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OXIDATION OF LIMONENE CATALYZED BY METAL(SALEN) COMPLEXES

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Abstract - The compound R-(+)limonene is available and cheap than its oxidized products. Consequently, the selective oxidation of R(+)limonene has attracted attention as a promising process for the production of compounds with a higher market value, such as cis/trans-1,2-limoneneoxide, cis/trans-carveol and/or carvone. One of the these processes, described in the recent literature, is submission of R-(+)limonene to an oxidation reaction catalyzed by neutral or cationic Metal(Salen) complexes, in the presence of effective terminal oxidants such as NaOCl or PhIO. These reactions are commonly carried out in organic solvents (dichromethane, ethyl acetate, acetonitrile or acetone). Thus, the main objective of the present work was to study the effect of several factors (type of oxidant, catalyst, solvent and time) on reaction selectivity for the high-priced compounds referred to above. For this purposes, experimental statistical multivariate analysis was used in conjunction with a complete experimental design. From the results it was observed that for the three targeted products (1,2-limoneneoxide, carveol or carvone) some factors, including the nature of the terminal oxidant and the catalyst, were significant for product selectivity (with a confidence level of 95%). Therefore, this statistical analysis proved to be suitable for choosing of the best reaction conditions for a specific desired product.

Keywords: R(+)-limonene; Salen; Experimental design; Catalysis; Oxidation.

INTRODUCTION

The catalytic transformation of olefins into oxidized products is probably the most important chemical process in industry with the exception of oil refining. Therefore, one attempts to use cheap and abundant feedstocks to produce scarcer, high-priced compounds (Cavaleiro et al., 1996; Silvestre et al., 1997).

In Brazil, the production of orange juice has been increasing over the past years. As a consequences the byproducts of this industry, including orange essential oil, which is very rich in R-limonene (>95% in most cases) are becoming increasingly abundant and cheap. This compound is therefore a particularly important substrate for the production of higher priced compounds, such as carvone, cis/trans-carveols and cis/trans-1,2-limoneneoxide (Silva et al., 2002; Gomes Jr. and Antunes, 2001; Gomes and Antunes, 1997; 1996a,b).

In Figure 1, the structures of limonene (1) and of the desired products, limoneneoxide (2), carveol (3) and carvone (4), are shown.

Olefin (biomimetic) oxidations catalyzed by Metal(Salen) complexes in the presence of efficient oxygen donors (iodosylbenzene or sodium hypochlorite) by a rebound mechanism reported to take place under room conditions (Gomes and

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Antunes, 1996a,b), appear to be very useful and compatible use under supercritical conditions (Lima et al., 2005).

Metal(Salen) complexes have attracted considerable attention because of their physical and chemical (especially catalytic) properties (Hobday and Smith, 1973). In addition, these complexes are easy to prepare and are consequently cheap; stable in water, even at high pHs; and with stable in a reasonable range of temperatures (Figure 2).

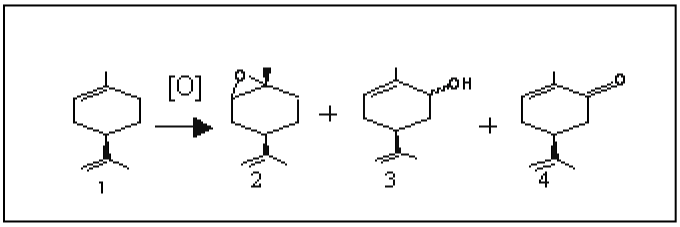

Figure 1: Limonene and its oxidized products

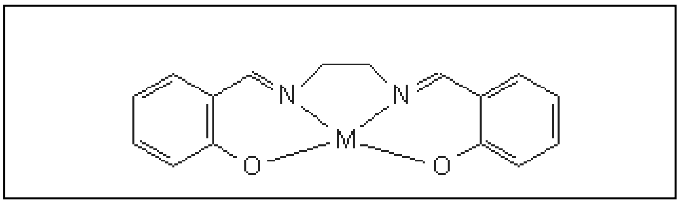

Figure 2: Metal(Salen) complex.

Salen is a Schiff base of ethylenediamine and salycilaldehyde. Many Metal(Salen) derivatives, including chiral ones, have already been described and used in different chemical processes (Hobday and Smith, 1973; Ito et al., 1998). Salen complexes of Cr(III) (Samsel and Katsuki, 1985), Mn(III) (Srinivasan et al., 1986; Chang *et al.,* 1994; Irie et al., 1991), Fe(III) (Jacob et al., 1989) and Co(III) (Reddy et al., 1995) have been shown to be active catalysts for olefinic oxidation.

