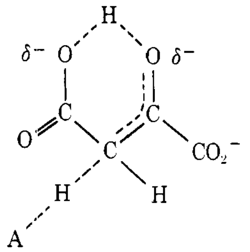
group is involved, then the mechanisms in Scheme I merge to one involving the transition state species III.



III

Registry No.—Oxaloacetic acid, 328-42-7; oxaloacetic acid enol, 7619-04-7; oxaloacetic acid hydrate (gem-diol), 60047-52-1; 4-ethyl oxaloacetate, 2401-96-9; 4-ethyl oxaloacetate enol, 63797-61-5.

References and Notes

(1) This work was supported in part by grants to M.C. and F.C.K. by the National Research Council of Canada.
(2) A. F. Hegarty and W. P. Jencks, *J. Am. Chem. Soc.*, **97**, 7188 (1975).
(3) E. S. Hand and W. P. Jencks, *J. Am. Chem. Soc.*, **97**, 6221 (1975).
(4) B. E. C. Banks, *J. Chem. Soc.*, 63 (1962).
(5) P. Y. Bruice and T. C. Bruice, *J. Am. Chem. Soc.*, **98**, 844 (1976).
(6) R. P. Bell and M. I. Page, *J. Chem. Soc., Perkin Trans. 2*, 1681 (1973).
(7) For a study of an oxaloacetate keto-enol tautomerase enzyme see, R. G. Annett and G. W. Kosicki, *J. Biol. Chem.*, **244**, 2059 (1969).
(8) L. Hellerman, O. K. Reiss, S. S. Parmar, J. Wein, and N. L. Lesser, *J. Biol. Chem.*, **235**, 2468 (1960). This reference claims to report a synthesis of 1-ethyl oxaloacetate, but the product is in fact the 4-ethyl oxaloacetate. Cf. ref 9.
(9) C. S. Tsai, Y. T. Lin, and E. E. Sharkawi, *J. Org. Chem.*, **37**, 85 (1972).
(10) W. Wislicenus and A. Endres, *Justus Liebigs Ann. Chem.*, **321**, 372 (1902); G. G. Kleinspehn and A. H. Corwin, *J. Am. Chem. Soc.*, **76**, 5641 (1954).
(11) K. J. Pedersen, *Acta Chem. Scand.*, **6**, 243 (1952).
(12) R. Hay, *Lab. Pract.*, **12**, 752 (1963).
(13) G. Kortum, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution", Butterworths, London, 1961.
(14) E. Gelles and R. W. Hay, *J. Chem. Soc.*, 3673 (1958).
(15) J. Pople, W. Schneider, and H. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, N.Y., 1959, Chapter 10.
(16) F. C. Kokesh, *J. Org. Chem.*, **41**, 3593 (1976).
(17) It has been reported that under some conditions the proton NMR spectrum of oxalo-2-propionic acid does not have separate signals due to enol, hydrate, and keto forms: N. Y. Sakkab and A. E. Martell, *J. Am. Chem. Soc.*, **98**, 5285 (1976).
(18) This treatment is valid because the contribution to the line width is additive when several parallel processes are involved in the proton exchange. See, E. Grunwald and M. Cocivera, *Discuss. Faraday Soc.*, 105 (1965).
(19) Because the fraction of OA present as enol is relatively pH independent (ref 16), $f \simeq$ the fraction of the enol present as monoanion, and therefore use of microscopic acid dissociation constants is unnecessary to estimate this fraction. For this reason, eq 1 and 2 could also be written in terms of the square of the enol concentration.
(20) The increase in Δ at pH <2 may represent a previously unreported pathway of H^+-catalyzed reaction of the enol of fully protonated OA.
(21) N. V. Raghavan and D. L. Leussing, *J. Am. Chem. Soc.*, **98**, 723 (1976).
(22) Data of Banks (ref 4) and Bruice (ref 5) are not sufficient to estimate α for general acid catalysis by carboxylic acids of the ketonization of the enol dianion.
(23) R. P. Bell, "The Proton in Chemistry", 1st ed, Cornell University Press, Ithaca, N.Y., 1959, p 171.
(24) For the ester, the pK_a is about 9.6; F. Kokesh, unpublished work. Benzoylacetone has a pK_a of 9.7, see ref 23.
(25) The value for β' for acetone is calculated using $\alpha' = 0.55$ from R. P. Bell and O. M. Lidwell, *Proc. R. Soc. London, Ser. A*, **176**, 88 (1940).
(26) The pK_a of the CH_2 protons of II should be about the same as that for the CH_2 protons of 4-ethyl oxaloacetate, which has a value of about 9.6 (ref 24). The value for the pK_a of the CH_2 protons of I is estimated to be about -1.1 in the following way. Since for OA^{2-} the value for $K_{\text{enol}} \approx [\text{enol}]/[\text{keto}]$ is 0.08 (at 38 °C, ref 16), the CH_2 protons of I are 12 times less acidic than the OH proton. Assuming that the latter is as acidic as the corresponding OH in protonated acetone (i.e., $pK_a = -2.2$, ref 27) the pK_a for the CH_2 protons is obtained as $-2.2 + \log 12$. A similar approach can be applied to acetone using $K_{\text{enol}} = 1.5 \times 10^{-8}$ (ref 28), pK_a of protonated acetone given above, and $pK_a = 20$ for acetone (ref 29).
(27) R. A. McCelland and W. F. Reynolds, *Can. J. Chem.*, **54**, 718 (1976).
(28) J. E. Dubois and J. Toullec, *Tetrahedron*, **29**, 2859 (1973).
(29) R. Pearson and R. Dillon, *J. Am. Chem. Soc.*, **75**, 2439 (1953).
(30) If the rate constant for OAH^- acting as a general acid toward E^{2-} is estimated in the same manner, the maximum contribution to Δ is 0.44 Hz at pH = pK_{a_2}. Since in this case substrate and catalyst are both negatively charged this may be an overestimate. A major contribution from this term would not be in agreement with eq 1.
(31) A similar procedure has been used to assess possible bifunctional catalysis by monoanions of dicarboxylic acids of the enolization acetone: G. E. Lienhard and F. H. Anderson, *J. Org. Chem.*, **32**, 2229 (1967).
(32) The fact that the experimental rate constant k_2 is considerably larger than an estimate obtained via a Brönsted relationship for general base catalysis in this case does *not* necessarily require that OAH^- is an exceptionally effective catalyst. It is a consequence of the kinetic equivalence of the mechanisms in Scheme I and their respective Brönsted coefficients that if an extrapolation (of data for acetic acid catalysis) in terms of the general acid-catalyzed pathway gives a rate constant near the experimental value, then the extrapolation via the general base-catalyzed pathway *must* give an estimated rate constant that appears to be too small. Nevertheless, this argument does not seem sufficient to preclude a process in which OAH^- acts as a bifunctional catalyst.
(33) R. P. Bell and P. de Maria, *Trans. Faraday Soc.*, **66**, 930 (1970).
(34) G. E. Lienhard and T. Wang, *J. Am. Chem. Soc.*, **91**, 1146 (1969).
(35) T. H. Fife, *J. Am. Chem. Soc.*, **87**, 1084 (1965).
(36) W. Dieckmann, *Ber.*, **55**, 2470 (1922).
(37) K. H. Meyer, *Justus Liebigs Ann. Chem.*, **380**, 212 (1911).
(38) We are grateful to a referee for noting our failure to make this point.

