, 6292 (1953).

(21) H. C. Brown and C. R. Smoot, *ibid.*, **78**, 6255 (1956).

(22) L. M. Stock and H. C. Brown, *ibid.*, **81**, 3323 (1959).

(23) H. Jungk, C. R. Smoot, and H. C. Brown, *ibid.*, **78**, 2185 (1956).

(24) H. C. Brown and H. Jungk, *ibid.*, **77**, 5584 (1955).

Additional information pertinent to the concept of activity was obtained from competitive oxygenation (heterogeneous) of benzene-toluene (Table VI). The relative rate $k_{\text{toluene}}/k_{\text{benzene}}$ was calculated²⁵ from the amounts of phenol and cresol formed by use of the equation $k_T/k_B = \text{cresol/phenol}$ (molar).

The average value of 9.6 (Table VI) compares favorably with the figure 6.1 calculated from Brown's equation on the assumption that the selectivity relationship is obeyed.^{21,22}

Table VI. Competitive Oxygenation with Diisopropyl Peroxydicarbonate^a

Benzene, moles	Toluene, moles	Phenolic product		
		Cresol + phenol, g.	Cresol: phenol, <i>M</i>	Residue, g.
1.7	1.7	2.8 ^b	8.7	0.13
1.4	1.4	3.6 ^b	10.4	0.09

^a Peroxide (0.07 mole), aluminum chloride (0.14 mole), 0°, 3 hr.; 50 ml. of the benzene-toluene mixture was used to dissolve the peroxide. ^b Less than 5% of the crude phenolic product consisted of high boiling distillate.

The relative rates are in the same range as the values reported for those reactions, *e.g.*, alkylations, entailing electrophiles of comparatively high activity (Table VII)

Table VII. Reactivity Ratios

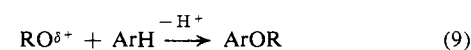
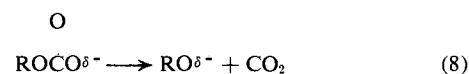
Reaction	Conditions	k_T/k_B	Ref.
Isopropylation	<i>i</i> -PrBr, GaBr ₃ , 25°	2	25
Amination	HN ₃ , AlCl ₃ , 26-28°	5	<i>a</i>
Sulfonation	H ₂ SO ₄ , 25°	5	<i>b</i>
Methylation	MeBr, GaBr ₃ , 25°	6	21
Mercuration	Hg(OAc) ₂ , HClO ₄ , 25°	8	<i>c</i>
Oxygenation	(<i>i</i> -PrOCO ₂) ₂ , AlCl ₃ , 0°	9	
Chlorination	Cl ₂ , HOAc, 24°	345	<i>d</i>
Bromination	Br ₂ , HOAc, 25°	465	<i>e</i>

^a P. Kovacic, R. L. Russell, and R. P. Bennett, *J. Am. Chem. Soc.*, **86**, 1588 (1964). ^b F. J. Stubbs, C. D. Williams, and C. N. Hinshelwood, *J. Chem. Soc.*, 1065 (1948). ^c H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2300 (1955). ^d P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 279 (1943). ^e E. Berliner and F. J. Bondhus, *J. Am. Chem. Soc.*, **70**, 854 (1948).

Information was obtained concerning the nature of the oxygenated product at the end of reaction. The ester form, ArOCO₂R, certainly is not present since almost all (93%) of the isopropyl groups were found in the hydrocarbon fraction. Also phenyl isopropyl carbonate undergoes decomposition in toluene at 0° in the presence of aluminum chloride. The essentially quantitative dealkylation yielded phenol and cymenes. Kane and Lowy²⁶ similarly alkylated benzene using diethyl carbonate under Friedel-Crafts conditions.

