Petroleum Chemistry, Vol. 45, No. 6, 2005, pp. 413–418. Translated from Neftekhimiya, Vol. 45, No. 6, 2005, pp. 447–452.

Hydrogen Peroxide Oxidation of Alkanes Catalyzed by the Vanadate Ion–Pyrazine-2-carboxylic Acid System in the Presence of Pyridine[1]

M. J. D. M. Jannini*, L. S. Shul'pina, U. Schuchardt*, and G. B. Shul'pin*****

**Instituto de Quimica, Universidade Estadual de Campinas,*
P. O. Box 6154, 13084-971, Campinas, SP, Brazil
***Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,*
ul. Vavilova 28, Moscow, 119991 Russia
****Semenov Institute of Chemical Physics, Russian Academy of Sciences,*
ul. Kosygina 4, Moscow, 119991 Russia

Received March 17, 2005

Abstract—Pyridine admixtures have a slight effect on the activity and selectivity parameters in the oxidation of alkanes with the O_2–H_2O_2–vanadate anion–pyrazine-2-carboxylic acid reagent in acetonitrile. This feature distinguishes this reagent, which oxygenates alkanes via the mechanism involving free hydroxyl radicals, from similar systems based on iron complexes that show unusual selectivity in alkane oxidation in the presence of pyridine (Gif systems). The data obtained may indirectly indicate that free hydroxyl radicals do not directly participate in alkane functionalization with the Gif system, at least in the principal reaction route.

INTRODUCTION

New catalyst systems for the oxidation of inert saturated hydrocarbons with dioxygen and hydrogen peroxide have been described in the last decades [1–7]. One of the systems that attracted the close attention of investigators is the so-called Gif system, consisting of an iron complex (frequently, $FeCl_3$) as a catalyst and hydrogen peroxide as an oxidant. The characteristic feature of the Gif system is the use as a solvent of either individual pyridine or acetonitrile in the presence of substituted pyridine; the presence of acetic acid is also necessary in many cases [8]. The reaction is markedly accelerated in the presence of picolinic acid. The unusual selectivity (preferred oxidation of secondary C–H bonds and preferred formation of ketones) and the specific behavior of the Gif system made Barton, who first described this system in 1983, suppose that the oxidation does not follow in this case the conventional route of the Fe(II)–H_2O_2 (Fenton's reagent) or Fe(III)–H_2O_2 mixtures involving the generation of free hydroxyl radicals but includes the intermediate formation of some organometallic species [9]. The nonradical mechanism in the alkane oxidation reaction catalyzed by iron complexes in the presence of pyridine has recently received new confirmation [10]. At the same time, it has been shown that iron complexes in acetonitrile in the absence of pyridine decompose hydrogen peroxide to yield free hydroxyl radicals and the generation of ferryl species (oxo derivatives of high-valence iron) is also possible during catalysis by $FeCl_3$ [11]. Analogous osmium derivatives also oxidize alkanes via the free radical mechanism [12]. Therefore, it was interesting to study whether a pyridine admixture would have a strong effect on the reaction rate and selectivity in the oxidation of saturated hydrocarbons with other systems that generate free hydroxyl radicals.

We have previously found a quite effective reagent for alkane oxidation under mild conditions, based on hydrogen peroxide as an oxidant and consisting of a catalyst, a vanadium derivative (most frequently, *n*-Bu_4NVO_3, compound **1**) and a cocatalyst, pyrazine-2-carboxylic acid (PCA), compound **2**) [13–18]. The primary product was alkyl hydroperoxide, which decomposed during the reaction to give the corresponding carbonyl compound (ketone or aldehyde) and alcohol. At the beginning of the reaction, especially at a low temperature, only alkyl hydroperoxide was detected in the solution. With the use of labeled molecular oxygen, it was shown that oxygen from ambient air entered into the alkyl hydroperoxide formed. It was demonstrated by the spin trapping technique that the interaction of hydrogen peroxide with the vanadium complex in the presence of PCA was accompanied by the formation of hydroxyl radicals. The study of the selectivity parameters in the oxidation of various alkanes, as well as the competing oxidation of benzene and some alcohols, has shown that the oxidizing action of this system is due to the formation of hydroxyl radicals, which attack alkane C–H bonds.