Nucleophilic Aromatic Substitution Promoted by Cobalt(III) Trifluoroacetate[1]

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A series of aromatics was subjected to oxidation by cobalt(III) trifluoroacetate in the presence of a variety of nucleophiles. In this manner benzene was successfully halogenated with chloride, bromide, and iodide, and toluene, chlorobenzene, and benzotrifluoride were also chlorinated. Attempts to substitute fluoride, cyanide, and nitrate onto benzene were thwarted by solvent interference. Nitrite ion was oxidized to nitrogen dioxide and no substitution products were formed. A mechanism involving aromatic radical cations is most consistent for the aromatic–chloride–cobalt(III) reactions. However, with many of the other nucleophiles an alternate reaction pathway involving ligand oxidation by metal ion appears more likely.

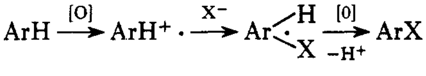
An interesting type of nucleophilic aromatic substitution can be accomplished by reacting nucleophiles with aromatic radical cations produced by an appropriate oxidant (eq 1). Both electrochemical oxidation[2] and chemical oxidizing agents such as xenon difluoride,[3,4] peroxydisulfate,[5,6] manganese(III) acetate,[7,8] and cobalt(III) acetate[9] have been effectively used in this manner. One of the limitations of these reactions, however, is the need to use aromatics of somewhat lower ionization potential (i.e., more electron rich).[8] Substitution of trifluoroacetate for acetate ligands on the cobalt complex was found to enhance its oxidative powers,[9-11] thus allowing radical cations to be formed from benzene and deactivated

Table I. Chlorination of Benzene

Reactant ratio	Products	
C_6H_6-Co(TFA)$_3$-LiCl	% C_6H_5Cl[a]	% C_6H_5OTF[a]
12:0:3	0	0
12:1:0	0	39
12:1:1	37	30
12:1:2	67	6
12:1:3	66	0
12:1:5	70	0
12:1[b]:3	<1	0

[a] Yield based on 0.5 mol of product produced per 1.0 mol of cobalt(III) consumed; OTF = O_2CCF_3. [b] Cobalt(III) acetate in acetic acid solvent.

aromatics such as chlorobenzene and benzotrifluoride. The radical cations of benzene and chlorobenzene underwent trifluoroacetoxylation with cobalt(III) trifluoroacetate.[10]



$$ArH \xrightarrow{[O]} ArH^+\cdot \xrightarrow{X^-} Ar\overset{H}{\underset{X}{<}}\cdot \xrightarrow[-H^+]{[0]} ArX \qquad (1)$$

The purpose of this study was to utilize the potent oxidant cobalt(III) trifluoroacetate with a series of aromatics (anisole, toluene, benzene, chlorobenzene, and benzotrifluoride) in the presence of a variety of nucleophiles (halides, cyanide, nitrate, and nitrite) in an effort to determine whether the corresponding nucleophilic substitution products could be obtained.