Further insight was gained by following the evolution of carbon dioxide from phenyl isopropyl carbonate-toluene-aluminum chloride during reaction and work-up. While the reaction was underway, 17% of the theoretical amount of carbon dioxide was evolved, whereas 75% was collected during subsequent

acid hydrolysis of the reaction mixture. These data support the conclusion that the oxygenated product from the peroxide reaction is present predominantly in the form ArOCO₂AlCl₂. Presumably, the small amount of decarboxylation gives rise to the structure C₆H₅-OAlCl₂.²⁷ In addition, only 22% of the theoretical amount of carbon dioxide was generated during oxygenation of toluene with diisopropyl peroxydicarbonate, while 59% was collected during hydrolysis. Therefore, it is reasonable to conclude that the carbon dioxide evolved during the peroxide reaction might well arise from decomposition of a nonperoxidic carbonic acid derivative. Alternatively, consideration should be given to limited participation of the process



A substantial body of evidence indicates that homolysis is not involved as part of the reaction pathway. A careful search revealed no products, *e.g.*, bibenzyl or α -substituted toluenes, of the type usually formed from toluene in systems containing free radicals. In addition, thermal decomposition of diisopropyl peroxydicarbonate in ethylbenzene²⁸ afforded carbon dioxide, isopropyl alcohol, and 2,3-diphenylbutane. Heating diethyl peroxydicarbonate in dichlorotoluene²⁹ gave tetrachlorobibenzyl, carbon dioxide, and ethyl alcohol.

In summary, an electrophilic substitution mechanism for the oxygenation is supported by the items: (1) necessity of a Lewis acid catalyst; (2) ability of the reaction to proceed at low temperatures, conditions under which the peroxide is stable; (3) isomer distribution-free-radical phenylation³⁰ characterized by relatively large amounts of *ortho* and *meta* isomers; (4) relative rate in the reaction involving the phenyl radical (k_T/k_B value is 1.9)³⁰; (5) absence of products usually arising from free-radical reactions.

This investigation provides the first method for the smooth, direct oxygenation of simple aromatic hydrocarbons leading to reasonably good yields of the corresponding monohydroxy derivatives. In prior work all attempts to oxygenate compounds of this type have led either to no reaction³¹ or to higher oxidation products, including dihydroxy derivatives, quinones, products from oxidative ring cleavage, and tar.⁵⁻⁷

It is tempting to speculate as to the reasons why diisopropyl peroxydicarbonate has proven so useful as an oxygenating agent. First, the electron-withdrawing power of the oxygens attached to the -C(=O)OOC-(=O)- group may favor heterolytic cleavage (*cf.* trifluoroperacetic acid *vs.* peracetic acid,⁷ and *p,p'*-dinitrobenzoyl peroxide *vs.* benzoyl peroxide¹⁰). Second, the incipient oxonium ion may be stabilized by

(27) G. Perrier, *Bull. soc. chim.*, [3] **9**, 1049 (1893).

(28) S. G. Cohen and D. B. Sparrow, *J. Am. Chem. Soc.*, **72**, 611 (1950).

(29) H. C. McBay, O. Tucker, and P. T. Groves, *J. Org. Chem.*, **24**, 536 (1959).

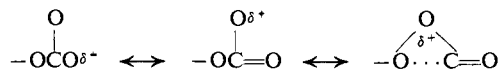
(30) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 484.

(31) J. Boeseken and G. Slooff, *Rec. trav. chim.*, **49**, 100 (1930).

(25) S. U. Choi and H. C. Brown, *J. Am. Chem. Soc.*, **81**, 3315 (1959).

(26) H. L. Kane and A. Lowy, *ibid.*, **58**, 2605 (1936).

resonance interaction



This would be expected to facilitate its formation and also to decrease its activity, thereby reducing multiple substitution and other undesirable side reactions. Third, the product appears to be protected from further attack by retention of the carbonate structure until hydrolysis. Experimental verification of this hypothesis was obtained. The theoretical amount of phenol was isolated from a reaction mixture containing diisopropyl peroxydicarbonate-phenyl isopropyl carbonate-toluene-aluminum chloride. This demonstrates that toluene is more prone to interaction with the peroxide than is the phenol ester. It is reasonable to presume that the phenol ester-aluminum chloride complex would exhibit decreased reactivity toward various electrophilic and radical reagents in comparison with the free phenol. On the other hand, only 84% of the phenol was recovered from the system diisopropyl peroxydicarbonate-phenol-toluene-aluminum chloride. The remainder of the phenol was converted to unidentified, higher molecular weight phenolic material. In most of the previous oxygenation procedures, e.g., those involving hydrogen peroxide³² and peracids,⁶ the oxygenated product is present as a free phenol which is highly vulnerable to subsequent attack by the peroxide. In contrast, it should be noted that phenol remained unchanged in the presence of diisopropyl peroxydicarbonate in toluene solution at 0°.