Allylic oxidation and epoxidation are two competing processes, either in vivo or in vitro (Sheldon and Kochi, 1981), that require different catalytic mechanisms. In contrast to epoxidation, which is mostly concerted, allylic oxidation has a radical character.

Supercritical fluids (SCFs) are attractive media for chemical reactions because of their unique properties. Many physical and transport properties of SCFs are intermediate between those of liquids and gases. An additional feature of SCFs that makes them appealing as a medium for chemical reactions is that their properties vary with density, which is a strong function of temperature and pressure in the critical region. Consequently, SCFs provide the opportunity to engineer the reaction environment by manipulating temperature and pressure. Specifically, the use of $SCCO_2$ as solvent offers the unique advantage of compatibility with green technology (Walther et al., 1999; Birbaum et al., 1999; Savage et al., 1995; Kerler and Martin, 2001; Dariva, 2000), although it cannot offer the advantage of tunable polarity that supercritical H_2O can (Kerler and Martin, 2001). Our findings on the use of supercritical CO_2 were been recently described (Lima et al. 2005).

The main objective of the present paper is to establish the principal reaction parameters which can affect selectivity for allylic oxidation or epoxidation using ordinary solvents.

EXPERIMENTAL

Materials and Methods

R-(+)-limonene (98%, Sigma), iodosylbenzene diacetate (98% pure, Aldrich), commercial sodium hypochlorite (12% commercial), ethylenediamine (98%, Carlo Erba), dichloromethane (99%, Carlo Erba), acetonitrile (99%, Jonhson Mattey), acetone (99.5%, Nuclear), ethyl acetate (99.5%, Mallinckrodt), ethanol (99.5%, VETEC), salicylaldehyde (99%, ACROS) and $MnCl_2$, $CoCl_2$ and $NiCl_2$ (98%, Synth) were used as received without any previous treatment.

The experimental procedure for synthesis of the catalysts and preparation of the terminal oxidant and the standard conditions for the reaction medium under room conditions were described in Gomes and Antunes (Gomes and Antunes, 1996a, b).

All reactions had a catalyst/oxidant/substrate molar ratio of 0.05/1(PhIO)/1 or 0.05/5(NaClO)/1. After the predetermined reaction time, samples were analyzed via GC. These analyses were performed in a Varian 3300 instrument, equipped with a FID detector with a 30 m DB-1 capillary column (0.25 mm ID), a 1.0 μm film thickness of 1 mL/min, H_2 as carrier gas, a split of ratio 1:100, an injector of temperature 483 K, a detector of temperature 513 K. Initial oven temperature was 333 K (5 K/min) and final temperature was 573 K.

In the present work, percent conversion is 100(moles converted feedstock/moles initial feedstock) and percent selectivity is 100(moles product/moles converted feedstock). Percent yield is 100(moles product/moles initial feedstock). Selectivities were calculated as the sum of both *cis* and *trans*-isomers.

RESULTS AND DISCUSSION

Reactions using Mn(Salen)Cl.H_2O, Co(Salen) and Ni(Salen) in different solvents were carried out in 4 and 24h. The results are presented in Tables 1 and 2, respectively.

It can be seen from these tables that the highest conversion (94.4%) under room conditions was observed for Mn(Salen)Cl.H_2O/NaOCl/ethyl acetate in 24h. However, the link between conversion and selectivity is much easier to find with multivariate analysis.

Under multivariate analysis the effect of the reaction parameters can be seen as a whole, therefore allowing visualization of the correlation of the variables under study for product formation.

From the results obtained above, multivariate analysis was undertaken using the STATISTICA® software with a confidence level of 95%. From this analysis, it was possible to observe the effect of the variables of the process on reaction conversion and selectivity.

Table 1: Experimental results with a reaction time of 4h.

No	CAT	OXI	SOLV	CONV	Product distribution (%)			
					2	3	4	other
1	Mn	PhIO	A	4.5	0.0	4.9	0.0	95.1
2			B	5.2	0.0	9.1	0.0	90.9
3			C	5.2	7.1	15.3	3.5	74.1
4			D	5.9	20.5	4.4	0.0	75.1
5		NaOCl	A	55.9	0.3	0.0	0.0	99.7
6			B	26.6	13.8	23.0	4.5	58.7
7			C	8.4	11.1	19.6	2.2	67.1
8			D	66.7	4.9	39.5	0.4	55.2
9	Ni	PhIO	A	7.9	34.9	10.8	2.5	51.8
10			B	10.7	14.8	8.9	3.8	72.5
11			C	3.3	18.4	25.3	0.0	56.3
12			D	3.2	6.0	16.1	0.0	77.9
13		NaOCl	A	48.1	0.5	0.0	0.0	99.5
14			B	37.7	0.0	27.0	0.0	73.0
15			C	4.5	43.4	20.7	0.0	35.9
16			D	17.8	0.9	0.0	0.0	99.1
17	Co	PhIO	A	6.0	39.8	10.8	0.0	49.4
18			B	7.2	32.2	13.8	0.0	54.0
19			C	8.4	25.3	4.8	0.0	69.9
20			D	10.4	16.8	16.9	0.0	66.3
21		NaOCl	A	49.1	0.5	0.0	0.0	99.5
22			B	5.3	12.7	21.0	0.0	66.3
23			C	5.3	3.2	7.2	1.6	88.0
24			D	4.7	3.0	26.3	1.7	69.0

