Oxidation by Metal Salts. XIII. Oxidation of Arylcarboxylic Acids by Cobaltic Acetate

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The oxidative decarboxylation of arylacetic acids by cobaltic acetate was shown to be an electron transfer process involving aromatic radical cation intermediates, rather than the free-radical process previously assumed. Evidence for this mechanism included the realtively high ρ value of -2.9 observed for the decarboxylation of substituted arylacetic acids, the detection of aromatic radical cations by ESR spectroscopy, and the exclusive formation of γ-phenylbutyrolactone in the cobaltic oxidation of γ-phenylbutyric acids.

The oxidative decarboxylation of saturated as well as aryl-substituted carboxylic acids by either electrochemical means (Kolbe reaction)[1] or by high-valent metal ions[2–5] has been extensively studied. The mechanism generally proposed for these decarboxylations has involved homolytic decomposition of the carboxylate anion into carbon dioxide, and alkyl radical, and the reduced form of the metal oxidant. In essence, this mechanism viewed oxidative decarboxylation as an electron transfer process from the carboxylate anion to the higher valent metal ion oxidant, even in the case of arylacetic acids (eq 1).

$$RCO_2^- \xrightarrow{-e} RCO_2\cdot \longrightarrow R\cdot + CO_2 \qquad (1)$$

Recent variations[5] which describe the transition state as highly polar with extensive carbon–carbon cleavage can still be classified as oxidations of the carboxylate group by the mechanism shown above.

Our previous work on the oxidation of alkylbenzenes by cobaltic acetate[6] clearly suggests that, whereas the above mechanism may indeed be correct for the oxidative decarboxylation of saturated carboxylic acids, an entirely different mechanism should be operative in the case of aryl-substituted carboxylic acids. We now wish to report our results which clearly demonstrate that the cobaltic acetate oxidation of aryl-substituted carboxylic acids involves attack at the aromatic center rather than at the carboxylate group, as shown in the following equations for the oxidative decarboxylation of phenylacetic acid.

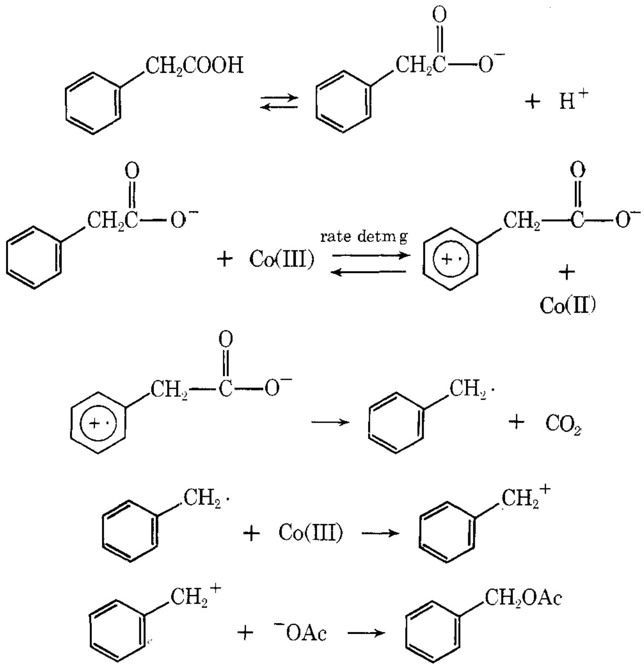


Table I
Formation of Benzylacetates from Arylacetic Acids

Arylacetic acid[a]	Acetate formed	Reaction time, min	Yield,[b] %
Phenylacetic acid	Benzyl	20	80
p-Methoxyphenylacetic	*p*-Methoxybenzyl	5	100
p-Tolylacetic	*p*-Methylbenzyl	15	90
m-Tolylacetic	*m*-Methylbenzyl	30	90
p-Chlorophenylacetic	*p*-Chlorobenzyl	30	70
m-Chlorophenylacetic	*m*-Chlorobenzyl	60	50

[a] Reaction conditions: 0.4 *M* arylacetic acid, 0.4 *M* $Co(OAc)_3$, 0.2 *M* $Cu(OAc)_2 \cdot H_2O$ in refluxing HOAc. [b] Yield based on cobaltic ion, assuming 2 mol per mole of acetate produced.