Results

Aromatic–Cobalt(III) Trifluoroacetate–Lithium Chloride. Initially, a control reaction in which benzene was treated with a solution of cobalt(III) trifluoroacetate[10,11] was performed. Phenyl trifluoroacetate was the only product observed (Table I), consistent with an earlier report.[10] The less than quantitative yield in the presence of excess benzene has been suggested to be due to polyphenylated materials arising from side reaction with excess aromatic.[10]

Inclusion of chloride ion (1:1 molar ratio with the cobalt(III) salt) led to a 37% yield of chlorobenzene and a somewhat reduced amount of phenyl trifluoroacetate. Increasing the ratio of chloride ion to cobalt(III) led predominantly or exclusively to chlorobenzene (Table I). Since the optimum reaction condition for chlorination was a 3:1 ratio of nucleophile-containing salt to cobalt(III), these conditions were adopted for most other reactions in the study.

A number of control reactions demonstrated the importance of this particular cobalt(III) salt. Treatment of benzene with chloride or with chloride and cobalt(III) acetate in acetic acid gave no substitution products (Table I).

Reaction of chlorobenzene using the same conditions as with benzene also resulted in chlorination (Table II). The dichlorobenzenes consisted of 19% ortho and 81% para isomers. Treatment of chlorobenzene with chlorine in this same solvent system both with and without cobalt(III) trifluoroacetate gave dichlorobenzenes with an isomer distribution of ortho/meta/para = 28/0.3/72.

Though little substitution was observed with benzotrifluoride under usual conditions, refluxing the mixture (65 °C) led to reduction of the cobalt(III) complex and nuclear chlorination products. The isomeric distribution was not determined.

The reaction with toluene resulted in a complex mixture of products including chlorinated toluenes, dimers, and trimers. With air present, the major chlorotoluene found was the nuclear substitution product (ortho/para = 41/59), while a small amount of the side-chain product, benzyl chloride, was observed. Under nitrogen, the major chlorinated product was benzyl chloride; chlorotoluenes were formed only in small quantities. Control reactions showed that in this solvent mixture chlorine reacted with toluene to give an ortho/para mixture of 65/35.

Unlike the other aromatics, the reaction of anisole with chloride ion and cobalt(III) trifluoroacetate gave rise to no chlorination products. Instead, *p*-methoxyacetophenone was formed in a very high yield and *p*,*p*′-dimethoxybiphenyl in yields of 46% (no other isomers found). All the cobalt(III) species was reduced in the reaction. A control reaction in which the cobalt(III) complex was omitted and lithium acetate added instead led to the acetophenone product. This suggested that the acetate ligands present in the cobalt salt solution were responsible for the major product observed.[12]

Control reactions showed that molecular chlorine, if present, would chlorinate anisole (ortho/para = 37/63). However, when equimolar amounts of chlorine and cobalt(III) trifluoroacetate were allowed to compete for a limited amount of anisole, no chlorination was observed (Table II).

Benzene–Cobalt(III) Trifluoroacetate–Other Nucleophiles. When benzene was reacted with lithium bromide in the presence of cobalt(III) trifluoroacetate, a good yield (60%) of bromobenzene was obtained, and no phenyl trifluoroacetate was noted (Table III). Molecular bromine itself in

Table II. Other Aromatics–Co(TFA)$_3$–Chloride[a]

Aromatic	Registry no.	Reagent	Products (% yield)[b]
PhCl	108-90-7	Co(TFA)$_3$–LiCl[c]	$C_6H_4Cl_2$ (43%, *o*/*p* = 19/81)
PhCl		Co(TFA)$_3$–Cl_2[d]	$C_6H_4Cl_2$[e] (*o*/*m*/*p* = 27/0.3/73)
PhCl		Cl_2	$C_6H_4Cl_2$[e] (*o*/*m*/*p* = 29/0.2/71)
$PhCF_3$	98-08-8	Co(TFA)$_3$–LiCl[c]	$ClC_6H_4CF_3$ (39%)[f]
$PhCH_3$	108-88-3	Co(TFA)$_3$–LiCl[c]	$ClC_6H_4CH_3$ (≃5%, *o*/*p* = 41/59) $C_6H_5CH_2Cl$ (<1%) $C_{14}H_{14}$[g] (≃5%) + $C_{21}H_{21}$[g] (≃7%)
$PhCH_3$		Cl_2	$ClC_6H_4CH_3$[b] (*o*/*p* = 65/35)
$PhOCH_3$	100-66-3	Co(TFA)$_3$–LiCl[c]	(*p*-$CH_3OC_6H_4$)$_2$ (46%) $CH_3COC_6H_4OCH_3$ (≃220%[h])
$PhOCH_3$[i]		Co(TFA)$_3$–Cl_2[d]	(*p*-$CH_3OC_6H_4$)$_2$[e] + $CH_3COC_6H_4OCH_3$[e]
$PhOCH_3$[j]		Co(TFA)$_3$–Cl_2[d]	(*p*-$CH_3OC_6H_2$)$_2$[e] + $CH_3COC_6H_4OCH_3$[e] $ClC_6H_4OCH_3$[e] (*o*/*p* = 21/79)
$PhOCH_3$		Cl_2	$ClC_6H_4OCH_3$[e] (*o*/*p* = 37/63)