OXI = Oxidant (PhIO or NaClO); SOLV = Solvent (A = acetone, B = acetonitrile, C = dichloromethane and D = ethyl acetate); CAT =catalyst (Mn = Mn(Salen)ClH_2O, Co = Co(Salen)ClH_2O and Ni = Ni(Salen)ClH_2O) for reaction time (t1 = 4h and t2 = 24h); CONV = overall conversion of limonene, Product Distribution = selectivity for limoneneoxide (2), carveol (3) and carvone (4).

Table 2: Experimental results with a reaction time of 24h.

No	CAT	OXI	SOLV	CONV	Product distribution (%)			
					2	3	4	other
1	Mn	PhIO	A	7.9	19.8	5.6	0.0	74.6
2			B	5.9	4.5	5.0	3.0	87.5
3			C	9.8	15.3	25.6	8.1	51.0
4			D	29.2	34.3	9.0	1.6	55.1
5		NaOCl	A	57.3	0.4	0.0	0.0	99.6
6			B	68.4	4.0	20.3	5.0	70.7
7			C	20.5	3.5	24.5	5.1	66.9
8			D	94.4	1.3	29.3	9.5	59.9
9	Ni	PhIO	A	8.2	10.7	8.1	3.7	77.5
10			B	11.7	19.6	11.7	2.0	66.7
11			C	9.3	37.4	4.2	1.4	57.0
12			D	4.8	25.3	12.7	6.9	55.1
13		NaOCl	A	55.4	0.4	0.0	0.0	99.6
14			B	54.0	2.6	31.4	3.7	62.3
15			C	34.4	19.0	10.7	0.3	70.0
16			D	29.8	1.4	19.4	6.2	73.0
17	Co	PhIO	A	24.8	40.3	19.9	0.4	39.4
18			B	11.6	40.7	16.6	1.5	41.2
19			C	12.8	24.0	20.9	6.8	48.3
20			D	25.1	46.3	19.9	0.7	33.1
21		NaOCl	A	56.6	0.4	0.0	0.0	99.6
22			B	13.9	4.5	29.9	0.0	65.6
23			C	7.7	3.9	23.5	2.6	70.0
24			D	14.1	4.3	30.1	12.1	53.5

OXI = Oxidant (PhIO or NaClO); SOLV = Solvent (A = acetone, B = acetonitrile, C = dichloromethane and D = ethyl acetate); CAT = catalyst (Mn = Mn(Salen)ClH$_2$O, Co= Co(Salen)ClH$_2$O and Ni = Ni(Salen)ClH$_2$O) for reaction time (t1 = 4h and t2 = 24h); CONV = overall conversion of limonene, Product Distribution = selectivity for limoneneoxide (2), carveol (3) and carvone (4).

Factor Analysis for Conversion of Limonene:

Independent variables: (SOLV), (CAT), (OXI) and (TIME).

Dependent variable: overall conversion of limonene.

All effects except the 4 fourth-order effects (limited by the number of degrees of freedom) were considered.

Statistical analysis: It can be observed that all the first-order effects were found to be statistically significant. For the second-order effects, the interactions SOLV × TIME and CAT × TIME were found to not be statistically significant and for the third-order interactions, only SOLV × CAT × OXI as found to be statistically significant.

Figures 3 and 4 contain details of the significant effects for overall conversion of limonene. Different behaviors were observed for different oxidants, although the Mn(Salen)Cl.H$_2$O/ethyl acetate/24 h reaction had the best results of all terminal oxidants used.

Mn(Salen)Cl.H$_2$O/ethyl acetate/24h with PhIO as the terminal oxidant (conversion 29.2%) and with NaOCl (conversion 94.4 %) were promising reactions. In general, acetone was shown to be a good solvent for achieving high conversions.

Factor Analysis of Selectivity for Limoneneoxide:

Independent variables: (SOLV), (CAT), (OXI) and (TIME).

Dependent variable: selectivity for limoneneoxide.

The effects of third and fourth order were not considered.

