Mendeleev Commun., 1991, 1(3), 115–116

The Efficient Oxidation of Alkanes by Hydrogen Peroxide in Pyridine Mixed Solvents Catalysed by Copper and Other Transition Metal Salts

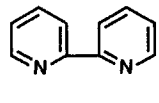
Derek H. R. Barton,[a] Dario Doller[a] and Yurii V. Geletii*[a,b]

[a] *Department of Chemistry, Texas A & M University, College Station, TX 77843-3255, USA*
[b] *Institute of Chemical Physics, USSR Academy of Sciences, Chernogolovka, Moscow Region 142 432, USSR*

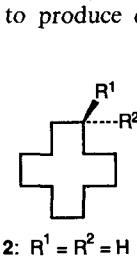
The catalytic activity of Cu^{II}, Fe^{III}, Co^{II}, Ru^{III}, Ni^{II} and other transition metal salts in the oxidation of cyclododecane by H_2O_2 was studied for several mixed solvent systems PyX–**S**–H_2O = 2:1:0.09 (volume ratio), where PyX is pyridine (Py) or substituted pyridines, and **S** = MeCN, Bu^{t}OH or acetone; the highest yield, *ca.* 25% of alkane conversion and 10% efficiency for H_2O_2, was found for Py–MeCN mixtures.

In previous publications we described in detail a family of chemical systems which share the rare property of functionalising saturated hydrocarbons under very mild conditions and with remarkable selectivity, the Gif systems.[1–3] In their original form, Gif systems include an electron source or reductant (Fe^0 or Zn^0 powder), dioxygen (ultimate oxidant) and an iron complex as the catalyst.[3] We have found that certain metal powders could replace the Fe^0, with pyridine and a carboxylic acid (as the reaction solvent) essential to maintain the characteristic Gif selectivity (*sec.* C–H > *tert.* C–H ≥ *prim.* C–H).[4] The dioxygen and reductant can be substituted by H_2O_2, and either Fe^{III} complexes (GoAgg^{II} or GoAgg^{III} systems) or Cu^{II} complexes (GoChAgg system) are both efficient reaction catalysts.[1,2] The side process in all Gif-type reactions is the oxidation of the solvent, *i.e.* pyridine, to hydroxy-pyridines, bipyridyls, *etc.*,[5] with decrease in the yield of alkane oxidation. We have found that the oxidation yield can be improved by substituting part of the easily oxidisable pyridine with a cosolvent like MeCN, more resistant to oxidation.[2b] In this study we examine: (*i*) the effect of replacing most of the pyridine by MeCN, Bu^{t}OH or acetone; (*ii*) the use of substituted pyridines as the reaction solvent and its influence on the oxidation yield; and (*iii*) the efficiency of different transition metal salts as catalysts.

The system PyX–**S**–H_2O = 2:1:0.09 (volume ratio) was chosen as the basic solvent mixture. Water was included as a cosolvent after previous observations showing that its addition to Cu^{II}-catalysed processes in pyridine resulted in improved oxidation yields.[2b] To eliminate the influence of the catalyst salt counterion, a three-fold excess of a strong ligand (2,2′-bipyridyl, **1**) was used. Recently, Co^{II} complexes were found to be efficient catalysts for alkane oxidation by H_2O_2 in Py–MeCN = 3:1 (molar ratio).[6] Iron complexes with 2,2′-bipyridyl have been studied as well, and found to produce efficient catalysis in Gif-systems.[7]



1



2: $R^1 = R^2 = H$
3: $R^1, R^2 = O$
4: $R^1 = H$; $R^2 = OH$

The results of the oxidation of cyclododecane **2** by H_2O_2 in a Py–MeCN mixture in the presence of different metal salts are summarised in Table 1. In addition to the salts presented there, Ce^{IV} $[(NH_4)_2Ce(NO_3)_6]$, Rh^{II} $[Rh(OAc)_2]$ and Mn^{II} $(MnCl_2 \cdot 4H_2O)$ salts were studied as well, although we did not find any catalytic activity with these salts. A superior efficiency was found for Cu^{II} catalysis; the Ni^{II} salt exhibited moderate activity as far as the reaction yield is considered, but the reaction was very slow (10 days). The ketone/alcohol ratio varied from 11.8 for Cu^{II} catalyst to 1.5 for Ru^{III} catalyst. This probably reflects the competition of two different pathways for the intermediate cyclododecyl-hydroperoxide.[8,9] The observed yields were not optimised.

At this point it is worth mentioning the efficient oxidation of cyclohexane by H_2O_2 catalysed by vanadium salts in acetic acid or trifluoroacetic acid.[8] The reaction mechanism proposed for this process does not include the sequence hydrogen atom abstraction–free alkyl radical formation.[8]

The effect of using substituted pyridines as the reaction solvent was examined in the case of the most efficient Cu^{II} catalyst. We replaced pyridine by 2,3,4-trimethylpyridine, 4-*tert*-butylpyridine, 2-chloropyridine, pentafluoropyridine and quinoline, and have found that in every case the reaction was much slower than in pyridine. For example, the reaction was complete in one day in the presence of pyridine, but was not complete after 2 weeks with other bases. The reaction rate was remarkably slow when chloro- and fluoro-derivatives were used. The yields of cyclododecane oxidation after 2 weeks are given in Table 2. No reasonable correlations were found for the oxidation yields or rates and some properties of pyridine derivatives, like basicity or steric hindrance.

