# Oxidation of Alcohols with Periodic Acid Catalyzed by Fe(III)/2-Picolinic Acid†

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Gif reactions[1] attempt to imitate the principle of the oxidations catalyzed by cytochrome P450.[2,3] Hydrocarbons[4] can be thus oxidized by $O_2$, $KO_2$, $H_2O_2$ and *t*-BuOOH with Fe(II) or Fe(III) being the catalyst. Numerous hypervalent iodine compounds[5] have been engaged in oxidation of alcohols. The oxidation of primary alcohols[6] into corresponding carboxylic acids proceed smoothly with periodic acid ($H_5IO_6$) catalyzed by $CrO_3$ in wet $CH_3CN$. Secondary benzylic methylenes[7] can be efficiently oxidized to ketonic products with $H_5IO_6/CrO_3$. Periodic acid[8] also oxidizes sulfides to sulfones with aid of a manganese catalyst. Accordingly, periodic acid with suitable catalyst shows very strong oxidation power to give the fully oxidized products of carboxylic acids,[6] ketones[7] and sulfones.[8]

## Experimental Section

**Materials and Method**. All the alcoholic substrates, periodic acid and other reagents were purchased from the major suppliers. Pyridin (99.9%) was used as received from Aldrich. Varian Gemini 2000 NMR spectrometer was employed for identification and the quantitative analysis of the reaction mixtures.

**Oxidations of the Alcoholic Substrates**. $FeCl_3\cdot 6H_2O$ (0.3 mmol) and 2-picolinic acid (0.6 mmol) were dissolved in $C_5H_5N$ (2.5 mL) that was stirred for 1/2h. A substrate (5 mmol) was added and $H_5IO_6$ (15 mmol) introduced slowly to give the total volume of *ca*. 5 mL that assumed dark brown color. After the reaction, the solvent was evaporated to dryness and $CH_2Cl_2$ (4 mL) was added that was subsequently subject to Silica gel column chromatography.

**Competition Reaction of Benzyl Alcohols**. $FeCl_3\cdot 6H_2O$ (0.06 mmol) and 2-picolinic acid (0.12 mmol) were dissolved in $C_5H_5N$ (0.5 mL) that was stirred for 1/2h. $C_6H_5CH_2OH$ (3 mmol) and $YC_6H_5CH_2OH$ (3 mmol) were added, and $H_5IO_6$ (3 mmol) introduced slowly. An aliquot of reaction mixture (~0.05 mL) was withdrawn and mixed with water (1 mL)/methylene chloride (1 mL). The methylene chloride layer was evaporated to dryness and $CDCl_3$/TMS was added for NMR analysis of $YC_6H_4CHO/C_6H_5CHO$.

## Results and Discussion

We'd like to herein report oxidation of various alcohols with periodic acid catalyzed by Fe(III)/2-picolinic acid (PA). Control experiments were designed to assess the catalytic activity of Fe(III) and PA. As indicated in Table 1, $H_5IO_6$ itself possesses some oxidative function that can be somewhat enhanced by presence of Fe(III). Addition of PA then greatly improves the oxidation power in terms of reaction time and yield. The dramatic effect of PA could be due to the bidentate character by which iron porphyrinlike structure[1] is attained between Fe(III) and two molecules of PA.

Secondary benzylic alcohol (entries 1-6) show efficient reactivities. The steric effects appear to be the dominating element in determining the rates. Particularly, presence of *t*-butyl may impose steric hinderance to drastically retard the reaction rate (entry 6). Simple benzyl alcohols (entries 7-9) and allylic alcohol (entry 12) were selectively oxidized to corresponding aldehydes. The oxidation of benzyl alcohols may be subject to minor substituent effects (entries 7-9). Competition reactions have been done with $YC_6H_4CH_2OH/C_6H_5CH_2OH$ for Y = *p*-$NO_2$, *m*-$NO_2$, *p*-Cl, H, and *p*-Me. However, Hammett correlation was hardly observed to give $\rho+ = -0.31$ with correlation coefficient r = 0.369. 2-cyclohexen-1-ol (entry 10) is very easily converted to 2-cyclohexen-1-one. Phenethyl alcohol undergoes also selective oxidation to give the aldehyde (entry 13). Cyclohexanol can be oxidized to cyclohexanone with good yield for a much longer period (entry 14). The reactivity decreases in the order of 2°-benzylic ≈ allylic > 1°-benzylic > aliphatic alcohols.