The first-order effects, catalyst and terminal oxidant, were found to be statistically significant. The second-order effects, the interactions CAT × OXI, SOLV × CAT and OXI × TIME, were also found to be statistically significant.

In Figures 5 and 6 the significant effects of selectivity for limoneneoxide are detailed.

Selectivity increased with time, using PhIO, except with Ni(Salen)Cl.H$_2$O/acetone. Co(Salen)Cl.H$_2$O showed improved selectivity in ethyl acetate. When using NaOCl, selectivity for limoneneoxide decreased with increasing time.

The best compromise between conversion and selectivity for limoneneoxide was achieved with Mn(Salen)Cl.H$_2$O/ PhIO/ethyl acetate/24h

(29.2%overall conversion and 34.3% for selectivity limoneneoxide), Co(Salen)Cl.H_2O/PhIO/ethyl acetate/24h (25.1% overall conversion and 46.3% for selectivity limoneneoxide) and Co(Salen) Cl.H_2O/PhIO/ acetone/24h (24.8% overall conversion and 40.3 for selectivity limoneneoxide). In general, the use of PhIO seemed to favor epoxidation.

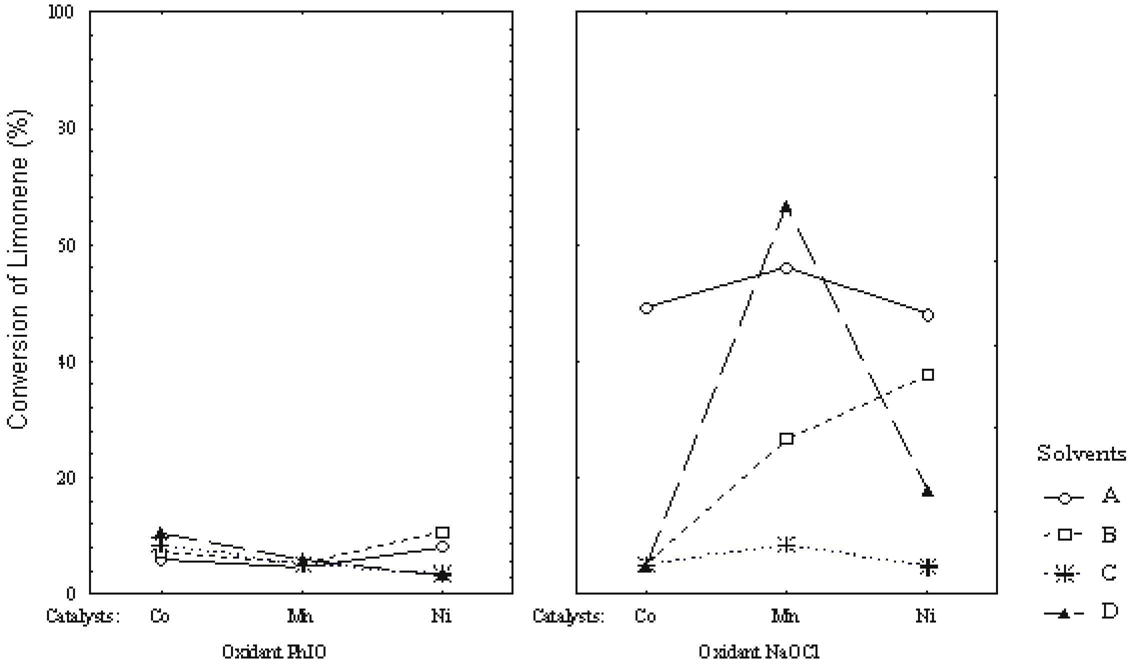

Figure 3: Variable independent media × overall conversion with a reaction time of 4h (t1).