When acetonitrile was replaced by acetone or Bu^{t}OH, lower reaction yields for cyclododecane oxidation were observed (Table 2).

Cyclododecane oxidation occurs in neat MeCN without any other cosolvents, but the ratio of ketone to alcohol is about 2:1. As alkanes were not very soluble in MeCN, water was not added to the reaction mixture (except that from H_2O_2 solution). Nevertheless, at the same concentration of cyclododecane the oxidation yields in MeCN or MeCN–Py were similar. In the latter case the reaction rate is about one order of magnitude higher.

The kinetic isotopic effect (KIE) for competitive oxidations of equimolar amounts of cyclo-C_6H_{12} and cyclo-C_6D_{12} under Cu^{II}-catalysis for MeCN–Py–H_2O, Bu^{t}OH–Py–H_2O, MeCN–(4-Bu^{t}Py)–H_2O and neat MeCN solution has been measured (Table 2). In every case the value of the KIE obtained was similar to those found for Gif-type systems, and differed from those for the oxidation by hydroxyl radical.[2b] The KIE value for the oxidation in MeCN was only slightly lower than that in the presence of pyridine.

When $CBrCl_3$ is added to GoAgg systems the formation of ketone is diverted to alkyl bromide production with comparable yield.[1] For the Cu-catalysed process (GoChAgg reaction) the bromination yield is much lower.[5] We analysed the possibility of improving the bromination reaction yield by using the mixed solvent MeCN–Py–H_2O. Indeed, 20 mmol of $CBrCl_3$ fully suppressed the oxidation of cyclododecane, leaving cyclododecyl bromide the only reaction product, but its yield was 6 times less than that for the ketonisation reaction. At lower $CBrCl_3$ concentrations mixtures of ketone and bromide were observed, the total yield diminishing with increasing amounts of $CBrCl_3$.

In conclusion, replacing most of the pyridine by less oxidisable cosolvents like Bu^{t}OH or MeCN does not alter significantly the unusual chemical characteristics of Gif-type systems. The oxidation yield increases when acetonitrile is used. However, substitution of pyridine with its derivatives decreased sharply the reaction rate, as well as the oxidation yield.

One of us (Yu. V. G.) is indebted to the Institute of Chemical Physics, USSR Academy of Sciences for sabbatical leave. We also are grateful to the NSF, BP and Quest Intl. for financial

Table 1 Oxidation of cyclo-$C_{12}H_{24}$ (2.0 mmol) by H_2O_2 (9.5 mmol, 30% in H_2O), catalysed by different metal salts (0.3 mmol) in the presence of 2,2′-bipyridyl (0.9 mmol) in MeCN–Py–H_2O = 2:1:0.09 (volume ratio); total volume 33.0 ml; room temp.

	Yield/mmol						
Catalyst	**2**	**3**	**4**	Σ[a]/mmol	**3/4**	Σ[b] (%)	Mass balance (%)
$Cu(ClO_4)_2 \cdot 6H_2O$	1.38	0.47	0.04	0.51	11.8	25.5	94.5
$FeCl_3 \cdot 6H_2O$	1.92	0.10	0.02	0.12	5.0	6.0	102.0
$RuCl_3 \cdot H_2O$[c]	1.88	0.03	0.02	0.05	1.5	2.5	96.5
$RuCl_3 \cdot H_2O$[d]	1.62	0.09	0.06	0.15	1.5	7.5	88.5
$Co(AcO)_2 \cdot 4H_2O$	2.01	0.05	0.01	0.06	5.0	3.0	103.5
$NiCl_2 \cdot 6H_2O$[c]	1.93	0.05	0.04	0.09	1.3	4.5	101.0
$NiCl_2 \cdot 6H_2O$[d]	1.52	0.18	0.057	0.25	2.6	12.5	88.5

[a] Combined yield of ketone plus alcohol. [b] Chemical yield of ketone plus alcohol based on the total amount of starting material. [c] After 1 day reaction time; H_2O_2 was not totally consumed. [d] After 10 days.