Table II
Competitive Experiments[a] Relative Reactivity of Substituted Arylacetic Acids at 65°

Acid A	Acid B	k_B/k_A[b]
Phenyl	*p*-Tolyl	6.9 ± 0.15
Phenyl	*m*-Tolyl	1.75 ± 0.15
Phenyl	*p*-Chlorophenyl	0.75 ± 0.02
Phenyl	*m*-Chlorophenyl	0.17 ± 0.01
p-Tolyl	*p*-Methoxyphenyl	53. ± 5

[a] Reaction conditions: 0.5 *M* total arylacetic acids, 0.05 *M* $Co(OAc)_3$, 0.2 *M* $Cu(OAc)_2 \cdot H_2O$, 65° in HOAc, reaction times 5–18 hr. [b] Values given are average of two or three independent experiments, each analyzed twice by vpc. Nonequimolar quantities of both acids were used to facilitate product analysis.

Such a mechanism has in fact been previously suggested for very special cases such as the ceric ion oxidation of methoxyphenylacetic acid[5] and the electrochemical oxidation of methoxyphenyl acetate and 10-methylanthracen-9-yl acetate;[7] although in all these cases the assertion was made that such a mechanism was not operative for simple phenylacetic acids.

The oxidative decarboxylation of arylacetic acids by cobaltic acetate in refluxing acetic acid,[8] containing added cupric acetate, resulted in the rapid formation of benzylacetates in very high yields, as shown in Table I.

In order to test our proposed mechanism, the competitive decarboxylation of a series of substituted arylacetic acids was studied. The relative rates of decarboxylation of these arylacetic acids were determined from the relative amounts of the corresponding benzylacetates produced under conditions where these acetates accounted for more than 80–90% of all products observed (Table II). These ratios were essentially independent of the extent of reaction, or the amount of cupric ion added.

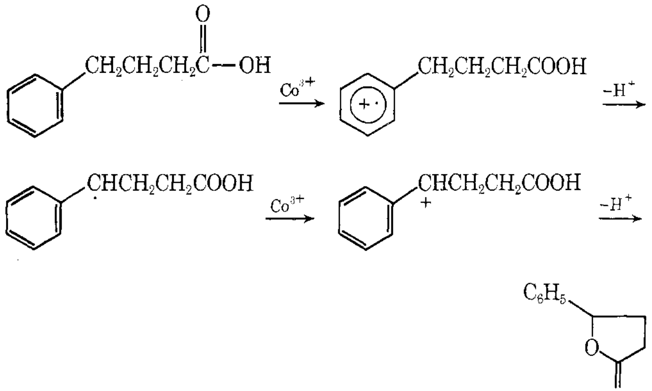
A Hammett σ–ρ plot of this data is presented in Figure 1. The good correlation with σ^+ values yielded a ρ of −2.9.

Note that the good correlation includes the data for the *p*-methoxy compound, indicating a common mechanism for all the arylacetic acids studied.

This high ρ value is inconsistent with any known free-radical process and indicates considerable positive charge development on the aromatic nucleus in the transition state. The large ρ value obtained agrees quite well with that observed by us for the cobaltic acetate oxidation of alkylaromatic hydrocarbons[6] (ρ = −2.4 at 65°), a process clearly shown to involve aromatic radical cation intermediates. The large ρ value of −2.9 stands in marked contrast to that reported[9] for the potassium persulfate promoted decarboxylation of substituted phenylacetic acids which gave a ρ of only −0.4. The small substituent effect in that case can best be rationalized by a mechanism involving the homolytic scission of a peroxidic intermediate such as $RC(=O)OOSO_3^-$ (formed by attack of a carboxylate anion on $S_2O_8^{2-}$) in a manner comparable to that suggested for the thermal decomposition of the corresponding *tert*-butyl peresters,[10] rather than by an electron transfer process, whether it be from the carboxylate anion[9] or the aromatic ring.[11]