From a mechanistic point of view, this novel procedure is particularly significant since it makes available for the first time data on the isomer distribution from toluene and the relative rates (k_T/k_B) for electrophilic oxygenation. Toluene is usually used as a standard for comparison in the various mechanistic categories.

Finally, it seems worthwhile to indicate similar processes involving aromatic substitution by heterolysis of related bond structures. The example of the chlorine molecule, leading to aromatic halogenation, is well known. One can also cite amination with hydroxylamines³³ and sulfuration with sulfonyl chlorides.³⁴ The favored route in the case of hypochlorites is chlorination.³⁵ In contrast, hydrazines display an intriguing inertness.³⁶ It is instructive to consider the first ionization energies (kcal./mole) for these elements³⁷: N, 335; O, 313.8; Cl, 300; C, 259.5; S, 238.8. Of course, it should be borne in mind that the concept of ionization energy constitutes an oversimplified picture.

Experimental³⁸

Materials. Commercial materials, usually of high purity, were used directly. Aluminum bromide of

(32) J. W. Cook and R. Schoental, *J. Chem. Soc.*, 47 (1950).

(33) P. Kovacic and J. L. Foote, *J. Am. Chem. Soc.*, 83, 743 (1961).

(34) H. Brintzinger and M. Langheck, *Ber.*, 86, 557 (1953).

(35) M. Anbar and D. Ginsberg, *Chem. Rev.*, 54, 925 (1954); C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.*, 82, 6108 (1960).

(36) P. Kovacic, R. P. Bennett, and J. L. Foote, *J. Org. Chem.*, 26, 3013 (1961).

(37) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1960, p. 57.

(38) Boiling points are uncorrected. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y.

technical grade was used. We are grateful to the Pittsburgh Plate Glass Co. for generous samples of diisopropyl peroxydicarbonate. *p*-Cymene (Matheson) was distilled before use. The following compounds, used as standards in analyses by infrared spectroscopy or gas chromatography, were purified by distillation *in vacuo*: phenol (Merck), *o*- and *m*-cresol (Eastman, practical), and *p*-cresol (Matheson).

Aromatic Oxygenation with Peroxides. General Procedure. A solution of the peroxide (ca. 0.07 mole) in a portion (50 ml.) of the aromatic reactant was added slowly during 75 min. to a mixture of aluminum chloride (19 g., 0.14 mole) and the remainder (100 ml.) of the aromatic in a three-necked flask fitted with a stirrer, thermometer, gas inlet for nitrogen, and condenser. The temperature was maintained at 0 ± 4° by means of an ice bath. A slow flow of nitrogen was maintained. In some cases the liberated hydrogen chloride was titrated with sodium hydroxide solution (phenolphthalein as the indicator). A maximum of about 2 moles of hydrogen chloride were evolved per mole of peroxide.

The reaction mixture was then added with stirring to a mixture of hydrochloric acid and crushed ice. After the layers were separated, the aqueous portion was washed with ether until the ether was colorless. The ether extracts were combined with the initial organic layer and washed with 0.1 *N* ferrous sulfate to remove unreacted peroxide. The ether was evaporated, and the residue was heated at reflux for 2 hr. with 10% sodium hydroxide under nitrogen. After being cooled, the layers were separated and the organic phase was washed with 10% sodium hydroxide until the basic extracts were colorless. The aqueous phase was acidified in the cold with hydrochloric acid, and then repeatedly extracted with ether. The ether was evaporated, and the residue distilled *in vacuo*. Yields are based on the peroxide.

Diisopropyl Peroxydicarbonate-Toluene-Aluminum Chloride. Product Identification. A solution (100 ml.) of diisopropyl peroxydicarbonate (29.4 g., 0.143 mole) in toluene was treated with aluminum chloride (38.0 g., 0.29 mole) in toluene (200 ml.) according to the general procedure. The addition required 2.25 hr. at 0°, and the mixture was stirred 3.75 hr. at the same temperature.