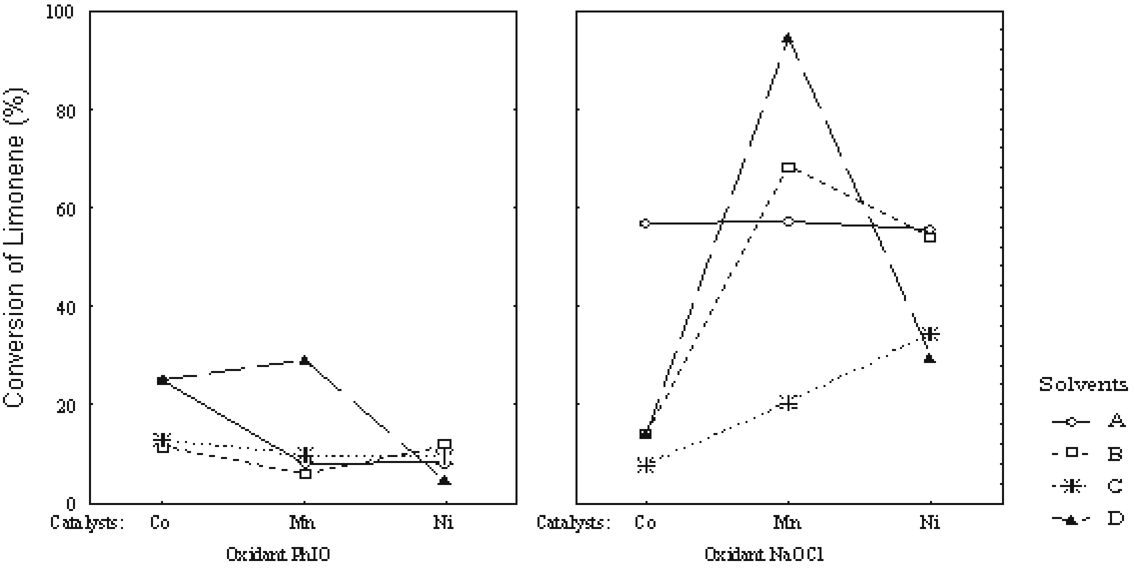

Figure 4: Variable independent media × overall conversion with a reaction time of 24h (t2).

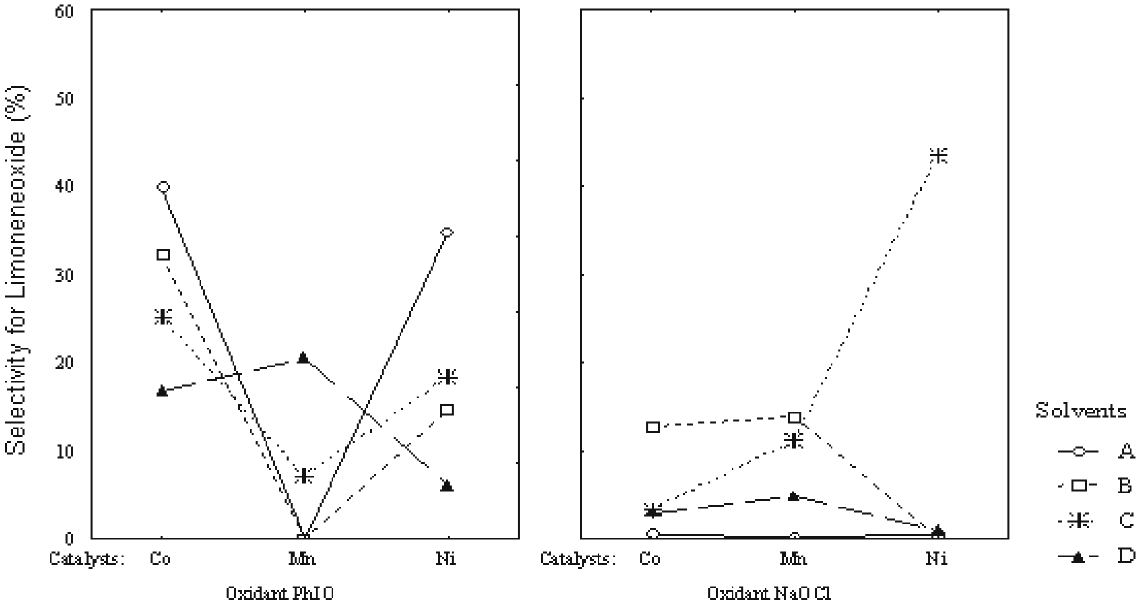

Figure 5: Variable independent media × selectivity for limoneneoxide with a reaction time of 4h (t1).