Additional support for the intermediacy of aromatic radical cations in the cobaltic oxidation of arylacetic acids comes from the direct observation of the ESR spectrum of the *p*-methoxyphenylacetic acid radical cation in a flow system using trifluoroacetic acid.[12]

Further support for the mechanism involving initial attack at the aromatic ring in aryl-substituted carboxylic acids can be found in the products obtained from the cobaltic acetate oxidation of γ-phenylbutyric acids. Here no oxidative decarboxylation was detected and the only product observed was γ-phenylbutyrolactone, the formation of which is depicted in the mechanism shown below.



The yield of lactone was 25% based on cobaltic ion used; however, this yield could be increased to 60% by the addition of some LiCl[6] or trifluoroacetic acid,[12] reagents previously shown to accelerate the electron transfer process to cobaltic ion. The formation of a single product in the case of cobaltic acetate contrasts sharply with the variety of products obtained using lead tetraacetate which, unlike cobaltic acetate, oxidatively decarboxylates acids, including aryl-substituted acids, via a homolytic process involving alkyl free radicals.[4,13] These compounds from the reaction of lead tetraacetate included the decarboxylation products, *n*-propylbenzene and 3-phenylpropyl acetate, in addition to only a small amount of lactone formed by hydrogen abstraction[13,14] from phenylbutyric acid.

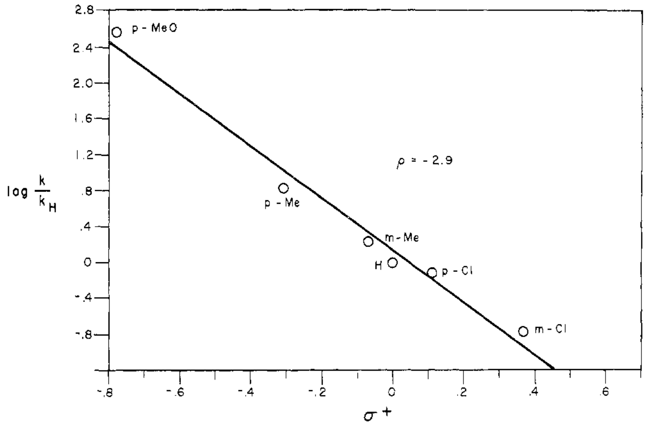


Figure 1. Relative rates of decarboxylation of arylacetic acids by cobaltic acetate at 65°.

These observations clearly demonstrate that the oxidation of arylcarboxylic acids by cobaltic ion involves electron transfer from the aromatic ring as the initial step. It is quite likely that other oxidants that undergo single electron transfer[15] will also follow this mechanism.

Experimental Section

Preparation of Cobaltic Acetate Solution. A dilute stream of ozone was bubbled overnight through a solution of 375 g (1.5 mol) of $Co(OAc)_2 \cdot 4H_2O$ and 567 ml (6 mol) of acetic anhydride in 3 l. of glacial acetic acid. The resulting deep green solution was flushed with nitrogen for 2 hr and filtered. Titration of this solution by sodium thiosulfate indicated a 0.44 *M* cobaltic ion concentration.

Cobaltic Oxidation of Arylacetic Acids. Formation of Benzyl Acetates. Solutions of arylacetic acid (0.4 *M*), cobaltic acetate (0.4 *M*), and $Cu(OAc)_2 \cdot H_2O$ (0.2 *M*) in glacial acetic acid were heated at reflux under a nitrogen atmosphere for a period of 5–60 min, at which time the green color had disappeared. An internal standard was added prior to extraction and the yields of benzyl acetates formed were determined by vapor phase chromatography. Yields based on cobaltic ion consumed were calculated on the assumption that 2 equiv were required per mole of benzyl acetate formed.