Distillation of the phenolic portion gave 7.66 g. of a slightly yellow liquid (characteristic cresol odor) and residue (0.18 g.). The distillate was analyzed by gas chromatography and found to contain 7.5 g. (49% yield, 96% recovery from crude phenolic product) of isomeric cresols, b.p. 85–95° (15 mm.); lit.³⁹ b.p. for *m*-cresol 85–87° (15 mm.).

Anal. Calcd. for C₇H₈O: C, 77.78; H, 7.46. Found: C, 78.07; H, 7.29.

Orientation data (infrared spectroscopy) from duplicate experiments gave: *ortho:meta:para* = 34:11:55, 36:10:54. The same retention time in gas chromatography was observed as for an identical mixture of authentic isomers.

The distillate also contained a small amount (about 2% of the crude phenolic product by g.l.c. analysis) of

Scouting work in this area was initiated by the senior author at E. I. du Pont de Nemours and Co. in 1949.

(39) F. Krollpfeiffer, *Ann.*, 430, 214 (1922).

a higher boiling component. This material, isolated by gas chromatography, exhibited a retention time and infrared spectrum similar to, but not identical with, the cymenols obtained from oxygenation of *p*-cymene with diisopropyl peroxydicarbonate-aluminum chloride (absorption maxima at 2.95 (s), 3.45 (s), 6.34 (m), 6.70 (s), 6.90 (s), 7.60 (s), 8.00 (s), 8.49 (s), 9.06 (s), 10.16 (w), 10.85 (w), 11.42 (m) in carbon tetrachloride).

Distillation of the neutral organic material gave the following fractions: (1) toluene, recovered, 210 ml.; (2) cymenes, 27 g. (0.20 mole), b.p. 68° (15 mm.), b.p. 174° (micro); lit.⁴⁰ b.p. 178° (*ortho*), 175° (*meta*), 177° (*para*) (the product exhibited essentially the same infrared spectrum and retention time in gas chromatography as did a mixture of the authentic isomers. *Anal.* Calcd. for C₁₀H₁₄: C, 89.49; H, 10.51. Found: C, 89.77; H, 10.43); (3) liquid, 5 g., b.p. 68–110° (1.5 mm.), consisting of a mixture of cymenes and 2,5-diisopropyltoluene (the higher boiling component, isolated by g.l.c., possessed the same infrared spectrum as did 3,5-diisopropyltoluene⁴¹; (4) residue, 1 g.

Diisopropyl Peroxydicarbonate and Toluene. A solution of diisopropyl peroxydicarbonate (20 g.) in toluene (150 ml.) was stirred for 3 hr. at 20–25°. The standard work-up yielded recovered toluene and no phenolic product (gas chromatographic analysis).

Diisopropyl Peroxydicarbonate-Phenol-Toluene. Phenol (10 g., 0.11 mole) in 100 ml. of toluene was cooled to 0° and 50 ml. of a solution of diisopropyl peroxydicarbonate (14.5 g., 0.070 mole) in toluene was added dropwise with stirring during 0.5 hr. No temperature rise was observed. The solution was stirred 2.5 hr. at the same temperature and then extracted with 10% aqueous sodium hydroxide. The extract was acidified in the cold and washed with ether, and the ether solution was evaporated. Distillation provided 9.5 g. (95% recovery) of phenol and a residue of 0.02 g.

Phenyl Isopropyl Carbonate. The ester was prepared by a modification of the procedure of Tarbell and Longosz.⁴² A solution of isopropyl chloroformate (30 g., 0.29 mole) and phenol (34 g., 0.36 mole) in 100 ml. of ether was cooled to 0° with stirring. Triethylamine (37 g., 0.36 mole) was added dropwise while the temperature was maintained at 0–10°. Stirring at 0° was continued for 0.5 hr. after the addition was completed.

After the amine salt was filtered and washed with ether, the liquid was washed successively with 1 *N* hydrochloric acid, 5% sodium hydroxide, and water. Following evaporation of the ether, distillation gave 38 g. (85%) of clear liquid, b.p. 96–100° (5 mm.), micro b.p. 209°, lit.⁴³ b.p. 220° (750 mm.). Gas chromatography showed a small amount of impurity.