[a] Reactions carried out in trifluoroacetic acid–trifluoroacetic anhydride (90/10) solvent with excess aromatic at 25 °C. [b] Based on 0.5 mol of product produced per mol of cobalt(III) consumed. [c] In 1:3 molar ratio. [d] In 1:1 molar ratio. [e] Yield not determined. [f] Isomers not determined. [g] Isomer mixtures; tentative identification based on similarity of GC retention times to authentics. [h] Yield based on available acetate is 73%. [i] Aromatic/Co(TFA)$_3$ molar ratio = 1:2. [j] Aromatic/Co(TFA)$_3$ molar ratio = 1:1.

Table III. Reaction of Other Nucleophiles with Benzene–Co(TFA)$_3$[a]

$C_6H_6 + Co\,(TFA)_3 \xrightarrow{X^-}$, X =	% C_6H_5X[b]	% $C_6H_5O_2CCF_3$[b]
Br^-	60	0
I^-	38	0
F^-	0	20
F^-[c]	0	30
CN^-	0	56
NO_2^-[d]	0	0
NO_3^-	0	20[e]
I_2	83[g]	0
I_2[f]	0	0
I^-[f]	0	0
Br_2[f]	251[g]	0

[a] Mole ratio of benzene/cobalt(III)/nucleophile = 12:1:3. [b] Yield based on 0.5 mol of product formed per mol of cobalt(III) consumed. [c] With added 15-crown-5. [d] Nitrogen dioxide fumes were observed. [e] In addition, nitrobenzene (>200%) was obtained; the limiting reagent in this process is the nitrate anion accounting for the high yield based on cobalt(III). [f] No Co(TFA)$_3$ used. [g] These yields are based on cobalt(III) in comparable runs; based on the halogens, they are 14% for I_2 and 42% for Br_2.

the same solvent system but without the cobalt(III) salt effectively produced bromobenzene (Table III).

The reaction of benzene with sodium iodide and cobalt(III) trifluoroacetate gave a moderate yield of iodobenzene (Table III). Three control reactions were performed in this solvent mixture with various potential iodinating species. Without cobalt(III) trifluoroacetate neither sodium iodide nor molecular iodine was able to cause iodination. However, iodobenzene was formed when molecular iodine was used in conjunction with cobalt(III) trifluoroacetate.

An attempt to fluorinate benzene by employing lithium fluoride along with the cobalt(III) salt was made. Fluorobenzene was not obtained; phenyl trifluoroacetate was the only substitution product observed (Table III). Even the use of the crown ether, 15-crown-5, with lithium fluoride in an effort to enhance the nucleophilic properties of the fluoride[13] did not promote fluorination.

None of the anticipated substitution product, benzonitrile, was detected when benzene was reacted with cyanide and the cobalt(III) salt. Instead, a 56% yield of phenyl trifluoroacetate was obtained (Table III).

Upon introduction of sodium nitrite into the cobalt(III) system, no substitution products of any type were formed. Instead, a brown gas (NO_2) was observed above the reaction mixture immediately after mixing.

An attempt was made to substitute nitrate onto benzene to form an aryl nitrate. Instead phenyl trifluoroacetate and a large yield of nitrobenzene were the only aromatic products (Table III). Nitrobenzene was also obtained in a control experiment involving all reactants with the exception of the cobalt(III) salt. This suggested the formation of an active migrating agent such as trifluoroacetyl nitrate,[14] 1, from nitrate and solvent (eq 2).

$$(CF_3CO)_2O + NO_3^- \rightarrow \underset{\mathbf{1}}{CF_3CONO_3} + CF_3CO_2^- \quad (2)$$