[1] This is part 15 of the series "Oxidations by the Reagent O_2–H_2O_2–Vanadium Derivative–Pyrazine-2-carboxylic Acid." For part 14, see [18].

EXPERIMENTAL

Alkanes were oxidized in a cylindrical glass vessel equipped with a jacket through which water from a thermostat was circulated; the solution volume was 10 ml. A 30% hydrogen peroxide aqueous solution was used. The reaction solution was sampled (0.5 ml) at certain intervals for further GLC analysis both before and after treatment (within 10–20 min) with an excess of solid triphenylphosphine (the method that we widely use to determine not only corresponding ketone and alcohol but also alkyl hydroperoxide is described in [4–6, 12–16, 19]).

Gas-chromatographic analyses were carried out on an HP Series 5890-II chromatograph (Carbowax 20M column, 25 m × 0.2 mm × 0.2 μm; helium as a carrier gas) and on a 3700 chromatograph (FFAP/OV-101, 20/80 w/w capillary column, 30 m × 0.2 mm × 0.3 μm; helium carrier gas). Chromatograms were preliminarily calibrated with authentic compounds—the alkane oxidation products.

RESULTS AND DISCUSSION

In this work, we studied the influence of relatively small admixtures of pyridine (and acetic acid) on the reaction of alkane oxidation by the O_2–H_2O_2–vanadate anion–pyrazine-2-carboxylic acid reagent in acetonitrile, in view of the fact that pyridine in the case of iron complexes used as catalysts in similar systems (Gif systems) is known to strongly affect the selectivity parameters and, presumably, leads to a change of the oxidation mechanism (from the radical mechanism in the absence of pyridine to a nonradical mechanism in the presence of pyridine even in small concentrations). It may be assumed that the pyridine additive in the case of our vanadium-containing reagent will also lead to dramatic changes in the selectivity parameters if this reagent and the Gif system oxidize alkanes via the same mechanism.

First, we studied the buildup of products in the cyclohexane oxidation reaction at 25, 40, and 50°C. The data obtained are listed in Table 1. Since it was evident *a priori* that pyridine must compete with cocatalyst **2** for the coordination site on the vanadium ion in compound **1**, we used a large excess of cocatalyst **2** with respect to catalyst **1**, unlike our previous works [14–18] (see also [20]). comparison of two experiments at 25°C conducted in the absence and presence of pyridine (entries 1–4 and 5–8, respectively, in Table 1) shows that pyridine (py) added at the ratios py/**1** = 182 and py/**2** = 6 only slightly (less than 10%) decreases the buildup rate of cyclohexane oxidation products (determined as the turnover number, TON, after certain time intervals). The alkyl hydroperoxide/ketone/alcohol product ratio varies insignificantly.

The reaction at 40°C was studied in more detail. In this case, the addition of pyridine in the ratios py/**1** = 150 and py/**2** = 6 (entries 9–13 and 14–16, respectively, in Table 1) leads to a twofold decrease in the initial reaction rate, whereas the composition of three products does not sharply vary. The simultaneous further increase in concentrations of pyridine and compound **2** (entries 17–22) does not lead to a significant decrease in the buildup rate of oxygenates. The simultaneous addition of acetic acid and pyridine leads to a slight decrease in the rate (entries 23–29). When the concentration of catalyst **1** was four times that in the previous experiments, the simultaneous addition of pyridine and acetic acid in the ratio py/CH_3COOH/**1**/**2** = 75 : 22.5 : 1 : 12.5 led to a threefold drop in the initial rate (entries 30–37 and 38–45). The experiments at 50°C (entries 46–81) showed that the addition of pure pyridine or its mixture with acetic acid did not lead to a strong decrease in the efficiency of cyclohexane oxidation. It is interesting that the addition of a rather large amount of acetic acid in the absence of pyridine (CH_3COOH/**1**/**2** = 45 : 1 : 25, entries 74–81) leads to a decrease in the initial rate by a factor of 2–3.

