Reaction of Phenyl Salicylates with Perbenzoic Acid. Formation of o-Alkoxyphenols and Catechol[1]

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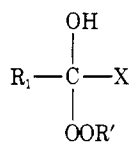
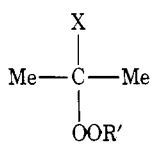
The reaction of phenyl salicylate with perbenzoic acid in 60 vol. % ethanol at pH >9 was found to afford o-ethoxyphenol and catechol together with other hydrolysis and alcoholysis products of the ester. The analogous reaction in aqueous methanol gave o-methoxyphenol; other phenyl salicylates substituted at the salicyl ring produced also o-alkoxyphenols, but the attempted reaction of other phenyl or methyl benzoates was unsuccessful. This novel alkoxylation seems to proceed *via* an aryl cation intermediate produced from phenyl salicylate and peracid.

The Baeyer–Villiger (B–V) reaction of ketones and aldehydes has been extensively studied,[2,3] but, so far as we know, there is no report on the similar reaction of esters. It is generally recognized that the migration of R_1 in the intermediate **1a**, an adduct of R'OOH to R_1COX, is accelerated by the adjacent oxygen atom.[4a] The similar acceleration of α oxygen atom was also observed for the rearrangement of 2-substituted 2-propyl *p*-nitroperbenzoates; *e.g.*, the relative rate for the rearrangement of **2b** *vs.* **2a** with R' = *p*-$O_2NC_6H_4CO$ is 1000.[4b]

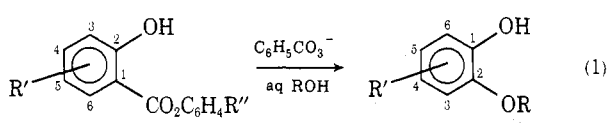


1a, X = R_2
b, X = OR_2



2a, X = Me
b, X = OMe

In view of the availability of two accelerating α oxygen atoms (**1b**), the B–V type reaction of esters seems to be possible. The present paper reports a novel reaction of some aromatic esters with perbenzoic acid (PBA), *i.e.*, the conversion of phenyl salicylates to o-alkoxyphenols (eq 1) which seems to be produced *via* aryl cations.



(1)

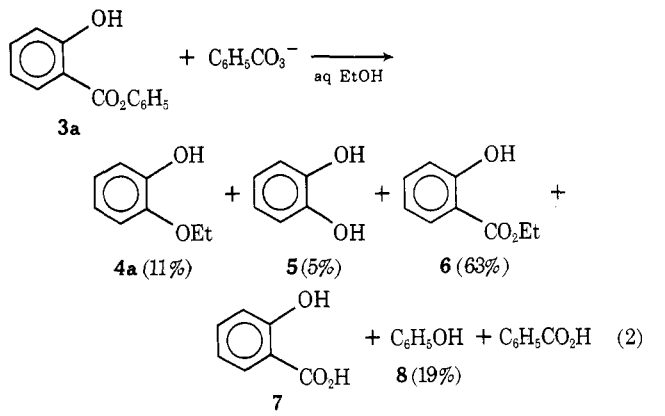
3a, R' = R'' = H
b, R' = 5-Me; R'' = H
c, R' = H; R'' = *p*-Me

4a, R' = H; R = Et
b, R' = H; R = Me
c, R' = 4-Me; R = Me

Results and Discussion

The reaction of phenyl salicylate (**3a**, 0.05 *M*) with perbenzoic acid (PBA, 0.05 *M*) was carried out in the presence of sodium carbonate (0.10 *M*, pH ~11) in 60 vol. % ethanol containing EDTA (5×10^{-4} *M*) to suppress spontaneous decomposition of PBA. This reaction affords o-ethoxyphenol (**4a**) and catechol (**5**) together with hydrolysis (**7** and **8**) and transesterification products (**6** and **8**) from the ester (eq 2).

The dependence of these products on the reaction time (Figure 1) shows that the decrease of ester **3a** is compatible with the increase of products, suggesting neither intervention of any stable intermediate nor interconversion between the products. The consumption of PBA is roughly comparable to that of **3a**, but, because of the further oxidation of produced phenols, the stoichiometry of PBA *vs.* **3a** is not clear and the yield of **4a** does not increase with excess PBA. The reaction at pH ~9 afforded a similar yield of **4a**, but the reaction did not occur at pH ~7.