Discussion

A number of possible mechanisms exist for systems in which an aromatic and a nucleophile are subjected to a strong oxidant. Equation 1 shows one possibility, a radical cation mechanism, where the oxidant is cobalt(III) trifluoroacetate. A second pathway would involve the preferential oxidation of nucleophile by the cobalt(III) salt (eq 3) followed by substitution (electrophilic or radical) of the resultant species onto the aromatic (eq 4).[15] Some controversy over which scheme is operative has appeared in the literature for a number of chlorination reactions.[6,16]

$$2X^- \xrightarrow[-2Co(II)]{2Co(III)} X_2 \quad (3)$$

$$X_2 + ArH \rightarrow ArX + HX \quad (4)$$

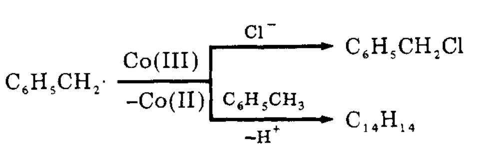
The mechanism felt to be most consistent with the results in the cobalt(III)–LiCl–aromatic reactions is the radical cation scheme (eq 1, [O] = Co(III), X^- = Cl^-). The net stoichiometry is shown in eq 5.

$$ArH + 2Co(O_2CCF_3)_3 + LiX \rightarrow ArX + 2Co(O_2CCF_3)_2 + CF_3CO_2H + LiO_2CCF_3 \quad (5)$$

Few reaction pathways are open to the radical cations formed from deactivated (electron poor) aromatics; thus chlorination by way of chloride ion attack (eq 1) was the major reaction with benzene, chlorobenzene, and benzotrifluoride. Chloride ion, being a better nucleophile than trifluoroacetate, effectively competed at lower concentrations and dominated trapping of the radical cation at higher concentrations (Table I). The need to react benzotrifluoride at elevated temperatures was consistent with its hesitancy towards radical cation production as measured by its higher ionization potential.[10]

Toluene is even more readily oxidized to a radical cation than is benzene, yet poorer substitution yields were noted. This is due primarily to the tendency of toluene radical cation, 2, to lose a proton-forming benzyl radical (eq 6). Evidence for this competing process was the identification of benzyl chloride (eq 7a) and oligomeric toluenes (eq 7b) among the products.[10]

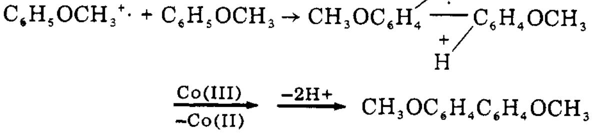
$$\underset{\mathbf{2}}{C_6H_5CH_3^{+}\cdot} \rightarrow C_6H_5CH_2\cdot \quad (6)$$



$$C_6H_5CH_2\cdot \xrightarrow[-Co(II)]{Co(III)} \begin{cases} \xrightarrow{Cl^-} C_6H_5CH_2Cl & (7a) \\ \xrightarrow[-H^+]{C_6H_5CH_3} C_{14}H_{14} & (7b) \end{cases}$$

The isomer distributions of the chlorotoluenes and dichlorobenzenes obtained from toluene and chlorobenzene, respectively, were different from those obtained from molecular chlorine in the same solvent system (Table II). This would be expected if a radical cation mechanism were involved.

The failure to observe chloroanisoles from anisole–lithium chloride–cobalt(III) trifluoroacetate was somewhat perplexing. Apparently the anisole radical cation undergoes reaction with another anisole molecule leading to the observed dimer (eq 8) more readily than it undergoes attack by the chloride



$$C_6H_5OCH_3^{+\cdot} + C_6H_5OCH_3 \rightarrow CH_3OC_6H_4\overset{H}{\underset{\overset{+}{H}}{\overset{\cdot}{—}}}C_6H_4OCH_3 \xrightarrow[-Co(II)]{Co(III)} \xrightarrow{-2H+} CH_3OC_6H_4C_6H_4OCH_3 \quad (8)$$

nucleophile (eq 1). Kochi has reported such a reaction for radical cations of electron-rich aromatics[10] and others have also noted the occurrence of dimerization for methoxy-substituted rings in radical cation systems.[17] Eberhardt[18] has observed the failure of the anisole radical cation to react with water as the nucleophile to yield the corresponding phenol, whereas with the radical cations of fluorobenzene and toluene this process proceeded smoothly.

An additional probe for the involvement of molecular chlorine was an experiment in which cyclohexene, which reacts readily with molecular chlorine,[19] was added to lithium chloride–cobalt(III) trifluoroacetate both with and without added benzene. In the former case no chlorinated cyclohexane products were found while in the latter cyclohexyl chloride was pinpointed among a complex product mixture. Apparently simple aromatics are oxidized in preference to chloride ion in this system.

With more readily oxidized ligands, the evidence for radical cation participation diminishes. Although bromination and iodination of benzene might involve the radical cation process (eq 1), the alternate scheme (eq 3 and 4) becomes more likely. In fact electrochemical iodinations occur by the latter mechanism.[20]

Molecular iodine itself and also the iodide ion were shown to be ineffective iodinating agents in the trifluoroacetic acid–anhydride media (Table III). However, when molecular iodine was added directly to the cobalt(III)–benzene system in the same solvent, iodination did in fact occur. Other studies have shown that aromatic iodinations require relatively reactive iodinating agents.[19] The bromination control also demonstrates that either process (eq 1 or eq 3 and 4) could account for the observed bromobenzenes.