To obtain information on the selectivity of the process, we carried out the oxidation of the linear alkane *n*-heptane in the absence and presence of pyridine (Table 2). Unlike the case of all our previous works, we determined concentrations of not only the isomeric alcohols produced but also carbonyl compounds (ketones, aldehyde, and acid). Only the initial period of the reaction (2.5 h at 40°C) was studied when isomeric alkyl hydroperoxides are almost exclusively formed. Since the products were determined after the reduction of the reaction mixture with triphenylphosphine, only corresponding alkanols and relatively small amount of heptanoic acid were found by the GLC technique. It is interesting that marked amounts of isomeric ketones were found in the reaction mixture containing pyridine. It may be assumed that pyridine induces the decomposition of alkyl hydroperoxides formed during the reaction and their conversion into corresponding ketones.

From the data on the distribution of all the *n*-heptane oxidation products, the normalized regioselectivity parameters were obtained and are given in Table 3 (note that these parameters had earlier been calculated only from the concentrations of isomeric alcohols). It follows from Table 3 that the regioselectivity parameters for the oxidation with the H_2O_2–**1**–**2** reagent in the absence and presence of pyridine have very low values, which agree well with the corresponding parameters obtained for other systems generating hydroxyl radicals (H_2O_2–$h\nu$ and H_2O_2–$FeSO_4$). These values are markedly lower than those obtained previously for *n*-heptane oxidation with the system based on the binuclear manganese(IV) complex [21–23], which functionalizes alkanes via a nonradical mechanism. Note that the selectivity parameters in the oxidation on the vanadium complex are slightly higher in the presence than in the absence of pyridine. This may be associated with the fact that pyridine induces another reaction route; however, the contribution of this route is small. Methylcyclohexane oxidation in the presence of pyridine also

Table 1. Cyclohexane oxidation with the O_2–H_2O_2–vanadate anion–prazine-2-carboxylic acid reagent in acetonitrile solution

No.	**1**, mmol	Temperature, °C	Additives, mmol			Reaction time, h	Products, mmol			Turnover number
			PCA (**2**)	Pyridine	CH_3COOH		$C_6H_{11}OOH$	$C_6H_{10}=O$	$C_6H_{11}OH$	
1	0.0033	25	0.1	0.0	0.0	4	0.16	0.009	0.016	54
2						24	0.47	0.036	0.056	168
3						46	0.62	0.044	0.066	218
4						100	0.86	0.056	0.065	293
5	0.0033	25	0.1	0.6	0.0	4	0.12	0.005	0.0006	37
6						24	0.49	0.02	0.015	157
7						46	0.58	0.03	0.019	188
8						100	0.73	0.03	0.017	232
9	0.0040	40	0.1	0.0	0.0	0.5	0.10	0.009	0.009	30
10						3	0.36	0.03	0.026	104
11						19	0.64	0.08	0.062	195
12						53	0.98	0.14	0.09	303
13						120	1.6	0.27	0.18	512
14	0.0040	40	0.1	0.6	0.0	0.5	0.03	0.005	0.007	13
15						3	0.19	0.018	0.017	67
16						19	0.43	0.045	0.036	153
17	0.0040	40	0.4	2.5	0.0	0.5	0.05	0.005	0.006	15
18						3	0.30	0.016	0.014	83
19						19	0.71	0.055	0.038	200
20	0.0040	40	0.8	6.2	0.0	0.5	0.04	0.005	0.006	12
21						3	0.19	0.012	0.010	53
22						19	0.47	0.039	0.028	134
23	0.0040	40	0.1	0.6	0.1	0.5	0.065	0.005	0.006	19
24						3	0.47	0.039	0.031	135
25						19	0.80	0.113	0.082	250
26						50	1.49	0.18	0.13	450
27	0.0040	40	0.1	0.6	0.54	0.5	0.037	0.004	0.006	12
28						3	0.09	0.009	0.011	27
29						72	1.50	0.15	0.12	442
30	0.0080	40	0.1	0.0	0.0	1	0.18	0.021	0.054	32
31						2	0.37	0.043	0.087	63
32						3	0.53	0.060	0.110	87
33						5	0.64	0.073	0.116	103
34						6	0.71	0.081	0.124	114
35						20	1.12	0.128	0.140	173
36						48	1.63	0.186	0.201	250
37						96	2.23	0.255	0.239	340
38	0.0080	40	0.1	0.6	0.18	1	0.003	0.004	0.056	12
39						2	0.010	0.011	0.012	15
40						3	0.014	0.016	0.022	22
41						5	0.023	0.026	0.023	34

Table 1. (Contd.)