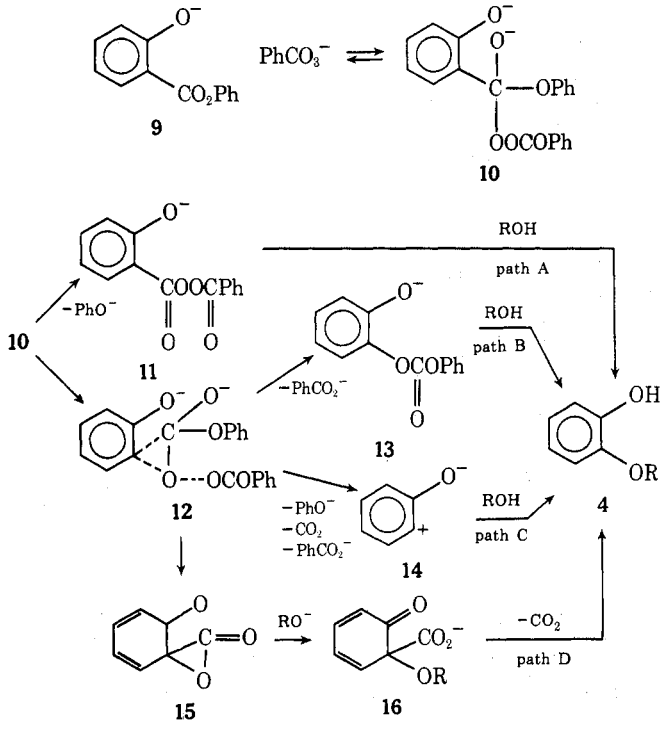
The reaction of **3a** with PBA in 60% methanol buffered by sodium bicarbonate also gave a similar yield of o-methoxyphenol (**4b**, *ca.* 9%). The same reaction of phenyl 2-hydroxy-5-methylbenzoate (**3b**) produces 2-methoxy-4-methylphenol (**4c**, 5%), but 2-methoxy-5-methylphenol was not obtained. The reaction of *p*-tolyl salicylate (**3c**) gave o-ethoxyphenol (**4a**) and o-methoxyphenol (**4b**) in aqueous ethanol and methanol, respectively. o-Alkoxyphenols were not obtained from the reaction of PBA with phenol, catechol, salicylic acid, and methyl or ethyl salicylate under the same conditions. These results indicate that the reaction of phenyl salicylate with PBA converts the carboalkoxyl group of the salicylate into the alkoxyl group from solvent alcohol.

The formation of o-alkoxyphenol from **3a** was not appreciable for the reaction with hydrogen peroxide or *tert*-butyl hydroperoxide in place of PBA. Attempted alkoxylation reaction under various conditions (pH, initial concentration, temperature, and time) were all unsuccessful for the reaction of phenyl o-methoxy-, *p*-hydroxy-, *p*-methoxy-, and *p*-chlorobenzoates, methyl o- and *p*-hydroxybenzoate, and o- and *p*-methoxybenzoates, transesterification being a main reaction. Thus, the alkoxylation reaction such as eq 1 is characteristic for phenyl salicylates.

Formation Mechanism of o-Alkoxyphenol. The reaction of phenyl salicylate with PBA to afford **4a** and **5** is interesting because no B–V type reaction of esters is known. Although the reaction proceeds at a comparable conversion rate at pH >9, it does not occur at pH <7, which shows that PBA anion is a reactive species, since the pK_a of PBA is 8.5 in 40% ethanol.[3c,5] The failure of formation of o- or *p*-alkoxyanisole from phenyl o- or *p*-methoxybenzoate indicates that the dissociation of the o-hydroxyl proton of **3a** is also necessary.[6] On the basis of these results several paths are conceivable for the formation of o-alkoxyphenol (paths A–D in Scheme I, etc.).