Table 2 Oxidation of cyclo-$C_{12}H_{24}$ by H_2O_2 (9.5 mmol, 30% in H_2O), catalysed by different metal salts in the presence of 2,2′-bipyridyl

Bu^{t}OH–Py–H_2O = 2:1:0.09 (volume ratio), **2** = 2.4 mmol, $FeCl_3 \cdot 6H_2O$ or $Cu(ClO_4)_2 \cdot 6H_2O$ = 0.3 mmol

	Yield/mmol							
Catalyst	**2**[a]	**3**	**4**	Σ[b]/mmol	**3/4**	Σ[c] (%)	Bal. (%)	KIE
Fe^{III}	2.25	0.13	0.03	0.16	4.3	6.7	100.0	—
Cu^{II}	2.14	0.24	0.02	0.26	12.0	10.8	100.0	2.3

Acetone–Py–H_2O = 2:1:0.09 (volume ratio), **2** = 2.0 mmol

	Yield/mmol						
Catalyst	**2**[a]	**3**	**4**	Σ[b]/mmol	**3/4**	Σ[c] (%)	Bal. (%)
Fe^{III}	1.98	0.05	0.01	0.06	5.0	3.0	102.0
Cu^{II}	1.86	0.16	0.01	0.17	16.0	8.5	101.0

MeCN–PyX–H_2O = 2:1:0.09 (volume ratio), **2** = 1.4 mmol, $Cu(ClO_4)_2 \cdot 6H_2O$ = 0.4 mmol

	Yield/mmol							
PyX	**2**	**3**	**4**	Σ[b]/mmol	**3/4**	Σ[c] (%)	Bal. (%)	KIE
Py	0.92	0.4	0.03	0.43	13.0	31.0	96.5	2.4
2,4,6-Me_3-Py	1.29	0.06	0.02	0.08	3.0	5.7	98.0	—
4-Bu^t-Py	1.04	0.29	0.02	0.31	14.5	22.0	96.5	2.5
Quinoline	1.25	0.08	0.01	0.09	8.0	6.5	96.0	—
2-Cl-Py	n.d.[d]	0.1	0.05	0.15	2.0	11.0	n.d.[d]	—
Py-F_5	1.3	0.1	0.05	0.15	2.0	11.0	103.5	—
MeCN[e]	0.76	0.17	0.08	0.25	2.0	25.0	101.0	2.2

[a] Recovered cyclo-$C_{12}H_{24}$. [b] Combined yield of **3** and **4**. [c] Yield based on starting **2**. [d] Not determined. [e] Neat MeCN, **2** = 1 mmol.

support of this work, and to Merck Sharp & Dohme for a post-doctoral fellowship (D. D.). We thank Professor D. T. Sawyer for a copy of reference 6 before its publication.

Received in USSR, 22nd May 1991
Received in UK, 14th May 1991: Com. 1/02315B

References

1 (*a*) D. H. R. Barton, M. J. Gastiger and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 1983, 41; (*b*) D. H. R. Barton and N. Ozbalik, *Selective Functionalization of Saturated Hydrocarbons by the 'Gif' and 'Gif-Orsay' Systems*, ch. IX, p. 281, in *Activation and Functionalization of Alkanes*, ed. C. L. Hill, Wiley, New York, 1989; (*c*) D. H. R. Barton, F. Halley, N. Ozbalik, M. Schmitt, E. Young and G. Balavoine, *J. Am. Chem. Soc.*, 1989, **111**, 7144; (*d*) D. H. R. Barton and D. Doller, *Pure Appl. Chem.*, in the press.

2 (*a*) Yu. V. Geletii, V. V. Lavrushko and G. V. Lubimova, *J. Chem. Soc., Chem. Commun.*, 1988, 936; (*b*) D. H. R. Barton, E. Csuhai, D. Doller and Yu. V. Geletii, *Tetrahedron*, in the press; (*c*) D. H. R. Barton, D. Doller and Yu. V. Geletii, *Tetrahedron Lett.*, 1991, **32**, 3811.

3 D. H. R. Barton, J. Boivin, W. B. Motherwell, N. Ozbalik and K. M. Schwartzentruber, *Nouv. J. Chim.*, 1986, **10**, 387.

4 (*a*) Yu. V. Geletii, G. V. Lubimova and A. E. Shilov, *Kinetika Katal.*, 1985, **26**, 1023; (*b*) Yu. V. Geletii, V. V. Lavrushko and A. E. Shilov, *Dokl. Akad. Nauk SSSR*, 1986, **288**, 139; (*c*) Yu. V. Geletii and A. E. Shilov, in *The Role of Oxygen in Chemistry and Biochemistry*, ed. W. Ando and Y. Moro-oka, Elsevier, Amsterdam, 1988, p. 293.

5 D. H. R. Barton, D. Doller and Yu. V. Geletii, in preparation.

6 C. Sheu, S. A. Richert, B. Cofre, B. Ross, Jr., A. Sobkowiak, D. T. Sawyer and J. R. Kanofsky, *J. Am. Chem. Soc.*, 1990, **112**, 1940.

7 W. Nam and J. V. Valentine, *New J. Chem.*, 1989, **13**, 677.

8 I. I. Moiseev, A. E. Gekhman and D. I. Shishkin, *New J. Chem.*, 1989, **13**, 683.

9 D. H. R. Barton, E. Csuhai, D. Doller and G. Balavoine, *J. Chem. Soc., Chem. Commun.*, 1990, 1737.