Phenyl Isopropyl Carbonate-Toluene-Aluminum Chloride. A solution of phenyl isopropyl carbonate (10 g., 0.055 mole) in toluene (50 ml.) was added dropwise to a stirred mixture of aluminum chloride (15 g., 0.11 mole) in toluene (100 ml.) at 0–5° during 1 hr. After an additional 2 hr. at 0–5°, the mixture was poured onto

(40) N. A. Lange, "Handbook of Chemistry," 9th Ed., Handbook Publishers, Inc., Sandusky, Ohio, 1956, p. 470.

(41) Infrared Spectral Data, American Petroleum Institute, 1956, serial no. 1748.

(42) D. S. Tarbell and E. J. Longosz, *J. Org. Chem.*, **24**, 774 (1959).

(43) P. Cazeneuve and A. Morel, *Bull. soc. chim. France*, **20**, 768 (1898).

ice-hydrochloric acid, the layers were separated, and the aqueous phase was washed with ether. Removal of the ether and toluene by distillation provided a residue which was subjected to gas chromatography. The two components were collected and shown to be phenol and cymenes by infrared analysis and g.l.c. retention times. None of the starting ester was present.

In a similar experiment carried out with a catalyst: ester ratio of one the carbonate ester was recovered unchanged.

Diisopropyl Peroxydicarbonate-Phenol-Toluene-Aluminum Chloride. Aluminum chloride (19.5 g., 0.14 mole) was added to a solution of phenol (5.0 g., 0.053 mole) in 100 ml. of toluene at 0°. After 0.5 hr. a toluene solution (50 ml.) of diisopropyl peroxydicarbonate (14.5 g., 0.07 mole) was added during 1.5 hr. at 0°. Stirring was continued for 1.5 hr. at this temperature, and the mixture was then mixed with ice-hydrochloric acid. The organic phase was extracted with base which was then acidified in the cold and extracted with ether. After evaporation of the ether the phenols were distilled under nitrogen, b.p. 175–188°, leaving 0.8 g. of residue. The distillable products were analyzed by g.l.c. and found to contain: phenol, 4.2 g. (84% recovery), cresols, 1.8 g., high-boiling material, 0.1 g.

Phenyl Isopropyl Carbonate-Diisopropyl Peroxydicarbonate-Toluene-Aluminum Chloride. Phenyl isopropyl carbonate (5.0 g., 0.028 mole) in 100 ml. of toluene was mixed with aluminum chloride (19.5 g., 0.14 mole) at 0°. After 0.5 hr., 50 ml. of a solution of diisopropyl peroxydicarbonate (14.5 g., 0.07 mole) in toluene was added at 0° during 1.5 hr. After an additional 1.5 hr. the mixture was worked up as in the previous experiment. Distillation gave 5.1 g. of distillable phenols, b.p. 169–191°, and 0.3 g. of residue. Analysis by g.l.c. showed: phenol, 2.6 g. (0.028 mole, 100% recovery from phenyl isopropyl carbonate), cresols, 2.5 g.

*Evolution of Carbon Dioxide.*⁴⁴ *A. From Phenyl Isopropyl Carbonate-Aluminum Chloride.* Phenyl isopropyl carbonate (6.3 g., 0.036 mole) in 50 ml. of toluene was added to aluminum chloride (9.5 g., 0.072 mole) in 100 ml. of toluene at 0° during 2.5 hr. The gases were swept out with nitrogen into a sodium hydroxide solution which was titrated on an automatic recording titrator. Carbon dioxide content was calculated from the volume of acid required to convert carbonate to bicarbonate. The amount of carbon dioxide evolved during reaction was found to be 0.006 mole (17%).

The gas was then trapped as before while the reaction mixture was hydrolyzed with hydrochloric acid during 0.5 hr. Carbon dioxide formed during this stage comprised 0.027 mole (75%).

B. From Diisopropyl Peroxydicarbonate-Toluene-Aluminum Chloride. Diisopropyl peroxydicarbonate (14.5 g., 0.070 mole) was allowed to react with aluminum chloride (19.5 g., 0.14 mole) and toluene (150 ml.) according to the general procedure. The carbon dioxide evolved during 3 hr. was determined to be 0.031 mole (22%). During hydrolysis, 0.083 mole (59%) of carbon dioxide was generated.