Competitive Oxidations of Substituted Arylacetic Acids. Competitive oxidations of pairs of substituted arylacetic acids were conducted at 65° under nitrogen atmosphere. The solutions, 0.5 *M* in total arylacetic acids, 0.05 *M* $Co(OAc)_3$, and 0.2 *M* $Cu(OAc)_2 \cdot H_2O$ in glacial acetic acid, were heated for a period of 5–18 hr. The solutions, some of which still contained cobaltic ion, were then poured into 1 l. of water and extracted into ether. After drying, the ether layer was stripped on a rotary evaporator and the residue analyzed by vapor phase chromatography on an OV-17 column. The ratios of benzyl acetates, which represented 80–90% of the observable products, were determined from their relative areas in the chromatogram after correction for variations in molar sensitivities. To facilitate analyses, nonequimolar quantities of arylacetic acids were used in some cases, most notably in the case of *p*-methoxyphenylacetic acid where 1:4 molar ratios were used.

Cobaltic Oxidation of Phenylbutyric Acid. A solution of 5.7 g (0.035 mol) of 4-phenylbutyric acid in 50 ml of a 0.7 *M* $Co(OAc)_3$ solution was heated at reflux for 2 hr, at which time the green color had disappeared. An internal standard was added to the reaction mixture which was then extracted with ether and water. The ether layer was dried and stripped on the rotary evaporator and the residue analyzed by vapor phase chromatography on an OV-17 column. Essentially only one product was observed, γ-phenylbutyrolactone (25% yield based on cobaltic ion used), whose spectra and retention time were identical with those of an authentic sample. In a similar experiment, 7.4 g of 4-phenylbutyric acid was dissolved in 100 ml of a 0.45 *M* cobaltic acetate solution containing 7.6 g of LiCl. The reaction mixture was maintained at room temperature for 22 hr, at which time the color had changed from green to blue. Analysis of the reaction residue again indicated one product, γ-phenylbutyrolactone, now obtained in 50% yield.

Replacement of LiCl with 100 ml of CF_3COOH also yielded γ-phenylbutyrolactone in 60% yield.

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Registry No.—Phenylacetic acid, 103-82-2; *p*-methoxyphenylacetic acid, 104-01-8; *p*-tolylacetic acid, 622-47-9; *m*-tolylacetic acid, 621-36-3; *p*-chlorophenylacetic acid, 1878-66-6; *m*-chlorophenylacetic acid, 1878-65-5; benzyl acetate, 140-11-4; *p*-methoxybenzyl acetate, 104-21-2; *p*-methylbenzyl acetate 2216-45-7; *m*-methylbenzyl acetate 17369-57-2; *p*-chlorobenzyl acetate, 5406-33-7; *m*-chlorobenzyl acetate, 21388-93-2; phenylbutyric acid, 1821-12-1; cobaltic acetate, 917-69-1.

References and Notes

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(14) The low yield of lactone produced by hydrogen abstraction was further dramatically reduced in the presence of 0.2 M cupric acetate, which simultaneously converted all of the propylbenzene to allylbenzene by oxidation of the intermediate 3-phenylpropyl radical.

(15) The data of ref 5, contrary to the conclusions stated therein, suggest that a similar mechanism is indeed operative in the case of ceric ion. The ρ value reported there, −2.9, is quite consistent with those we observed in the oxidation reactions of cobaltic ion. The high rate reported for the ceric oxidation of *p*-methoxyphenylacetic acid, which must have been extremely difficult to measure accurately by NMR, is just about what would have been expected for a reaction with such a large ρ. The high reactivity of the *m*-methoxy compound, which definitely does not fit the Hammett correlation (which we also found in our system, it being only slightly less reactive than *p*-tolylacetic acid), is exactly what would be expected on the basis of aromatic radical cation formation and the ease of electron transfer from anisole and its derivatives. On the basis of molecular orbital theory, it is clear that the symmetry of the highest occupied molecular orbital of the radical cation of *m*-methoxyphenylacetic acid differs from all the other derivatives in terms of electronic symmetry relative to the carboxymethylene group. Consequently, a *m*-methoxy substituent is not a minor perturbation of the aromatic ring and should not fit a Hammett plot.