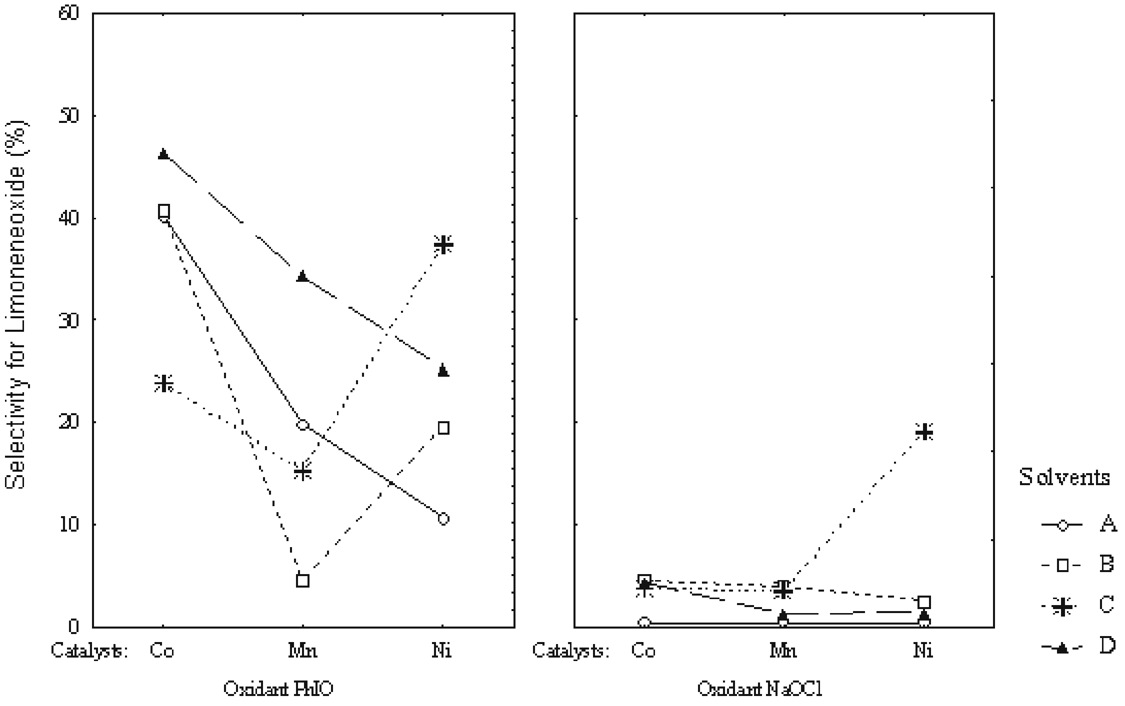

Figure 6: Variable independent media × selectivity for limoneneoxide with a reaction time of 24h (t2).

Factor Analysis Selectivity for Carveol:

Independent variables: (SOLV), (CAT), (OXI) and (TIME).

Dependent variable: selectivity for carveol.

The third- and fourth-order effects were not considered in the statistical analysis selectivity for carveol. The first-order effects, SOLV and OXI, were shown to be significant. Of the second-order effects, just the SOLV × OXI interaction was proved to be statistically significant.

Figures 7 and 9 show the significant effects of selectivity for carveol. It can be seen that with the use of PhIO as terminal oxidant, longer reaction times favored selectivity for carveol [except with Ni(Salen)Cl.H_2O]. However, NaOCl was shown to be more effective selectivity for carveol, demonstrating the favorable effect of this terminal oxidant on of radicals generation.

In many cases increasing time was shown to be deleterious to the desired selectivity. Increasing formation of by-products was the dominant effect in several reactions.

The highest selectivity for carveol was found with Mn(Salen)Cl.H_2O/ NaOCl/ethyl acetate /4 h (39.5%). The best yields, 26.3% (4h reaction) and 27.7% (24h reaction), were found as well.

Factor Analysis of Selectivity for Carvone:

Independent variables: (SOLV), (CAT), (OXI) and (TIME).

Dependent variable: selectivity for carvone.

Effects of third and fourth order not considered in statistical analyses for carvone selectivity. The first-order effect, SOLV and TIME, were shown to be statistically significant. The second-order effects, the interactions SOLV × OXI and SOLV × TIME, were also found to be statistically significant. Carvone is expected to be produced from carveol. Therefore, as expected, longer reaction times favored its formation (Figures 9 and 10). NaOCl favored selectivity for carvone.