Firstly, the possibility of o-alkoxyphenol formation *via* path A may be denied from the following examination. o-

Scheme I



Hydroxybenzoyl peroxide (protonated **11**) synthesized from salicyloyl chloride and PBA was considerably stable in 20% chloroform–80% ethanol, its half-life being *ca.* 3 hr at 25°, while the formation of **4a** by the reaction of **3a** with PBA was almost complete within 1 hr (Figure 1). Moreover, *o*-ethoxyphenol was not obtained from the decomposition of **11** in the same solvent at 25 or 80°. These results deny the intervention of **11**. The formation of **11** from **10** would be prevented, probably because the departure of perbenzoate ion from **10** is more effective than that of phenolate ion because of the higher acidity of PBA ($\Delta pK_a = 2$).[7]

Secondly, the B–V type rearrangement might give carbonate **13** *via* the transition state **12** (path B). The alcoholysis of aryl carbonates as well as hydrolysis, however, is generally known as acyl–O fission to give phenols,[8,9] and *o*-oxy anion in the carbonates effectively catalyzes the hydrolysis to give catechols.[9] Moreover, the B–V reaction of salicylaldehyde gives a high yield of catechol *via* the same carbonate **13**[3b] but not **4**. Hence, the formation of **4** *via* carbonate **13** cannot be substantiated.

Thirdly, path C assumes the intermediacy of an aryl cation from the B–V type transition state **12**. If this is the case, cation **14** should be trapped by solvent alcohol to give alkoxyphenol **4**. This mechanism seems to be most probable as discussed in the following. The cationic character of the migration group is important for the B–V reaction[3] and other rearrangements of peroxides.[2-4] The ionic decomposition of *tert*-butyl *p*-nitroperbenzoate in methanol gave *tert*-butyl methyl ether and isobutylene, which are formed from *tert*-butyl cation.[4b] The anchimeric assistance of α oxygen atom is large owing to its electron-donating resonance in the B–V rearrangement.[4a] Since carbonyl adduct **10** has two α oxygen atoms, the electron-donating power to stabilize the transition state **12** should be large.[10] Moreover, the aryl cation is stabilized by a strongly electron-donating *o*-HO or *o*-O$^-$ group as exemplified for the case of the NH_2 group.[11]

Fourthly, another path to **4** involves a spirodienone intermediate **15** (path D).[12a] With this α-lactone mechanism it is difficult to explain why the alkoxylation is specific for phenyl salicylates and unsuccessful for the case of phenyl *p*-hydroxybenzoate or methyl salicylate. Further, we cannot see why **15** should be formed instead of the well-established B–V type conversion to the more stable carbonate **13**. Moreover, it is not clear that its conversion to **4** is very facile at 25°.[12b]

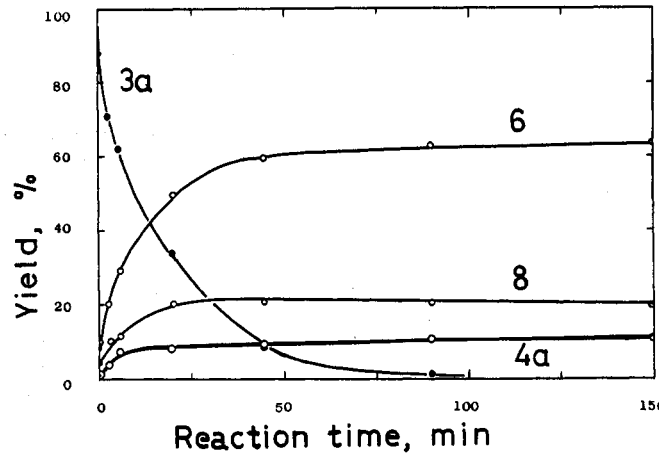


Figure 1. The reaction of phenyl salicylate (**3a**) with PBA in 60% ethanol at 25°. Initial concentrations: [**3a**] = [PBA] = 0.05 *M*, $[Na_2CO_3] = 0.1$ *M*, and [EDTA] = 5×10^{-4} *M*.

Finally, a nucleophilic substitution (SN2) by RO$^-$ on the aromatic ring of **10** is less probable on the basis of the observed similar yields of **4** from the reaction at pH 9 and 11, and of the absence of any electron-attracting group on the ring. Another path involving radical reaction to give **4** would be a coupling of phenoxy and alkoxy radicals. However, a radical attack on alcohols gives α-hydroxyalkyl radicals but not alkoxy radical;[13] further, there has been no indication of *o*-alkoxyphenol formation from a radical reaction of phenol and alcohol.

Hence, although a decisive choice of path C or D is still impossible, path C seems to be most appropriate. Trapping of **14** by acetonitrile leading to *o*-(*N*-acetylamino)-phenol was unsuccessful in these aqueous alcohols, and the reaction does not occur in pure acetonitrile.