No.	**1**, mmol	Temperature, °C	Additives, mmol			Reaction time, h	Products, mmol			Turnover number
			PCA (**2**)	Pyridine	CH_3COOH		$C_6H_{11}OOH$	$C_6H_{10}=O$	$C_6H_{11}OH$	
42						6	0.020	0.023	0.024	31
43						20	0.068	0.077	0.058	101
44						48	0.131	0.150	0.104	195
45						96	0.152	0.173	0.118	226
46	0.0040	50	0.1	0.0	0.0	0.5	0.31	0.008	0.023	85
47						1	0.61	0.016	0.055	170
48						2	0.84	0.032	0.072	236
49						3	0.98	0.041	0.078	274
50						5	0.87	0.082	0.100	262
51						6	0.98	0.095	0.111	298
52						7	1.20	0.117	0.136	362
53						8	0.94	0.107	0.115	290
54						24	1.00	0.175	0.157	332
55	0.0040	50	0.1	0.6	0.0	0.5	0.10	0.009	0.009	30
56						2	0.57	0.026	0.027	157
57						5	0.58	0.09	0.05	178
58						8	1.0	0.095	0.07	300
59						24	1.2	0.07	0.04	328
60	0.0040	50	0.1	0.6	0.09	0.5	0.22	0.003	0.002	56
61						2	0.67	0.009	0.010	172
62						3	0.85	0.013	0.013	219
63						5	0.94	0.034	0.032	250
64						8	1.22	0.048	0.050	330
65						24	1.08	0.120	0.073	317
66						144	1.66	0.163	0.102	480
67	0.0040	50	0.1	2.5	0.0	0.5	0.057	0.013	0.008	19
68						2	0.185	0.022	0.019	56
69						3	0.28	0.034	0.027	85
70						5	0.31	0.040	0.031	95
71						8	0.50	0.076	0.068	160
72						24	0.58	0.066	0.044	172
73						144	0.95	0.11	0.056	278
74	0.0040	50	0.1	0.0	0.18	1	0.19	0.022	0.060	34
75						2	0.34	0.038	0.106	60
76						3	0.47	0.053	0.112	80
77						5	0.55	0.062	0.115	90
78						6	0.61	0.070	0.121	100
79						20	1.03	0.118	0.145	162
80						48	1.53	0.175	0.181	235
81						96	2.11	0.242	0.213	320

Note: In all runs, 14.7 mmol of hydrogen peroxide (30% aqueous solution) and 9.3 mmol of cyclohexane were used. Total solution volume was 10 ml. The turnover number is the number of moles of all products formed at a given time per mole of catalyst **1**.

Table 2. *n*-Heptane oxidation catalyzed by complex **1** in the presence of cocatalyst **2** and in the absence and presence of pyridine

Pyridine, mmol	Heptanoic acid	Heptanal	Heptanone-4	Heptanone-3	Heptanone-2	Heptanol-4	Heptanol-3	Heptanol-2	Heptanol-1
0.00	0.08	0.00	0.00	0.00	0.00	1.04	2.39	2.45	1.00
3.75	0.29	0.05	0.65	0.77	0.68	2.18	4.33	3.00	1.00

Note: An acetonitrile solution (total volume, 5 ml) of *n*-heptane (0.4 ml), 30% H_2O_2 aqueous solution (0.5 ml), *n*-Bu_4VO_3 complex (**1**) (0.01 mmol) and pyrazine-2-carboxylic acid (**2**) (0.2 mmol) was heated at 40°C for 2.5 h. The concentrations of isomeric products were determined after reduction of the reaction mixture with an excess of triphenylphosphine. The number in the product specifies the position of the functional group in the alkane chain. The concentrations of isomeric compounds are given with respect to heptanol-1, whose concentration is taken to be unity.

