Communications

Three-Electron Oxidations. 15. Chromic Acid Oxidation of Mandelic Acid[1,2]

Summary: The observation that mandelic acid is oxidized to an about equimolar mixture of benzaldehyde and benzoic acid is interpreted by a mechanism according to which an intermediate cyclic complex of mandelic acid and chromic acid decomposes in a three-electron oxidation–reduction step with synchronous C–C and C–H bond cleavage.

Sir: Heckner, Grupe, and Landsberg[3] reported that the chromium(VI) oxidation of mandelic acid yields benzaldehyde and benzoic acid but no phenylglyoxylic acid and that the deuterio compound, $C_6H_5CD(OH)CO_2H$, exhibits a large kinetic isotope effect ($k_H/k_D = 8.4$).

These two findings are irreconcilable with any usual one- or two-electron oxidation mechanism.[4] Oxidation on the carbon–hydrogen bond should result in a deuterium isotope effect, but would yield phenylglyoxylic acid. Oxidation on the carbon–carbon bond would give benzaldehyde, but no appreciable isotope effect. We were intrigued by this contradiction and decided therefore to investigate the reaction in detail.

Kinetic measurements have shown that the chromic acid oxidation of mandelic acid (MA) follows the rate law

$$-\mathrm{d}[\mathrm{Cr(VI)}]/\mathrm{d}t = [\mathrm{HCrO_4}^-][\mathrm{MA}](k_1 + k_2[\mathrm{H}^+] + k_3[\mathrm{MA}])$$

At 25 °C the rate constants have the values: $k_1 = 9.24 \times 10^{-4}$ M^{-1} s^{-1}, $k_2 = 7.62 \times 10^{-2}$ M^{-2} s^{-1}, $k_3 = 7.21 \times 10^{-2}$ M^{-2} s^{-1}.

At high mandelic acid concentrations the reaction is second order in mandelic acid and the reaction products are phenylglyoxylic acid, benzaldehyde, and carbon dioxide (Table I). The observed kinetic isotope effect ($k_H/k_D = 7.6$ at $[H^+] = 0.005$ M, [MA] = 0.8 M) is therefore easily understood.

Under first-order conditions (low mandelic acid concentration, high acidity, cf. Table I) the main products are benzaldehyde and benzoic acid in almost equal amounts, while only a low yield of phenylglyoxylic acid is formed. Nevertheless, the kinetic isotope effect is even higher ($k_H/k_D = 9.0$ at $[H^+] = 0.5$ M, [MA] = 0.005 M). These results are in essential agreement with those reported by Landsberg.[3] The formation of a higher oxidation product, benzoic acid, in a stoichiometric yield (~0.5 mol/Cr(VI)) is surprising and provides the clue to the understanding of the reaction mechanism.

Landsberg[3] assumed that benzoic acid is formed by the further oxidation of benzaldehyde. If that were the case, it would be most unlikely that benzaldehyde and benzoic acid would be found consistently in almost precisely equimolar amounts. Moreover, benzaldehyde reacts 20.5 times slower with chromium(VI) than does mandelic acid. The oxidation of mandelic acid to benzaldehyde and carbon dioxide would not give rise to any appreciable isotope effect. Further, when *m*-methylmandelic acid was oxidized in the presence of benzaldehyde, the yield of *m*-toluic acid was essentially unaffected and only minute amounts of benzoic acid were formed (Table II). Finally, when the reaction products are analyzed as a function of time, one finds that the benzaldehyde/benzoic acid ratio remains constant throughout the reaction. Although an induction period would be expected if benzoic acid were formed through a stable intermediate, none is observed.

Phenylglyoxylic acid would seem to be a somewhat more likely reaction intermediate. It reacts with chromic acid 3.2 times faster than mandelic acid and its formation in the rate-limiting step would lead to a significant isotope effect. However, the difference in reactivity between phenylglyoxylic acid and mandelic acid with respect to Cr(VI) is by far not

Table I. Product Yields in the Chromic Acid Oxidation of Mandelic Acid (MA)[a]

$[H^+]$, M	[MA], M	yield, mol/mol Cr(VI)			
		$C_6H_5COCO_2H$	$C_6H_5CO_2H$	C_6H_5CHO	CO_2
0.005	0.8	0.44	0.037	0.968	0.94
0.005	0.5	0.433	0.046	0.961	0.94
0.1	0.005	0.138	0.424	0.497	1.00
0.5	0.005	0.140	0.442	0.470	1.00

[a] 25 °C; initial [Cr(VI)] = 5×10^{-4} M; solutions purged with nitrogen for 10 min.