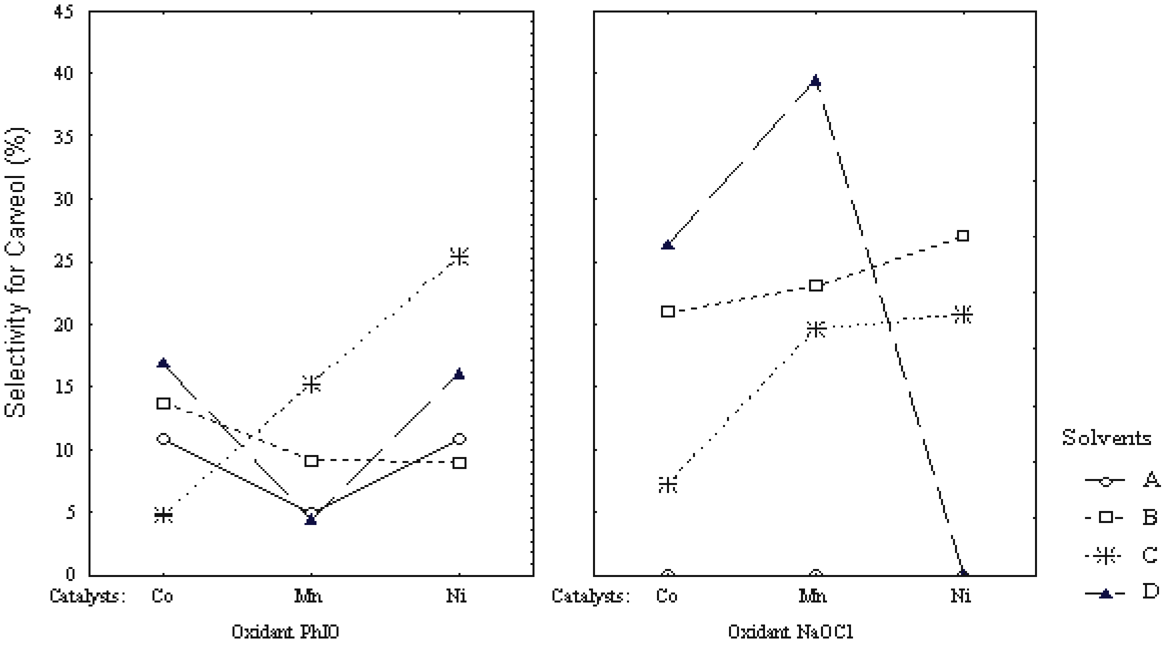

Figure 7: Variable independent media × selectivity for carveol with a reaction time of 4h (t1).

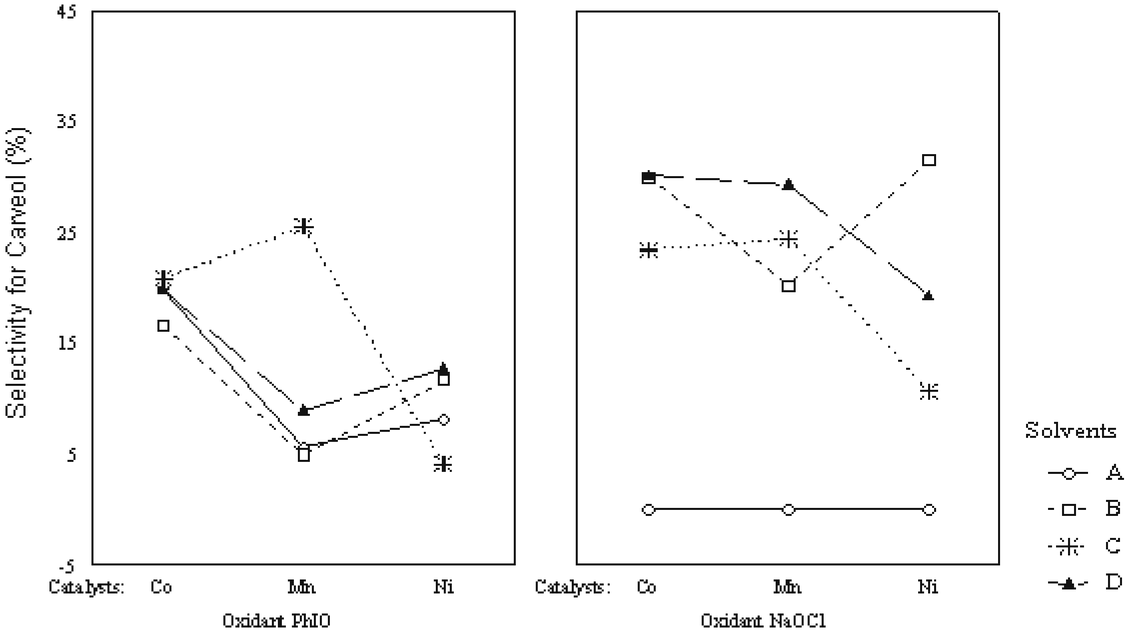

Figure 8: Variable independent media × selectivity for carveol with a reaction time of 24h (t2).