Copper(I)-Induced Reductive Dehalogenation, Hydrolysis, or Coupling of Some Aryl and Vinyl Halides at Room Temperature

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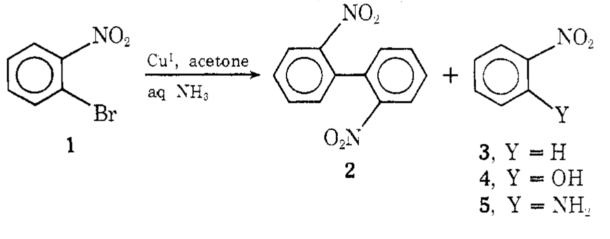
The room temperature reactions of some activated aryl and vinyl halides with acetone solutions of copper(I) trifluoromethanesulfonate, ammonia (aqueous or dry), and various quantities of copper(II) trifluoromethanesulfonate have been studied. Conditions have been found for the following conversions in good yield: *o*-bromonitrobenzene to 2,2′-dinitrobiphenyl, nitrobenzene, or *o*-nitrophenol; methyl *o*-iodobenzoate to methyl salicylate or methyl benzoate; diethyl iodofumarate to *trans,trans*-1,2,3,4-tetracarbethoxy-1,3-butadiene or diethyl fumarate; diethyl iodomaleate to diethyl maleate. Reductive dehalogenation and phenol formation are favored, respectively, by the presence of ammonium tetrafluoroborate and a substantial quantity of cupric ion. The retention of configuration observed for the protolysis products of the organocopper intermediates derived from the vinyl iodides has been interpreted as ruling out vinyl radicals as intermediates.

It was recently reported from this laboratory that the Ullmann coupling,[1] which is usually performed with copper powder at elevated temperatures, can, in the case of certain activated aryl halides, be performed at room temperature in homogeneous solutions containing copper(I) trifluoromethanesulfonate[2] (triflate) dissolved in equal volumes of acetone and 5% aqueous ammonia.[3] For example, while *p*-nitro- and *o*-fluoroiodobenzene failed to react, *o*-iodonitrobenzene and 2,4-dinitroiodobenzene coupled in a few minutes to form 2,2′-dinitrobiphenyl (**2**) and 2,2′,4,4′-tetranitrobiphenyl, respectively. However, with *o*-bromonitrobenzene (**1**) as substrate, under the same conditions, the reaction took far longer (about 24 hr) and only produced a 15% yield of biaryl (**2**) in addition to *o*-nitroaniline (**5**), the other significant product. Methyl *o*-iodobenzoate (**6**) was about as reactive as *o*-bromonitrobenzene (**1**) but, under these conditions, it produced mainly methyl anthranilate and no discernible coupling product. We summarize here a survey of reaction conditions for bromide displacement in *o*-bromonitrobenzene (**1**) and we report satisfactory conditions for the formation of good yields of any of the following products: biaryl (**2**), *o*-nitrophenol (**4**), or nitrobenzene (**3**). Conditions for halide displacement reactions in methyl *o*-iodobenzoate (**6**), diethyl iodofumarate (**10**), and diethyl iodomaleate (**13**) are also reported.

We have found that in the case of *o*-bromonitrobenzene far better yields of biaryl can be obtained by using a smaller volume of more concentrated aqueous ammonia. The yields can be further enhanced by the presence of a small quantity of copper(II) triflate. On the other hand, the presence of a much larger quantity of copper(II) triflate leads to a 74.6% yield of *o*-nitrophenol (**4**). A selection of our re-



1

2

3, Y = H
4, Y = OH
5, Y = NH2