Table II. Effect of Benzaldehyde and Phenylglyoxylic Acid on Product Yields in the Chromic Acid Oxidation of *m*-Methylmandelic Acid (MeMA) at 25 °C[a]

[MeMA], M	$[C_6H_5CHO]$, M	$[C_6H_5COCO_2H]$, M	yield, mol/mol Cr(VI)				
			$C_6H_5CO_2H$				
			calcd[b]	found	*m*-$MeC_6H_4CO_2H$	*m*-MeC_6H_4CHO	*m*-$MeC_6H_4COCO_2H$[c]
0.005	0.0	0.0			0.445	0.464	0.114
0.05	0.0	0.0			0.424	0.556	0.122
0.005	0.0025	0.0	0.023	0.014	0.435	0.415	0.117
0.0	0.0025	0.0		0.012[d]			
0.005	0.0	0.00025	0.134	0.110	0.352	0.471	0.119
0.01	0.0	0.00025	0.075	0.055	0.389	0.509	0.127
0.02	0.0	0.00025	0.037	0.034	0.410	0.520	0.130
0.05	0.0	0.00025	0.015	0.018	0.406	0.535	0.143

[a] Initial Cr(VI) = 5×10^{-4} M (0.001 mmol); $[H^+] = 0.5$ M; solutions purged with nitrogen for 10 min. [b] Calculated from Cr(VI) oxidation rate constants for benzaldehyde ($k_{exptl} = 8.49 \times 10^{-6}$ s^{-1}), phenylglyoxylic acid ($k_{exptl} = 5.61 \times 10^{-4}$ s^{-1}), and *m*-methylmandelic acid ($k_{exptl} = 1.82 \times 10^{-4}$ s^{-1}) at 25 °C, $[HClO_4] = 0.5$ M, and [substrate] = 5×10^{-3} M. [c] Estimated from LC analysis using the phenylglyoxylic acid calibration curve. [d] Solution quenched with oxalic acid–*i*-PrOH mixture at time required for the complete oxidation of the α-hydroxy acid in absence of the aldehyde.

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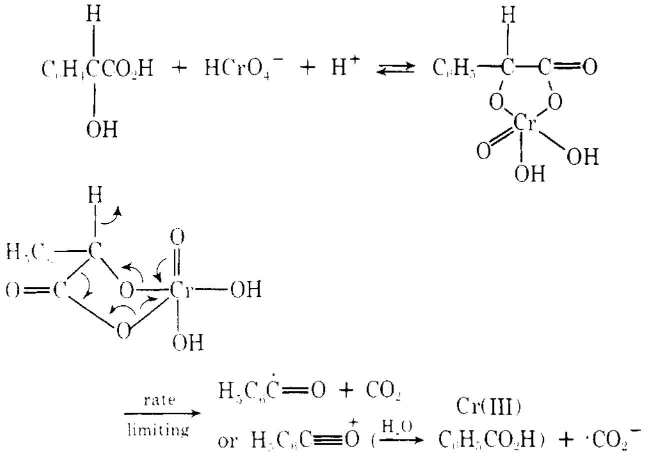
large enough to explain the very low yield of phenylglyoxylic acid and the high yield of benzoic acid, unless one of the chromium intermediates, Cr(IV) or Cr(V), had a much higher selective preference for the keto acid. We oxidized *m*-methylmandelic acid in the presence of phenylglyoxylic acid, assuming that a *m*-methyl substituent will have only a minimal effect on the reactivity of either the hydroxy or the keto acid and will therefore serve as a noninterfering label. The results in Table II show that the yields of *m*-toluic acid are only slightly reduced and those of *m*-tolylglyoxylic acid only slightly increased if an equivalent amount of phenylglyoxylic acid ((0.5 mol/Cr(VI)) is added. The yields of benzoic acid are in good agreement with calculated values based on the relative reactivities of phenylglyoxylic and *m*-methylmandelic acids toward chromium(VI).

Our results provide convincing evidence that neither benzaldehyde nor phenylglyoxylic acid is an intermediate in the formation of benzoic acid. In order to explain the formation of benzoic acid one has to postulate that it is formed through a reactive intermediate of a higher oxidation level and the formation of which involves the breaking of the carbon–hydrogen bond. Both requirements are met by $C_6H_5\dot{C}{=}O$ or $C_6H_5C{\equiv}O^+$, either of which can be formed in a three-electron oxidation of mandelic acid.