This novel alkoxylation is limited to phenyl salicylates and failed for the case of other phenyl and methyl benzoates. Two factors seem to contribute to the success only with the case of phenyl salicylates: (i) stabilization of phenyl cation by the *o*-O$^-$ group;[14a] (ii) stabilization of the C=O adduct **10**, *i.e.*, the increase of [**10**] by the electron-attracting phenoxy group.[14b] No formation of **4** by the reaction with hydrogen peroxide or *tert*-butyl hydroperoxide suggests that the O–O heterolysis induced by PhCO is important for the formation of aryl cation. The sole formation of **4c** from **3b** indicates that the produced aryl cation is not of a bridged structure such as benzene epoxide.

Mechanism for the Formation of Catechol. The conceivable paths for the catechol formation are paths A–D together with PBA oxidation of phenol. The formation of catechol and hydroquinone by peracid oxidation of phenol is well known.[15] The PBA oxidation of phenyl salicylate gave catechol and hydroquinone in a molar ratio of 30:1, while the PBA oxidation of phenol under the same conditions resulted in a ratio of 2:1. This large difference indicates that the main path affording catechol in this reaction is not the PBA oxidation of phenol.

Although unsymmetrical benzoyl peroxides are known to give phenols by a carboxy inversion process,[16,17] the intermediacy of **11** is not probable as mentioned in the pre-

vious section. Hence catechol is formed by hydrolysis of carbonate **13** (path B) or the trapping of **14** (path C) or **16** (path D) by water. Although the choice might be possible by the presence or absence of catechol for the reaction in absolute ethanol, the reaction failed because of the solubility of reactants in the solvent and hence the choice remains unanswered.

Experimental Section

Materials. PBA was synthesized by the reaction of benzoyl peroxide with alkaline hydrogen peroxide[18] and crystallized from *n*-hexane. Phenyl salicylate is of commercial origin and its purity (>98%) was checked by glc. Phenyl hydroxybenzoates were obtained by the preparation using phosphoryl chloride;[19] phenyl methoxybenzoates were prepared by the Schotten–Baumann method.[20] Substituents and melting points of phenyl-substituted benzoates are as follows: *p*-MeO, 58–59°; *o*-MeO, 59–60°; *p*-HO, 173–175°; 2-HO-5-Me, 86–88°. *o*-Hydroxybenzoyl peroxide was obtained by the usual method;[21,22] pyridine was dropped into a mixture of salicyloyl chloride and PBA at −30 to −40°. Its purity was *ca.* 30% on the basis of iodometric titration and further purification was unsuccessful: ir 3230 (OH), 1790 and 1765 (diacyl peroxide C=O), 700 and 760 (monosubstituted benzene), and 745 cm^{-1} (ortho-disubstituted benzene).

Authentic *o*-ethoxyphenol (**4a**) and *o*-methoxyphenol (**4b**) were synthesized from the B–V reaction of *o*-ethoxy- and *o*-methoxybenzaldehyde with peracetic acid in the presence of acetate buffer in 30% ethanol for 3 hr at 40°. Authentic 2-methoxy-4-methylphenol (**4c**) was synthesized from 2-hydroxy-4-methylactophenone obtained by the Fries rearrangement of *m*-cresyl acetate,[23] followed by methylation with dimethyl sulfate, B–V reaction, and hydrolysis. 2-Methoxy-5-methylphenol was obtained similarly from *p*-cresyl acetate.

Typical Reaction and Product Analysis. Phenyl salicylate (**3a**, 1 mmol), PBA (1 mmol), and Na_2CO_3 (2 mmol) were allowed to react in 60% ethanol (20 ml) in the presence of EDTA (0.01 mmol) for 2.5 hr at 25°. The reaction mixture was acidified by acetic acid after the addition of *p*-cresol and *p*-methoxytoluene as internal standards for glc analysis. Catechol was converted to *o*-dimethoxybenzene by dimethyl sulfate and extracted. Identification and determination of products were carried out mainly by glc analysis using a Yanagimoto gas chromatograph, Model 550F: a 1.2-m column of 15% Apiezon grease on Celite 545 and/or a 1.2-m column of PEG on Chamelite CS.

o-Ethoxyphenol was extracted with chloroform from the diluted reaction mixture buffered at pH 5, chromatographed on silica gel using chloroform eluent, and confirmed by identification with ir, uv, and tlc analysis in comparison with the authentic sample: uv λ_{max} (0.1 *N* NaOH) 239 and 290 nm; λ_{max} (H_2O) 214 and 274 nm; ir 3500 (OH), 740 cm^{-1} (ortho-disubstituted benzene).