A definitive example of preferential interaction of the cobalt(III) complex with the nucleophile rather than with the aromatic occurred when nitrite was incorporated into the system. Oxidation to nitrogen dioxide (eq 9) took place as evidenced by the brown gas above the reaction mixture. No aromatic substitution products were formed, implying that all the cobalt(III) was reduced by nitrite.

$$NO_2^- \xrightarrow[-\mathrm{Co(II)}]{\mathrm{Co(III)}} NO_2 \qquad (9)$$

The rationale for failure to substitute fluoride or cyanide ions under the influence of cobalt(III) trifluoroacetate is probably due to their protonation by the strongly acid solvent, thus greatly reducing their nucleophilicity. Solvent interference also prevented nitrate substitution by formation of trifluoroacetyl nitrate (eq 2), an eventual nitrating agent (vide supra). In all three cases only the trifluoroacetate ligand was left to react with the radical cation.

Experimental Section

The organic reagents, shown to be greater than 99% pure by GC, were used directly as were the reagent grade inorganic salts. Cobalt(III) acetate was prepared from the corresponding cobalt(II) salt by ozonolysis[11] and was shown to be 84% pure by iodometric titration.

Authentic aryl trifluoroacetates were prepared from the appropriate phenol (0.05 mol) and trifluoroacetic anhydride (0.071 mol) and purified by direct distillation. In this manner, phenyl trifluoroacetate (bp 145–146 °C), *o*-methoxyphenyl trifluoroacetate (bp 191–193 °C), *m*-methoxyphenyl trifluoroacetate (bp 195–196 °C), and *p*-methoxyphenyl trifluoroacetate (bp 196–199 °C) were prepared. *p*-Methoxyacetophenone was prepared from *p*-hydroxyacetophenone and dimethyl sulfate.[21] Most other compounds needed as authentics in this study were commercially available.

For all reactions run in this study, the cobalt(III) trifluoroacetate salt was formed "in situ" by dissolving cobalt(III) acetate in a mixture of trifluoroacetic acid and trifluoroacetic anhydride.[10,11] Verification of ligand exchange to produce the desired species was obtained from visible spectra.

Reaction of Aromatics with Cobalt(III) Trifluoroacetate and a Nucleophile. General Procedure. The aromatic to be reacted (0.047–0.065 mol) was dissolved in a portion of trifluoroacetic acid (15–40 mL). Whenever a nucleophile was also to be reacted, it was added as the sodium or lithium salt (0.005–0.015 mol) to this same portion of solvent. The cobalt(III) acetate (0.005 mol) was dissolved in a second portion of solution (10–15 mL) consisting of a mixture of trifluoroacetic acid and trifluoroacetic anhydride (50% by volume). When dissolution of solids was complete, the two solutions were rapidly mixed and allowed to react to completion at a temperature of 25 °C. In general, the presence of oxygen did not affect the reaction. The only exception was the case with toluene as the reactant.

The completeness of reaction was judged by color change (the cobalt(II) complex is violet whereas the cobalt(III) complex is green) as well as by iodometric titration to determine cobalt(III) remaining.

The reaction vessel was heated to 65–70 °C whenever the reaction did not proceed readily at 25 °C.

In reactions in which crown ethers were used, the appropriate crown ether (15-crown-5) was added to the reaction in small amounts, while all other reaction conditions remained constant.

Control reactions involving only cobalt(III) trifluoroacetate, halogen, or the nucleophile with the aromatic were run under analogous conditions.

Identification of Organic Products. Comparison of GC retention times of products from the reaction mixtures directly or from base-washed ether extracts to those of the appropriate authentics constituted one method of product analysis. A Hewlett-Packard Model 5830A GC equipped with dual columns (1.67 ft × 0.125 in. stainless steel UCW-982/Chromosorb W and 6 ft × 0.125 in. stainless steel OV-225/Chromosorb W), hydrogen flame ionization detectors, and programmable console was used for this purpose.

In addition the ether extracts of most reaction mixtures (after base extraction) were subjected to GC–MS analysis (Finnegan Model 3000 with quadrupole mass filter operated at 70 eV and coupled with a 3% OV-1/Chromosorb W GC column).

Where authentics were available, consistency between product mass spectra and authentic mass spectra confirmed identity. In this manner phenyl trifluoroacetate (molecular ion at *m/e* 190, base peak at *m/e* 69), chlorobenzene (molecular ions at *m/e* 113–115, base peak at *m/e* 51), bromobenzene (molecular ions at *m/e* 156–158, base peak at *m/e* 77), iodobenzene (molecular ion at *m/e* 204, base peak at *m/e* 51), *p*-methoxyacetophenone (molecular ion at *m/e* 150, base peak at *m/e* 65), and nitrobenzene (molecular ion at *m/e* 123, base peak at *m/e* 77) were identified. Due to relatively low yields of clorotoluenes and benzyl chloride from toluene and *o*- and *p*-dichlorobenzene from chlorobenzene no mass spectra were obtained. In these cases, identification of these products was based only on comparison of retention times with authentics on two dissimilar GC columns.