The only known example of a three-electron oxidation of a single molecule is the recently reported oxidation of 2,7-dihydroxyheptanoic acid,[2] in which the two reacting centers are separated by a long chain of methylene groups. *The chromic acid oxidation of mandelic acid represents the first example of a three-electron oxidation of a molecule in which a C–C and a C–H bond on the same carbon atom are broken simultaneously in the rate-limiting step.*

The free-radical intermediates formed in the rate-limiting step would be expected to reduce chromium(VI) to chromium(V). In order to account for the observed reaction products one must assume that chromium(V) [directly or after disproportionation to chromium(VI) and chromium(IV)] will oxidize mandelic acid to benzaldehyde and carbon dioxide

$$\mathrm{Cr(VI)} + C_6H_5\dot{C}{=}O\ (\text{or}\ \cdot CO_2H) \rightarrow \mathrm{Cr(V)} + C_6H_5CO_2H\ (\text{or}\ CO_2)$$

$$C_6H_5CH(OH)CO_2H + \mathrm{Cr(V)} \rightarrow C_6H_5CHO + CO_2 + \mathrm{Cr(III)}$$

This reaction sequence leads to the observed 1:1 benzoic acid/benzaldehyde ratio.

References and Notes

(1) Support for this investigation by a grant of the National Science Foundation is gratefully acknowledged.

(2) Part 14: S. Ramesh, J. Roček, and D. A. Schoeller, *J. Phys. Chem.*, in press.

(3) K. H. Heckner, K. H. Grupe, and R. Lansberg, *Z. Phys. Chem. (Leipzig)*, **242**, 225 (1969); *ibid.*, **247**, 91 (1971); *J. Prakt Chem.*, **313**, 161 (1971).

(4) The mechanism proposed by Lansberg[3] postulates a two-electron oxidation of mandelic acid to benzaldehyde. No explicit explanation for the observed deuterium isotope effect is given, although the proposed reaction scheme indicates a breaking of the carbon–hydrogen bond during the formation of benzaldehyde.

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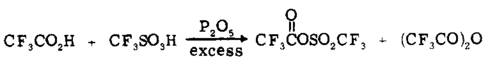
Trifluoroacetyl Triflate: An Easily Accessible, Highly Electrophilic Trifluoroacetylating Agent

Summary: Trifluoroacetyl triflate (TFAT, 3) is easily prepared and isolated. It is a powerful electrophile capable of uncatalyzed trifluoroacetylation of reactive aromatic rings as well as attack at chlorine of covalent chlorides and reaction with other nucleophiles.

Sir: Studies of mixed anhydrides of carboxylic acids and trifluoromethanesulfonic (triflic) acid (2) have shown them to be extremely powerful acylating agents.[1] However, no reports of perfluoroacyl analogues have appeared. Mixed anhydrides of perfluorocarboxylic acids and fluorosulfonic acid have been reported.[2,3] The possible application of these in synthesis has not been explored. Although salts involving the trifluoroacetylium ion have been reported,[4] further work[5] showed these not in fact to be acylium salts but covalent acyl fluoride complexes.

Trifluoroacetyl triflate (TFAT, 3) is conveniently prepared by the action of a threefold excess of phosphorus pentoxide on an equimolar mixture of trifluoroacetic acid (1) and triflic acid (2). The mixture is boiled for 2 h and distilled. A fractional redistillation from phosphorus pentoxide gives trifluoroacetic anhydride (4, 23%, bp 37.5–40.5 °C) and TFAT (3,[6] 52%, bp 62.5 °C). Surprisingly, no triflic anhydride was observed.



$$CF_3CO_2H + CF_3SO_3H \xrightarrow[\text{excess}]{P_2O_5} CF_3\overset{O}{\overset{\|}{C}}OSO_2CF_3 + (CF_3CO)_2O$$

1 2 3 (TFAT) 4

Pure TFAT (3) is a colorless liquid which is stable indefinitely at room temperature in the absence of moisture. It can be repeatedly distilled from P_2O_5 without any detectible reequilibration to form the symmetrical anhydrides. It reacts almost explosively with water, but does not react at room temperature with the sterically hindered base 2,6-di-*tert*-butyl-4-methylpyridine (5).[7,8]

The utility of 3 as a trifluoroacetylating agent is demonstrated in the reaction with anthracene (6) to give 81%[9] of 9-(trifluoroacetyl)anthracene (7) when a mixture of 1.1 equiv of 3 and 1.1 equiv of 5 were heated in benzene at 80 °C with 6 for 44 h. The mild conditions used for this reaction are to be contrasted with those used previously by Pirkle[10] for making 7, which involved heating anthracene with trifluoroacetic anhydride in benzene at 200 °C for 15 h in a sealed tube to yield 73% of the product.

$$Ph_3CCl + \mathbf{3} \longrightarrow Ph_3C^+\ {}^-OSO_2CF_3 + CF_3COCl$$

12 13 14

Cyclohexanone is converted to enol ester 9 (72%) upon slow addition to a mixture of 2 equiv of 3 and 1 equiv of 5 in dry CH_2Cl_2 at 0 °C.[12] The trifluoroacetylation by 3 at atoms other

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