(44) We are grateful to Mrs. Leslie Mornewick of the Sohio Research Laboratories for these analyses.

C. *From Sodium Bicarbonate.* Sodium bicarbonate (11.8 g., 0.14 mole) in 100 ml. of water was treated during 1.5 hr. at 0° with dilute hydrochloric acid (0.3 mole), and the solution was stirred for 1.5 hr. The carbon dioxide amounted to 0.12 mole (87%).

Diisopropyl Peroxydicarbonate-o-Cymene-Aluminum Chloride. A *p*-cymene solution (50 ml.) of diisopropyl peroxydicarbonate (14.5 g., 0.07 mole) was treated with aluminum chloride (19 g., 0.14 mole) in *p*-cymene (100 ml.) according to the general procedure. The addition required 1 hr. at -12°, and the mixture was stirred 2 hr. at the same temperature.

Distillation of the phenolic product gave 2.3 g. of an orange oil with a phenolic odor, b.p. 90-100° (15 mm.). Gas chromatography showed two major components, the first being cresols (identified by g.l.c. and the infrared spectrum). The second peak (a doublet), attributed to cymenols, possessed the same retention time as did the high boiling fraction from toluene-aluminum chloride-diisopropyl peroxydicarbonate.

Anal. Calcd. for C₁₀H₁₄O: C, 79.95; H, 9.39. Found: C, 80.25; H, 9.44.

The infrared spectrum displayed peaks (in μ) at 2.81 (s), 3.40 (s), 8.00 (s), 8.22 (s), 8.60 (s), 9.06 (s), 9.78 (s), 10.72 (w), 11.64 (w), 11.87 (w), 12.48 (s) (in carbon disulfide).

Isomerization and Recovery Studies. A. Isomerization. A solution of isomeric cresols (10 g., 28% *ortho*, 13% *meta*, 59% *para*) in toluene (50 ml.) was added dropwise to aluminum chloride (19 g., 0.14 mole) in toluene (100 ml.) to which water (1 ml.) and isopropyl alcohol (1 ml.) had been added, and the mixture was stirred for 3 hr. at 0°. After treatment with acid-ice, the toluene was distilled from the organic portion. The recovered cresol mixture was compared to the starting material by infrared spectroscopy and was found to be isomerically identical.

B. Recovery. (1) A known mixture of isomeric cresols (8 g., 44% *ortho*, 12% *meta*, 44% *para*) was dissolved in toluene (150 ml.) and subjected to the usual work-up procedure. Distillation gave recovered

cresols (7.27 g.) with 0.13 g. of hold-up in the distilling head, representing 92.5% recovery. The residue amounted to 0.04 g. According to infrared spectroscopy, the recovered cresols were found to be essentially identical in isomer distribution to the starting material.

(2) A known mixture of cresols (45% *ortho*, 10% *meta*, 45% *para*) was exposed to the standard conditions of gas chromatography. The collected material was shown by infrared spectroscopy to have essentially the same isomeric composition as that injected.

Analytical Procedures. A. Peroxides. An iodometric method was used.⁴⁵ The commercial diisopropyl peroxydicarbonate exhibited a purity of >95% based on this procedure.

B. Phenolic Products. The isomer distribution of the cresols was determined by infrared spectroscopy with a Beckman IR 8 spectrophotometer according to the baseline method.⁴⁶

The analyses of the phenol cresol mixtures obtained from competitive oxygenation experiments and of the cresol yield in some experiments were performed on an Aerograph A-90-P gas chromatograph. A 10 ft. \times 0.25 in. copper column, packed with 15% Apiezon L on acid-washed Chromosorb P (35/80 mesh), was used under the indicated operating conditions: helium flow rate at 175°, 100 ml./min.; block temperature, 250°; injector temperature, 300°; column temperature, 175°. Known mixtures of phenol and cresol of isomeric composition similar to that found in the reaction product were prepared in toluene. A plot was made of the ratio of peak areas vs. the weight ratio, and the unknown mixtures were compared to this plot. In the cases where cresol yield was to be determined, a known amount of phenol was added to all or an aliquot of the reaction product.

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(46) R. L. Bohon, R. Isaac, H. Hoftiezer, and R. J. Zellner, *Anal. Chem.*, **30**, 245 (1958).