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The Carboxylation of Saturated Hydrocarbons by Gif Systems. (Fe^{III} trispicolinate/P(OMe)₃/CO/H₂O₂ 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/H₂O₂ in pyridine-acetic acid. Optimisation of the reaction conditions and mechanistic 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^{III}-OOH reagent which evolves into an Fe^V species by elimination of water. The chemistry that results is considered to take place in the Fe^{III}-Fe^V manifold.¹ There is extensive evidence that carbon radicals are not involved in this manifold. The tertiary position of adamantane is an exception.² On the contrary, there is a second manifold based on Fe^{II}-Fe^{IV} 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 H₂O₂ in the presence of chloride ion gives alkyl chloride in a yield equivalent to that of the ketone obtained previously.³ 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.

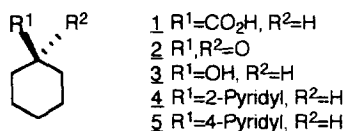
Recently⁴ we have shown that anionic coupling is commonplace in the the Fe^{II}-Fe^{IV} manifold and azides, bromides, thiocyanates and nitro-compounds can be formed readily. If the addition of H₂O₂ is made portionwise then as soon as all the Fe^{II} has been converted to Fe^{III} the formation of anion derived products stops and the usual slower ketonisation process of the Fe^{III}-Fe^V manifold takes over.

We are now reexamining the various Gif reactions 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.⁵ When cyclohexane (20 mmol) in pyridine-acetic acid (10:1; 33 ml) containing triphenylphosphine (10 mmol) and Fe^{III}trispicolinate (1 mmol) was treated with H₂O₂ (10 mmol) in a stream of carbon monoxide at variable temperature (20°C down to -40°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 Fe^{II} 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°C . The superior convenience of the trimethyl phosphite was thus established. Titration showed that with both of these P^{III} compounds on addition of H_2O_2 the Fe^{III} was reduced to Fe^{II} . Moreover, a kinetic study showed that the carboxylic acid formation was a fast reaction which ceased when all the Fe^{II} has been oxidised to Fe^{III} . At this point the normal ketonisation reaction associated with the Fe^{III} - Fe^{V} manifold took over (Fig. 1).

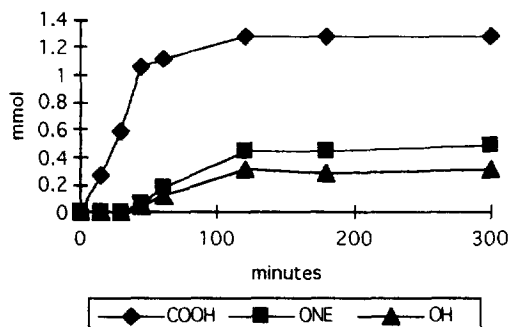
Table 1 Optimisation of the reaction conditions of the $\text{Fe}(\text{Pa})_3/\text{H}_2\text{O}_2/\text{CO}$ system.



Entry	Conditions	1	2	3	4	5
1	A+Pyr(33ml)+P(OMe) ₃ (4mmol) at 0°C	0.52	nd	nd	0.03	0.05
2	A+Pyr(30ml)+AcOH(3ml)+P(OMe) ₃ (4mmol) at 0°C	1.40	0.07	0.08	0.16	0.22
3	A+Pyr(33ml)+PPh ₃ (4mmol) at -40°C	0.26	nd	nd	0.06	0.04
4	A+Pyr(30ml)+AcOH(3ml)+PPh ₃ (4mmol) at -40°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, $\text{Fe}(\text{Pa})_3$ 1 mmol, H_2O_2 5x2mmol each 15min, under CO.

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



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

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^{IV}-carbon bond breaks to give a free carbon radical the attached carbon monoxide ligand inserts to give the acyl-Fe^{IV} species.⁷

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References:

- 1- Bardin, C.; Barton, D. H. R.; Hu, B.; Rojas-Wahl, R.; Taylor, D. K. *Tetrahedron Lett.* **1994**, *35*, 5805-5808.
- 2- Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504-512.
- 3- Barton, D. H. R.; Beviere S. D., *Tetrahedron Lett.* **1993**, *34*, 5689.
- 4- Barton, D. H. R.; Chabot, B. M.; Delanghe, N. C.; Hu, B.; Le Gloahec, V. N.; Rojas-Wahl, R. U. *Tetrahedron Lett.* **1995**, *36*, 7007-7010.
- 5- Barton, D. H. R.; Cshai, E., Doller, D. *Tetrahedron Lett.* **1992**, *33*, 4389-4392.
- 6- Ryu, I. ; Kusano, K.; Yamazaki, H.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5003-5005. Ryu, I. ; Kusano, K.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1990**, *112*, 1295-1297.
Typically temperatures of 80°C at 65-80 atm. of carbon monoxide are needed for radical addition to carbon monoxide
- 7- General reaction conditions and workup procedure: 1 mmol of Fe(Pa)₃ was dissolved in pyridine-acetic acid (10:1; 33 ml) under a stream of carbon monoxide, then cyclohexane and PPh₃ or P(OMe)₃ (4mmol) were added. The reaction mixture was cooled down at least at 0°C before adding portionwise H₂O₂ (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 N₂ as a carrier gas. The column used for chromatography was a DB-WAX(30m x 0.32mm, 0.25µ). 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 HCl solution(20%) and extracted with ether. The organic phases were dried over MgSO₄, 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 NaHCO₃.

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