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## The Carboxylation of Saturated Hydrocarbons by Gif Systems. $(Fe^{II1} trispicolinate/P(OMe)_3/CO/H_2O_2 in Pyridine-Acetic Acid).$

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**Abstract:** Saturated hydrocarbons are transformed into the corresponding homologous carboxylic acids by treatment with  $Fe(Pa)_3/P(OMe)_3/CO/H_2O_2$  in pyridine-acetic acid. Optimisation of the reaction conditions and mechanistics studies are reported.

Our work on the oxidation of saturated hydrocarbons to ketones using iron based Gif chemistry has been interpreted on the hypothesis of the formation of an Fe<sup>III</sup>-OOH reagent which evolves into an Fe<sup>V</sup> species by elimination of water. The chemistry that results is considered to take place in the Fe<sup>III</sup>-Fe<sup>V</sup> manifold.<sup>1</sup> There is extensive evidence that carbon radicals are not involved in this manifold. The tertiary position of adamantane is an exception.<sup>2</sup> On the contrary, there is a second manifold based on Fe<sup>II</sup>-Fe<sup>IV</sup> chemistry where carbon radicals do play a major role. They are readily detected by coupling to the solvent which is pyridine.

Clearly transition from one manifold to the other can change dramatically the chemistry observed. For example, the addition of chloride ion up to saturation to reactions in the  $Fe^{III}$ - $Fe^{V}$  manifold does not interfere with the normal ketonisation. However, the addition of triphenyl phosphine to the  $Fe^{III}$  catalyst followed by  $H_2O_2$  in the presence of chloride ion gives alkyl chloride in a yield equivalent to that of the ketone obtained previously.<sup>3</sup> This chemical effect is due to the reduction of  $Fe^{III}$  to  $Fe^{II}$  which then produces carbon radicals which react with  $Fe^{III}$ -Cl to give the alkyl chloride. In the absence of chloride ion and oxygen the  $Fe^{II}$ - $Fe^{IV}$  manifold produces only radical coupling to pyridine.

Recently <sup>4</sup> we have shown that anionic coupling is commonplace in the the  $Fe^{II}$ - $Fe^{IV}$  manifold and azides, bromides, thiocyanates and nitro-compounds can be formed readily. If the addition of H<sub>2</sub>O<sub>2</sub> is made portionwise then as soon as all the Fe<sup>II</sup> has been converted to Fe<sup>III</sup> the formation of anion derived products stops and the usual slower ketonisation process of the Fe<sup>III</sup>-Fe<sup>V</sup> manifold takes over.

We are now reexamining the various Gif rections to establish in which manifold they take place. Previously, we had studied the iron powder-carbon monoxide-oxygen reaction which converts saturated hydrocarbons into carboxylic acids in very poor yield.<sup>5</sup> When cyclohexane (20 mmol) in pyridine-acetic acid (10:1; 33 ml) containing triphenylphosphine (10 mmol) and Fe<sup>III</sup>trispicolinate (1 mmol) was treated with H<sub>2</sub>O<sub>2</sub> (10 mmol) in a stream of carbon monoxide at variable temperature (20<sup>o</sup>C down to - 40<sup>o</sup>C) for 3 hours up to 1 mmol of cyclohexane-carboxylic acid was formed as well as minor amounts of pyridine-cyclohexyl coupling products. This

experiment indicated that FeII had again been produced.

Encouraged by this result we decided to compare trimethyl phosphite with triphenylphosphine (Table 1). The presence of acetic acid was necessary in both cases. The use of triphenyl phosphine works best at  $-40^{\circ}$ C. The superior convenience of the trimethyl phosphite was thus established. Titration showed that with both of these P<sup>III</sup> compounds on addition of H<sub>2</sub>O<sub>2</sub> the Fe<sup>III</sup> was reduced to Fe<sup>II</sup>. Moreover, a kinetic study showed that the carboxylic acid formation was a fast reaction which ceased when all the Fe<sup>II</sup> has been oxidised to Fe<sup>III</sup>. At this point the normal ketonisation reaction associated with the Fe<sup>III</sup>-Fe<sup>V</sup> manifold took over (Fig.1).

Table 1 Optimisation of the reaction conditions of the Fe(Pa)<sub>3</sub>/H<sub>2</sub>O<sub>2</sub>/CO system.



<u>1</u> R<sup>1</sup>=CO<sub>2</sub>H, R<sup>2</sup>=H <u>2</u> R<sup>1</sup>,R<sup>2</sup>=O <u>3</u> R<sup>1</sup>=OH, R<sup>2</sup>=H <u>4</u> R<sup>1</sup>=2-Pyridyl, R<sup>2</sup>=H <u>5</u> R<sup>1</sup>=4-Pyridyl, R<sup>2</sup>=H

Entry	Conditions	1	2	3	4	5
1	A+Pyr(33ml)+P(OMe) <sub>3</sub> (4mmol) at $0^{\circ}$ C	0.52	nd	nd	0.03	0.05
2	A+Pyr(30ml)+AcOH(3ml)+P(OMe) <sub>3</sub> (4mmol) at 0 <sup>0</sup> C	1.40	0.07	0.08	0.16	0.22
3	A+Pyr(33ml)+PPh <sub>3</sub> (4mmol) at - 40 <sup>0</sup> C	0.26	nd	nd	0.06	0.04
4	A+Pyr(30ml)+AcOH(3ml)+PPh <sub>3</sub> (4mmol) at - 40 <sup>0</sup> C	1.33	0.04	nd	0.14	0.22

All the results are in mmol. AcOH: acetic acid. nd: not detected. A: Cyclohexane 20 mmol, Fe(Pa)<sub>3</sub> 1 mmol, H<sub>2</sub>O<sub>2</sub> 5x2mmol each 15min, under CO.