Registry No. 3a, 118-55-8; PBA, 93-59-4; phenyl *p*-methoxybenzoate, 4181-97-9; phenyl *o*-methoxybenzoate, 10268-71-0; phenyl *p*-hydroxybenzoate, 17696-62-7; phenyl 2-hydroxy-5-methylbenzoate, 10268-64-1; *o*-hydroxybenzoyl peroxide, 42806-89-3.

References and Notes

(1) Contribution No. 199.
(2) (a) C. H. Hassall, *Org. React.*, **9**, 73 (1957); (b) A. G. Davies, "Organic Peroxides," Butterworths, London, 1961, p 144; (c) P. A. S. Smith, "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, p 579; (d) S. B. Lee and B. C. Uff, *Quart. Rev., Chem. Soc.*, **21**, 429 (1967).
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(4) (a) E. Hedaya and S. Winstein, *Tetrahedron Lett.*, 563 (1962); (b) E. Hedaya and S. Winstein, *J. Amer. Chem. Soc.*, **89**, 1661 (1967).
(5) If PBA is a reactive species, the rate should decrease with increasing pH.
(6) The pK_a value of **3a** is 8.80 in water: B. Capon and B. C. Ghosh, *J. Chem. Soc. B*, 472 (1966).
(7) This is similar to the fact that in spite of the strong nucleophilicity of HOO^- esters are not perhydrolyzed by HOO^- because of its stronger departing ability compared to HO^-: K. B. Wiberg, *J. Amer. Chem. Soc.*, **77**, 2519 (1955).
(8) (a) G. D. Cooper and B. Williams, *J. Org. Chem.*, **27**, 3717 (1962); (b) G. D. Cooper and H. T. Johnson, *ibid.*, **30**, 3989 (1965).
(9) T. H. Hife, J. E. C. Hutchins, and D. M. McMahon, *J. Amer. Chem. Soc.*, **94**, 1316, 2837 (1972).
(10) The reaction of salicylaldehyde with PBA in aqueous ethanol gave catechol and its formate but not *o*-ethoxyphenol. This shows that two α oxygen atoms in **10** are necessary for the formation of the aryl cation **14.**
(11) E. M. Evleth and P. M. Horowitz, *J. Amer. Chem. Soc.*, **93**, 5636 (1971).
(12) (a) A referee's suggestion. (b) A α-lactone intermediate was suggested in the alcoholysis of α-halocarboxylate ion, which gave α-alkoxycarboxylic acid: J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1956, p 118. A dienonecarboxylic acid intermediate similar to **16** was suggested for the acid-catalyzed decarboxylation of salicylic acid: A. V. Willi, *Trans. Faraday Soc.*, **55**, 433 (1959); *Z. Phys. Chem.*, **30**, 285 (1961). Hence, the reaction sequence **15** → **16** → **4** may presumably be facile. However, a similar α-lactone intermediate from the induced decomposition of acetyl benzoyl peroxide was converted to substituted benzoic acid but not to solvolytic decarboxylation: C. Walling and Z. Cekovic, *J. Amer. Chem. Soc.*, **89**, 6681 (1967).
(13) For example, see C. Walling, "Free Radicals in Solutions," Wiley, New York, N. Y., 1957, pp 412 and 479.
(14) (a) The order of *o*-MeO > *p*-MeO for the B–V reaction was suggested as an indication for the stronger electron-donating power of the ortho substitutent.[3a] (b) The carbonyl addition of peroxide anion is less sensitive to steric retardation.[3b] Since EtO^- is probably more sensitive to steric effect than HO^- and hence than PBA anion, the following reason for the failure of the reaction with methyl salicylate cannot be neglected. That is, while the carbonyl addition of EtO^- and PBA anion to phenyl salicylate is competitive, methyl salicylate is consumed by a preferential attack of EtO^- on the carbonyl, since the steric retardation by its methoxy group is smaller than that by the phenoxy group of phenyl salicylate.
(15) (a) J. Boseken and C. F. Metz, *Recl. Trav. Chim. Pays-Bas*, **54**, 345 (1935); (b) Y. Ogata and M. Mineno, *Kogyo Kagaku Zasshi*, **73**, 1849 (1970).
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