No chlorobenzotrifluoride or *p,p'*-dimethoxybiphenyl authentics were available; thus mass spectra data alone were used to determine product identity. The chlorinated benzotrifluoride mass spectra (molecular ion at *m/e* 180–182, base peak at *m/e* 59, others in decreasing intensity at *m/e* 77, 69, and 146) and the *p,p'*-dimethoxybiphenyl mass spectra (molecular ion at *m/e* 214, base peak also at 214, others in decreasing order at *m/e* 198, 169, 126, 137, 154) were a basis for identification. The melting point for the biphenyl product (173 °C) matched that of the literature value.[22]

Whenever these two techniques left some doubt as to the identity of a product, a larger scale reaction was run and products were isolated by vacuum distillation. IR and NMR spectra of the products were taken and found to be consistent with the structures proposed.

Quantitative product analysis was performed on a measured aliquot of the original reaction mixtures by GC after adding an appropriate internal standard (chlorobenzene, bromobenzene, iodobenzene, or methyl benzoate). Yields were obtained by comparing the relative peak areas of the products to those of the internal standard and correcting by means of response factors, calculated from mixtures containing known concentrations of authentic products (where available) plus the marker. Each reaction mixture was marked twice and the average value was taken as the product yield. Percent yield was based on the stoichiometry of 0.5 mol of product per mol of cobalt(III), the limiting reagent (eq 5).

Registry No.—C_6H_6, 71-43-2; $Co(TFA)_3$, 50517-80-1; phenol, 108-95-2; *o*-methoxyphenol, 90-05-1; *m*-methoxyphenol, 150-19-6; *p*-methoxyphenol, 150-76-5; trifluoroacetic anhydride, 407-25-0; phenyltrifluoroacetate, 500-73-2; *o*-methoxyphenyl trifluoroacetate, 31083-15-5; *m*-methoxyphenyl trifluoroacetate, 31083-16-6; *p*-methoxyphenyl trifluoroacetate, 5672-87-7; bromobenzene, 108-86-1; iodobenzene, 591-50-4; *p*-methoxyacetophenone, 100-06-1; nitrobenzene, 98-95-3; chlorobenzotrifluoride, 52181-51-8; *p,p'*-dimethoxybiphenyl, 2132-80-1.

References and Notes

(1) Presented at the American Chemical Society Great Lakes Regional Meeting, Evanston, Ill, June 1976.

(2) For a recent summary, see S. D. Ross, M. Finklestein, and E. J. Rudd, "Anodic Oxidation", Organic Chemistry Series, Vol. 32, A. T. Blomquist and H. H. Wasserman, Ed., Academic Press, New York, N.Y., 1975, pp 82–116; M. J. Allen, "Organic Electrode Processes", Chapman and Hall, London, 1968, pp 142–163.

(3) S. R. Anand, L. A. Quarterman, H. H. Hyman, K. G. Migliorese, and R. Filler, *J. Org. Chem.*, **40**, 807–809 (1975).
(4) S. P. Anand, L. A. Quarterman, P. A. Christian, H. H. Hyman, and R. Filler, *J. Org. Chem.*, **40**, 3796–3797 (1975).
(5) C. Walling and D. M. Camaioni, *J. Am. Chem. Soc.*, **97**, 1603–1604 (1975).
(6) A. Ledwith and P. J. Russell, *J. Chem. Soc., Perkin Trans. 2*, 1503–1508 (1975); however, see also R. Filler and R. C. Rickert, *J. Chem. Soc., Chem. Commun.*, 133–134 (1976).
(7) P. J. Andrulis, Jr., M. J. S. Dewar, R. Dietz, and R. L. Hunt, *J. Am. Chem. Soc.*, **88**, 5473–5478 (1966).
(8) E. I. Heiba, R. M. Dessau, and W. J. Koehl, Jr., *J. Am. Chem. Soc.*, **91**, 138–145 (1969).
(9) E. I. Heiba, R. M. Dessau, and W. J. Koehl, Jr., *J. Am. Chem. Soc.*, **91**, 6830–6837 (1969).
(10) J. K. Kochi, R. T. Tang, and T. Bernath, *J. Am. Chem. Soc.*, **95**, 7114–7123 (1973).
(11) R. Tang and J. K. Kochi, *J. Inorg. Nucl. Chem.*, **35**, 3845–3856 (1973).
(12) We feel that a mixed anhydride, **1**, formed by reaction of trifluoroacetic anhydride with acetic acid liberated from ligand exchange of cobalt(III) acetate acts as an effective acylating agent with the electron-rich aromatic, anisole. The limiting reagent in this reaction is the acetate ligand rather than the cobalt(III) complex which explains why the yield based on cobalt(III) is greater than 100% (300% possible on this basis, Table II).
(13) C. L. Liotta and H. P. Harris, *J. Am. Chem. Soc.*, **96**, 2250–2252 (1974).
(14) E. J. Bourne, M. Stacey, J. C. Tatlow, and J. M. Tedder, *J. Chem. Soc.*, 1695–1696 (1952).
(15) A referee has suggested a third possible mechanism involving electrophilic aromatic substitution by a positively charged cobalt(III) species similar to that reported for thallium(III) (A. McKillop and E. C. Taylor, *Adv. Organomet. Chem.*, **11**, 147 (1973)) and lead(IV) salts (R. Criegee, *Oxid. Org. Chem.*, K. B. Wiberg, Ed., Academic Press, New York, N.Y., 1965, p 326). While we cannot discount this pathway, we feel that the other mechanisms are more probable in this study.
(16) J. K. Kochi, *Tetrahedron Lett.*, 4305 (1974); E. Baciocchi and G. Illuminati, *ibid.*, 2265 (1975).
(17) V. D. Parker and A. Ronlan, *J. Am. Chem. Soc.*, **97**, 4714–4721 (1975); A. Nishinaga, H. Hidetoshi, and T. Matsura, *Bull. Chem. Soc. Jpn.*, **47**, 1813–1814 (1974).
(18) M. K. Eberhardt, *J. Org. Chem.*, **42**, 832 (1977).
(19) W. McCrae, "Basic Organic Reactions" Heyden and Sons, New York, N.Y., 1973, p 120 ff.
(20) L. L. Miller, E. P. Kyawa, and C. B. Campbell, *J. Am. Chem. Soc.*, **92**, 2821–2825 (1970).
(21) A. I. Vogel, "Elementary Practical Organic Chemistry", Part II, Longmans, Green and Co., New York, N.Y., 1957, p 277.
(22) R. C. Weast, Ed., "CRC Handbook of Chemistry and Physics", 54th ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1974, p C-206.