**Table 1**. Oxidation of *p*-$CH_3OC_6H_4CH_2OH$ in the Absence and Presence of Fe(III) and PA into *p*-$CH_3OC_6H_4CHO$[a]

$$p\text{-}CH_3OC_6H_4CH_2OH\ (5\ \text{mmol}) \xrightarrow[\text{Pyridine (2.5 mL)}]{} p\text{-}CH_3OC_6H_4CHO$$

| $H_5IO_6$[b] | $FeCl_3\cdot 6H_2O$ | PA | Time (h) | Isolated Yield (%) |
|---|---|---|---|---|
| 15 mmol | 0.3 mmol | 0.6 mmol | 1.5 | 80 |
| 15 mmol | 0.3 mmol | – | 26 | 38 |
| 15 mmol | – | – | 36 | 28 |

[a]The product were identified with NMR. [b]Periodic acid (99.999%) was available from Aldrich.

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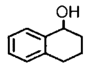
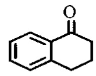
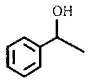
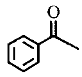
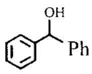
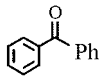
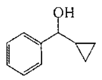
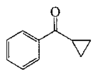
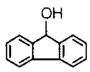
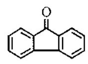
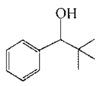
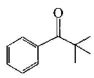
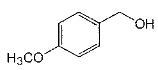
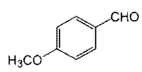
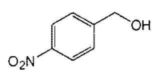
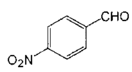
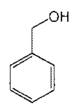
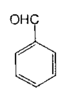
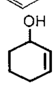
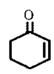
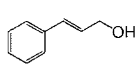
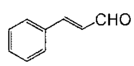
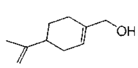
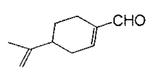
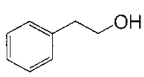
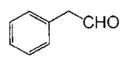
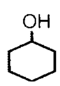
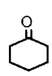
**Table 2.** Oxidation of Alcohols by Periodic Acid Catalyzed by Fe(III)/PA

$Fe^{III}$ / PA / $H_5IO_6$ / Pyridine / substrate
0.3 mmol 0.6 mmol 15 mmol 2.5 mL 5 mmol

| Entry | Substrate | Time(h) | Product [a] | Isolated Yield (%) |
|---|---|---|---|---|
| 1 |  | 10 min |  | 80 |
| 2 |  | 20 min |  | 92 |
| 3 |  | 1 |  | 82 |
| 4 |  | 2 |  | 89 |
| 5 |  | 6 |  | 90 |
| 6 |  | 20 |  | 82 |
| 7 |  | 1.5 |  | 80 |
| 8 |  | 2.5 |  | 70 |
| 9 |  | 4 |  | 74 |
| 10 |  | 10 min |  | 81 |
| 11 |  | 1 |  | 30 (60)[b] |
| 12 |  | 5 |  | 84 |
| 13 |  | 7 |  | 78 |
| 14 |  | 24 |  | 80 |

[a]Products were identified by NMR (Varian Gemini 2000). [b]Cinnamic acid.

In conclusion, $H_5IO_6$/Fe(III)/PA in pyridine is an efficient and selective reagent that can convert the alcohols to their aldehydes and ketones. The process utilizing $H_5IO_6$/Fe(III) should be environmentally benign.

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