Table 3. Selectivity parameters in alkane oxidation with various systems in acetonitrile

Alkane	Oxidizing system	Selectivity parameters
n-Heptane		C(1) : C(2) : C(3) : C(4)
	H_2O_2–*h*ν	1.0 : 7.3 : 6.3 : 8.1
	H_2O_2–$FeSO_4$	1.0 : 5.0 : 4.8 : 4.6
	H_2O_2–**1**–**2**	1.0 : 3.4 : 3.3 : 2.9
	H_2O_2–**1**–**2**–pyridine	1.0 : 4.2 : 5.9 : 6.6
	$[L_2Mn_2O_3]^{2+}$–$MeCO_2H$–H_2O_2	1 : 46 : 35 : 35
Methylcyclohexane		1° : 2° : 3°
	H_2O_2–**1**–**2**	1 : 6 : 18
	H_2O_2–**1**–**2**–pyridine	1 : 4 : 21
	$[L_2Mn_2O_3]^{2+}$–$MeCO_2H$–H_2O_2	1 : 26 : 200
cis-1,2-Dimetylcyclohexane		*trans*/*cis*
	H_2O_2–*h*ν	0.9
	H_2O_2–$FeSO_4$	1.3
	H_2O_2–**1**–**2**	0.75
	H_2O_2–**1**–**2**–pyridine	1.2
	$[L_2Mn_2O_3]^{2+}$–$MeCO_2H$–H_2O_2	0.34

Note: The (C1) : (C2) : (C3) : (C4) parameter is normalized (i.e., calculated taking into account the number of hydrogen atoms at each position) relative to the reactivity of hydrogen atoms in the 1-, 2-, 3- and 4-positions of the carbon chain; the parameter 1° : 2° : 3° is normalized relative to the reactivity of hydrogen atoms on primary, secondary, and tertiary carbon atoms, respectively; the parameter *trans*/*cis* = [*trans-tert-ol*]/[*cis-tert-ol*], where [*trans-tert-ol*] and [*cis-tert-ol*] are the concentrations of corresponding tertiary alcohols produced in *cis*-1,2-dimethylcyclohexane oxidation. The selectivity parameters for *n*-heptane oxidation with the H_2O_2–**1**–**2** and H_2O_2–**1**–**2**–pyridine systems was calculated from the concentrations of only resulting isomeric alcohols. For comparison, the oxidation with $[LMn^{IV}(O)_3Mn^{IV}L]^{2+}$, where L is the 1,4,7-trimethyl-1,4,7-triazacyclononane in the presence of acetic acid, is also represented [21–23].

leads to selectivity values that are close to the parameters of the reaction in the absence of pyridine. Finally, as the reaction in the absence of pyridine, the oxidation of *cis*-1,2-dimethylcyclohexane in the presence of pyridine is not stereoselective (Table 3).

In summary, on the basis of all the obtained data, it may be concluded that pyridine additives have a slight effect on the activity and selectivity parameters in the oxidation with our earlier proposed O_2–H_2O_2–vanadium complex–pyrazine-2-carboxylic acid reagent in acetonitrile. In this property, the given reagent markedly differs from the systems based on iron complexes and hydrogen peroxide. The difference may be due to the fact that oxidation follows different mechanisms in these two cases. However, there may be a situation when both ions, iron and vanadium, lead to the same intermediates, whose further transformations are different because iron and vanadium can induce secondary processes that differ from each other. For example, alkyl hydroperoxide can readily be transformed into corresponding ketone by the action of pyridine and the iron ion, whereas pyridine in the presence of vanadate ions cannot induce this conversion.

ACKNOWLEDGMENTS

This work was supported by the Research Foundation of São Paulo State and the Brazil National Council

on Scientific and Technological Development. G.B. Shul'pin thanks FAPESP (grant no. 2002/8495-4), CNPq (grant no. 300601/01-8), the Institute of Chemistry, Campinas State University, and the Faculty of Chemistry, Campinas Catholic University, for the invitation as a professor at these universities where this work was in part carried out. This study was also supported by the Chemistry and Materials Science Division Program "Theoretical and experimental study of the nature of chemical bonding and mechanisms of the most important chemical reactions and processes" of the Russian Academy of Sciences and by the Russian Foundation for Basic Research.

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