## Fig.1: Kinetics of the formation of the carboxylic acid.



Cyclohexane 20 mmol;  $Fe(Pa)_3$  1 mmol;  $P(OMe)_3$  4 mmol;  $H_2O_2$  5x2 mmol each 15 min; pyridine 30 ml; acetic acid 3 ml; under CO at  $O^0$ C to room temperature (Pa=picolinic acid).

When adamantane was the starting hydrocarbon, functionalization in the secondary position was predominent: 0.32 mmol of adamantane-2- carboxylic acid against 0.045 of adamantane-1- carboxylic acid were obtained, which results in a  $C^2/C^3$  ratio of 1.24 (Table 2). In the presence of methanol in the reaction mixture, one third of the carboxylic acid was replaced by the methyl carboxylate, in agreement with the intermediacy of a R-CO-Fe<sup>IV</sup> species (Fig.2, ligands on metal are omitted for clarity).<sup>5</sup>

Table 2: Selectivity for Adamantane.



6 R<sup>5</sup>=CO<sub>2</sub>H, R<sup>3</sup>=R<sup>4</sup>=H
7 R<sup>3</sup>=CO<sub>2</sub>H, R<sup>4</sup>=R<sup>5</sup>=H
8 R<sup>5</sup>=OH, R<sup>3</sup>=R<sup>4</sup>=H
9 R<sup>3</sup>=OH, R<sup>4</sup>=R<sup>5</sup>=H
10 R<sup>4</sup>, R<sup>5</sup>=O, R<sup>3</sup>=H
11 R<sup>3</sup>=2-Pyridyl, R<sup>4</sup>=R<sup>5</sup>=H
12 R<sup>3</sup>=4-Pyridyl, R<sup>4</sup>=R<sup>5</sup>=H
13 R<sup>5</sup>=2-Pyridyl, R<sup>3</sup>=R<sup>4</sup>=H
14 R<sup>5</sup>=4-Pyridyl, R<sup>3</sup>=R<sup>4</sup>=H

Substrate	6	7	8	9	10	11	12	13	14
Adamantane	0.320	0.045	0.025	0.010	0.052	0.250	0.130	0.110	0.033

All the results are in mmol. Conditions of the reaction: Adamantane 10 mmol, Fe(Pa)<sub>3</sub> 1mmol, P(OMe)<sub>3</sub> 4 mmol, H<sub>2</sub>O<sub>2</sub> 5x2mmol each 15 min, pyridine 30 ml, acetic acid 3 ml, under CO at 0 °C to room temperature.

Fig.2: Proposed reaction mechanism for the carboxylation of alkanes by Fe(Pa)<sub>3</sub>/P(OMe)<sub>3</sub>/H<sub>2</sub>O<sub>2</sub>/CO system.



The fact that carbon radicals are normally produced from saturated hydrocarbons in the  $Fe^{II}$  - $Fe^{IV}$  manifold raises again <sup>5</sup> the question as to whether such radicals react fast enough with free carbon monoxide to explain this new carboxylation reaction. The previous experimental work <sup>5</sup> coupled with other studies of this reaction <sup>6</sup> suggest that the carbon monoxide-carbon radical reaction is not operative. The coupling of carbon radicals to a carbonyl group still bonded to iron can still be considered, but this does not explain easily the formation of the methyl ester in the presence of methanol. Hence we consider that before the Fe<sup>IV</sup>-carbon bond breaks to give a free carbon radical the attached carbon monoxide ligand inserts to give the acyl-Fe<sup>IV</sup> species.<sup>7</sup>

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- 7- General reaction conditions and workup procedure: 1 mmol of Fe(Pa)<sub>3</sub> was dissolved in pyridine-acetic acid (10:1; 33 ml) under a stream of carbon monoxide, then cyclohexane and PPh<sub>3</sub> or P(OMe)<sub>3</sub> (4mmol) were added. The reaction mixture was cooled down at least at 0<sup>o</sup>C before adding portionwise H<sub>2</sub>O<sub>2</sub> (5x2mmol each 15 minutes). All yields (in mmol) were determined by G.-C. using a Hewlett Packard 5890 series II instrument equipped with flame ionisation detectors, with N<sub>2</sub> as a carrier gas. The column used for chromatography was a DB-WAX(30m x 0.32mm, 0.25u). In order to quantify the acid formed, an acidic work up was made: a 1ml aliquot of the reaction mixture was taken and poured into cold HCI solution(20%) and extracted with ether. The organic phases were dried over MgSO<sub>4</sub>, filtered and analysed by G.-C. after the introduction of an appropriate standard. For the quantification of the coupling product with pyridine, a basic work up was made via the same procedure but using a saturated solution of NaHCO<sub>3</sub>.

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