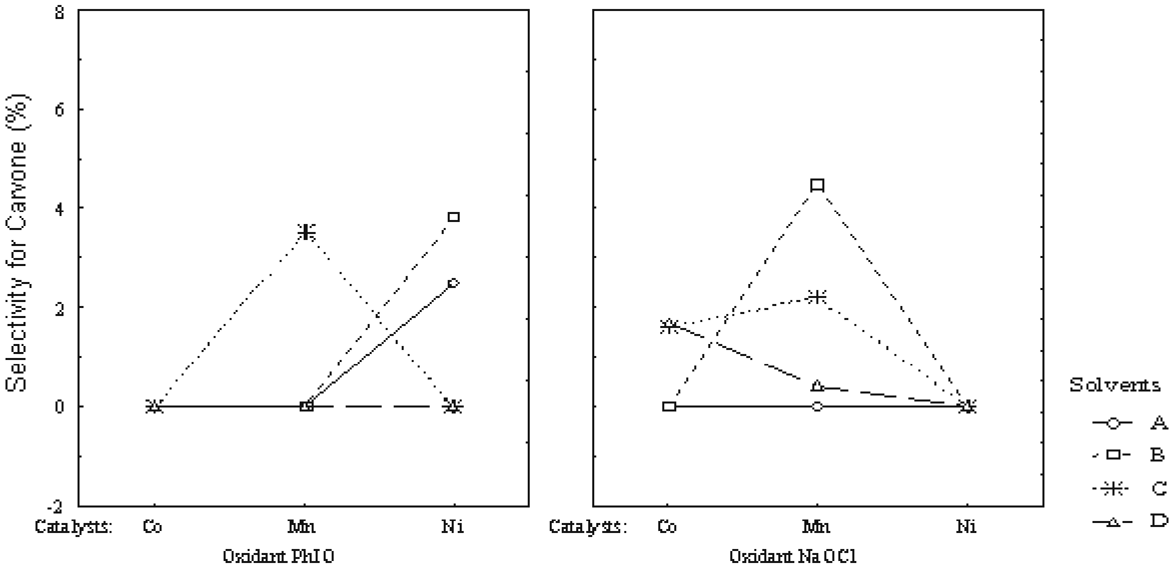

Figure 9: Variable independent media × selectivity for carvone with a reaction time of 4h (t1).

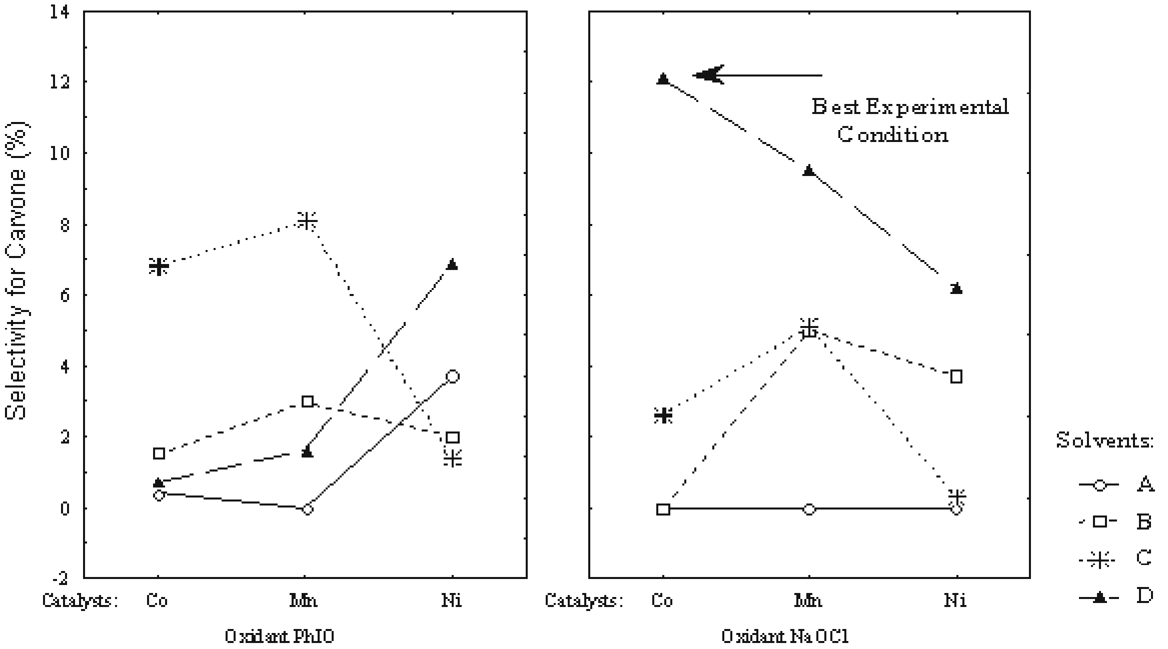

Figure 10: Variable independent media × selectivity for carvone with a reaction time of 24h (t2).

CONCLUSIONS

In general, the use of multivariate analysis to analyze selectivities for limoneneoxide [Mn(Salen)Cl.H_2O/PhIO/ethyl acetate], carveol [Mn(Salen)Cl.H_2O/NaOCl/ethyl acetate/4 h (39.5%)] and carvone (longer reaction times and the use of NaOCl) was conclusive under the conditions studied. NaOCl appeared to favor allylic oxidation and PhIO, epoxidation. In general, longer times, resulted in a lager number of side products, although in some cases increased the selectivity and/or yield of a particular compound. Ethyl acetate showed the best results in terms of conversion and selectivity for both epoxidation and for allylic oxidation.

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