Generation and Reactivity of an Unstabilized Carbohydrate Phosphorane

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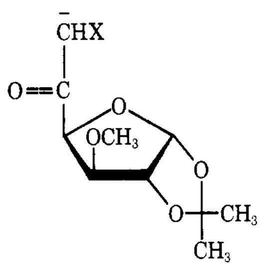
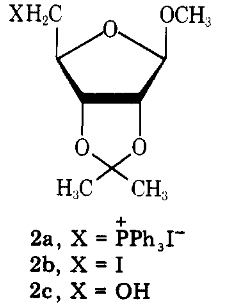
Generation of the ylide of methyl 5-deoxy-2,3-*O*-isopropylidene-5-(triphenylphosphonio)-β-D-ribofuranoside iodide (**2a**) is described. Treatment of the ylide with aldehydes affords good yields of olefinic products of the α-L-*lyxo* configuration, resulting from epimerization of the ylide prior to reaction. Ketones do not react cleanly with the ylide. Addition of a proton source to the ylide under appropriate conditions allows the formation of good yields of a self-condensation product **14**.

The Wittig reaction has been extensively utilized as a method of chain extension in the carbohydrate field.[1] Both aldehydo and keto sugars have proven amenable to the action of stabilized as well as unstabilized phosphorus ylides, and many unique and interesting chain-extended and branched-chain carbohydrates have been synthesized in this manner. The concept of reversing the roles of the two partners in the Wittig reaction, that is, the combination of a carbohydrate ylide and an aliphatic or aromatic carbonyl compound, has received only scant attention. Zhdanov[2,3] has generated the stabilized carbohydrate-containing phosphorane **1a** as well as one other carbonyl-stabilized example. Both phosphoranes have very low reactivity, as would be expected, and only condense with a few activated aromatic aldehydes (*p*-nitro- and *o*-hydroxybenzaldehyde). Recently, an analogous stabilized carbohydrate sulfur ylide **1b** has been prepared and found to react with acrolein and acrylonitrile.[4] To further explore the potential of unstabilized carbohydrate ylides, we have examined the generation and reactivity of the ylide derived from methyl 5-deoxy-2,3-*O*-isopropylidene-5-(triphenylphosphonio)-β-D-ribofuranoside iodide (**2a**). Though phosphorus-containing carbohydrates have been well studied,[5] the only examples of triphenylphosphonium salts appear to be those employed as leaving groups in studies on the synthesis of α-glycosides.[6,7]



1a, X = $\overset{+}{P}Ph_3$
1b, X = $\underset{CH_3}{\overset{+}{S}}$—$CH_2Ph$

The major obstacle in the use of an unstabilized carbohydrate phosphorane is the presence of a leaving group β to the phosphorus in the vast majority of carbohydrates. Generation of the phosphorane might then be rapidly followed by elimination to form a vinylphosphonium salt. In principle, this problem can be approached through experimental manipulations (solvents, temperature) as well as by decreasing the ability of the β substituent to leave. The selection of **2a**, with the β substituent additionally attached through the carbon chain, should provide a particularly favorable case, since intramolecular closure to regenerate the ylide should be possible.



2a, X = $\overset{+}{P}Ph_3I^-$
2b, X = I
2c, X = OH
2d, X = OTs